

Cost-Effectiveness of Quadrivalent HPV Vaccination of Adult Women

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Cost-effectiveness of HPV vaccination

- Vaccination of 12-year-old girls is cost-effective
 - Consistency across models
- More uncertainty, less precision in cost-effectiveness estimates for:
 - Vaccination of adult women
 - February 2008 ACIP, June 2008 ACIP
 - Vaccination of males
 - June 2009 ACIP, October 2009 ACIP

Outline

- Review of cost-effectiveness ratios, QALYs
 - Other vaccines
 - Other health interventions
- Summary of 3 cost-effectiveness models for adult women in US
 - Kim & Goldie (N Engl J Med 2008)
 - Merck (based on Elbasha et al., Emerg Inf Dis 2007)
 - Chesson et al. (based on Emerg Inf Dis 2008)

Vaccination cost-effectiveness

- Often expressed in terms of cost per QALY gained

Cost per QALY gained by adding HPV vaccination to screening:

$(\text{Vaccine cost} + \text{administration cost}) - (\text{cost of illness averted by vaccination})$

Number of QALYs gained by vaccination

QALY: Quality-adjusted life year

- QALYs account for quality and length of life
 - One year in perfect health = 1 QALY
 - Death = 0 QALY
 - One year of life in less than perfect health is given a value between 0 and 1 QALY

Cost-effectiveness thresholds

- No consensus on appropriate cost-per-QALY threshold for determining cost-effectiveness of public health interventions in the US
 - Grosse (2008), Weinstein (2008)
- In the US:
 - \$50,000 to \$100,000 threshold often cited^a
 - Described as arbitrary, w/o empirical or theoretical justification^a
- Globally:
 - Per-capita GDP suggested by WHO^{a,b}
 - < Per-capita GDP very cost-effective
 - < 3 times per-capita GDP cost-effective
 - US per-capita GDP ≈ \$50,000
 - Described as lacking theoretical rationale^a

GDP: Gross Domestic Product WHO: World Health Organization QALY: Quality-adjusted life year.

^a Grosse (2008). See also Weinstein et al. (2010) for additional incremental QALY threshold interpretation.

^b WHO cost-effectiveness threshold is for disability-adjusted life years (DALYs).

Cost per outcome gained for selected childhood vaccines in the US

Vaccine	Cost per outcome gained (compared to no vaccine)	Source
DTaP, Hib, MMR, Polio, Varicella	<\$0 per QALY (cost-saving) Individually and as a group	Ekwueme (2000), Zhou (2004, 2005, 2008), Cochi (1985), White (1985), Thompson (2006), Preblud (1985)
Influenza (LAIV)	≈ \$10,000 per QALY	Prosser (2006)
Hepatitis A	≈ \$10,000 to \$30,000 per QALY	Das (1999), Rein (2007)
Meningococcal	≈ \$120,000 per QALY	Shepard (2005)
Pneumococcal	≈ \$10,000 to \$105,000 per LYS	Ray (2006, 2009) and Lieu (2000)
Rotavirus	≈ \$135,000 to \$225,000 per LYS	Cortese (2009) and Widdowson (2007)

QALY: quality-adjusted life year. LYS: life-year saved.

Updated to 2009 US dollars. Meningococcal estimate is for vaccination at age 1 year. This table shows a collection of point estimates; the ranges shown for hepatitis A, pneumococcal, and rotavirus vaccination reflect base case results of more than one study. For each vaccine, the actual range of plausible cost-effectiveness estimates varies (not shown). See source studies for details.

Cost per QALY gained for selected adolescent vaccines in the US

Vaccine	Target group	Cost per QALY gained (compared to no vaccination)
Hepatitis B	College freshmen	<\$0 (cost-saving) to ≈ \$10,000
Hepatitis A	College freshmen	<\$0 (cost-saving) to ≈ \$15,000
HPV	12-year-old females	≈ \$3,000 to \$45,000
Influenza (LAIV)	12- to 17-year olds, high risk	≈ \$10,000
Tdap	All 11-year-olds	≈ \$25,000
Meningococcal (MCV4)	All 11- to 17-year-olds	≈ \$105,000
Influenza (LAIV)	12- to 17-year olds, healthy	≈ \$140,000
Meningococcal (MCV4)	All 11-year-olds, routine	≈ \$140,000

Source: Ortega-Sanchez et al. *Pediatrics* (2008), except HPV (see notes).

