Cost-effectiveness of Influenza Vaccination: Updated Estimates for Children Aged 2-4 Years

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Conflict of Interest Statement:

All authors declare no known conflict of interest.

Introduction

- New data comparing live attenuated and inactivated influenza vaccines
  - Comparative effectiveness
  - Possible increased incidence of adverse events for live attenuated vaccine
    - Fever
    - Wheezing
   - Hospitalization

Objectives

- Evaluate the cost-effectiveness of influenza vaccination for children aged 2-4 years in the United States

  – Update previously published cost-effectiveness model with current cost data

  – Incorporate possible increased incidence of adverse events for live attenuated vaccine

Alternatives

- Strategies evaluated:
  - Inactivated influenza vaccine (IIV)
  - Live attenuated influenza vaccine (LAIV) for eligible age/risk groups
  - No vaccination

Methods: Target population

- Computer simulation to estimate costs and effects for influenza-related illness for:
  - children aged 2 to 4 years
    - 2 years
    - 3-4 years
  - stratified by risk status: high risk/ non-high risk
  - cohorts of 1,000 children for each age/risk group

Model Schematic
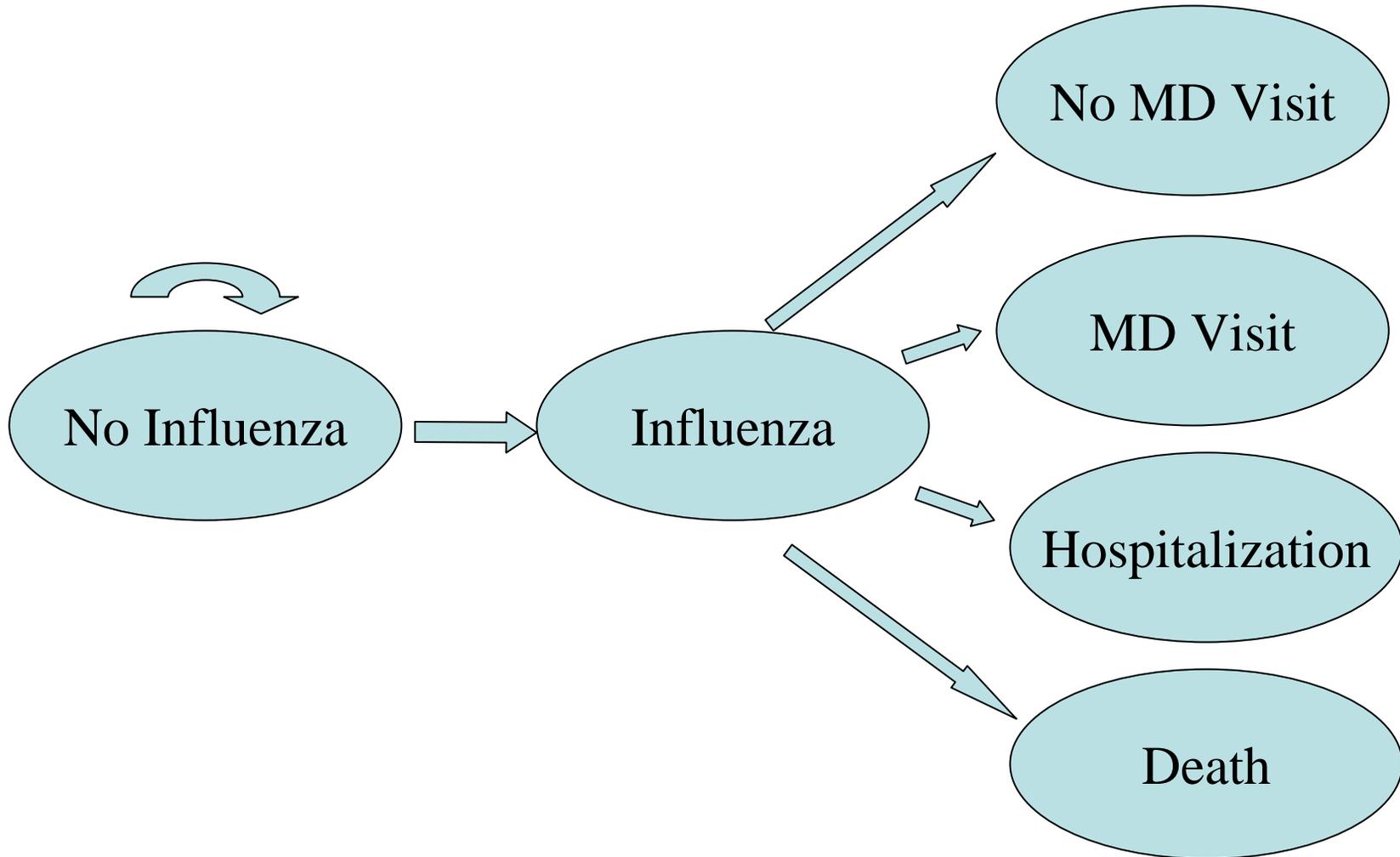
Economic Model: Analysis Plan

