

# Comparative Analysis of Strategies for JE Vaccination for U.S. Travelers to Asia

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DISCLAIMER: The results and conclusions presented here are those of the authors and are not necessarily those of the Centers for Disease Control and Prevention

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# Objective

To compare numbers needed to vaccinate and cost-effectiveness of strategies for JE vaccination for U.S. travelers to Asia

# Design

- Modeling approach: Decision Tree
- Hypothetical population
  - Compare cases in vaccinated and unvaccinated cohorts of 1 million individuals
- Strategy/assumptions
  - 2-dose primary vaccination schedule
  - All individuals travel in year 1
  - Some individuals travel again after year 1
  - Repeat travelers may receive booster dose
- Analytic horizon
  - 6 years but productivity losses evaluated over average life-expectancy

# Analytic Perspectives\*

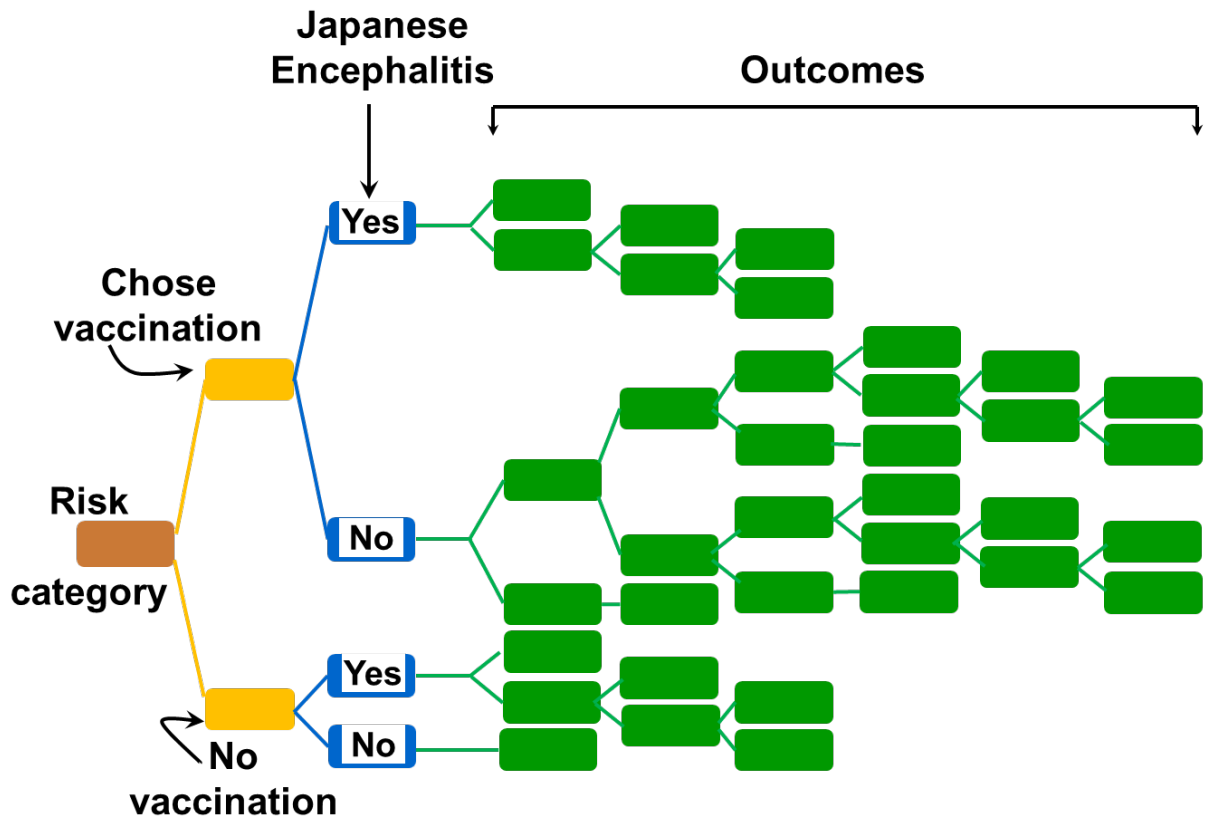
	<b>Societal</b>	<b>Travelers'</b>
Vaccine cost per dose	Included	Included
Vaccine administration cost	Included	Included
Vaccine adverse event costs per vaccinee	Included	Included <sup>†</sup>
Short-term and long-term medical costs	Included	-
Productivity costs with complete recovery	Included	Included
Productivity costs with mild sequelae	Included	Included
Life-time productivity costs with severe sequelae	Included	Included
Life-time productivity costs with death	Included	-

