

Cost-Effectiveness of Cervical Cancer Screening Strategies: Examples from Different World Regions

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Cervical Cancer Control

- **Public health success** in countries with cytology (Pap smear) screening programs where mortality has been reduced by 75%
- **Public health failure** in developing countries where ~90% of all cervical cancer deaths occur
 - infrastructure and technological expertise for cytology programs not available
 - three visits for screening, diagnosis, and treatment not feasible

Overview of Decision-Analytic Methods

- Develop mathematical model of the natural history of disease.
- Synthesize clinical and economic data from multiple sources (clinical trials, cohort studies, national surveys, databases).
- *Calibrate* model to achieve the best fit to epidemiological data; *validate* model by predicting outcomes consistent with observations from independent data.
- “Simulate” different interventions to estimate consequences (e.g., life-expectancy, quality of life, costs).

Objectives

- To develop and validate models of the natural history of cervical cancer in developed and developing country populations.
- To conduct formal cost-effectiveness analysis of alternative cervical cancer screening strategies.

Example 1

Cost-Effectiveness of Management Strategies for Atypical Squamous Cells of Undetermined Significance in the United States*

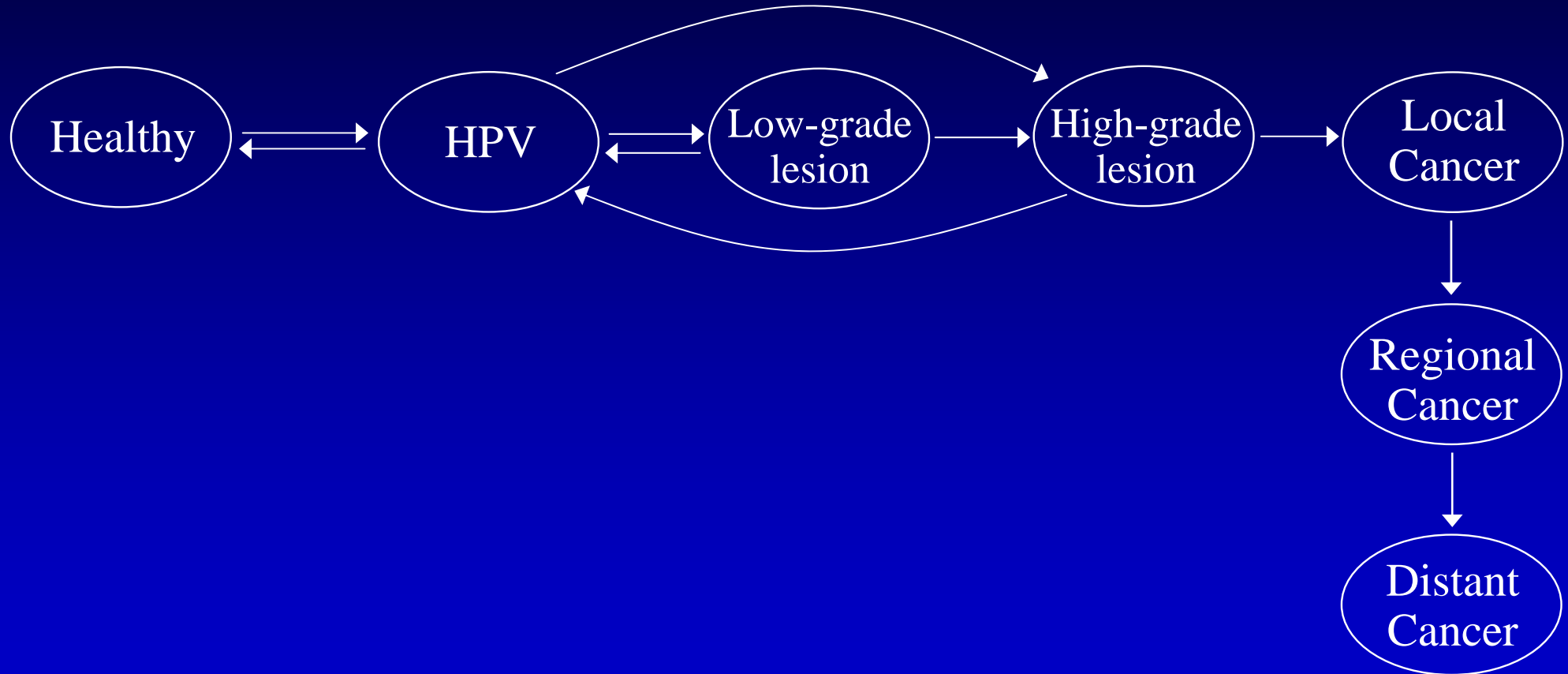
Jane J. Kim, PhD; Thomas C. Wright, MD; Sue J. Goldie, MD, MPH