Updated to 2009 US dollars. For HPV, lower and upper bound estimates obtained from Elbasha (2007) and Kim (2008), respectively. This table shows a collection of point estimates; the range shown for HPV reflects base case results of two studies; and the ranges shown for hepatitis A & B reflect base case results from two perspectives. For each vaccine, the actual range of plausible cost-effectiveness estimates varies (not shown). See source studies for details.

Cost per QALY gained for selected health interventions in the US

Vaccine	Cost per QALY gained
Chlamydia screening	≈ \$3,000 to \$40,000
Cervical cancer screening	
Every 2 years vs. never	≈ \$25,000
Annual vs. every 2 years	≈ \$725,000
Breast cancer screening	
Every 2 years vs. never	≈ \$40,000
Annual vs. every 2 years	≈ \$65,000 to \$160,000

QALY: quality adjusted life year. Updated to 2009 US dollars.

Chlamydia screening is annual (compared to no screening), for sexually active women aged 15-24 years (Hu 2004, lower bound estimate) and for women aged 15 to 34 years (Gift 2008, upper bound estimate). Cervical cancer screening, beginning at age 21: Cytology (followed by HPV DNA testing for ASC-US results) for women under 30; HPV DNA testing as an adjunct to cytology for women 30 and older. ASC-US: atypical squamous cells of undetermined significance. Estimates extrapolated from Goldhaber (2008) and consistent with other estimates [Tengs 1995; Goldie 2004,2006; Kulasingam 2006; and Kim 2002]. Breast cancer screening (every year vs. every 2 years, and every 2 years vs. every year) was estimated to cost approximately: \$40,000 and \$160,000, respectively, by Ahern (2009)(extrapolated), for combined mammography and clinical breast exam for ages 40 to 79 years; and \$40,000 to \$65,000, respectively, by Stout (2006)(extrapolated), for mammography for ages 40 to 80 years, per QALY. Ranges (where given) reflect point estimates from more than one study. For each intervention, the actual range of plausible cost-effectiveness estimates varies (not shown). See the source studies for more details.

Comparison of selected model features

All models examined female-only vaccination and assumed lifelong vaccine protection

	Kim & Goldie (2008) <i>N Engl J Med</i>	Merck (Unpublished)	Chesson et al. (Unpublished)
Total vaccine cost per series	\$500 (includes patient time and transport costs)	\$400	\$500
Includes cervical cancer, CIN, genital warts, non-cervical cancers, RRP*	Yes	Yes	Yes
Includes male health outcomes (indirect benefit of female vaccination)	Not in this application of model	Yes	Yes
Quality of life impact of CIN	No	Yes	Yes
Includes indirect effects (herd immunity)	Yes (for HPV 16 & 18)	Yes	Yes, with simplified model

CIN: Cervical intraepithelial neoplasia.

*No evidence to date of vaccine efficacy against recurrent respiratory papillomatosis (RRP) or all non-cervical cancers included in the analyses (e.g., oropharyngeal cancer). All models include juvenile-onset RRP (JORRP); Merck model also includes adult-onset RRP.