\*Medical payer perspective included in Appendix

<sup>†</sup>Costs partially attributed to the traveler with remainder to the medical payer



# Decision Tree: Schematic



# Epidemiologic Data: Disease Incidence By Risk

<b>Category</b>	<b>Incidence of JE (per million travelers)</b>
Risk group I*	0.53
Risk group II†	0.25
Risk group III‡	0.04

\*Travelers who plan to spend  $\geq 1$  month in JE endemic areas

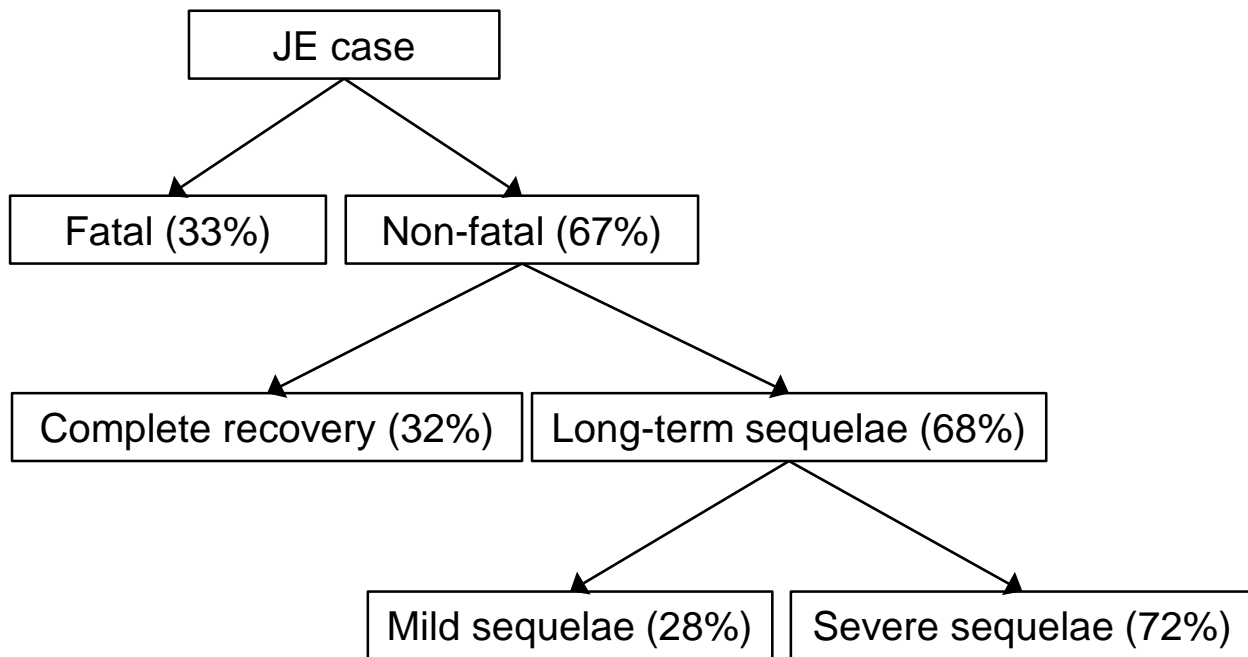
†Shorter-term travelers (<1 month) who plan to spend >20% time doing outdoor activities in rural areas

‡Remaining travelers to JE endemic areas not in risk group I or II

**Sources:** Hills SL. CDC Yellow Book 2018; US National Travel and Tourism Office; Duffy M. J Travel Med 2013 (unpublished data); CDC. MMWR Rec Rep 2010.



