High Dose Influenza Vaccine Utilization at Inland Hospital in Waterville, Maine

High Dose Influenza Vaccine

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Disclosures

- None

Influenza Burden

- Annual hospitalizations: 140,000-710,000
- Annual deaths: 12,000-56,000
- Adults over 65 years are at increased risk
  - 90% of influenza-related deaths

Efficacy of Influenza Vaccine

- Standard dose influenza vaccine efficacy:
  - Children: up to 94%
  - Adults 18-65: up to 75%
  - Adults >65 up to 58%
- Decline in immune function with aging affects the ability to resist influenza and respond to vaccination

High-Dose Influenza Vaccine

- High-dose, trivalent, inactivated influenza vaccine (IIV3-HD)
- 4 times more hemagglutinin antigen than is contained in standard-dose vaccines (60 µg versus 15µg).
- FDA approval for adults 65 years and older since 2009.

The NEW ENGLAND JOURNAL of MEDICINE

Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults

- Double blinded randomized control trial in 2015
  - HD Vaccine: N=15,5991
  - SD Vaccine: N=15,998
- Primary Outcome:
  - Laboratory-confirmed influenza in association with a influenza-like illness.
  - 228 cases (1.4%) in IIV-HD versus 301 cases (1.9%) in IIV-SD
  - Relative efficacy 24.4%

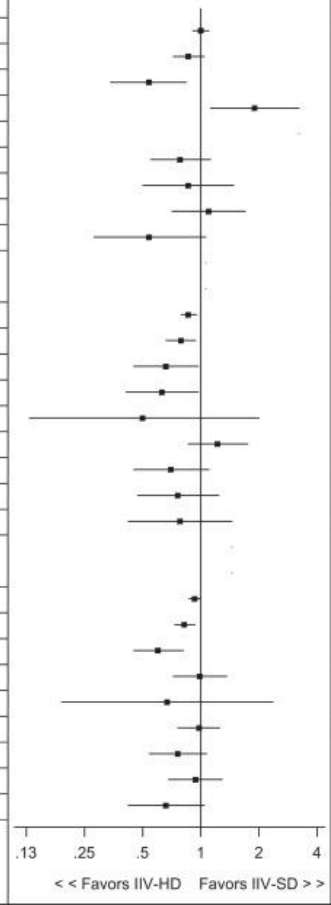
- The study was funded by Sanofi Pasteur – the manufacturer of Fuzone high-dose influenza vaccine

Prevention of Serious Events in Adults 65 years of age or older: A comparison between high-dose and standard-dose inactivated vaccine

- Same data and authors as the previous study, published in 2015 in the journal Vaccine. Analysis for influenza complications.

- Cardio-respiratory Events:
  - 428 cases in IIV-HD versus 520 cases in IIV-SD
  - 17.7% reduction
- Pneumonia:
  - 71 cases in IIV-HD versus 118 cases in IIV-SD
  - 39.8% reduction
- All-cause Hospitalizations:
  - 1530 cases in IIV-HD versus 1643 cases in IIV-SD
  - 6.9% reduction

	Rate Ratio (95% CI)
YEAR 1	
All-cause hospitalization	1.00 (0.91; 1.10)
Serious cardio-respiratory events	0.86 (0.72; 1.04)
Pneumonia events	0.54 (0.34; 0.84)
Asthma/COPD/bronchial events	1.90 (1.12; 3.22)
Influenza events	NA
Coronary artery events	0.78 (0.55; 1.12)
Congestive heart failure	0.86 (0.50; 1.48)
Cerebrovascular events	1.10 (0.71; 1.70)
Other respiratory events	0.54 (0.28; 1.06)
YEAR 2	
All-cause hospitalization	0.86 (0.79; 0.95)
Serious cardio-respiratory events	0.79 (0.66; 0.94)
Pneumonia events	0.66 (0.45; 0.97)
Asthma/COPD/bronchial events	0.63 (0.41; 0.97)
Influenza events	0.50 (0.13; 2.00)
Coronary artery events	1.22 (0.86; 1.75)
Congestive heart failure	0.70 (0.45; 1.10)
Cerebrovascular events	0.76 (0.47; 1.24)
Other respiratory events	0.78 (0.42; 1.45)
COMBINED (YEAR 1 AND YEAR 2)	
All-cause hospitalization	0.93 (0.87; 1.00)
Serious cardio-respiratory events	0.82 (0.73; 0.93)
Pneumonia events	0.60 (0.45; 0.81)
Asthma/COPD/bronchial events	0.99 (0.72; 1.36)
Influenza events	0.67 (0.19; 2.36)
Coronary artery events	0.98 (0.76; 1.25)
Congestive heart failure	0.76 (0.54; 1.07)
Cerebrovascular events	0.94 (0.68; 1.29)
Other respiratory events	0.66 (0.42; 1.04)



