Incremental Cost-Effectiveness of Using Two Instead of Three Primary Doses in the 13-valent Pneumococcal Conjugate Vaccination Schedule

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Objective

- **Evaluate cost effectiveness of switching PCV13 schedule from 3+1 to 2+1**
  - Model removal of the dose at 6 months
  - Program cost savings
  - Increases in disease, medical costs, and nonmedical costs

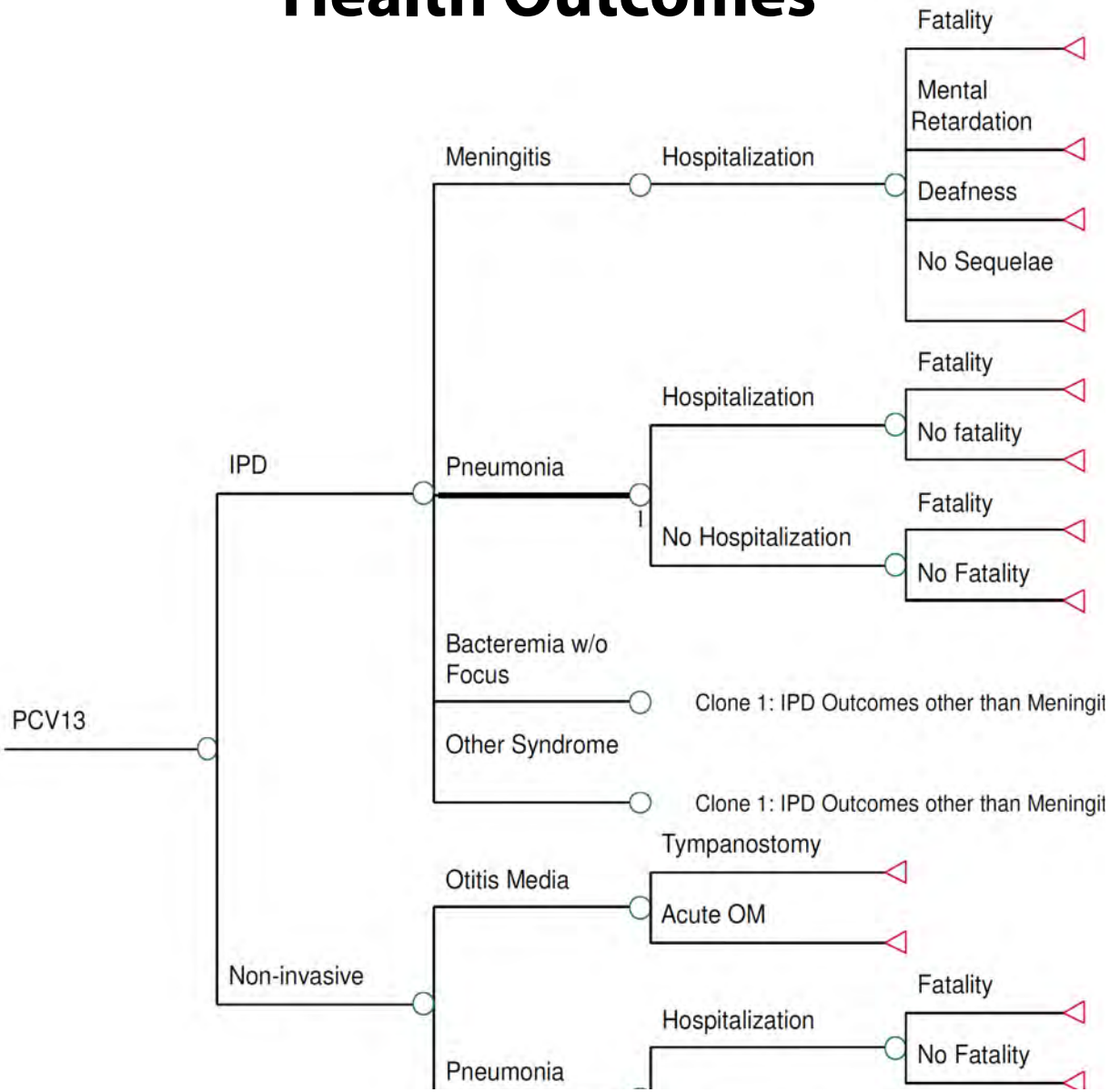
This presentation reports results previously published in: Stoecker, Charles, Lee M. Hampton, Ruth Link-Gelles, Mark L. Messonnier, Fangjun Zhou, and Matthew R. Moore. "Cost-effectiveness of using 2 vs 3 primary doses of 13-valent pneumococcal conjugate vaccine." *Pediatrics* 132.2 (2013): e324-e332.

