BIOE 301

Lecture Thirteen

October 11, 2009

Success of AIDS Vaccine Trial Is at Issue

By DONALD G. McNEIL Jr.

When AIDS researchers released results last month from a six-year trial in Thailand of a new AIDS vaccine, they said it showed some promise for new avenues of research, though they freely admitted their data was weak.

Now two published accounts citing anonymous AIDS researchers who were given confidential briefings about the trial results have reported that the data, released on Sept. 24, may be even weaker than the authors admitted — essentially, instead of being 31 percent better than nothing, the vaccine might be only 26 percent better.

The accounts were on Science magazine's Web site and in The Wall Street Journal.

The debate is over which participants in the study should be counted — all 16,395 Thais who participated at some point or only the ones who got all the doses of the vaccine and stayed in the study for the full time.

The researchers said last month that the vaccine seemed to work 31 percent better than a placebo — and there was only a 4 percent chance that that 31 percent difference was simply a fluke. To some it seemed that a promising step had been made in the long search for a vaccine against AIDS, which has killed more than 25 million people.

But others who have seen the research say that a "per protocol" analysis, that is, how the vaccine worked among the Thais who got all six vaccine shots at the right time and were followed up to the trial's end, would show that the results were not statistically significant

The Science report calling into question the results was on its Web site on Oct. 5, and was written by Jon Cohen, the author of the 2001 book "Shots in the Dark," a history of the search for an AIDS vaccine. The Wall Street Journal report was published on Saturday.

Dr. Anthony S. Fauci, director of one of the National Institutes of Health, which financed the trial, agreed that different analyses of the data could show a weaker effect. But he said the one released on Sept. 24, which included every participant in the trial, was "the gold standard."

HIV/AIDS Vaccine Update

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Putting several biostatistical analyses in a news release "would have confused everybody," Dr. Fauci said, and suggesting that the researchers were engaging in a cover-up is "absurd."

"They couldn't be that stupid," he said. "They were already planning to give confidential briefings to experts. They were about to publish everything in a journal. And they were heading to Paris in three weeks to present the results to the world."

Dr. Fauci said he had not been consulted on how to release the results, which were released in Thailand by United States military and Thai researchers. But he was asked to join a news briefing in Washington the next day because he oversaw the financing and is good at explaining complex science.

In retrospect, he said, the Army's decision to brief other players in the field before the late October Paris conference "backfired."

Health Care Reform Update

- http://www.npr.org/templates/story/story.php?storyId=113781751&ps=rs

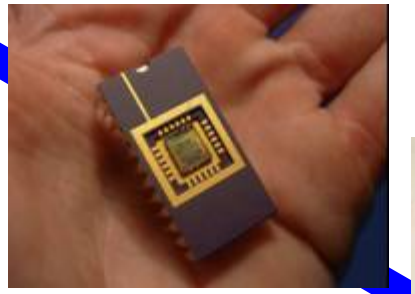
Review of Cancer Lectures

- What is the goal of cancer screening?
- Successful cancer screening examples?
- Can screening hurt more people than it helps?
- What are the challenges in cancer screening?
- Is cancer screening a good investment?

