Cost-effectiveness of HPV vaccination in the U.S.

Summary of cost-effectiveness estimates focusing on age at vaccination

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Atlanta, GA
June 2008

HPV vaccination of 12-year-old girls

- Cost-effective by usual standards
  - $3,000 to $50,000 per QALY gained
- Consistency across range of different models
  - Cost-effectiveness estimates for 12-year-olds less sensitive to uncertainty in natural history, epidemiology of HPV, assuming long duration of protection

QALY: quality-adjusted life year

Cost-effectiveness of HPV vaccination of females over age 12 years in the U.S.

- Kim/Goldie model
  - Kim et al., *Am J Epid* 2007
  - Goldhaber-Fiebert et al., *J Natl Cancer Inst* 2008
  - Goldhaber-Fiebert et al., *Population Health Metrics* 2007
- Merck model
  - Elbasha, Dasbach, Insinga, *Emerg Infect Dis* 2007
  - Elbasha, Dasbach, Insinga, *Bull Math Biol* 2008

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Merck model: Methods

- Utilized transmission dynamic model from previously published cost-effectiveness study of vaccination of ages 12-24 years in U.S.
  - *Elbasha et al., Emerg Infect Dis 2007; 13:28-41.*

- Extended model to address vaccination of women 25-44 years of age

Merck model: Assumptions

- Degree of protection for 3 doses of vaccine
  - HPV 16/18, HPV 6/11: against infection ≈ 90%
  - HPV 16/18, HPV 6/11: against CIN ≈ 95%
  - HPV 6/11: against genital warts ≈ 99%
- Degree of protection for < 3 doses: 0%
- Duration of protection: lifelong
- Vaccine cost: $360 per series

CIN: cervical intraepithelial neoplasia

Merck model: Assumptions, continued

- Annual probability of vaccination*:
  - <12 years: 70%
    - Increases linearly to 70% over the first five years of vaccination
  - 12-19 years: 35%
  - 20-29 years: 19%
  - 30-44 years: 5%
- Compliance:
  - 75% of those receiving 1st dose received 2nd dose
  - 75% of those receiving 2nd dose received 3rd dose
- Health outcomes included:
  - CIN, cervical cancer, genital warts
    - Including prevention of genital warts in males as a result of female vaccination

*Among those not previously vaccinated. Not adjusted for compliance; 56% of persons receiving first dose will receive all 3 doses.

CIN: cervical intraepithelial neoplasia

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

Ages vaccinated	Incremental ages added	Incremental cost per QALY gained
No vaccination	-	-
12-24	12-24	$8,600
12-29	25-29	$46,400
12-34	30-34	$103,600
12-39	35-39	$156,400
12-44	40-44	$225,300

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

Includes indirect effects (herd immunity), including impact of female vaccination on genital warts in males

Merck, unpublished results. Preliminary.

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Why do the cost-effectiveness estimates differ?

- Different model structures, assumptions
- Complexity of HPV
  - Uncertainty in natural history of HPV
- Incremental health impact of HPV vaccination decreases as cutoff age of catch-up vaccination increases

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Comparison of selected model features

Model feature	Merck	Kim/Goldie
Type of model	Dynamic	Hybrid: Dynamic + individual-based simulation
HPV types modeled	6/11, 16/18	16, 18, other high risk HPV types, low risk HPV types
Includes indirect effects (herd immunity)	Yes	Yes
Selection of base case parameter values	Literature, expert review, vaccine trial data	Literature, likelihood-based calibration

Comparison of selected model features, continued

Model feature	Merck	Kim/Goldie
Cervical cancer screening	Yes	Yes Model tracks individual-level history of screening, treatment
Age at which acquisition of new sex partners ceases	85 years	50 years
Time horizon of analysis	100 years	Lifetimes of birth cohorts who were alive during first 10 years of vaccination program