Model

Cohort Model

- **Cohort**
  - Size of 2010 U.S. birth cohort
- **Events**
  - Tracked annually
    - Except first year which is tracked separately in two six month periods
  - Occur within first 10 years of life
  - Consequences counted over expected lifetime
- **Societal perspective, costs in 2011$, Discount rate 3%**
- **New Steady State**

Health Outcomes



Assumptions

6 Key Assumptions

1) Both schedules have similar direct effects against IPD
2) Both schedules have identical herd effects
3) Both schedules have identical replacement disease
4) 2+1 provides zero direct protection against OM and all-cause pneumonia between 6-11 months
5) 2+1 provides same direct protection against OM and all-cause pneumonia as 3+1 after the booster dose
6) No price response from vaccine manufacturer

Pre-PCV7 Baseline Rates (per 100k population)

Age (yrs)	Acute Otitis Media[1]	Tymp. Tube Placement[1]	Outpatient Pneumonia[1]	Inpatient Pneumonia[1]	IPD[2]
0-<0.5	32,264	121	4,500	649	34.3
0.5-<1	92,086	477	4,500	649	41.6
1-<2	124,350	4,680	9,000	1,297	32.6
2-<3	80,475	2,370	6,500	418	15.9
3-<4	36,600	1,130	4,000	418	10.1
4-<5	36,600	1,020	4,000	418	9.5

[1] Non-IPD rates for children younger than 5 are adapted from Ray et al 2009. Incidence rates in the first year of life are broken into 6-month categories by the proportions reported in Ray et al 2006.

[2] IPD incidence rates are averages from 2006–2008 Active Bacterial Core surveillance data (Centers for Disease Control and Prevention, unpublished data, September 2011).

Assumed Percent Reduction in Pneumococcal Disease by Syndrome, Age, and Schedule

Disease	Ages (yrs)	2+1	3+1
Acute Otitis Media[1,2]	0-<0.5, 1+	14.6	14.6
	0.5-<1	6.7	14.6
Tympanostomy Tube Placement[1,2]	0-<0.5, 1+	25.1	25.1
	0.5-<1	11.5	25.1
Outpatient Pneumonia[1,3]	0-<0.5, 1+	6.3	6.3
	0.5-<1	0	6.3
Inpatient Pneumonia[1,3]	0-<0.5, 1+	13.8	13.8
	0.5-<1	7.5	13.8
Invasive Pneumococcal Disease (Vaccine Serotypes)[4]	0-<1	96	96
	1+	98	100

[1] Adapted from Ray et al 2009.
[2] Adapted from Fireman et al 2003.
[3] Adapted from Pelton et al 2010.
[4] Adapted from Whitney et al 2006.

Vaccine Costs

Item	Cost
Vaccine Price Public[1]	$97
Vaccine Price Private[1]	$121
Public Share[2]	65%
Wastage[3]	5%
Vaccine Administration[4]	$15

[1] CDC vaccine price list 2011.
[2] CDC Biologics Surveillance Data (unpublished), 2010.
[3] Ching 2007.
[4] Zhou et al 2005.

