Update on cost effectiveness of rotavirus vaccination in the United States

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Justification

- **Previous analysis for 3-dose pentavalent vaccine (RotaTeq) presented Feb 2006**

- **Results of last analysis likely broadly applicable to 2-dose monovalent vaccine, but analysis performed to address several potential differences**

  1) **Published efficacies of 2-dose monovalent vaccine are slightly different**

  2) **2-dose vaccine would provide full efficacy by 4 months of age (compared to 6 months of age with 3-dose vaccine)**

  3) **Administration costs may be different for a 2-dose vaccine**

  4) **Dose 1 efficacy of both 2-dose and 3-dose vaccines may be higher than previously estimated**

Objective

- **Assess if the cost effectiveness of a 2-dose monovalent rotavirus vaccine is different than a 3-dose pentavalent vaccine, per case averted and life-year saved, from both healthcare and societal perspectives.**

Methods

- **Cohort model**

  - Same model Widdowson et al: Pediatrics, 2007:119:684-697

  - Cumulative number of rotavirus disease outcomes in cohort of 100 000 children followed 0 to 59 months

  - Number of outcomes in the cohort fully vaccinated at 2m, 4m

  - Medical and non-medical costs of each outcome type

  - Costs of vaccine program and adverse reactions

Model input – disease burden

	Cumulative number events by age 59 months, US population*	
	Median	**5th-95th percentile**
Death	30	21–39
Hospitalization	67,033	47,365 – 91,921
Emergency room	213,946	144,103 – 291,015
Hospital outpatient	36,929	16,859 – 72,653
Physician office	387,351	200,299 – 675,958
No medical care	2,280,594	1,811,518 – 2,720,689
Any rotavirus	3,010,500	2,609,100 – 3,411,900

* US birth cohort 2004 = 4,010,000   For model, convert to rates per 100,000

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Model input – Vaccine efficacy

	3-dose vaccine effectiveness Median % (95% confidence Interval)*		2-dose vaccine effectiveness Median % (95% confidence interval)	
	One season follow-up	CE analysis (Min-Max)§	One season follow-up†	CE analysis (Min – max)
Death	No data	**90 (80-98)**	No data	**90 (80-100)**
Hospitalization	96 (91-98)	**90 (80-98)**	100 (81.8- 100)	**90 (80-100)**
ER	93 (86-96)	**90 (80-98)**	No data	**90 (80-100)**
Office / hospital outpatient	86 (74-93)	**85 (70-90)**	92 (84 -96)‡	**85 (70-90)**
Mild / moderate	71 (63-78)	**65 (55-75)**	78 (?-?)	**70 (65-75)**

* Widdowson et al, Pediatrics 2007 † Vesikari et al Lancet 2007

Example of program costs using current and 2006 retail price of both vaccines

	Cost in 2008$ (full course)	Cost in 2006$ (full course)	Potential Intussusception (1:50 000)	Administration cost ($) $10 per dose	Total in 2006$ (full course)
Course of 2-dose vaccine	205.50*	187.50†	0.25	20	208
Course of 3- dose vaccine	206.52	187.50	0.25	30	218

*Personal communication Dr M. Rennels

† Estimated

Cost effectiveness
Per case averted
Health care perspective
(Medical costs)

Cost

$500

$300

$100

($100)

($300)

($500)