Comparison of selected model features, continued

Model feature	Merck	Kim/Goldie
Cost per vaccine series	$360	$360
Cost per vaccinated person	≈ $500 Accounting for compliance	$500 Accounting for administrative costs, patient costs, etc.
Includes patient time & travel costs	No	Yes
Health outcomes include cervical cancer, CIN, genital warts in females	Yes	Yes RRP and non-cervical cancers also addressed in additional analyses
Includes impact of CIN on quality of life	Yes	No
Includes genital warts in males	Yes	No

CIN: cervical intraepithelial neoplasia; RRP: recurrent respiratory papillomatosis

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Comparison of selected model features, continued

Model feature	Merck	Kim/Goldie
Vaccine coverage: Annual probability of vaccination, by age	< 12 years: 70%* coverage increases linearly in first five years from 0% to 70% Older ages: 12-19: 35% 20-29: 19% 30-44: 5% Not adjusted for compliance	Age 12: 25% in years 1-5 75% in years 6-10 Older ages: 25%

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Parameters for modeling HPV incidence
(Selected examples)

Percentage of men, women in each sexual activity group, by age

Number of new partners per year in each sexual activity group

Sexual mixing matrix

HPV transmission probability

Vaccine efficacy

Probability of HPV clearance

Probability of natural immunity

Degree of protection offered by natural immunity

Progression of invasive cancer

Cancer survival probabilities

Parameters for modeling HPV-related health outcomes
(Selected examples)

Progression of HPV to CIN 1

Progression of HPV to CIN 2/3

Progression of CIN 1 to CIN 2/3

Progression of CIN 2/3 to invasive cancer

HPV clearance

CIN1 , CIN 2/3 regression

Probability of natural immunity

Degree of protection offered by natural immunity

Progression of invasive cancer

Cancer survival probabilities

Probability of symptom detection

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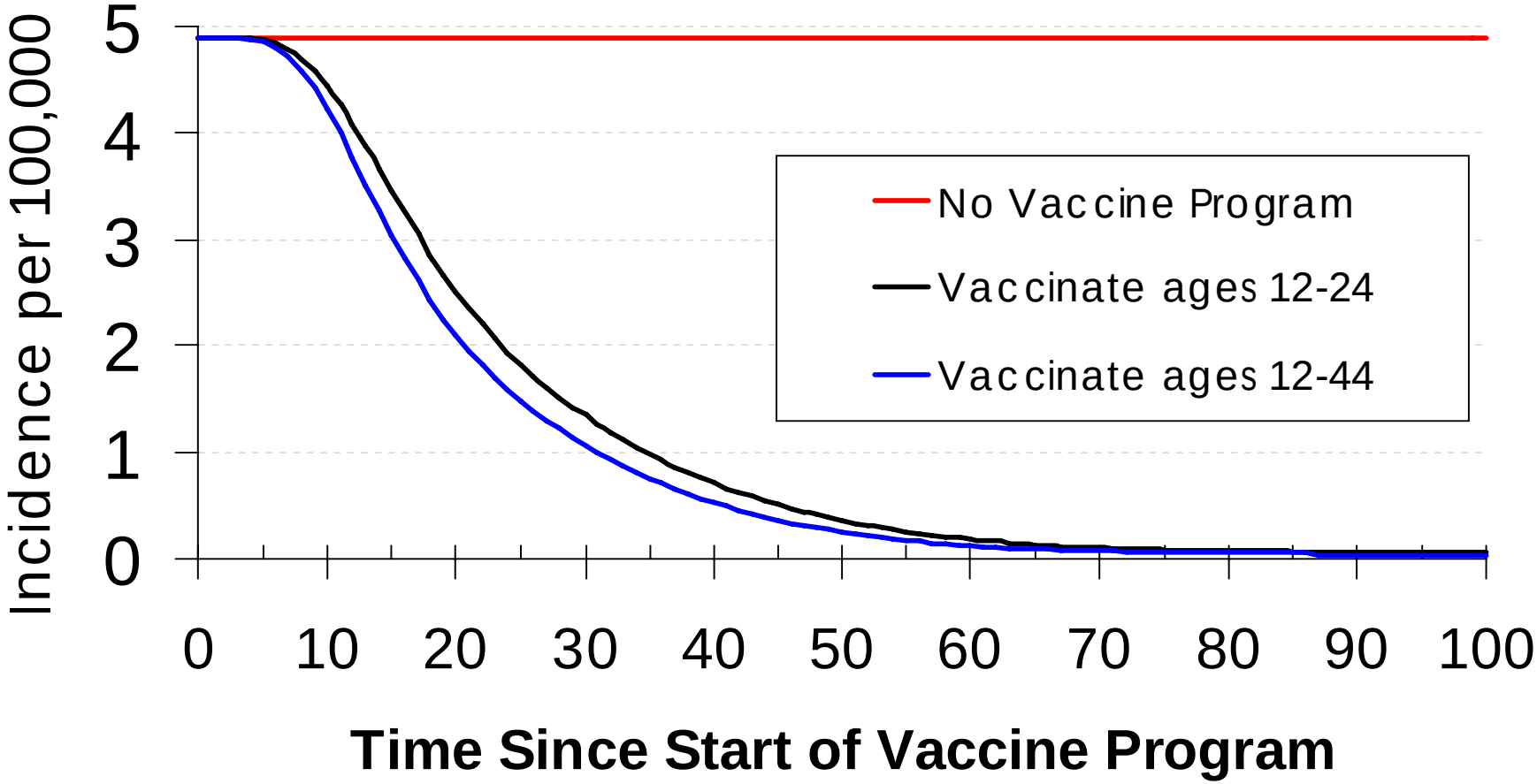
Why do the cost-effectiveness estimates differ?