Disease Costs

Item	Medical	Non-Medical
Inpatient Pneumonia, age 0-5 yrs[1]	$7,763	$371
Inpatient Pneumonia, age 5+ yrs[1,2]	$5,329	$749
Outpatient Pneumonia[1]	$248	$371
Acute Otitis Media[1]	$59	$147
Tympanostomy Tube Placement[1]	$2,556	$367
IPD, Meningitis, age 0-5 yrs[1]	$18,189	$2,603
IPD, other, age 0-5 yrs[1,2]	$3,471	$497
IPD, age 5+ yrs[1,2]	$13,591	$749
Deafness[3]	$34,230	$110,240
Disability[3]	$182,700	$123,107

[1] Ray et al 2009.
[2] Non-medical costs from hospital stay length from ABCs data 2001 and lost wages from Widdowson et al 2007.
[3] MMWR 53(3) 2004 and MMWR 55(32) 2006.

QALY Loss per Episode of Disease

Item	QALY
Acute Otitis Media	0.005
Tympanostomy Tube Placement	0.005
Inpatient Pneumonia	0.006
Outpatient Pneumonia	0.004
IPD, Meningitis	0.0232
IPD, other	0.0079
Deafness	0.73
Disability	0.68

QALY decrements assembled by Rubin et al 2010.

Results

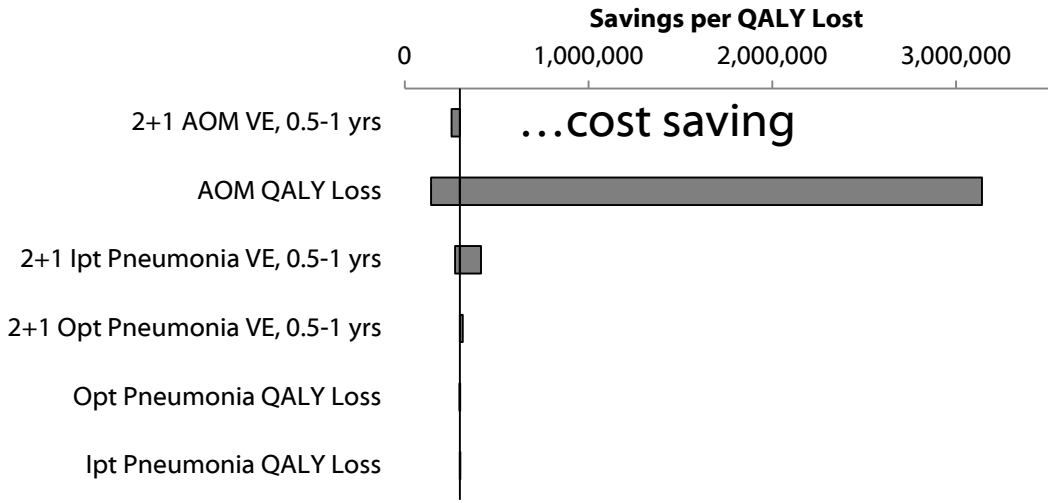
Disease and Cost Changes when Switching to 2+1

	2+1 Identical to 3+1 vs All Syndromes
Cases	
IPD	0
Hospitalized pneumonia	0
Non-hospitalized pneumonia	0
Tymp. tube placement	0
Otitis media	0
Deaths	0
Total Cost (savings) in millions	($500)
Savings/QALY lost	Cost Saving
Savings/Life-year lost	Cost Saving

Disease and Cost Changes when Switching to 2+1

	Base Case	(%)
Cases		
IPD	44	(8)
Hospitalized pneumonia	1,453	(1)
Non-hospitalized pneumonia	10,136	(1)
Tymp. tube placement	2,318	(1)
Otitis media	261,324	(2)
Deaths	2.5	(1)
Total Cost (savings) in millions	($421)	(~25)
Savings/QALY lost	$300,000	
Savings/Life-year lost	$6,014,000	