Comparative effectiveness of high-dose versus standard-dose influenza vaccines in US residents aged 65 years and older from 2012 to 2013 using Medicare data: a retrospective cohort analysis

Hector S Izurieta*, Nicole Thadani*, David K Shay, Yun Lu, Aaron Maurer, Ivo M Foppa, Riley Franks, Douglas Pratt, Richard A Forshee, Thomas MaCurdy, Chris Worrall, Andrew E Howery, Jeffrey Kelman

- Retrospective cohort study
  - HD vaccine: N= 929,730
  - SD vaccine: N= 1,615,545
  - US Medicare beneficiaries 65 years and older who received influenza vaccine in a community pharmacy
- Primary outcome: probable episode of influenza-related illness with positive rapid influenza test followed by dispensing of oseltamivir within a 2-day period
- The study was also funded by Sanofi Pasteur

Results

High dose vaccine:

- 22% reduction in influenza-associated illness
- 22% reduction in influenza hospitalizations

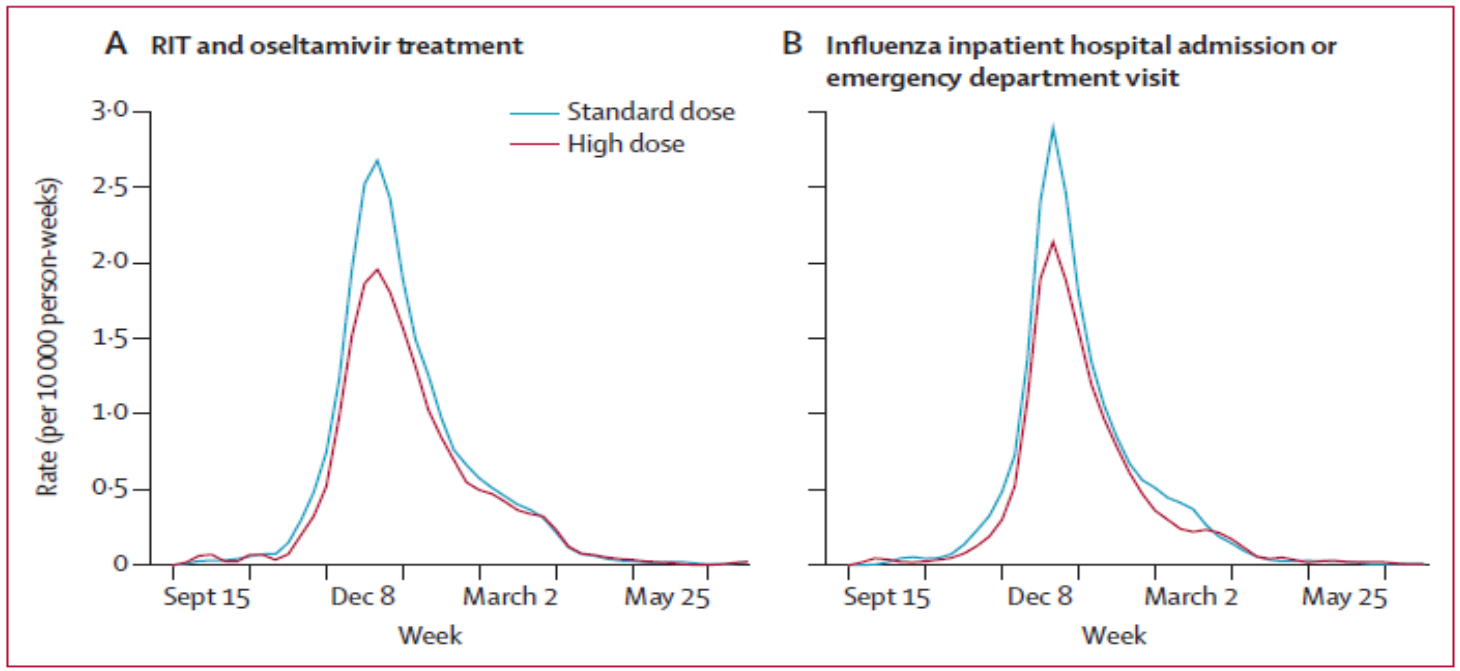


Figure 1: Influenza outcome rates by vaccine type during the 2012–13 influenza season

Comparative Effectiveness of High-Dose Versus Standard-Dose Influenza Vaccines Among US Medicare Beneficiaries in Preventing Postinfluenza Deaths During 2012–2013 and 2013–2014