* *JAMA* (2002)

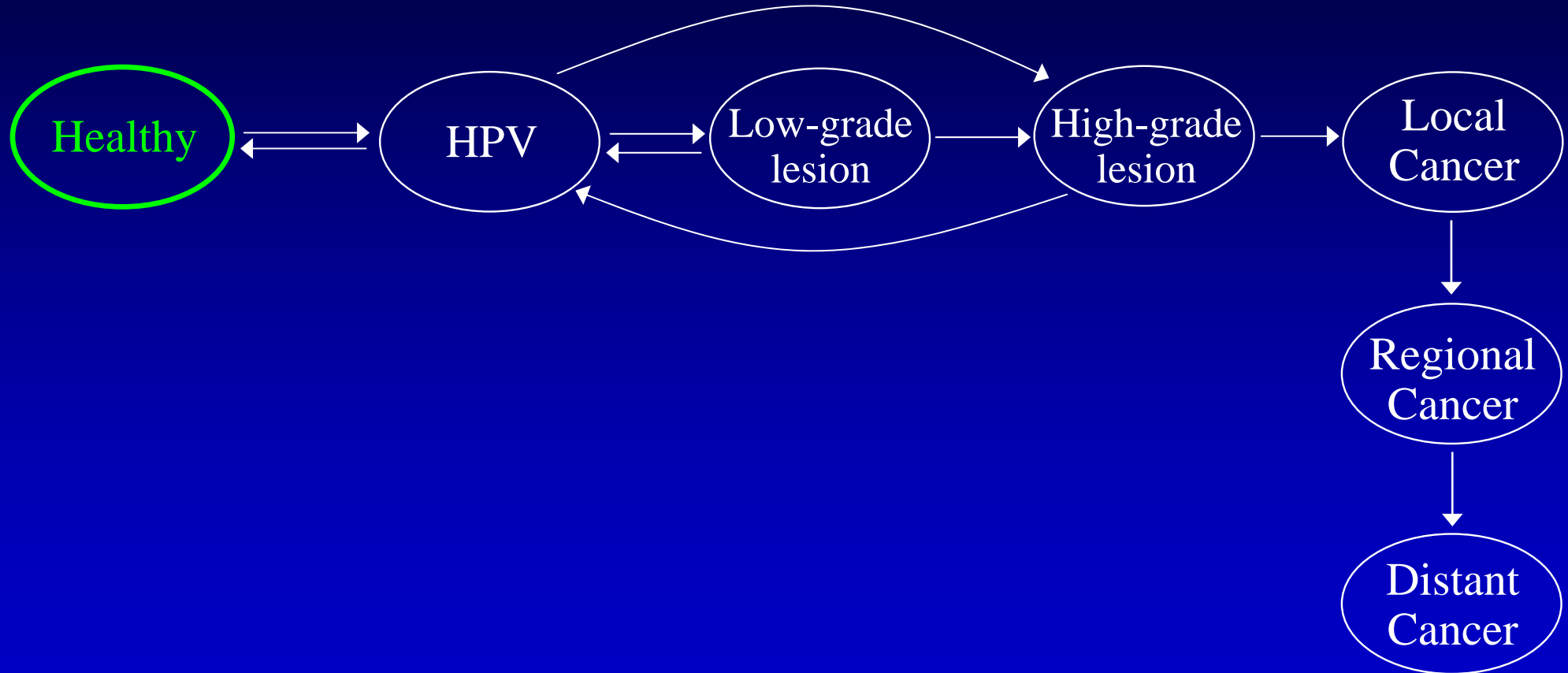
Introduction

- Cervical cancer control has been largely successful in the U.S., where annual screening is recommended.
- More than 2 million U.S. women are diagnosed with an equivocal result referred to as “atypical squamous cells of undetermined significance” (**ASCUS**).
- The clinical response to an ASCUS result varies widely and has been the subject of heated debate.