Science of Understanding Disease

Bioengineering

Emerging Health Technologies



Preclinical Testing

Ethics of research

Clinical Trials

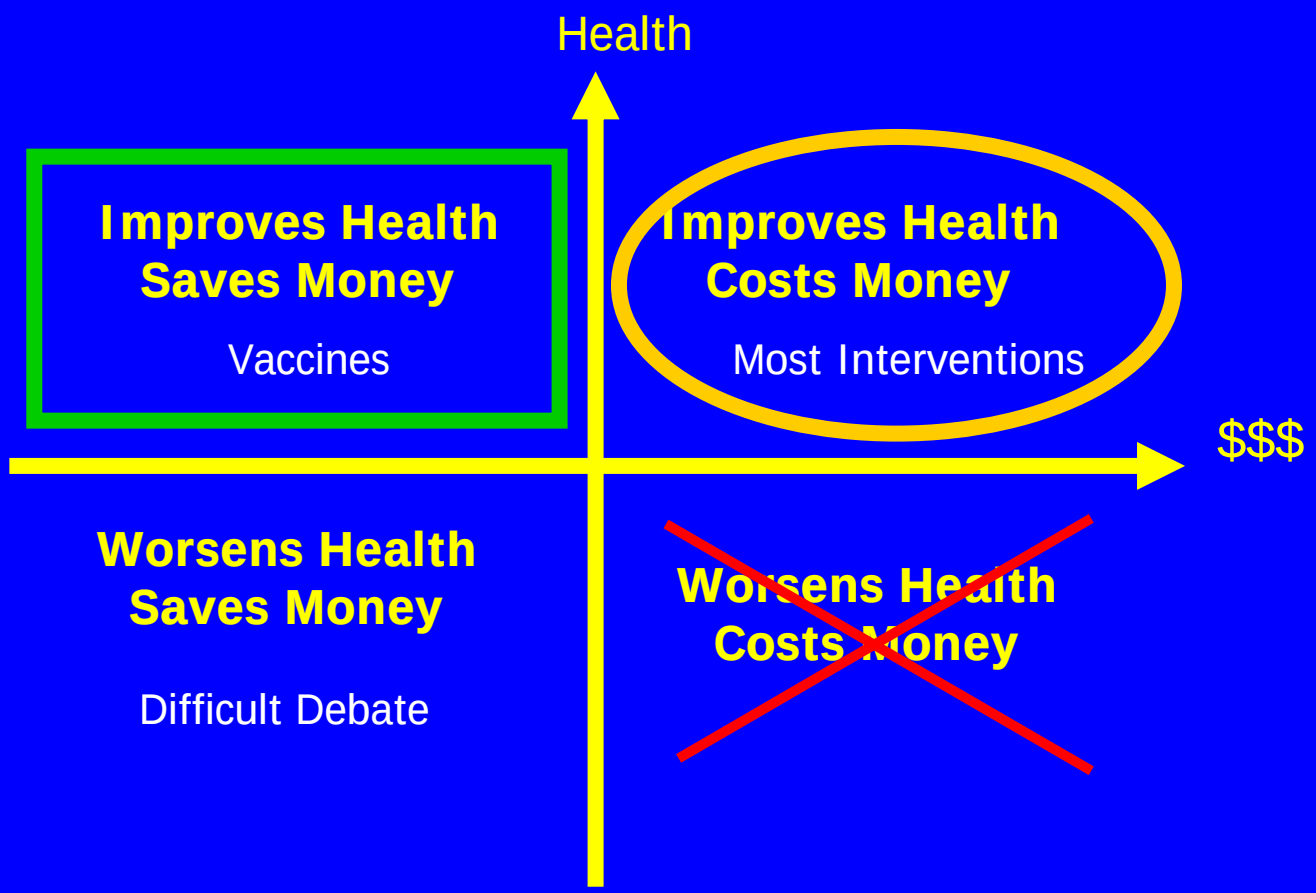
Cost-Effectiveness

Adoption & Diffusion

Abandoned due to:

- poor performance
- safety concerns
- ethical concerns
- legal issues
- social issues
- economic issues

Health Policy Space



Health Care Reform in Oregon

- Health services ranked according to cost-effectiveness

$$priorityrating = \frac{CostofTreatment}{NetExpectedBenefit \times DurationofBenefit}$$

$$/DALY or $$/QALY

- What does a DALY measure?
- How much are we willing to spend to gain a year of life?
- Name two health interventions that result in cost SAVINGS.