- Different model structures, assumptions
- Complexity of HPV
  - Uncertainty in natural history of HPV
- Incremental health impact of HPV vaccination decreases as cutoff age of catch-up vaccination increases
  - Impact on cost-effectiveness estimates

Impact of quadrivalent vaccination on HPV-16/18-related cervical cancer (age 12+)



Merck, unpublished results. Preliminary.

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Merck model results

Strategy (ages vaccinated)	Incremental ages added	ΔCosts ($1,000)	ΔQALYs (1,000)	Cost per QALY
No Vaccine	-	-	-	-
12-24	12-24	$14,700,000	1,711	$8,600
12-29	25-29	$2,900,000	62	$46,400
12-34	30-34	$1,000,000	10	$103,600
12-39	35-39	$1,100,000	7	$156,400
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Vaccinating women over age 24 years provides less than 5% of the QALYs gained by vaccinating women 12-24 years old.

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Vaccinating women over age 24 years provides less than 5% of the QALYs gained by vaccinating women 12-24 years old, at over 40% of the cost of vaccinating women 12-24 years old.

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Health impact and cost-effectiveness ratios

- Potential for divergent cost-effectiveness estimates can increase as health impact decreases

$$\text{Cost-effectiveness ratio} = \frac{\text{Net increase in health care cost}}{\text{Net gain in health effect}}$$

Conclusions

- Cost-effectiveness of catch-up vaccination varies across the two models
- Wide range of results across different models not unexpected
  - Uncertainty of natural history, epidemiology of HPV
  - Different modeling assumptions, methods

Conclusions (continued)

- Vaccination becomes less cost-effective as cutoff age of catch-up vaccination increases
- Extending vaccination beyond mid-20's would account for small percentage of overall benefits of vaccination
  - Decreasing incremental health impact as cutoff age of catch-up vaccination is increased

Acknowledgements

Elamin Elbasha, Merck
Erik Dasbach, Merck

Jane Kim, Harvard
Sue Goldie, Harvard

Eileen Dunne, CDC
Lauri Markowitz, CDC