Tornado Diagram of Most Influential Inputs



Sensitivity Analysis: AOM Assumptions

	Base Case	OM QALY = 0.011	2+1 Identical to 3+1 vs AOM
Cases			
IPD	44	44	44
Hospitalized pneumonia	1,453	1,453	1,453
Non-hospitalized pneumonia	10,136	10,136	10,136
Tymp. tube placement	2,318	2,318	0
Otitis media	261,324	261,324	0
Deaths	2.5	2.5	2.5
Total Cost (savings) in millions	($421)	($421)	($482)
Savings/QALY lost	$300,000	$143,000	$3,919,000
Savings/Life-year lost	$6,014,000	$6,014,000	$6,886,000

Sensitivity Analysis: VE against other Syndromes

	2+1 Identical to 3+1 vs IPD	2+1 Identical to 3+1 vs IPT Pneumonia	2+1 Identical to 3+1 vs OPT Pneumonia
Cases			
IPD	0	44	44
Hospitalized pneumonia	1,453	0	1,453
Non-hospitalized pneumonia	10,136	10,136	0
Tymp. tube placement	2,318	2,318	2,318
Otitis media	261,324	261,324	261,324
Deaths	1.9	0.6	2.5
Total Cost (savings) in millions	($422)	($433)	($428)
Savings/QALY lost	$305,000	$323,000	$314,000
Savings/Life-year lost	$7,673,000	$30,929,000	$6,114,000

Sensitivity Analysis: Increases in PCV13 Coverage

	Base Case Coverage (83.3%)	Expanded Coverage (86%)	Expanded Coverage (93%)
Cases			
IPD	44	(82)	(410)
Hospitalized pneumonia	1,453	831	(780)
Non-hospitalized pneumonia	10,136	8,091	2,790
Tymp. tube placement	2,318	(450)	(7,624)
Otitis media	261,324	201,596	46,745
Deaths	2.5	(0.5)	(8.1)
Total Cost (savings) in millions	($421)	($434)	($466)
Savings/QALY lost	$300,000	$446,000	Cost Saving
Savings/Life-year lost	$6,014,000	Cost Saving	Cost Saving

Coverage denotes coverage with complete recommended schedule.

Discussion

Limitations

- 2+1 vs 3+1 comparative effectiveness based on observation studies
  - RCT evidence that effectiveness is similar for invasive disease
- No RCT evidence of PCV13 efficacy
  - estimates adjusted from PCV7 to match PCV13 serotypes
- Evidence of herd immunity based on international comparisons and immunogenicity
- Data quality of effectiveness of 2+1 against non-invasive disease is especially limited
- Great uncertainty around how important OM outcome is
  - This is a key input for cost effectiveness
- Does not model continuing 3+1 for high risk groups

3rd Primary Dose of PCV13 vs. Other Interventions

Intervention	2011 Cost/QALY
HPV 3 doses for boys	43,000
PCV13 3+1 instead of 2+1: Otitis Media QALY loss = 0.011 instead of 0.005	**140,000**
MCV4 doses at age 11 and age 16	160,000
Tdap revaccination at age 16 (favorable assumptions)	180,000
Lyme disease in areas with attack rate >0.5%	190,000
PCV13 3+1 instead of 2+1: Base case	**300,000**
Value of a Statistical Life Year	450,000
PCV13 3+1 instead of 2+1: Equal protection against Otitis Media	**3,920,000**

Conclusions

- Compared to a 2+1 schedule, the current 3+1 schedule is less cost-effective than other routinely recommended preventive services
- The cost-effectiveness of the third dose in the 3+1 schedule could fall into the range of other routinely recommended services if the QALY loss associated with otitis media were 0.011 (4 days) instead of 0.005 (1.8 days)
- If the effectiveness of 2+1 and 3+1 against otitis media are equivalent, then the cost-effectiveness of the 3+1 schedule falls far outside the range of other services considered to be cost-effective.

Thank you!

Contributors:

Lee Hampton
Ruth Link-Gelles
Mark Messonnier
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Matt Moore