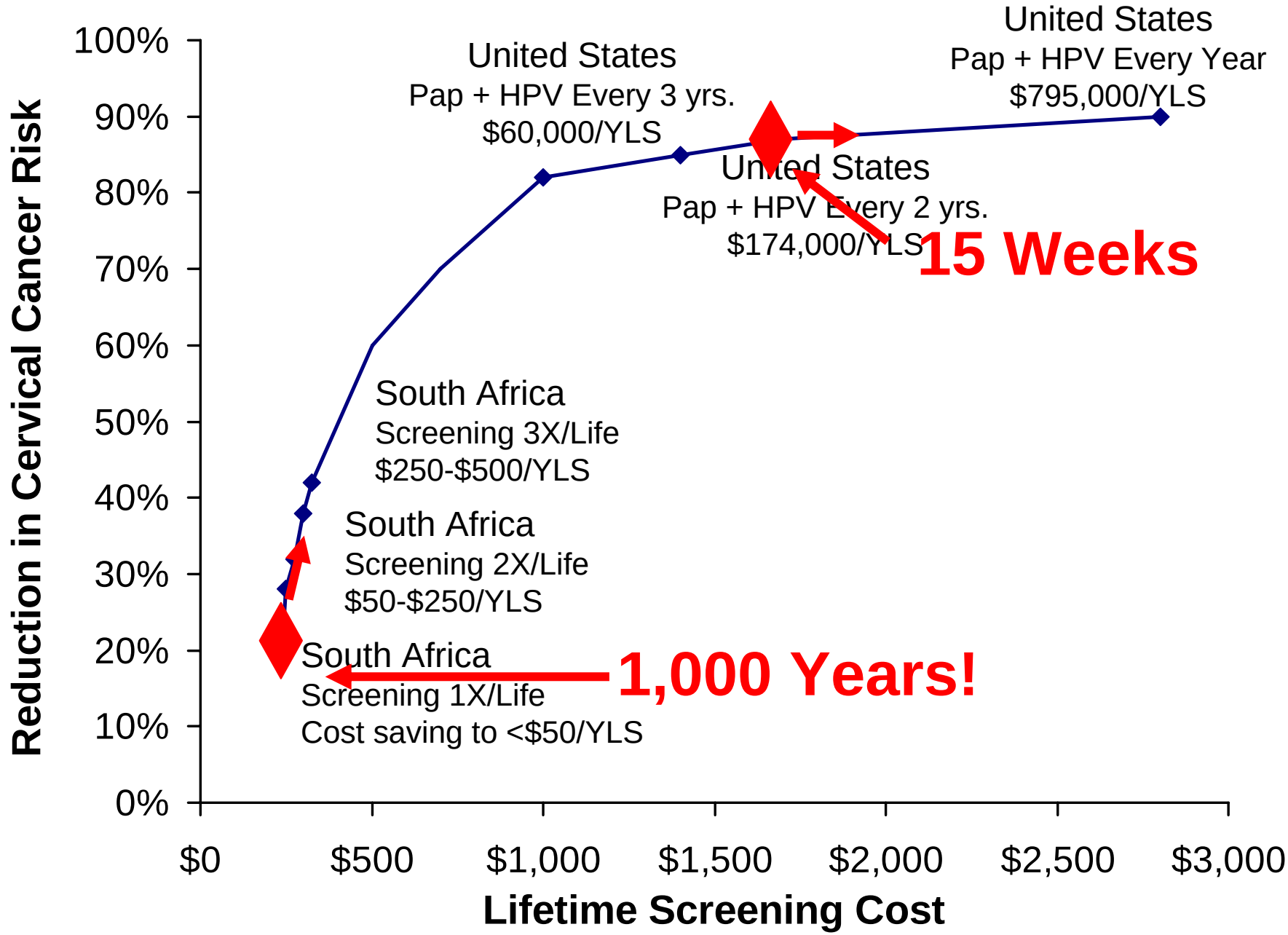
League Table

Intervention	Cost-Effectiveness Ratio
Pneumococcal vaccine for adults over 65 years of age	Cost saving
Tobacco cessation counseling	Cost saving to $2,000/QALY saved
Chlamydia screening for women 15-24 years old	$2,500/QALY saved
Colorectal cancer screening for people >50 years old	$13,000/QALY saved

What is Society's Threshold Ratio?

- No correct answer
- Common guesses:
  - $20,000-$100,000 / QALY
  - Median estimate = about $150,000/QALY
  - [Hirth RA, et al. What should society be willing to pay for a QALY? Evidence from the value of life literature (abstract). Medical Decision Making 1999;18:459.]

How Much Life Can $50,000 Buy?



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  - [Hirth RA, et al. What should society be willing to pay for a QALY? Evidence from the value of life literature (abstract). Medical Decision Making 1999;18:459.]
- What about in developing countries?
  - Very cost-effective:
    - amount to gain one QALY is < per person GDP
  - Cost-effective:
    - amount to gain one QALY is < 3 x per capita GDP

Cost-Effectiveness Assessment

- Define the problem
- Identify the perspective
- Identify the alternatives
- Analyze the effectiveness
- Analyze the costs
- Perform discounting
- Perform sensitivity analysis
- Address ethical issues
- Interpret the results

Example: Cervical Cancer Screening for Elderly Women

- 1988:
  - Medicare did not cover cervical cancer screening
  - Elderly accounted for 40% of cervical CA deaths
- Question:
  - Should Medicare pay?