# Epidemiologic Data: Disease Outcome Probabilities



Source: Hills SL. *Am J Trop Med Hyg* 2010.

# Epidemiologic Data: Vaccine Effectiveness By Year

<u>Year post-vaccination</u>	<u>Effectiveness*</u>
Year 1	0.91
Without booster dose	
Year 2	0.75
Year 3	0.68
Year 4	0.72
Year 5	0.69
Year 6	0.64
With booster dose	
Years 2–6	0.96

\*Proportion of vaccinees with protective neutralizing antibodies

**Sources:** Schuller E. *Vaccine* 2008; Dubischar-Kastner K. 60th  
ASTMH Annual Meeting 2011; Paulke-Korinek M. *Vaccine* 2015.





# Epidemiologic Data: Assumptions\*

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Likelihood of annual return travel to JE endemic areas	40%
<u>Likelihood of receiving booster dose, given return travel</u>	<u>100%</u>

\*Extensive sensitivity analyses were performed on these parameters

# Economic Data: Medical Costs

	Estimated costs (US 2016 \$)
Vaccine cost per dose	\$292
Vaccine administration fee per dose	\$46
Vaccine adverse effects per vaccinee	\$0.01 <sup>†</sup>
Short-term medical costs of JE treatment*	\$29,992
Long-term medical costs of mild sequelae*	\$1,687
Long-term medical costs of severe sequelae*	\$8,437

<sup>†</sup>See appendix for details

\*Assumes clinical syndrome of encephalitis

**Sources:** *Drug Topics Red Book. Medical Economics Co, 1995, online;*  
*Coleman MS. Vaccine 2005; Staples JE. Am J Trop Med Hyg 2014.*



# Economic Data: Productivity Costs\*

	<b>Estimated costs (US 2016 \$)</b>
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Short-term productivity costs <sup>†</sup>	
Complete recovery	\$59,090
Mild sequelae	\$59,090
 Lifetime productivity costs	
Severe sequelae <sup>†</sup>	\$1,183,294
Death <sup>‡</sup>	\$1,688,566
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\*Assumes median age of JE case is 33 years

<sup>†</sup>Based on market productivity

<sup>‡</sup>Based on total productivity (household + market)

**Sources:** Grosse SD. *Med Care* 2009; Staples JE. *Am J Trop Med Hyg* 2014 (Table 5).



# Results

## Results:

# Numbers needed to vaccinate to prevent one JE-related health outcome

Health outcome	Risk group I	Risk group II	Risk group III
JE case	735,994	1,560,306	9,751,912
Long-term sequelae	1,615,439	3,424,729	21,404,548
Death	2,230,284	4,728,201	29,551,248

<u>Category</u>	<u>Incidence</u>
Risk group I	0.53 per million
Risk group II	0.25 per million
Risk group III	0.04 per million



# Results:

## Cost per outcome averted (\$ millions)

### Societal perspective

Health outcome	Risk group I	Risk group II	Risk group III
JE case	\$596	\$1,264	\$7,905
Long-term sequelae	\$1,307	\$2,774	\$17,351
Death	\$1,805	\$3,830	\$23,954

<u>Category</u>	<u>Incidence</u>
Risk group I	0.53 per million
Risk group II	0.25 per million
Risk group III	0.04 per million