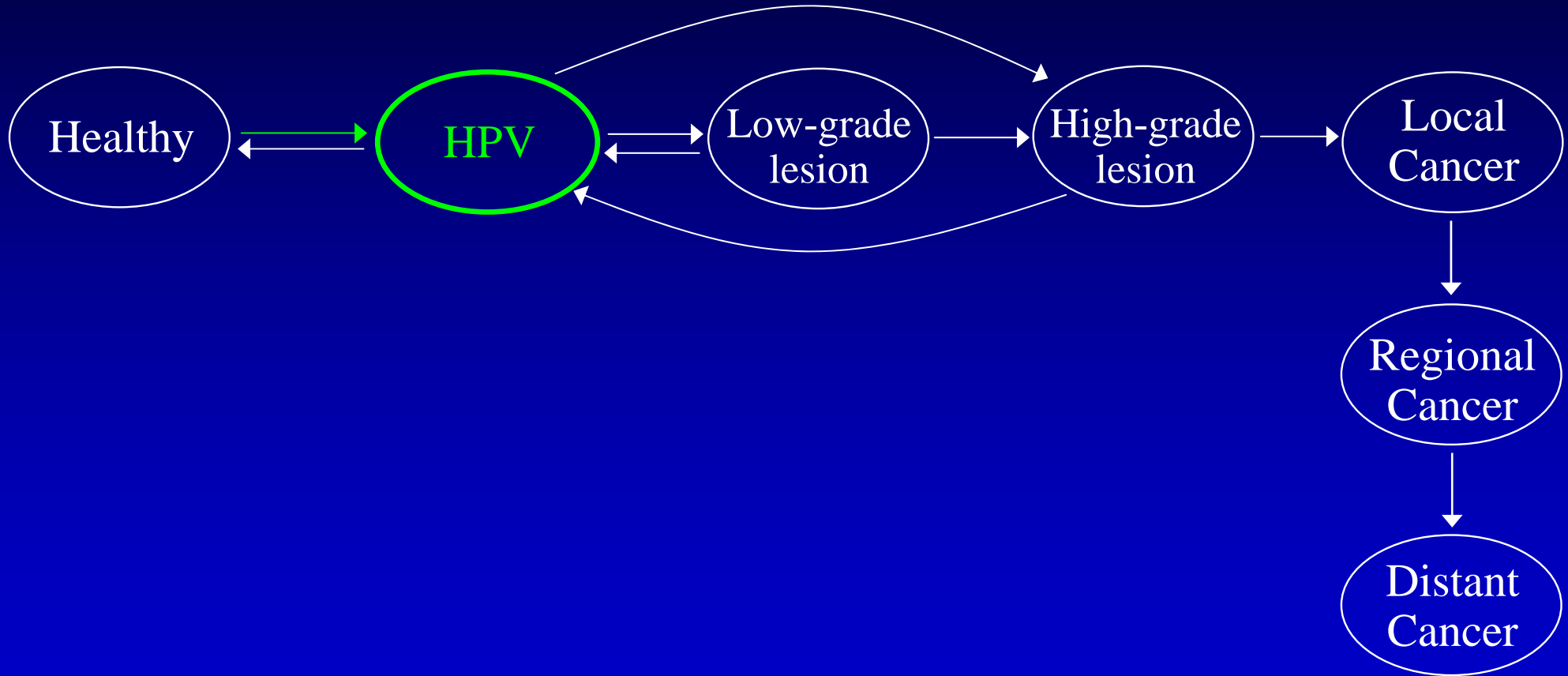
Cervical Cancer Model



