

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 randomised controlled trial

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Conflicts of interest statements

- Ayman Chit and Carlos DiazGranados are employees of Sanofi Pasteur
- Debbie Becker and Michael Maschio are employees of Optum which was contracted by Sanofi Pasteur to conduct this economic evaluation
- Eddy Yau was an employee of inVentive Health Clinical at the time this economic evaluation was conducted. inVentive Health Clinical was contracted by Sanofi Pasteur to assist with the primary analysis of the FIM12 trial
- Michael Drummond was a Principal Consultant at Optum at the time this economic evaluation was conducted

Methods: Study question

- Assess the economic value of Fluzone® High Dose vaccine - an inactivated split virus influenza vaccine containing 4 times the antigen of standard dose vaccine
- Estimate the cost-effectiveness of:
 - Fluzone High-Dose vaccine**versus**
 - Standard-dose Fluzone vaccine
- Evaluation based on data collected during the FIM12 trial¹
- Analysis was conducted from two perspectives:
 - U.S. healthcare payer perspective
 - U.S. societal perspective

¹DiazGranados GA, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. N Engl J Med 2014; 371(7): 635-45.

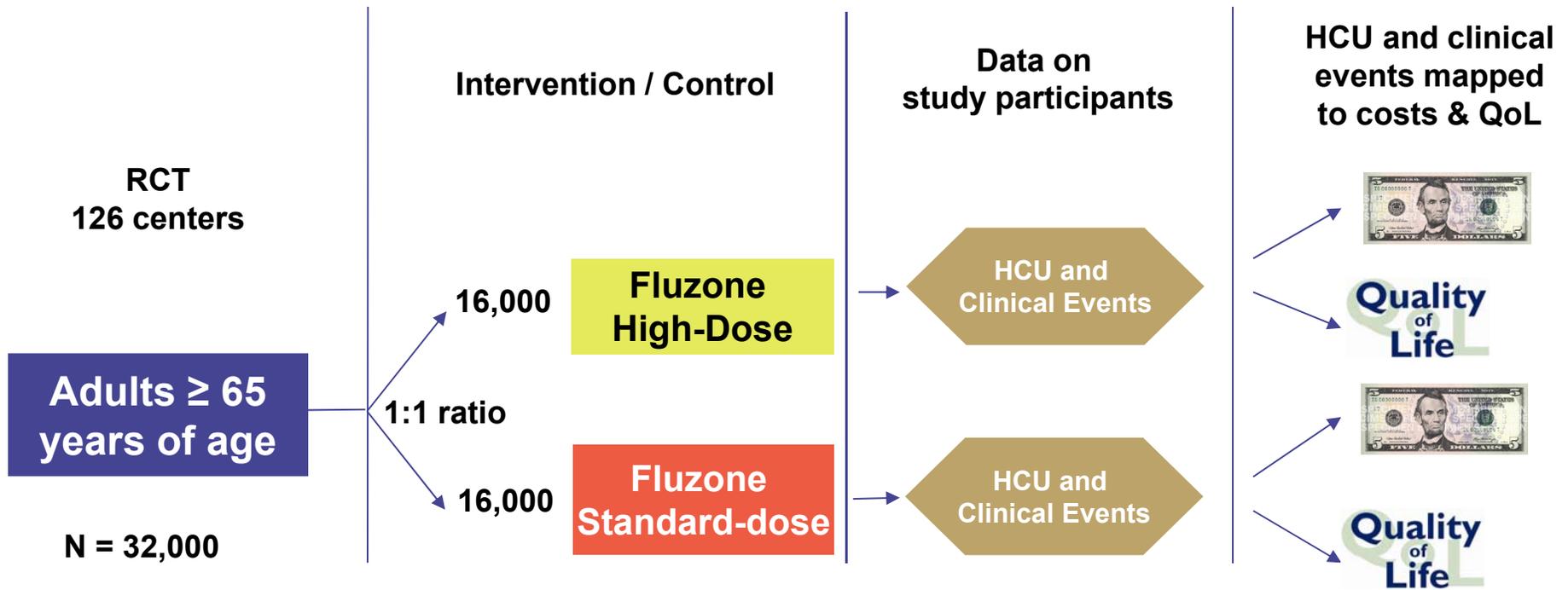
Methods: Interventions, timeframe & discounting