# Results:

## Cost per outcome averted (\$ millions)

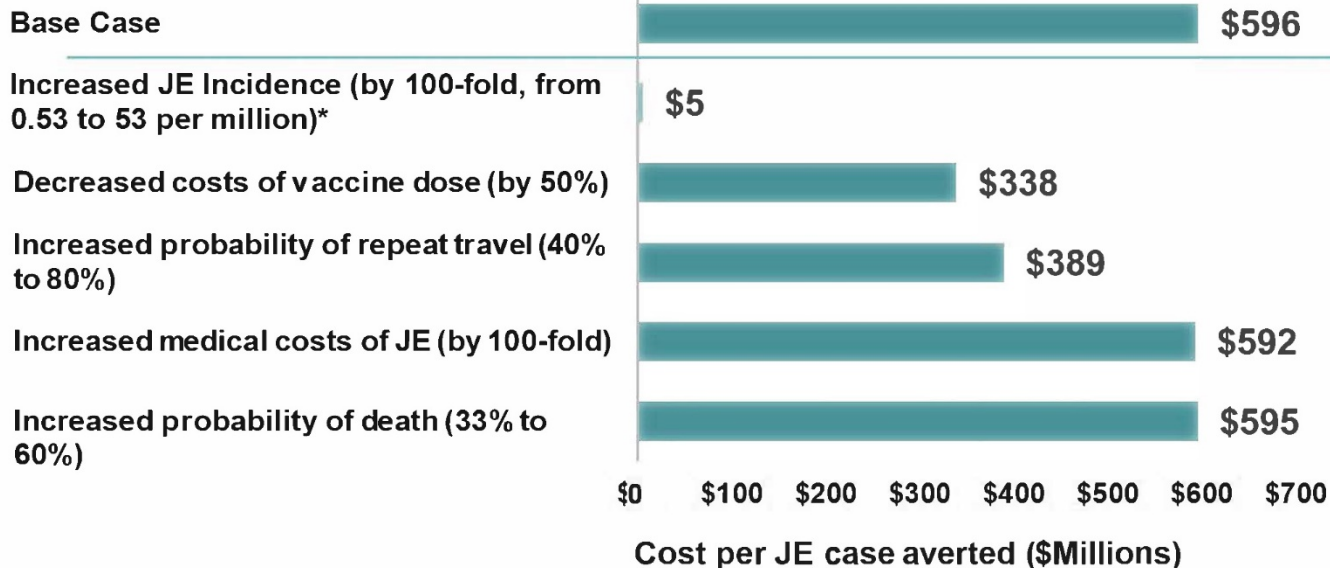
### Travelers' perspective

Health outcome	Risk group I	Risk group II	Risk group III
JE case	\$596	\$1,265	\$7,905
Long-term sequelae	\$1,309	\$2,776	\$17,352
Death	\$1,807	\$3,832	\$23,956

<u>Category</u>	<u>Incidence</u>
Risk group I	0.53 per million
Risk group II	0.25 per million
Risk group III	0.04 per million



# Sensitivity analysis: Cost per case averted (\$ millions) Risk group I, Societal perspective



\*Allowing a 100-fold increase in JE incidence allows for the potential effects of underreporting and variability in true incidence





# Sensitivity analysis: Cost per JE case averted (\$ millions) with increased disease incidence

## Societal perspective

<u>JE Incidence</u>	<u>Risk group I</u>	<u>Risk group II</u>	<u>Risk group III</u>
Base incidence	\$596	\$1,264	\$7,905
10 times higher	\$59	\$125	\$790
100 times higher	\$5	\$12	\$78

<u>Category</u>	<u>Base incidence</u>
Risk group I	0.53 per million
Risk group II	0.25 per million
Risk group III	0.04 per million



# Sensitivity analysis: Cost per JE case averted (\$ millions) with increased medical costs

## Societal perspective

<b>Costs</b>	<b>Risk group I</b>	<b>Risk group II</b>	<b>Risk group III</b>
Base medical costs	\$596	\$1,264	\$7,905
10 times higher*	\$595	\$1,264	\$7,905
100 times higher*	\$592	\$1,261	\$7,902