0   50   100   150   200   250   300

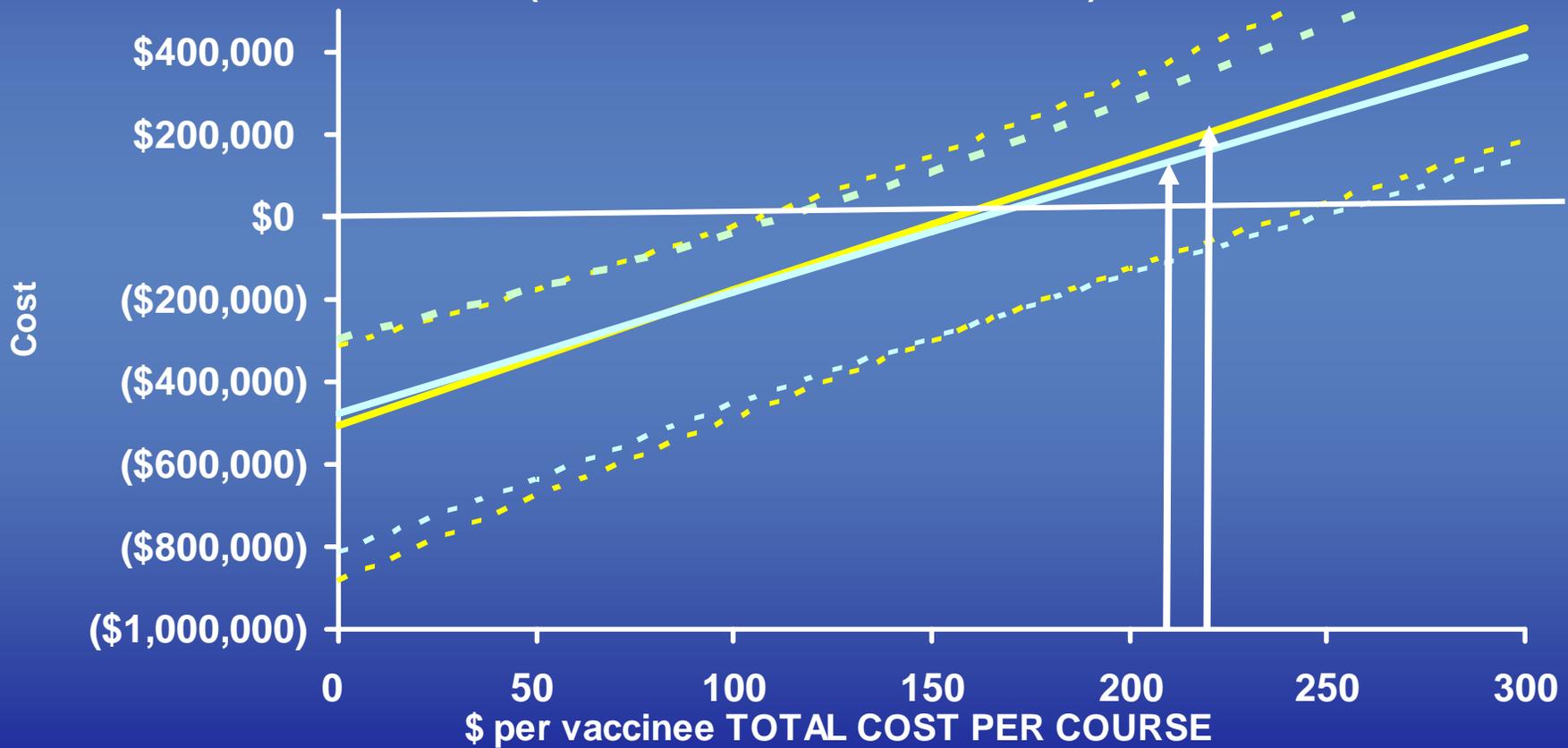$ per vaccinee TOTAL COST OF COURSE