- This economic evaluation compares:
 - Single-dose Fluzone High-Dose vaccine

versus

 - Single-dose Fluzone vaccine
- Evaluation timeframe:
 - The time horizon was one influenza season for
 - Analysis of health care utilization (HCU) and corresponding costs
 - For assigning disutilities to clinical events
 - For analysis of life years (LYs) and quality-adjusted life years (QALYs), a lifetime horizon was used
- Discount rate:
 - 3% per year
 - Applied to outcomes that occurred after the first year (i.e., LYs and QALYs)

Methods: Economic analysis



- FIM12 trial conducted over two influenza seasons
- Health care resources utilized by FIM12 participants captured by study centers
- Health care resource use and clinical events were mapped to cost and utility data
- “Modeling” techniques were used to estimate LYs and QALYs
- Health care costs (in 2014 USD) and outcomes then compared between both study groups

Methods: Populations/Subgroups

- Primary Population (Scenario 1):
 - Included the broadest scope of costs and clinical events
 - Costs of vaccine, medications and hospitalizations (for any reason) reported by all subjects, and ER visits/non-routine/urgent care for new respiratory illness
 - Disutility values applied related to each respiratory illness, serious medical condition, and hospitalization (for any reason); only disutility of most severe event was applied in instances where a patient experienced overlapping events
 - All deaths considered, regardless of reason
- Cardio-respiratory Outcomes Population (Scenario 2):
 - Considered a subset of clinical outcomes, selected by study physicians based on the plausibility of their relation to influenza before the unblinding of FIM12.
- Complication Risk Subgroups
 1. Subjects with one or more defined, pre-specified high-risk comorbid conditions for influenza or influenza complications
 2. Subjects ≥ 75 years of age

Methods: Inputs

Variable	Value	Source
Unit Costs		
Fluzone Vaccine	\$12.04	CMS Seasonal Influenza Vaccines Pricing List
Fluzone High-Dose Vaccine	\$31.82	CMS Seasonal Influenza Vaccines Pricing List
Non-Rx Ibuprofen	\$0.14 (200 mg TID/QID, 4 days)	Optum's EncoderPro Database
Rx Ibuprofen	\$0.24 (600 mg TID, 4 days)	Optum's EncoderPro Database
Oseltamivir	\$110.60 (75 mg BID, 5 days)	Optum's EncoderPro Database
Azithromycin	\$29.88 (500 mg day 1, 250 mg days 2-5)	Optum's EncoderPro Database

Methods: Inputs

Variable	Value	Source
Unit Costs		
ER Visit	\$177.42/visit	Medicare Physician's Fee Schedule
Non-routine Medical Office / Urgent Care Visit	\$72.81/visit	Medicare Physician's Fee Schedule
Hospitalization	Range: \$1,214/day to \$9,140/day	Healthcare Cost and Utilization Project (HCUP) database; 2011 values inflated to 2014 \$
Lost productivity (mean hourly wage)	\$22.33/hour	US Bureau of Labor Statistics

Methods: Inputs

Variable	Value	Source
Other Inputs		
Life Expectancy	Age- and gender-dependent	U.S. 2009 Life Tables, U.S. Department of Health and Human Services
Average Utility Values for U.S. Adult Population (age 70-79)	Males: 0.802 Females: 0.771	Hanmer et al., 2006
Daily Disutility Value for Respiratory Illness	Range: 0.60957 (Day 1) to 0.05824 (Day 21)	Turner et al., 2003
Daily Disutility Value for Serious Medical Condition (inpatient days)	0.4272 (first 3 days) and 0.2832 (remaining days)	McPhail and Haines, 2010
Daily Disutility Value for Serious Medical Condition (outpatient days)	0.0696 (following discharge or not requiring hospitalization) to 0.2136 (days prior to hospitalization)	McPhail and Haines, 2010