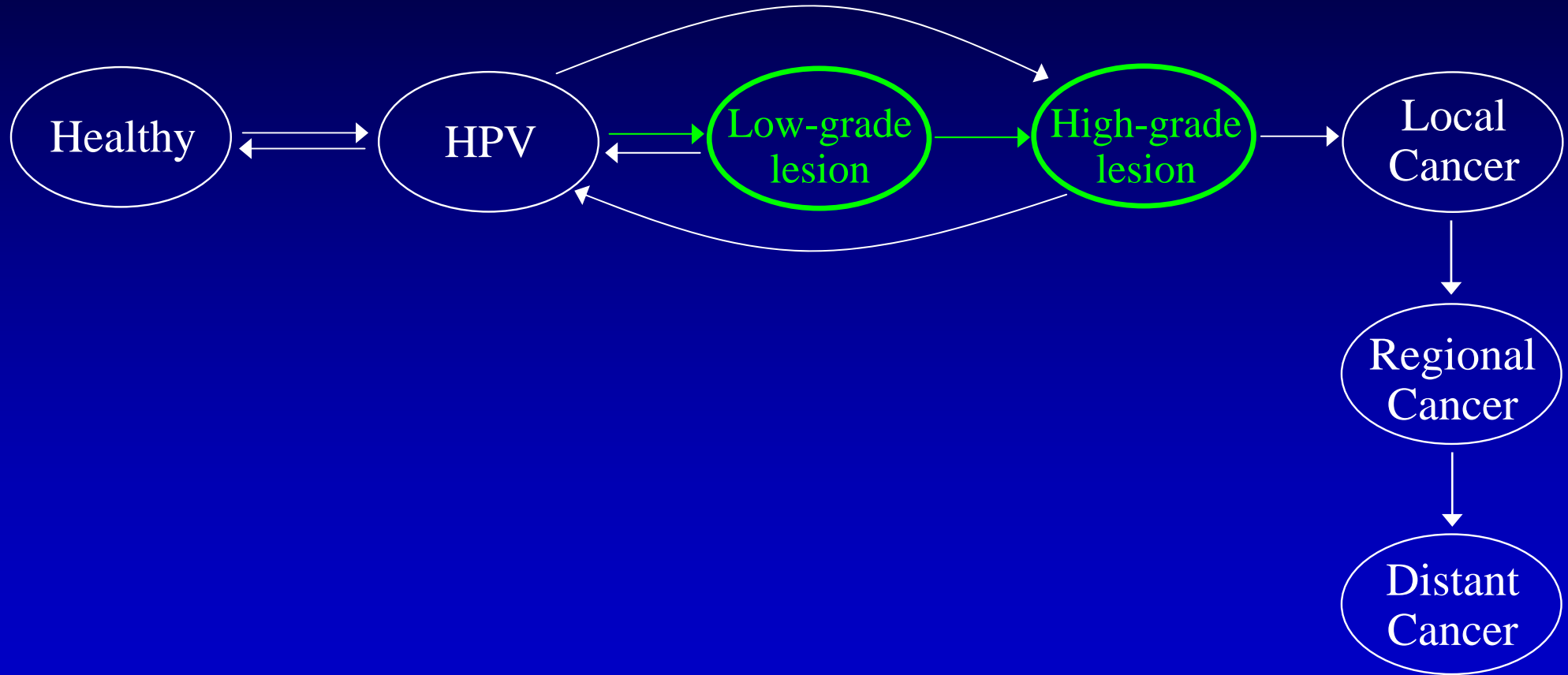
Cervical Cancer Model