- Incremental cost-effectiveness analysis:
  - $ / influenza episode avoided
  - $ / hospitalization averted
  - $ / death averted
  - $ / QALY gained

$$\text{C/E Ratio} = \frac{\text{Costs}_{\text{Vaccination}} - \text{Costs}_{\text{No Vaccination}}}{\text{Events}_{\text{Vaccination}} - \text{Events}_{\text{No Vaccination}}}$$

- Sensitivity Analyses

Model Inputs

- Inputs from primary and secondary data sources
  - Natural history of influenza in children
  - Effects (reduced incidence rates, adverse events)
  - Costs (direct medical costs, opportunity costs)
  - Adjustment for quality-of-life
- Societal perspective
- Timeframe: One year (except death, long-term sequelae)
- Discount rate: 3%

Model Inputs: Influenza-related probabilities
2 yrs, Non-high-risk

Variable	Base Case Value	Range (95% CI)
Prob. of influenza illness	0.155	0.02 - 0.35
Hospitalizations, per 10,000	17.1	0.5-56.8
Deaths from influenza, per million	1.5	0 – 11.4

Sources: 1-15

Model Inputs: Influenza-related costs (2006$) 2 yrs, Non-high-risk

Event	Base Case Value	Range
Non-medically-attended influenza	$3	-
Influenza-related MD visit	$38	$12 - 98
Influenza-related hospitalization	$5,100	$2,500 – 12,200

Sources: 16-19

Model Inputs:
Preferences for influenza-related events

Event	Time Trade-off Amount		Quality-adjusted life years lost (95% CI)
	Median	Mean	
Influenza	0 days	68 days	0.005 (0.002, 0.009)
Otitis media	7 days	265 days	0.042 (0.023, 0.065)
Pneumonia hospitalization	1 year	2.7 years	0.076 (0.054, 0.100)

Sources: 20-21

Model Inputs:
Vaccination-related probabilities, IIV, 2 yrs

	Probability	Range
Vaccine effectiveness	0.69	0.40-0.90
Injection site reaction	0.003	0.0008-0.006
Systemic reaction	0.011	0.002-0.014
Anaphylaxis	1 in 4 million	0-0.000001
GBS	1 in 1 million	0-0.00001

Sources: 8, 22-23

Model Inputs:
Vaccination-related probabilities, LAIV, 2 yrs

	Probability	Range
Vaccine effectiveness	0.84	0.60-0.96
Systemic reaction	0.03	0.005-0.04
Anaphylaxis	1 in 4 million	0-0.000001
GBS	1 in 1 million	0-0.00001
Wheezing Episode	0.0037	0.0016-0.01
Hospitalization following vaccination	0.000157	0-0.2

Sources: 23-26

Model Inputs:
Vaccination-related costs, IIV, 2 years

	Direct Medical Costs	Range
Vaccine dose costs	$13.52 (under 3) $14.32(3 and older)	Varied as part of total vaccination costs
Injection site reaction	$69	$34-773
Systemic reaction	$38	$12-98
Anaphylaxis	$3,000	$60-15,500
GBS	$26,400	$7,500-89,300

Sources: 19, 27

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Model Inputs:
Vaccination-related costs, LAIV, 2 yrs

	Direct Medical Costs	Range
Vaccine dose costs	$17.90	Varied as part of total vaccination costs
Systemic reaction	$38	$12-98
Anaphylaxis	$3,000	$60-15,500
GBS	$26,400	$7,500-89,300
Wheezing Episode	$186	$118-220
Hospitalization following vaccination	$5100	$2,500-12,200