Comparison of selected model features, continued

	Kim & Goldie (2008) <i>N Engl J Med</i>	Merck (unpublished)	Chesson et al. (unpublished)
Cervical cancer screening	Yes (model tracks individual-level history of screening, treatment)	Yes	Not modeled directly; assumed to be reflected in cervical cancer rates
Warts quality of life, duration	0.91 utility, 3 months	0.91 utility, ≈ 8 months	≈ 0.94 utility, ≈ 6 months
Vaccine efficacy against recurrence	0%	0%	0%
Degree & duration of natural immunity	HPV 16: 75%, lifelong HPV 18: 70%, lifelong	Female: 80%, lifelong Male: 50%, lifelong (for those seropositive)	100%, lifelong
Time horizon	Lifetimes of relevant birth cohorts	100 years	100 years

Kim & Goldie model results: Cost-effectiveness of female vaccination by age

Ages vaccinated	Incremental ages added	Cost per QALY
No vaccination	-	-
12	12	\$34,900
12-18	13-18	\$81,000
12-21	19-21	\$101,300
12-26	22-26	\$133,600

Includes cervical outcomes and genital warts (females)

Cost per QALY (quality-adjusted life year) of each strategy is the incremental cost-effectiveness ratio of the strategy when compared to the preceding strategy. All strategies include cervical cancer screening.

Kim & Goldie model results: Cost-effectiveness of vaccination after age 30

- In another application of model, Kim et al. focused on women 35 to 45 years old
- Compared with current screening, HPV vaccination was less cost-effective than other, well-accepted interventions in US

Merck model results: Cost-effectiveness of female vaccination by age

Ages vaccinated	Incremental ages added	Cost per QALY
No vaccination	-	-
9 to 26	9-26	\$7,800
9 to 34	27-34	\$51,900
9 to 44	35-44	\$142,000

Includes cervical, vulvar & vaginal outcomes; genital warts (males and females)

Cost per QALY (quality-adjusted life year) of each strategy is the incremental cost-effectiveness ratio of the strategy when compared to the preceding strategy. All strategies include cervical cancer screening.

Degree of protection against infection based on anytime DNA detection endpoint efficacy. By age 18, 75% of females received at least one dose of vaccine. No vaccine benefits assumed for less than three vaccine doses. Vaccine cost per dose = \$133. Results preliminary.

Incremental cost-effectiveness ratios by HPV disease prevented

Merck model results: Base case cost per QALY estimates

HPV Diseases	Female-only 9–26	+ 27–34 females	+ 35–44 females
Cervical	\$17,500	\$84,000	\$224,000
+ Vulvar and vaginal	\$16,000	\$77,000	\$205,200
+ Genital warts	\$7,800	\$51,900	\$142,000
+ Anal	\$6,200	\$41,600	\$113,400
+ Head & neck	\$4,300	\$31,700	\$87,800
+ Penile	\$4,200	\$30,900	\$85,700
+ RRP	\$2,300	\$28,900	\$83,300