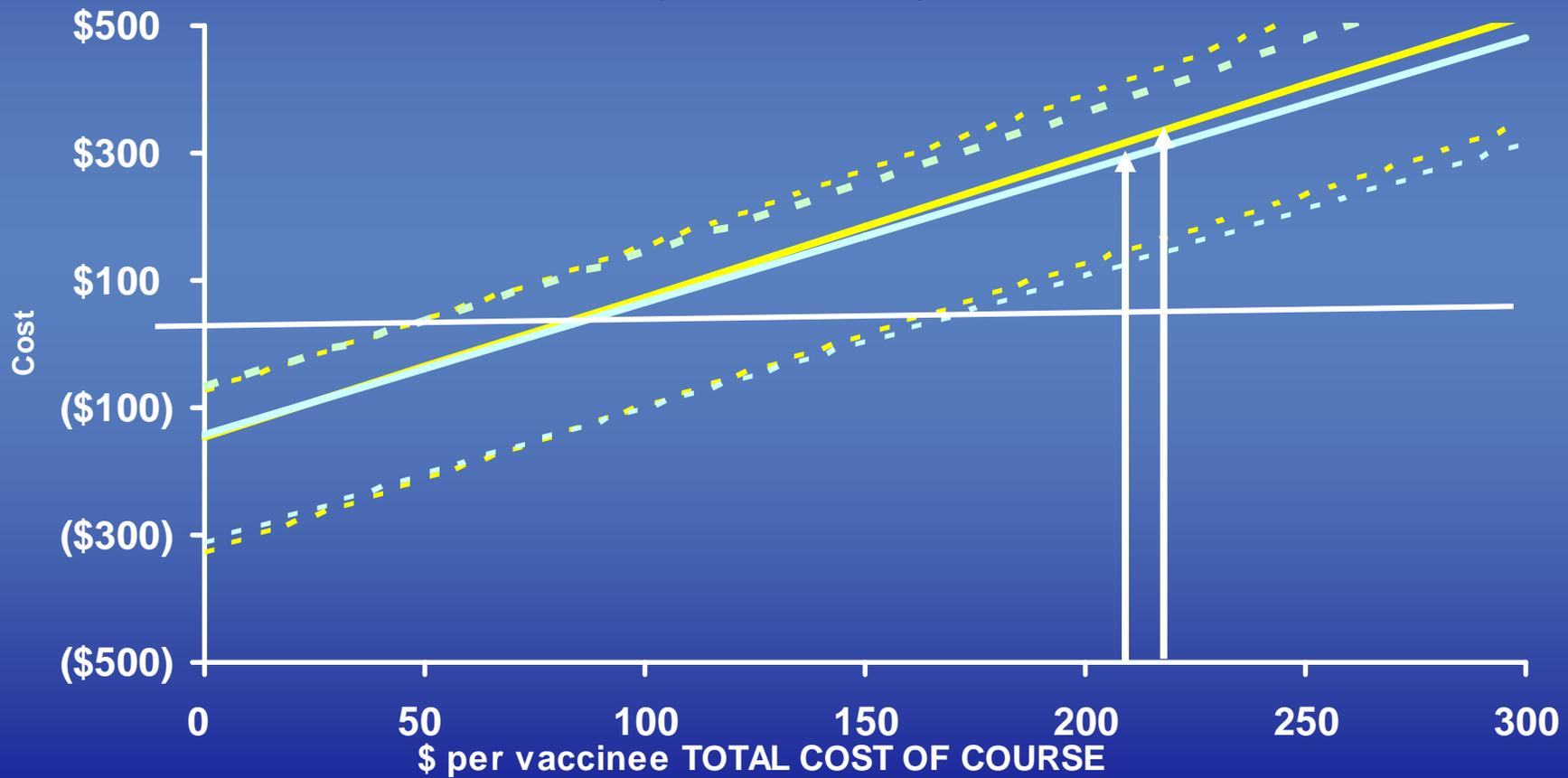
- - - - 3-dose:5th   ——— 3-dose:median   - - - - 3-dose:95th