Sources: 19, 27-29

Model Inputs:
Vaccination-related costs, IIV, 2 yrs

Vaccine dose costs	
1-2 doses	$21
Administration costs	
0-2 visits	$29
Parent time costs	
0-2 visits	$33
Adverse event costs	**$4**
Total Vaccination Costs	**$88***
(Range)	**($30-$110)**

Sources: 27, 30-31

Model Inputs: Preferences for vaccination-related events (QALYs lost)

	QALYs lost	Range
Injection site reaction	None	-
Systemic reaction	None	-
Anaphylaxis	0.02	0.006-0.041
GBS	0.141	0.092-0.199
Wheezing Episode	0.0018	0.0003-0.005
Hospitalization following vaccination	0.076	0.054-0.100

Sources: 20-21, 32

Results: Mean outcomes per 1,000 (95% CI) 2 yrs, Non-high-risk

|	Inactivated vaccine	Live attenuated vaccine
Net costs	59K (7K, 97K)	64K (5K, 105K)
Episodes averted	107 (15, 276)	130 (20, 322)
Hosps averted	1.2 (0.1, 4.2)	1.4 (0.1, 4.9)
Deaths averted	0.001 (0, 0.005)	0.001 (0, 0.005)
QALYs saved	2.4 (0.3, 7.3)	2.9 (0.3, 8.2)

Results: Mean $/Event Avoided (95% CI) 2 yrs, Non-high-risk

	IIV	LAIV
$/influenza event	$600 ($35-5,000)	$500 ($20-4,300)
$/hospital-ization	$50,000 ($2,000-723,000)	$45,000 ($1,000-644,000)
$/death	$58m ($2.4m-2b)	$52m ($1.3m-1.9b)
$/QALY	**$25,000 ($1,000 - 271,000)**	**$23,000 ($1,000 - 236,000)**

Results: Mean C/E Ratios, $/QALY (95% CI)

	IIV, High risk	IIV, Non-high risk	LAIV, Non-high risk
2 yrs	CS (CS; 122,000)	$25,000 (1,000; 271,000)	$23,000 (1,000; 236,000)
3-4 yrs	$2,000 (CS; 171,000)	$37,000 (6,000; 290,000)	$33,000 (5,000; 306,000)

CS = Cost savings

Sensitivity Analysis:
2 yrs, LAIV, Non-high-risk

Influenza illness rate (0.02 - 0.35) — $5,341 | $242,028

Influenza-related hospitalizations, per 10,000 children (0 - 56.8) — $5,758 | $35,627