QALY: quality-adjusted life year

Incremental cost-effectiveness ratios by HPV disease prevented

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↑ Evidence of vaccine efficacy in females ↑			
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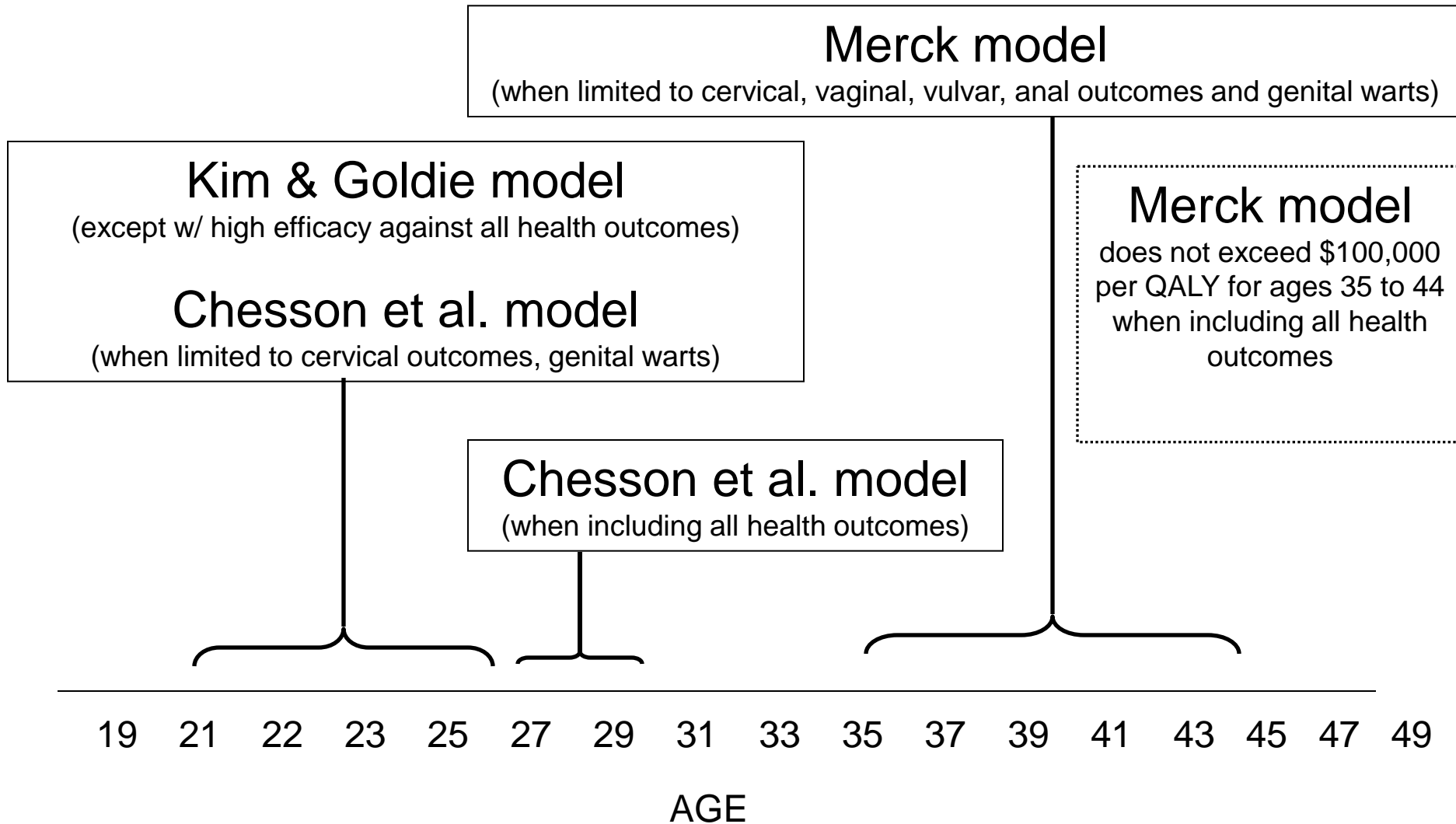
QALY: quality-adjusted life year

Chesson et al. model results: Cost-effectiveness of female vaccination by age

Ages vaccinated	Incremental ages added	Cost per QALY	
		Cervical, warts	All outcomes
12	12	\$8,000	\$3,000
12-18	13-18	\$26,000	\$17,000
12-21	19-21	\$55,000	\$38,000
12-26	21-26	\$119,000	\$85,000
12-29	27-29	\$254,000	\$179,000
12-34	30-34	\$449,000	\$305,000

Cost per QALY (quality-adjusted life year) of each strategy is the incremental cost-effectiveness ratio of the strategy compared to the preceding strategy. Cost per QALY of vaccinating 12-year-olds is as compared to no vaccination (screening only). All strategies include cervical cancer screening. Results preliminary.