Cost-Effectiveness Assessment

- Define the problem:
  - Is cervical cancer screening for elderly women cost-effective?
- Identify the perspective
  - Societal perspective
- Identify the alternatives
  - No screening
- Analyze the costs & effectiveness
  - Real clinical trial
  - Projected costs and benefits

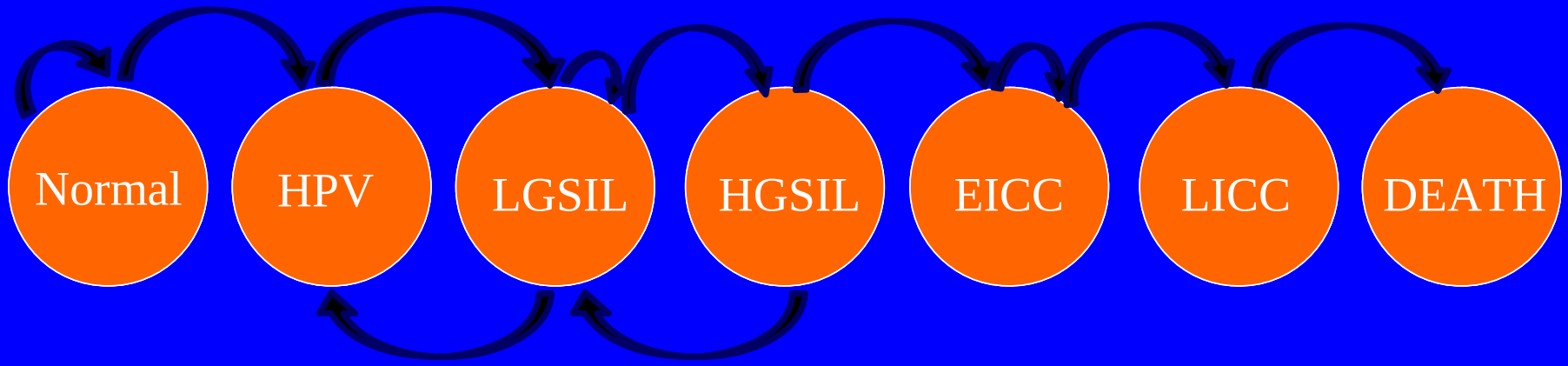
Cost-Effectiveness Assessment

- Perform discounting
  - 5% discount rate
- Perform sensitivity analysis
  - Screening would be cost-saving in elderly women who had never been screened
- Address ethical issues
  - Is it ethical for Medicare to pay for smears only for women who have never been screened?
- Interpret the results

Summary of Study

- New Technology:
  - Pap screening in low-income, elderly women
- Alternative:
  - No screening
- Number of tests performed:
  - 816
  - 25% had never had a Pap smear
  - 11 abnormal Paps, 2 patients with cancer
- Costs of Screening + Treatment:
  - $59,733

Markov Model



- Would have cost more to treat women in the absence of screening
  - Would have cost $107,936 to treat if cancers detected when symptomatic
  - Gained 30.33 years of life by screening
  - Gained 36.77 QALYs by screening

Summary of Study

- Benefits of Technology:
  - 30.33 life years gained
  - 36.77 QALYs gained
- Net Costs of Intervention:
  - $59,733-$107,936 = -$48,203
  - Intervention SAVES money
- Cost-effectiveness:
  - SAVE $1311/QALY

Impact of Study

- 1990:
  - Medicare extended to cover triennial screening with Pap smears for all women with no upper age limit
- Study was a one-time screen in population with limited prior access to screening!
- Should results be generalized?
  - $2,254/QALY gained for triennial screening in elderly women in US

Cost-Effectiveness Study of Cervical Cancer Screening for Low-Income, Elde

"I previously worked in the Harlem community and other New York City neighborh very poor in resources: housing, healthcare, and other resources. The issue I wa was whether we should screen older women for cervical cancer. The reason I, someone else, did this is that I was the only person in the primary care clinic who gynecologic examinations, and I was the first person in 10 years to observe that tables had stirrups! This was the beginning of my life's work.