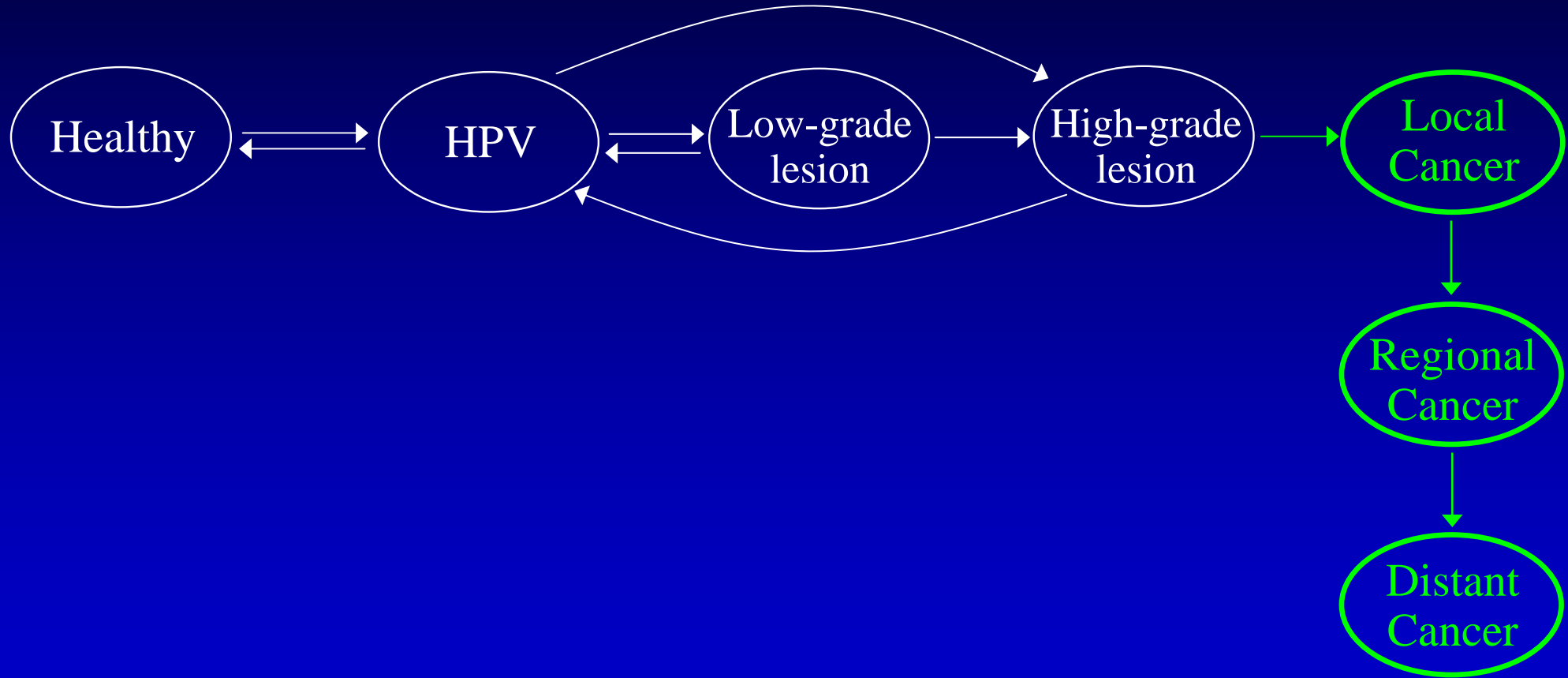
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