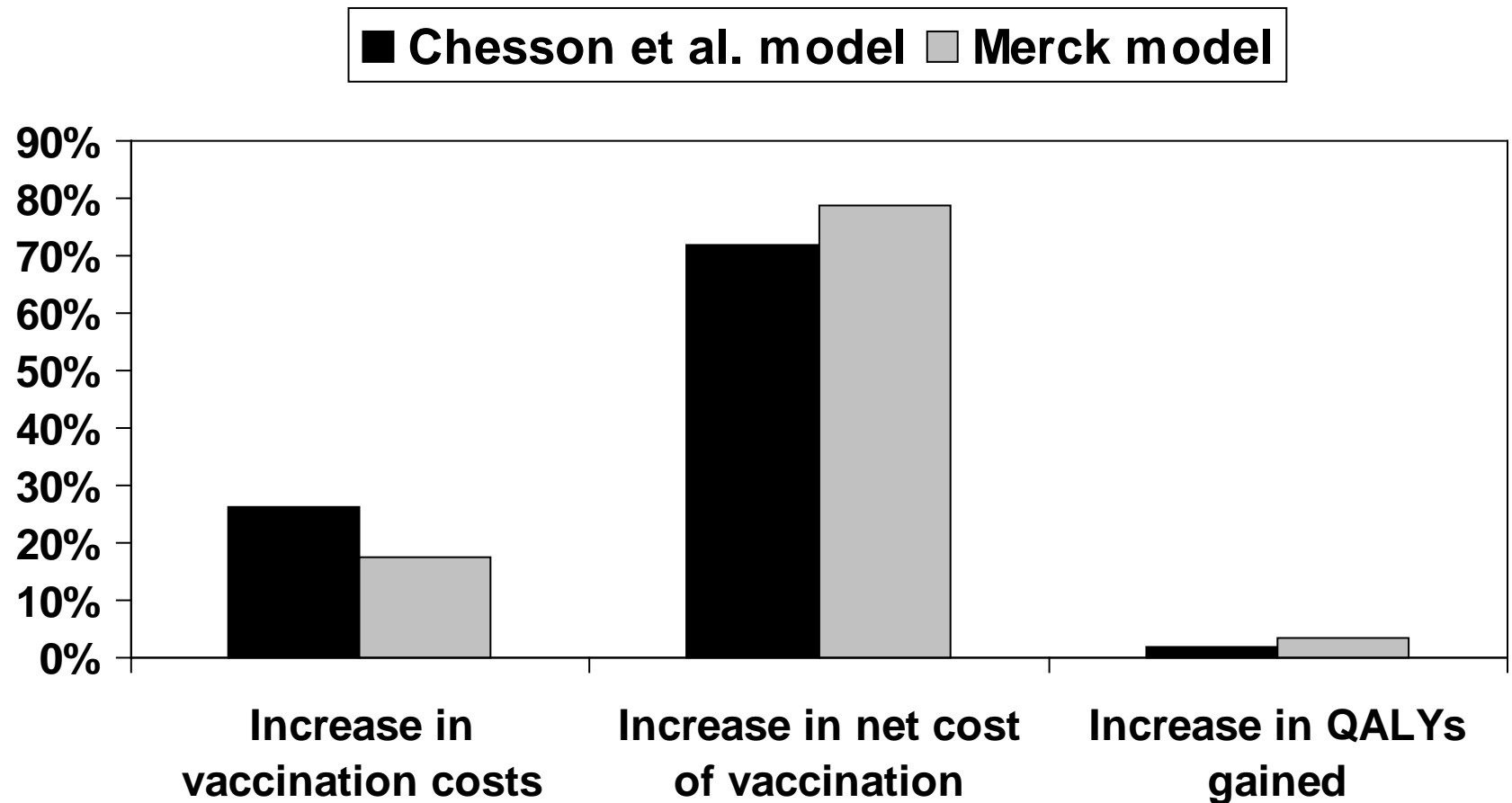
Age group at which female vaccination exceeds \$100,000 per QALY



Factors that contribute to differences in model results

- Compared to Kim & Goldie model, Merck model:
 - Uses a lower cost per vaccine series
 - Assumes greater quality of life impact of CIN, genital warts
 - Includes more health outcomes
 - Outcomes in males; adult-onset RRP
- Differences in how screening is modeled
- Differences in model structure

Change in costs and benefits when expanding cut-off age of vaccination from 26 to 44 years



Net cost of vaccination = (Vaccine cost + administration cost) – (cost of illness averted by vaccination)