In the first few years of our screening program, the nurse practitioner and I screened more than 800 women. They were on average 74 years old and had largely been unscreened previously. As a result, we found that screening these women actually saved lives as well as health care costs (3.72 lives and $5907 saved for every 100 Pap smears done)-an ideal program.

But then serendipity came into play. We were doing this work at a time when there was an explosion in the growth of the older population and members of congress were receiving a lot of pressure from their older constituents to include preventive services.

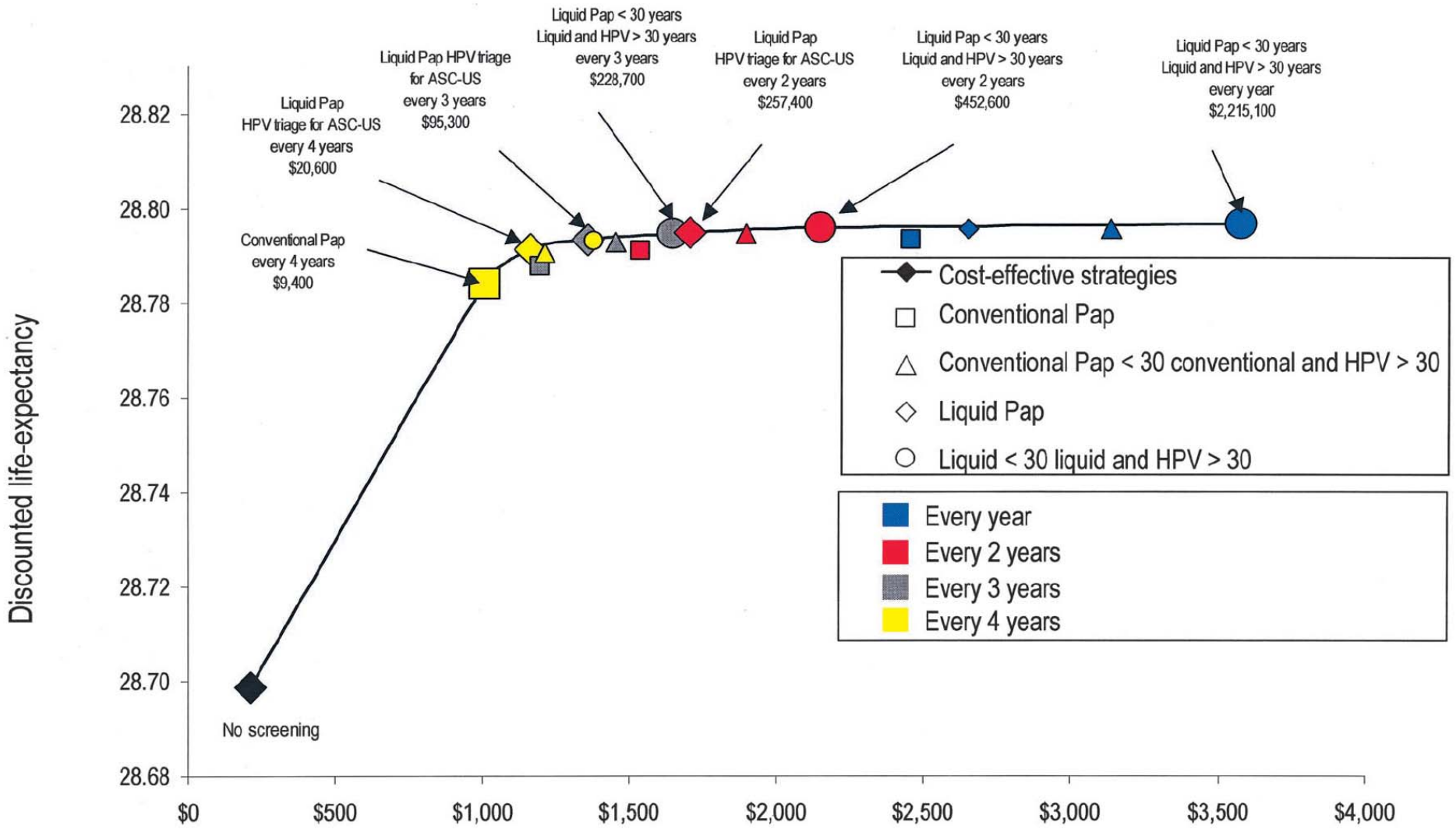
Along I came with my Pap smear analysis and showed that if we were to screen the average elderly population at that point Pap smear screening would be a good buy. It would cost about $2,200 per year of life saved. Of great importance was that we could save money if we targeted screening to women who had not been screened previously, but the cost-effectiveness would worsen by more than 10-fold if screening were applied to women who had already been regularly screened.