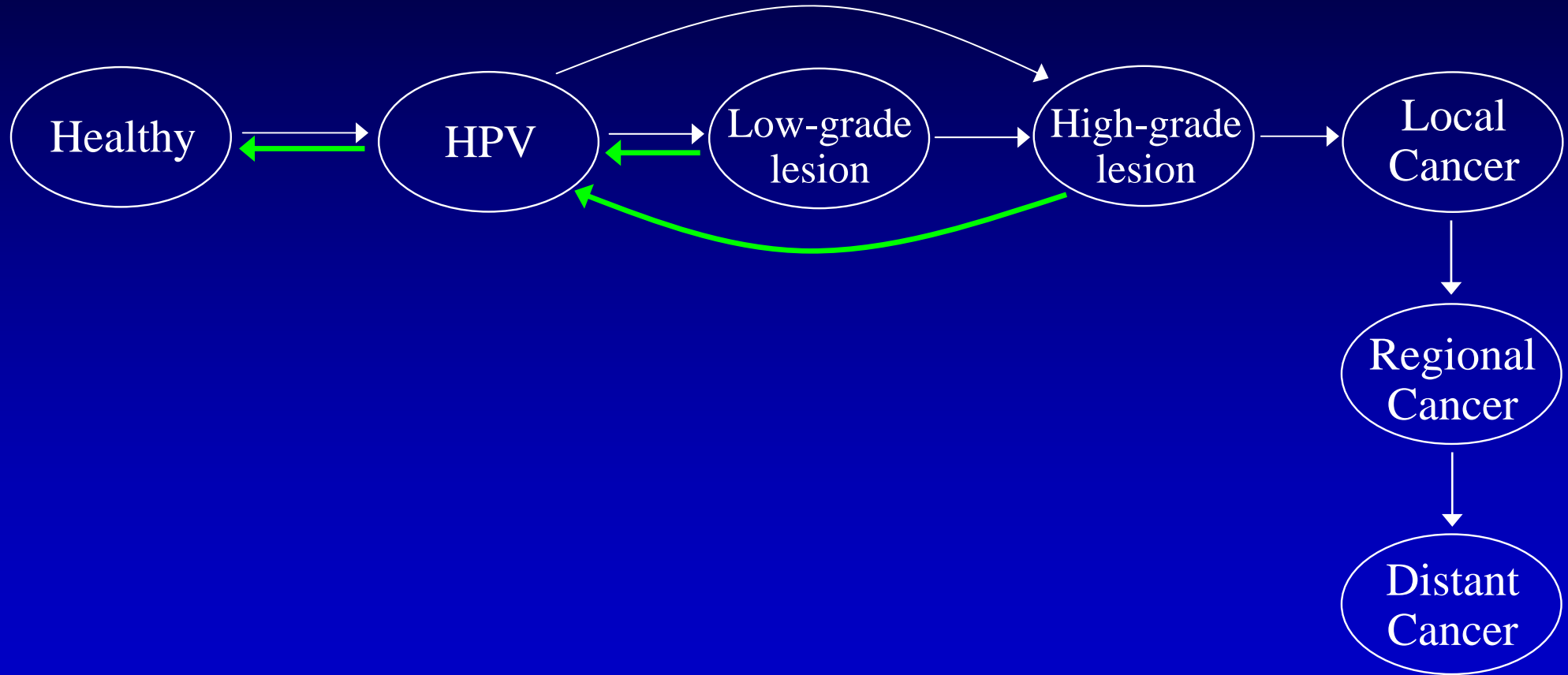
Cervical Cancer Model