- - - - 2-dose:5th   ——— 2-dose:median   - - - - 2-dose:95th

Cost effectiveness Per life-year saved — Societal perspective (Medical and nonmedical costs)

Cost effectiveness of 2-dose and 3-dose rotavirus vaccines

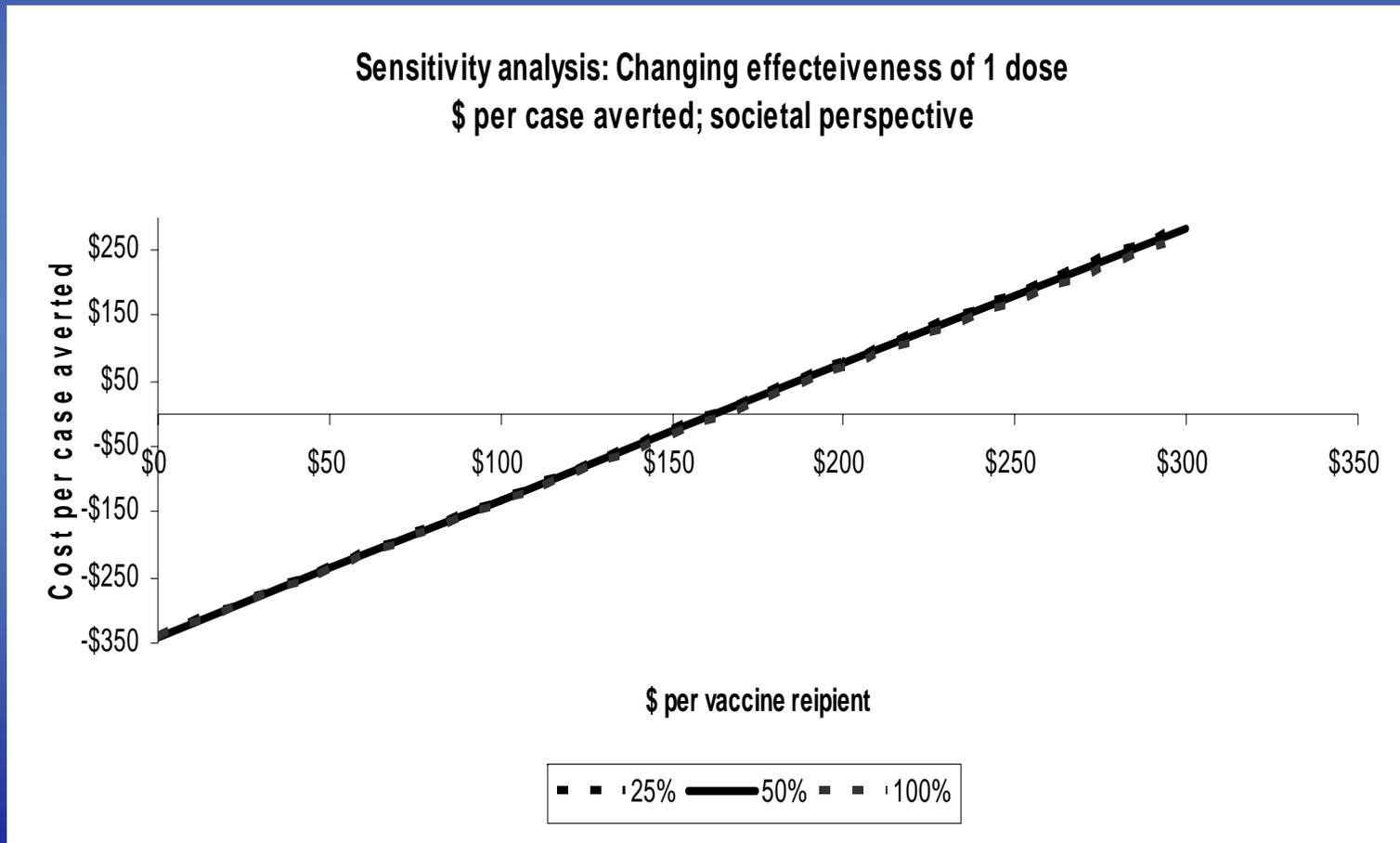|	3-dose vaccine $218 per course*	2-dose vaccine $208 per course*
Health care perspective		
Median $ per case averted 5th and 95th percentile	**338** 116 - 438	**290** 125 – 381
Median $ per life-year saved 5th and 95th percentile	**472,672** 218,892 – 741,611	**392,550** 170,353 – 624,673
Societal perspective		
Median $ per case averted 5th and 95th percentile	**139** (42) - 261	**94** (81) - 206
Median $ per life-year saved 5th and 95th percentile	**198,546** (66,988) – 411,104	**128,400** (115,049) - 304,864

***2006 price $62.50 pr dose plus $10 per dose administration fee
Parentheses indicate cost-saving**

CDC

Sensitivity: impact of efficacy of dose one

Sensitivity analysis: Changing effecteiveness of 1 dose
$ per case averted; societal perspective

Discussion and Conclusions

- **Median estimates in this model suggest small increased cost-effectiveness of 2-dose monovalent vaccine over 3-dose pentavalent vaccine**