What were our responsibilities and what were the issues that came out of this work? When we presented this work to the OTA, we proposed considering cervical cancer screening as a targeted benefit and perhaps even including benefits to do outreach to women who have never been screened. The OTA said that under Medicare, benefits must be included for all (or no) women, so our recommendation could not be implemented….The actual cost-effectiveness for Medicare might not be as favorable as it could have been if targeted to the highest-risk women."

New Technologies for Cervical CA Screening

Technology	Sensitivity	Specificity	Cost per Test
Liquid Cytology	84%	88%	$71
Pap	69%	97%	$58
HPV	88%	95%	$49
HPV + cytology	94%	93%	

New Technologies for Cervical CA Screening



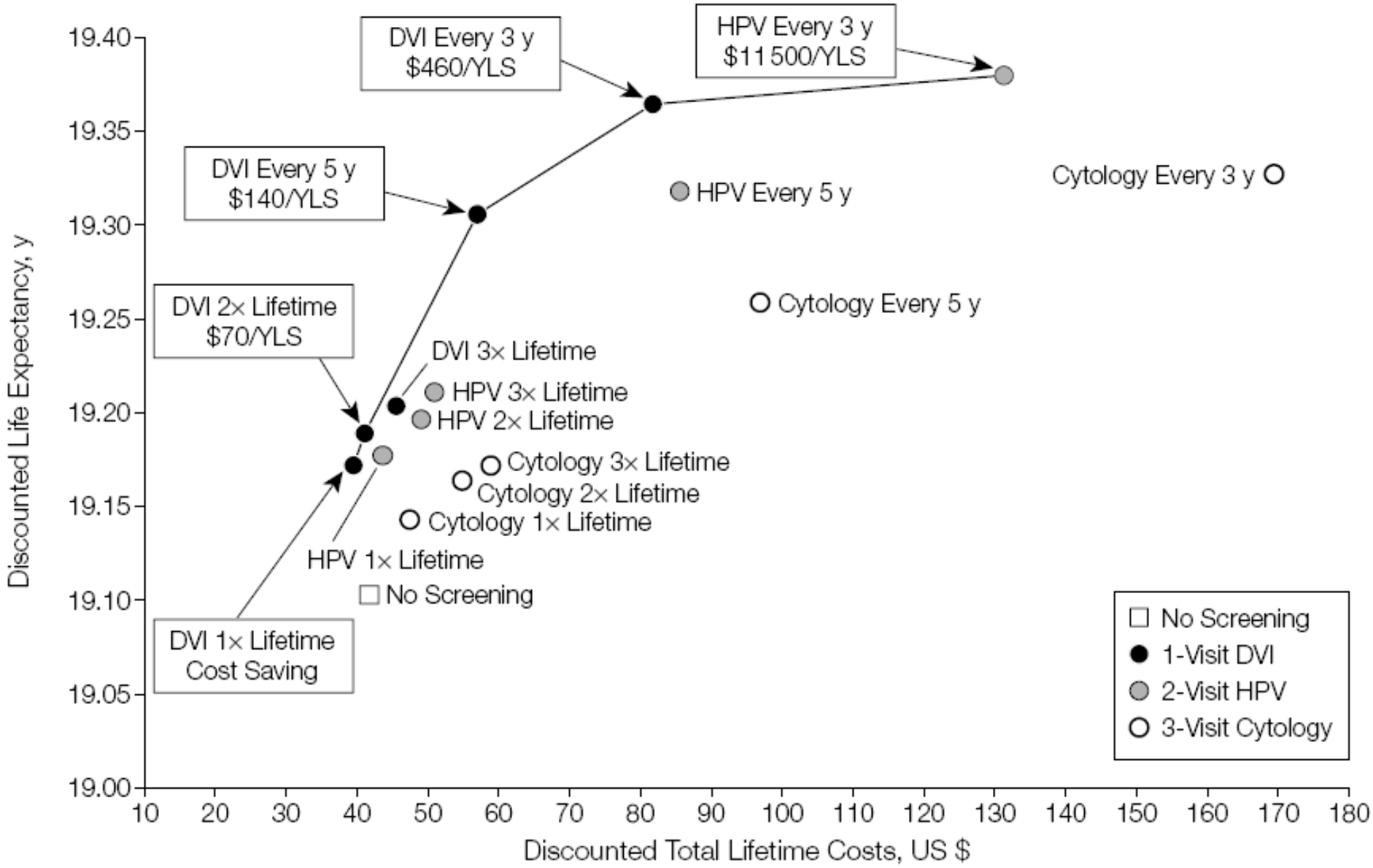
New Technologies for Cervical CA Screening