Results: Costs

Full analysis set (Scenario 1) – Cost/Subject

Item/Outcome	Fluzone High Dose	Fluzone	Difference
Study Vaccine	\$31.81	\$12.06	\$19.75
Prescription Medications	\$5.65	\$5.61	\$0.04
ER Visits	\$2.32	\$2.26	\$0.06
Non-routine/Urgent Care Visits	\$16.43	\$15.87	\$0.56
Hospitalizations	\$1,320.51	\$1,456.85	-\$136.34
Total Health Care Payer Costs	\$1,376.72	\$1,492.64	-\$115.92
Non-prescription Medications	\$0.11	\$0.15	-\$0.04
Productivity Losses	\$129.64	\$141.71	-\$12.07
Total Societal Costs	\$1,506.48	\$1,634.50	-\$128.02

Results: Incremental Cost-effectiveness Ratios

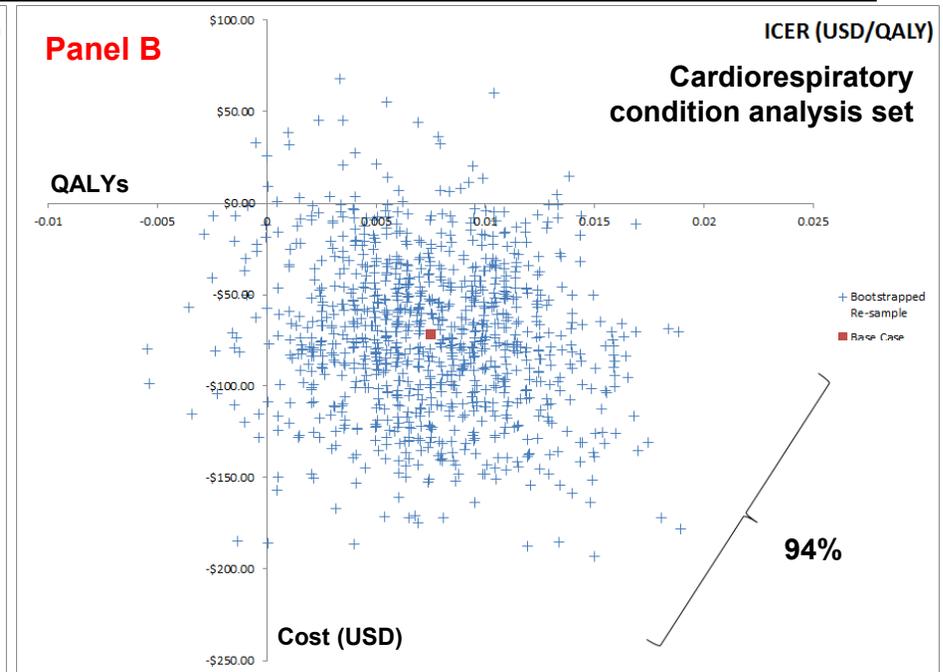
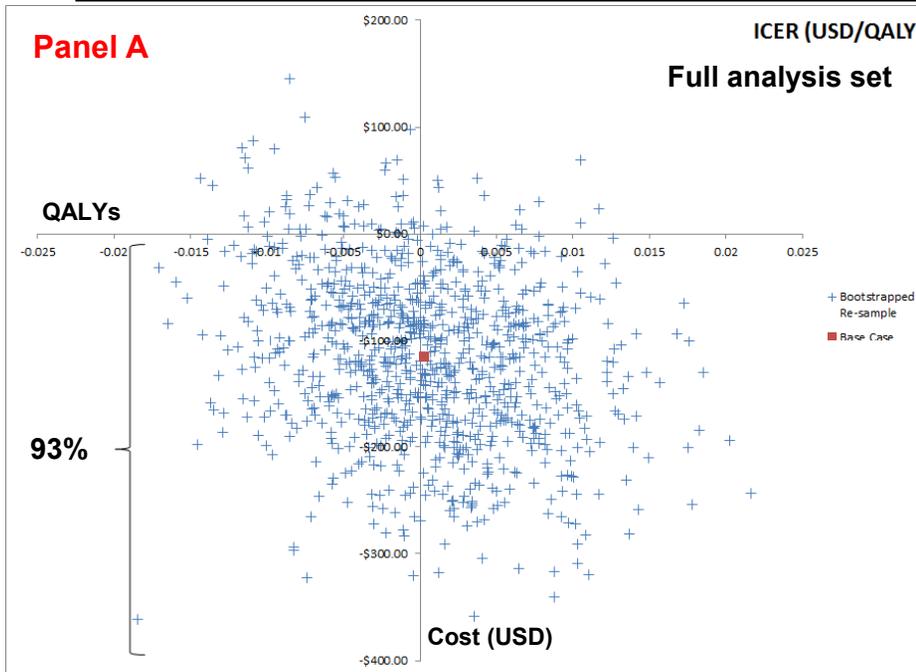
Full analysis set (Scenario 1)