- **Difference between vaccines is unlikely significant due to uncertainty of factors between vaccines**
  - True cost of each vaccine not known
    - e.g. VFC and commercial arrangements
  - Cost of administration / shipping
    - e.g. 2-dose requires reconstitution
  - Vaccine efficacy
    - e.g. high dose 1 vaccine efficacy for 3-dose will make more comparable to 2-dose

Overall Conclusion

- **Overall cost-effectiveness of rotavirus vaccination not appreciably changed with 2-dose vaccine**

Limitations

- No assessment of herd immunity
- Do not know the field effectiveness of 2-dose vaccine – may not perform similarly to trials.
- Field cost-effectiveness for both vaccines may be higher if first dose has high efficacy in children that do not complete course.

Older vaccines more cost-effective

Immunization	Reference	Results
MMR	Hatziandreu, 1994	Cost saving (societal & healthcare payer)
DTaP	Ekwueme, 2000.	Cost saving (societal & healthcare system)
Hep B	Margolis, 1995.	Cost saving (societal) $1522 / YOL for infants (healthcare payer)
Varicella	Lieu, 1994	Cost saving (societal) $2500 / YOL (healthcare payer)
Pneumococcal conjugate	Lieu, 2000	$80,000 / YOL @ $58/dose (societal)
IPV (vs OPV)	Miller, 1996	$3(m) / VAPP (incremental costs)

CDC

Comparing rotavirus with other vaccines

From the societal perspective:

	$ / case prevented	$ / LY year saved
Varicella 1 dose	Saving	Saving
Hepatitis B	Saving	Saving
Pneumococcal	200[*]	80,000
Meningococcal	223,000	127,000**
Rotavirus[†]	138	197,000

*Includes otitis media, pneumonia, meningitis, and bacteremia.
**Incl. herd immunity – Ortega-Sanchez et al, Clin Infect Dis 2008
† Widdowson et al, Pediatrics, 2007

Anonymous CDC review comments

- **Justification for redoing analysis for the 2-dose vaccine is not clear**

- **Cost-effectiveness ratios should be presented and the high cost per life year saved made explicit**

Methods

- **Cost effectiveness ratio**

$$= \frac{\text{Costs of program} - \text{Costs saved with program}}{\text{No. outcomes saved}}$$

- **Two perspectives**
  - Health care payer (medical costs)
  - Societal (medical and non-medical costs)
- **Costs discounted at 3%**

Methods

- **Cohort model**

  - Cumulative number of rotavirus disease outcomes in cohort of 100 000 children followed 0 to 59 months

  - Number of outcomes in the cohort fully vaccinated at 2m, 4m

  - Medical and non-medical costs of each outcome type

  - Costs of vaccine program and adverse reactions

  - Same model Widdowson et al: Pediatrics, 2007:119:684-697

Model input – medical costs

	Cost in 2004 dollars		
	Median	Mean	5th- 95% percentile
Hospitalization (median duration =2 days)	2962	3496	1181–7426
Emergency room	332	487	79–1402
Hospital outpatient	200	394	35–1161
Physician office	63	69	32–124
Medication*	22	37	4–117