\*Includes short-term and long-term medical costs

<b>Category</b>	<b>Base incidence</b>
Risk group I	0.53 per million
Risk group II	0.25 per million
Risk group III	0.04 per million



# Sensitivity analysis: Cost per case averted with varying probability of medical costs and disease incidence (\$ millions) Risk group I, Societal perspective

		Incidence		
		Base	10x higher	100x higher
Medical costs	Base	\$596	\$59	\$5
	10x higher*	\$595	\$58	\$5
	100x higher*	\$592	\$55	\$2

\*Includes short-term and long-term medical costs



# Sensitivity analysis: Cost per JE case averted (\$ millions) with reduced vaccine cost\*

## Societal perspective

<b>Vaccine dose costs</b>	<b>Risk group I</b>	<b>Risk group II</b>	<b>Risk group III</b>
Base cost (\$292 per dose)	\$596	\$1,264	\$7,905
50% reduced (\$146 per dose)	\$338	\$717	\$4,487
90% reduced (\$29 per dose)	\$131	\$279	\$1,752

\*Includes vaccine administration (\$45.66) and adverse event (\$0.01) costs per vaccinee



# Sensitivity analysis: Cost per case averted with varying probability of yearly travel and receiving a booster dose

## Risk group I

Cost per case averted (\$ millions), societal perspective

		Probability of getting the booster				
		0	0.2	0.4	0.6	0.8
Probability of travel	0					
	0.2	800	807	814	821	
	0.4	562	571	580	588	
	0.6	434	444	453	461	
	0.8					

Cost per case averted:

- Decreases with increased probability of yearly travel
- Increases with probability of getting the booster

# Sensitivity Analyses: Mixed cohort\*

## Incremental cost effectiveness analysis

### Societal perspective

Risk group vaccinated in traveler cohort	Cases averted per 1 million traveler cohort*	Cost of vaccination per 1 million traveler cohort (\$ millions)**	Cost per case averted (\$ millions)*@	Incremental cost effectiveness ratio (\$ millions)†
Risk group I	0.26	\$185	\$596	-
Risk group I+II	0.43	\$426	\$850	\$1,562
Risk group I+II+III	0.48	\$949	\$1,673	\$14,569

\*Mixed cohort: 1 million, 19.5% in Risk group I; 25.4% in Risk group II; 55.1% in Risk group III

#Cost of vaccination: *first year*—2 vaccine doses, admin. costs and adverse effects; second year (40% repeat travelers) — 1 vaccine booster dose and admin. and adverse effects costs

@Cases averted: measured over 6 years (duration of immunity, assuming repeat travel likelihood of 40% each year)

†Additional cost to prevent one additional JE case by expanding the vaccination program to another risk group

<u>Category</u>	<u>Base incidence</u>
Risk group I	0.53 per million
Risk group II	0.25 per million
Risk group III	0.04 per million



# Limitations

- Results affected by uncertainty regarding JE incidence
- Current proportion of travelers who get JE vaccine is unknown
- Only includes possible vaccine booster dose in Year 2
- Long-term medicals costs only include costs for the first 5 years

# ACIP Guidelines

- Study performed according to ACIP guidelines and underwent peer-review inside CDC
- Main comments from peer-review were:
  - Clarify assumptions regarding number of doses administered to vaccinees
  - Increase breadth of sensitivity analyses regarding vaccine administration costs and medical costs
  - Explain why medical costs were not discounted



# Conclusions

- Cost per JE case averted: \$596M (Risk group I) to \$7,905M (Risk group III) (Societal perspective)
- Number needed to vaccinate: ~736,000 (Risk group 1) to ~9.8 million (Risk group III)
- Most important variable: incidence
- Smaller impact of other variables including:
  - increased likelihood of returning travel
  - increased medical costs
  - decreased likelihood of getting booster