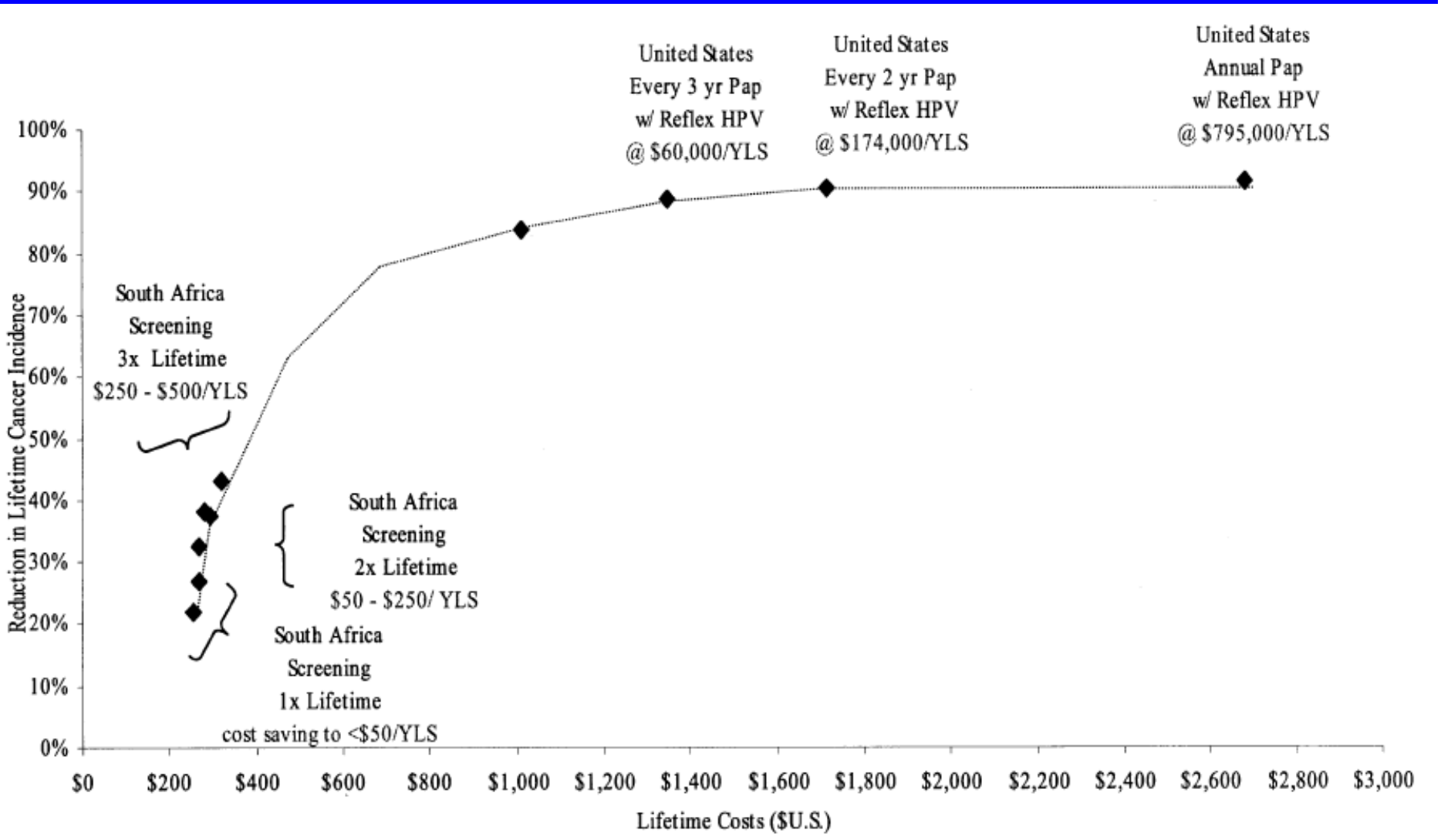
Intervention	Sensitivity	Specificity
VIA	76%	81%
Pap	63%	94%
HPV DNA	88%	93%