* Added to physician office & hospital outpatient visit cost
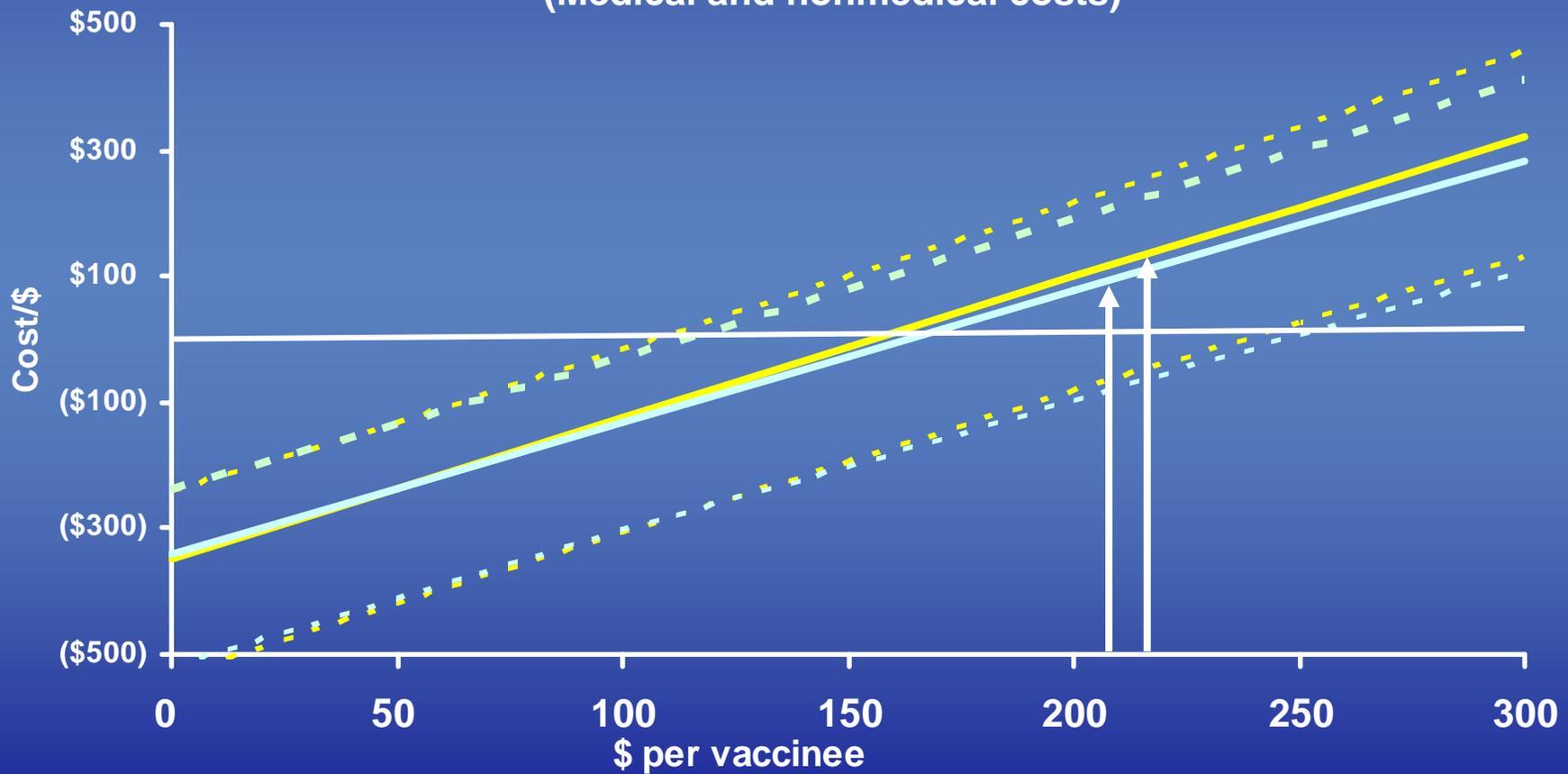
Model input – non-medical costs

	Days off work	Cost in 2004 dollars		
		Median	Mean	5th– 95% percentile
Parental days off work @ $118/ day				
Home care	1.0	---	---	---
Office & Hospital outpatient	1.3	---	---	---
Emergency room & Hospitalization	2.0	---	---	---
Death	10.0	---	---	---
Travel for episode needing health care	---	19	19	1–68
Extra diapers (all episodes except death)	---	9	9	1–19
Special food, ORS (all episodes)	---	24	24	1–71
Childcare costs (all episodes)	---	9	9	1–66
Lifetime productivity loss of child death	---	--	1,167,789	--