Total vaccination costs ($30 - $110) — $3.683 | $31.685

Probability of an outpatient visit for child with influenza (0.15 - 0.81) — $15,145 | $39,098
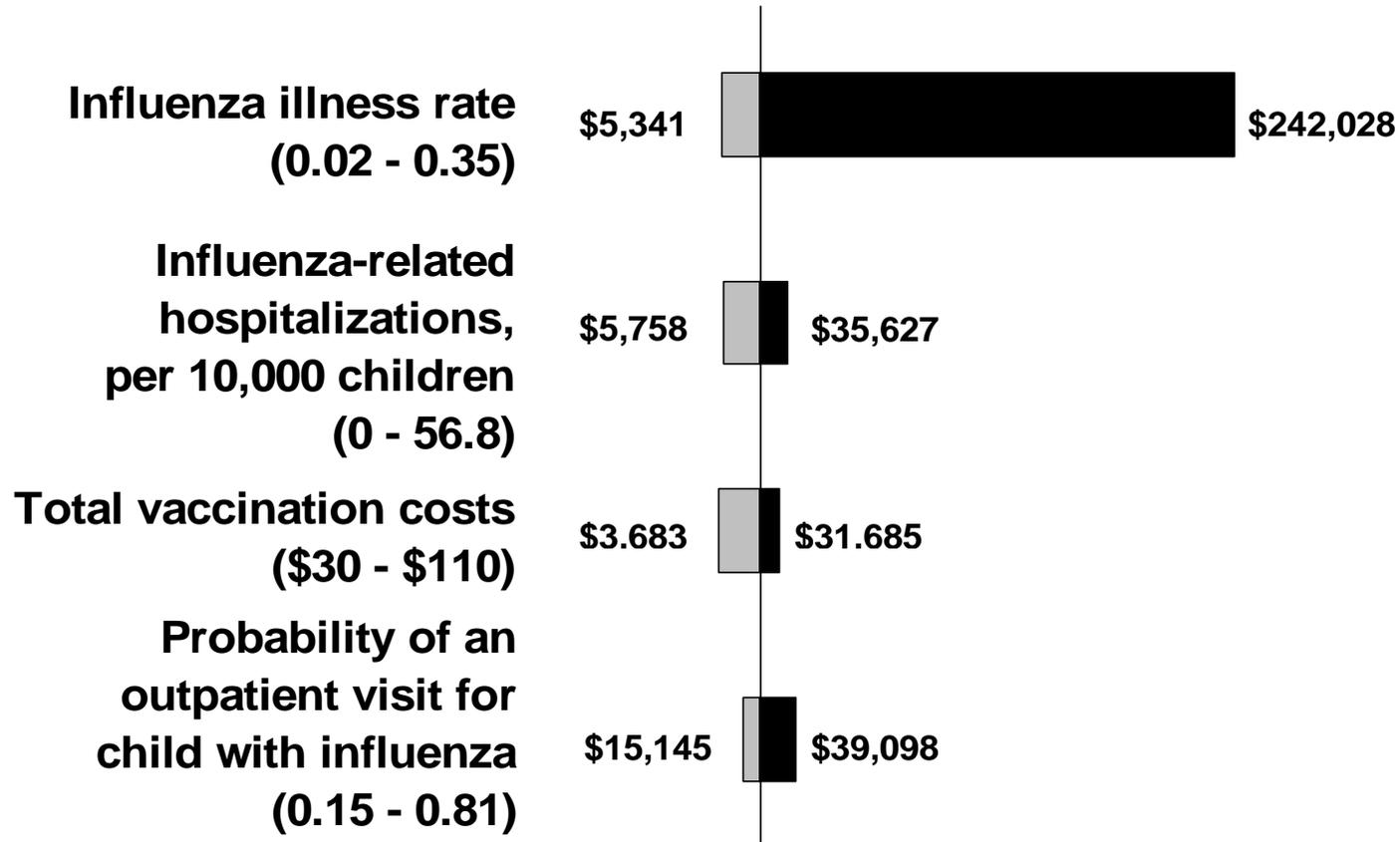
Sensitivity analysis:
Probability of hospitalization following LAIV
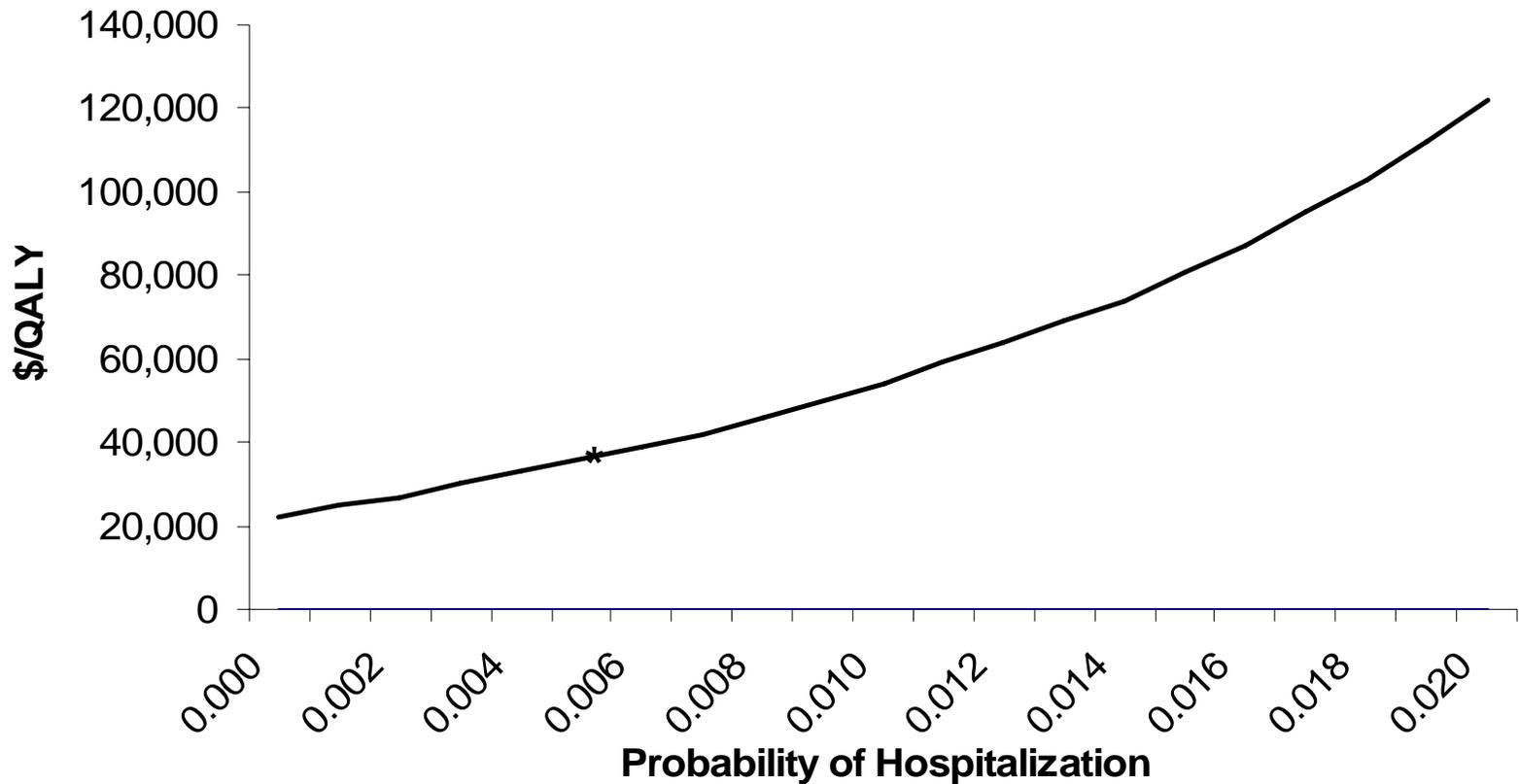
*Dominated by inactivated vaccine (LAIV is more costly yet saves QALYs).