New Technologies for Cervical CA Screening

Characteristic	India	Kenya	Peru	South Africa	Thailand
Total population (millions)	1,016	30	26	44	61
Rural population (% of total)	72.34	64.11	27.23	44.51	68.86
Population density (no. of persons/km²)	341.69	52.87	20.26	36.03	118.87
Women 35–39 yr of age (% of total population)	3.28	2.18	3.21	3.35	4.10
Literacy rate among women ≥15 yr of age (%)	45.39	76.02	85.24	84.56	90.52
Women employed in informal sector (% of women employed)	86	83	58	58	54
Average hourly wage rate (2000 international dollars)†	0.48	1.94	2.26	9.90	2.59
Female life expectancy at birth (yr)‡	63.56	47.37	71.69	48.97	71.06
Cervical-cancer incidence (age-standardized incidence per 100,000)§	186.50	200.10	238.30	174.80	129.60
HIV prevalence among adults (% of total population)	0.70	14	0.40	19.90	2.20
Per capita gross domestic product (2000 international dollars)†	2,430	1,005	4,747	9,486	6,373

* Data are from the World Bank,[9] the International Labor Office,[10] and the U.S. Department of Commerce.[11]
† The international dollar is a unit of currency that minimizes the consequences of differences in price levels existing among countries.
‡ The average life expectancy for women who reach 35 to 40 years of age in Kenya is 67.9 years and in South Africa 68.8 years.
§ Age-standardized incidence is computed as a weighted average of age-specific cancer rates, with the population proportions of a global standard age pattern used as weights.


DVI Every 3 y
$460/YLS
HPV Every 3 y
$11 500/YLS
DVI Every 5 y
$140/YLS
HPV Every 5 y
Cytology Every 3 y
Cytology Every 5 y
DVI 2× Lifetime
$70/YLS
DVI 3× Lifetime
HPV 3× Lifetime
HPV 2× Lifetime
Cytology 3× Lifetime
Cytology 2× Lifetime
Cytology 1× Lifetime
HPV 1× Lifetime
No Screening
DVI 1× Lifetime
Cost Saving
No Screening
1-Visit DVI
2-Visit HPV
3-Visit Cytology
Discounted Life Expectancy, y
19.40
19.35
19.30
19.25
19.20
19.15
19.10
19.05
19.00
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
Discounted Total Lifetime Costs, US $


United States
Every 3 yr Pap
w/ Reflex HPV
@ $60,000/YLS
United States
Every 2 yr Pap
w/ Reflex HPV
@ $174,000/YLS
United States
Annual Pap
w/ Reflex HPV
@ $795,000/YLS
South Africa
Screening
3x Lifetime
$250 - $500/YLS
South Africa
Screening
2x Lifetime
$50 - $250/ YLS
South Africa
Screening
1x Lifetime
cost saving to <$50/YLS
Reduction in Lifetime Cancer Incidence
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
$0
$200
$400
$600
$800
$1,000
$1,200
$1,400
$1,600
$1,800
$2,000
$2,200
$2,400
$2,600
$2,800
$3,000
Lifetime Costs ($U.S.)

Summary

- Cost-effectiveness analysis can aid in decision making in all countries
  - Can answer clinical questions
  - Can answer policy questions
- New cost-effective technologies can:
  - Improve health globally
  - Reduce disparities in health

Project Proposal

- Thursday, October 22nd
- Schedule & rubric are posted on Owlspace
- Max of 5 slides, 5 minutes
  - Design Criteria
  - Brainstorming
  - Decision Matrix
  - Proposed Solution
  - Schedule for rest of semester