Cost effectiveness
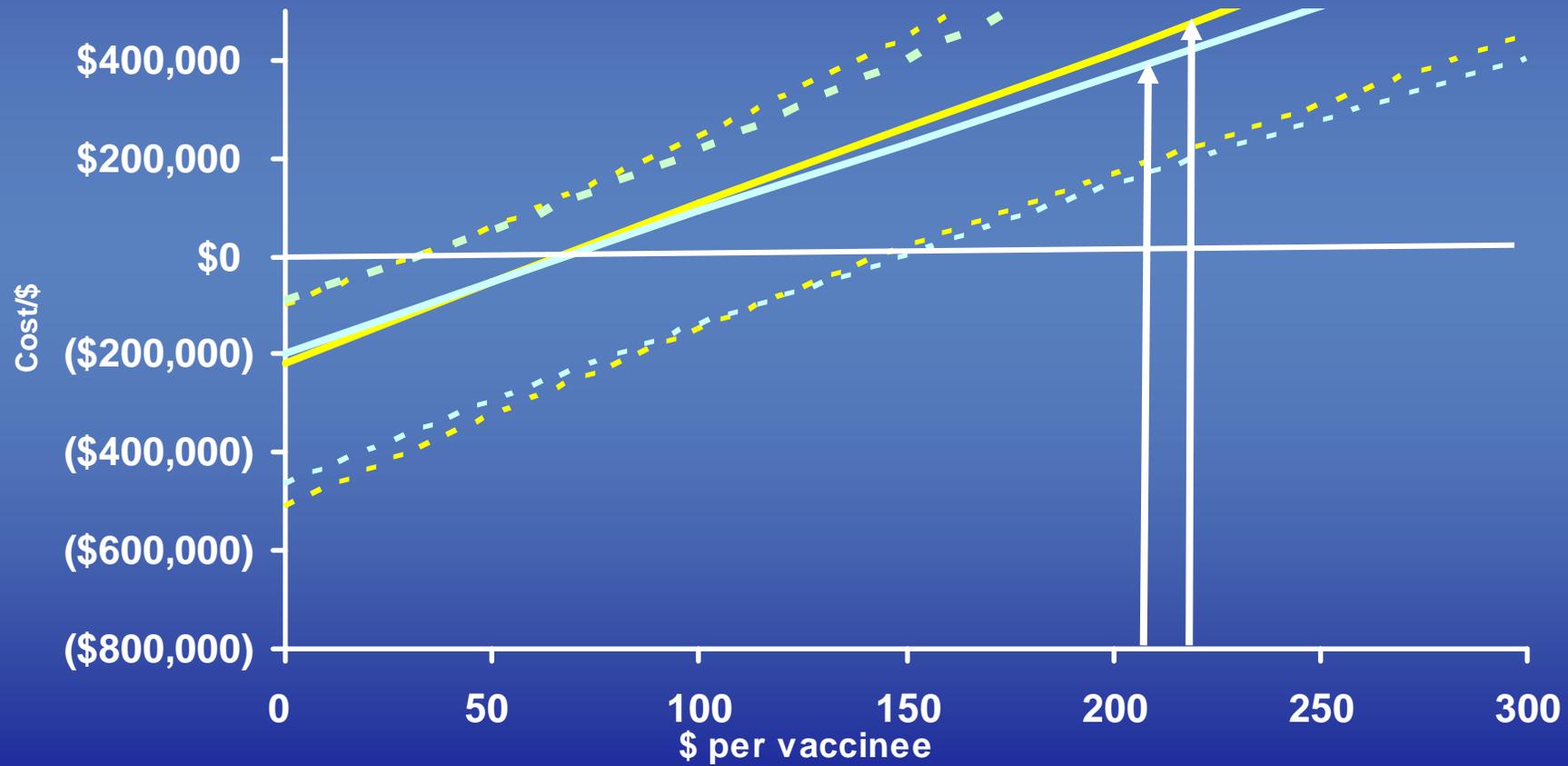# Per case averted
Societal perspective
(Medical and nonmedical costs)

Sensitivity: Relative importance of input distributions @ $62.50/dose

Hospital $/case
ER visit $/case
Extra childcare $/case
% children w/ RV disease by 59m
Diets / ORT $/case
% RV positive hospital
Hospital outpatient $/case
% RV positive outpatient
Travel to care $/case
Outpatient drugs $/case
% RV positive ER

0   0.2   0.4   0.6   0.8   1