Perspective	Treatment Group	Cost /Subject	Δ Cost	QALYs /Subject	Δ QALYs	ICER (cost/QALY)
Payer Perspective	Fluzone High Dose	\$1,377		8.1502		
	Fluzone	\$1,493	\$116	8.1499	-0.0004	Dominated by Fluzone High Dose
Societal Perspective	Fluzone High Dose	\$1,506		8.1502		
	Fluzone	\$1,635	\$128	8.1499	-0.0004	Dominated by Fluzone High Dose

Results: Fluzone HD dominated Fluzone in each scenario analysis, and in each subgroup analysis

		Full analysis set (Scenario 1)					Cardiorespiratory outcomes analysis set (Scenario 2)				
Population	Treatment Group	Cost /Subject	Δ Cost	QALYs /Subject	Δ QALYs	ICER (cost/QALY)	Cost /Subject	Δ Cost	QALYs /Subject	Δ QALYs	ICER (cost/QALY)
Healthcare Payer Perspective											
All subjects	Fluzone HD	\$1377	..	8.1502	\$401	..	8.1873
	Fluzone	\$1493	\$116	8.1499	-0.0003	Dominated	\$473	\$72	8.1798	-0.0075	Dominated
Subjects with one or more comorbid condition	Fluzone HD	\$1701	..	8.1370	\$512	..	8.1841
	Fluzone	\$1807	\$106	8.1357	-0.0013	Dominated	\$618	\$106	8.1730	-0.0111	Dominated
Subjects aged ≥75 years	Fluzone HD	\$1846	..	8.1187	\$539	..	8.1791
	Fluzone	\$1858	\$12	8.1134	-0.0053	Dominated	\$617	\$78	8.1631	-0.0160	Dominated
Societal Perspective											
All subjects	Fluzone HD	\$1506	..	8.1502	\$427	..	8.1873
	Fluzone	\$1635	\$128	8.1499	-0.0003	Dominated	\$507	\$80	8.1798	-0.0075	Dominated
Subjects with one or more comorbid condition	Fluzone HD	\$1858	..	8.1370	\$546	..	8.1841
	Fluzone	\$1977	\$119	8.1357	-0.0013	Dominated	\$663	\$117	8.1730	-0.0111	Dominated
Subjects aged ≥75 years	Fluzone HD	\$2007	..	8.1187	\$575	..	8.1791
	Fluzone	\$2029	\$22	8.1134	-0.0053	Dominated	\$662	\$88	8.1631	-0.0160	Dominated

Results: PSA Scatterplot



Fluzone High-Dose is less costly than Fluzone

PANEL A Quadrants	Δ Cost	Δ QALYs	Percentage of the points
Upper left	Positive	Negative	5%
Upper right	Positive	Positive	2%
Lower left	Negative	Negative	43%
Lower right	Negative	Positive	50%

Reduction in cardiorespiratory complications are the major driver of cost savings and health benefits offered by Fluzone High-Dose

Results: Influential variables

- Hospitalizations represent greater than 95% of the total costs to the healthcare payer and greater than 87% of the total societal cost
- The difference in total cost between vaccine groups is driven by:
 - Hospitalization costs (\$136/participant higher in Fluzone vaccine group)
 - Vaccine cost (\$20/participant lower in Fluzone vaccine group)
 - Indirect costs (\$12/participant higher in Fluzone vaccine group)

Limitations

- Limitations inherent to the FIM12 RCT apply to this economic analysis
- Not all elements required for the economic analysis were collected in FIM12, therefore, necessary to combine trial data with data from other sources.
 - E.g., utility data, unit cost data, productivity losses
- Grouping diagnostic codes was necessary when assigning disutilities and hospital per diem costs to serious medical condition, since it was not possible to collect values specific to each diagnosis
- Disutilities and costs were limited to those experienced during the trial period

Thank You

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