Conclusion

- Routine HPV vaccination of 12-year-old girls is cost-effective
- For adult women, vaccination less cost-effective as age at vaccination increases
 - HPV incidence decreases, probability of previous exposure increases
- Extending vaccination beyond age 26 years would account for small percentage of total vaccine benefits

Conclusion, continued

- Precise age at which vaccine no longer “cost-effective” is uncertain
 - Depends on many factors
 - Health outcomes included, screening assumptions, other modeling assumptions, etc.
 - Results can vary within and across models
 - Uncertainties in natural history of HPV
 - Other uncertainties
 - Cost and impact on quality of life of HPV-related outcomes
 - Differences in model structure

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References

- Ahern CH, et al. *Cancer Epidemiol Biomarkers Prev.* 2009;18:718-725.
- Chesson HW, et al. *Emerg Infect Dis.* 2008;14:244-251.
- Cochi SL, et al. *JAMA.* 1985;253:521-529.
- Cortese MM, et al. *MMWR Recomm Rep.* 2009;58:1-25.
- Das A. *Hepatology.* 1999;29:548-552.
- Dasbach et al. In Haddix et al. *Prevention Effectiveness.* Oxford Univ Press, 1996.
- Ekwueme DU, et al. *Arch Pediatr Adolesc Med.* 2000;154:797-803.
- Elbasha EH, et al. *Emerg Infect Dis.* 2007;13:28-41.
- Gift TL, et al. *Sex Transm Dis.* 2008;35:S66-S75.
- Goldhaber-Fiebert JD, et al. *J Natl Cancer Inst.* 2008;100:308-320.
- Goldie SJ, et al. *Obstet Gynecol.* 2004;103:619-631.
- Goldie SJ, et al. *Vaccine.* 2006;24 Suppl 3:S3-164-S3/170.
- Grosse SD. *Expert Rev Pharmacoeconomics Outcomes Res.* 2008;8(2):165-78
- Hu D, et al. *Ann Intern Med.* 2004;141:501-513.
- Kim JJ, et al. *JAMA.* 2002;287:2382-2390.
- Kim JJ, et al. *N Engl J Med.* 2008;359:821-832.
- Kim JJ, et al. *Ann Intern Med.* 2009;151:538-545.
- Kulasingam SL, et al. *Obstet Gynecol.* 2006;107:321-328.
- Lieu TA, et al. *JAMA.* 2000;283:1460-1468.

References, continued

- Ortega-Sanchez IR, et al. *Pediatrics*. 2008;121 Suppl 1:S63-S78.
- Preblud SR, et al. *Postgrad Med J*. 1985;61 Suppl 4:17-22.
- Prosser LA, et al. *Emerg Infect Dis*. 2006;12:1548-1558.
- Ray GT, et al. *Pediatr Infect Dis J*. 2006;25:494-501.
- Ray GT, et al. *Vaccine*. 2009;27:6483-6494.
- Rein DB, et al. *Pediatrics*. 2007;119:e12-e21.
- Shepard CW, et al. *Pediatrics*. 2005;115:1220-1232.
- Stout NK, et al. *J Natl Cancer Inst*. 2006;98:774-782.
- Tengs TO, et al. *Risk Anal*. 1995;15:369-390.
- Thompson KM, et al. *Risk Anal*. 2006;26:1423-1440.
- Weinstein MC. *Med Care* 2008; 46:343-345
- Weinstein MC et al. *New Engl J Med* 2010; 362:460-465
- White CC, et al. *Am J Public Health*. 1985;75:739-744.
- Widdowson MA, et al. *Pediatrics*. 2007;119:684-697.
- Zhou F, et al. *J Infect Dis*. 2004;189 Suppl 1:S131-S145.
- Zhou F, et al. *Arch Pediatr Adolesc Med*. 2005;159:1136-1144.
- Zhou F, et al. *J Infect Dis*. 2008;197 Suppl 2:S156-S164.