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Results

- For children 2-4 years, updated cost-effectiveness results remained similar to previous results
  - LAIV has similar or better cost-effectiveness than IIV for this age group (IIV currently recommended)
- Inclusion of possible new adverse events for LAIV had varying effects on cost-effectiveness
  - Not sensitive to inclusion of wheezing
  - Very sensitive to possible increased probability of hospitalization
- Results sensitive to probabilities of key outcomes and vaccination costs

Limitations

- Herd immunity effects not considered

- Limited data regarding some key assumptions

- Quality adjustments for adverse events may not reflect increased value associated with causing harm

Reviewer Comments

- Comment: Additional description of methods for determining parent time costs requested

  - Response: Text and references added.

- Comment: Add discount rate to slide

  - Response: Added as requested

- Comment: Revise model schematic

  - Response: Unable to include full model schematic on slide but included in technical report

- Comment: $/hosp and $/death not included in technical report

  - Response: Not considered primary endpoints for the analysis, but can be calculated directly from data in Table 3.

Mean C/E Ratios, $/QALY

	IIV, High Risk	IIV, Non-high risk	LAIV, Non-high risk
2 years	CS	$25,000	$23,000
3-4 years	$2,000	$37,000	$33,000
5-11 years	$18,000	$104,000	$90,000
12-17 years	$25,000	$157,000	$136,000

New Recommendations, 2004-2006
Advisory Committee on Immunization Practices

Program	Age Group	$/QALY*
Rotavirus	Infants	Cost saving
Pertussis	Adolescents	21,000
HPV	Adol girls	25,000
Influenza (LAIV)	2-4 yrs, non-high-risk	26,000
Hepatitis A	2 yrs	28,000
Varicella 2nd dose	5 yrs	109,000
Meningococcal	Adolescents	131,000

*Converted to 2006 dollars

Summary

- Inclusion of higher rates of adverse events had little impact on cost-effectiveness results with the exception of a possible increase in all-cause hospitalization

- LAIV was more costly but more effective than IIV unless risk of hospitalization is considerable

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