- Retrospective cohort study
  - HD vaccine (60 mcg of hemagglutinin per strain): N= 1,039,645
  - SD vaccine (15 mcg of hemagglutinin per strain): N= 1,683,264
  - US Medicare beneficiaries 65 years and older who received influenza vaccine in a community pharmacy
- Primary outcome: death in the 30 days following an inpatient or emergency department encounter listing an influenza code
- Results:
  - Rates of post-influenza death were 0.028/10,000 person-weeks for high-dose vaccine and 0.038/10000 person-weeks in standard-dose recipients.
  - Comparative effectiveness was 24.0%
- Funding from CDC and FDA

Comparative Effectiveness of High-Dose Versus Standard-Dose Influenza Vaccination in Community-Dwelling Veterans

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Darren R. Linkin for the Centers for Disease Control and Prevention Epicenter Program

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- Retrospective cohort study
  - HD vaccine (60 mcg of hemagglutinin per strain): N= 25,714
  - SD vaccine (15 mcg of hemagglutinin per strain): N= 139,511
  - patients who receive primary care at Veteran Health Administration (VHA) medical centers, and who received influenza vaccine in the 2010–2011 influenza season
- Primary outcome: hospitalization for influenza or pneumonia
- No potential conflicts of interest from funding sources.

Efficacy in VA population

- In the subgroup of patients ≥85 years of age, receiving HD vaccine was associated with lower rates of hospitalization for influenza or pneumonia (0.30% and 0.66%, respectively).

- No difference in hospitalization rate from influenza or pneumonia in other age groups.

Safety of High-Dose Influenza Vaccine

- Increased in adverse events when compared with standard dose vaccine

	High Dose	Low Dose	% increase with IIV3-HD
Injection site pain	35.6%	24.3%	**11.3%**
Injection site erythema	14.9%	10.8%	**4.1%**
Injection site swelling	8.9%	5.8%	**3.1%**
Malaise	18.0%	14.0%	**4.0%**
Myalgia	21.4%	18.3%	**3.1%**
Headache	16.8%	14.4%	**2.4%**
Fever	3.6%	2.3%	**1.3%**

Summary

- All studies I found show some benefit
- Depending the study, high-dose influenza vaccine reduces:
  - Incidence of influenza
  - Hospitalizations
  - Pneumonia
  - Cardio-respiratory events
  - Mortality from influenza
- Drawbacks:
  - Increased rate of post-injection adverse effects
  - More expensive (high dose $32, standard dose $12)
  - Statistically significant benefits are not found by every study.

Inland Hospital

- Inland offers both high-dose and standard-dose influenza vaccine in outpatient settings.
- Only standard-dose vaccine is available in the inpatient setting.

References

- CDC. Flu Vaccine Effictiveness: Questions and Answers for Health Care Professionals. Last updated 01/29/2016. Accessed 10/23/2017. https://www.cdc.gov/flu/professionals/vaccination/effectivenessqa.htm
- Chit A et al. Cost-effectiveness of high-dose versus standard-dose inactivated influenza vaccine in adults aged 65 years and older: an economic evaluation of data from a randomized controlled trial. Lancet Infect Dis. 2015;15(12):1459-1466. http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(15)00249-2/abstract
- DiazGranados CA et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. N Engl J Med. 2014;371(7):635-645. http://www.nejm.org/doi/full/10.1056/NEJMoa1315727
- DiazGranados CA et al. Prevention of serious events in adults 65 years of age or older: A comparison between high-dose and standard-dose inactivated influenza vaccines. *Vaccine*. 2015;33(38):4988-4993 http://www.sciencedirect.com/science/article/pii/S0264410X15009342
- Food and Drug Administration. Highlights of Prescribing Information: Fluzone High Dose. 03/02/17 v. 0.1 https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM305079.pdf
- Izurieta HS et al. Comparative effectiveness of high-dose versus standard dose influenza vaccines in US residents aged 65 years and older from 2012 to 2013 using Medicare data: a retrospective cohort analysis. *Lancet Infect Dis*. 2015;15(3):293-300. http://dx.doi.org/10.1016/S1473-3099(14)71087-4
- Shay, David et al. Comparative Effectiveness of High-Dose Versus Standard-Dose Influenza Vaccines Among US Medicare Beneficiaries in Preventing Postinfluenza Deaths During 2012–2013 and 2013–2014, The Journal of Infectious Diseases, Volume 215, Issue 4, 15 February 2017, Pages 510–517, https://doi.org/10.1093/infdis/jiw641