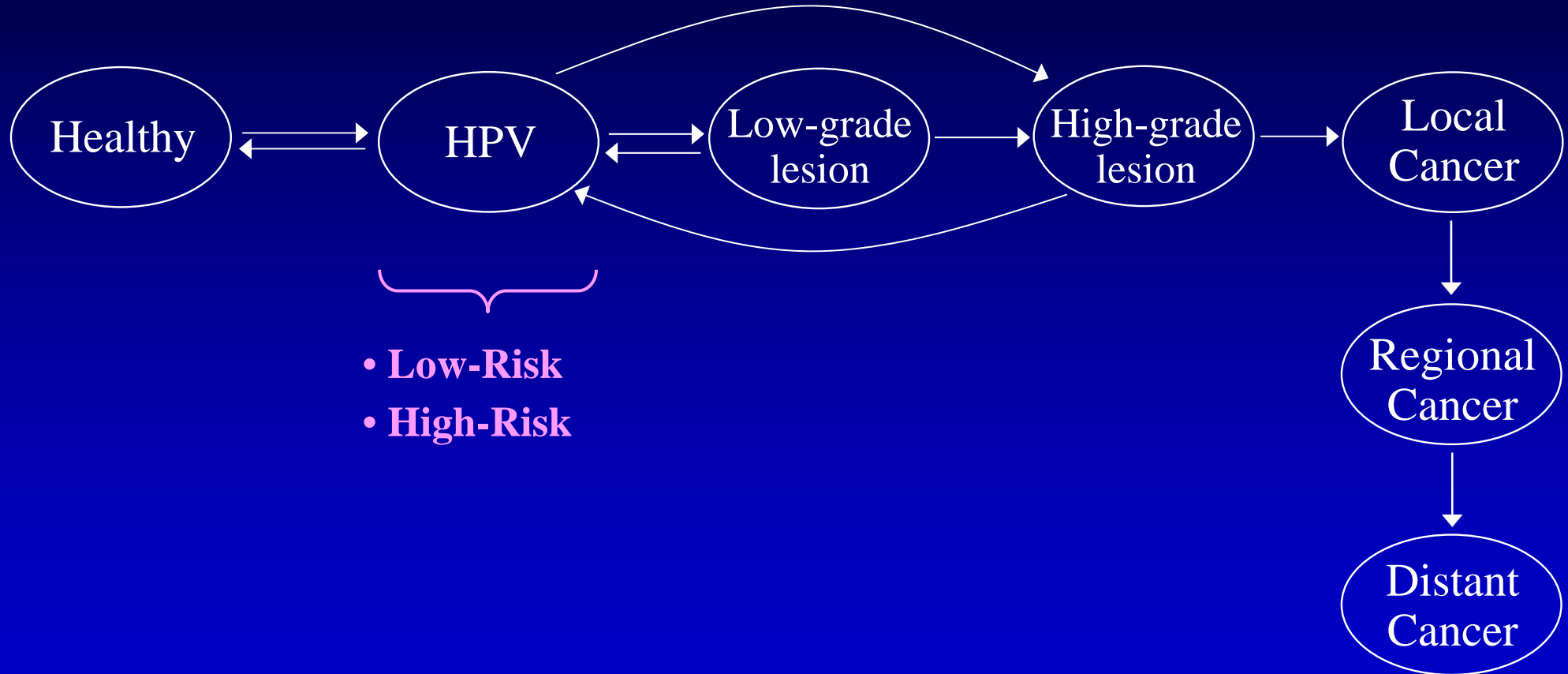
Cervical Cancer Model



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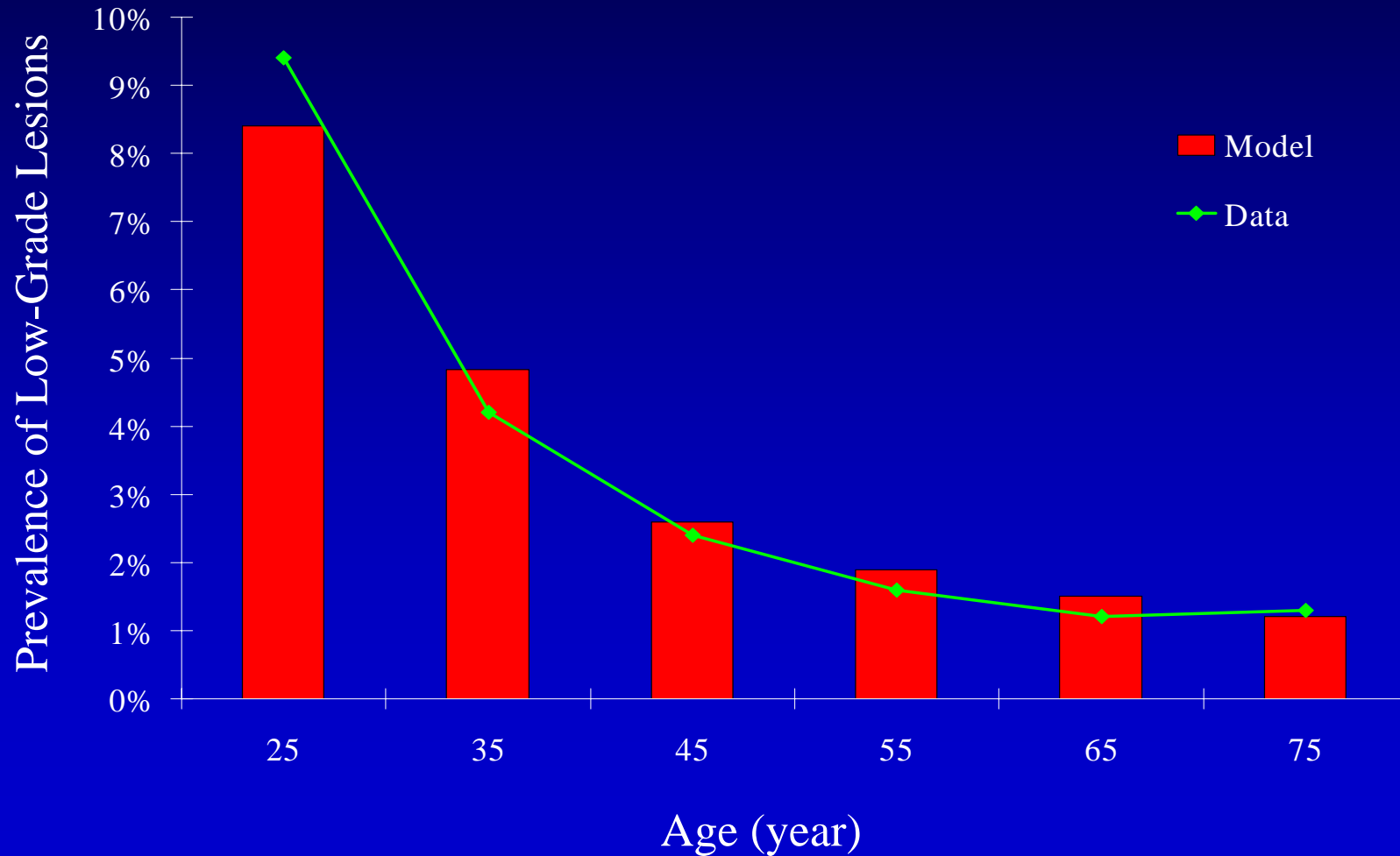
Cervical Cancer Model



Predictive Validity (1)



Predictive Validity (2)



Strategies

1. Ignore ASCUS result (least aggressive)
2. Immediate colposcopy (most aggressive)
3. Repeat Pap smear at 6-month intervals (most common)
4. Human Papillomavirus (HPV) DNA testing (new)

Routine Pap Smear Screening

Screening Test	Sensitivity (CIN 1)	Sensitivity (CIN 2,3)	Specificity	Cost
Liquid-based	70% (55-90)	80% (60-95)	95% (92-98)	\$30 (17-45)
Conventional	56% (50-70)	64% (55-75)	95% (92-98)	\$17 (13-30)

Incremental Cost-Effectiveness Ratio

Net increase in health care cost

Net gain in health effect

- measure of “value” for resources
- data for comparative analysis

Cost-Effectiveness Results

(2-year Liquid-Based Pap)

Strategy	Costs (US \$)	LE (years)	C/E (\$/YLS)	C/E (\$/QALY)
No Screen	210	28.6987	---	----
Ignore ASCUS	1,420	28.7874	13,700	12,300
HPV Test	1,710	28.7939	44,400	36,100
Repeat Paps	1,820	28.7937	dominated	dominated
Colposcopy	1,870	28.7941	905,300	667,300

Interpreting Cost-Effectiveness Results

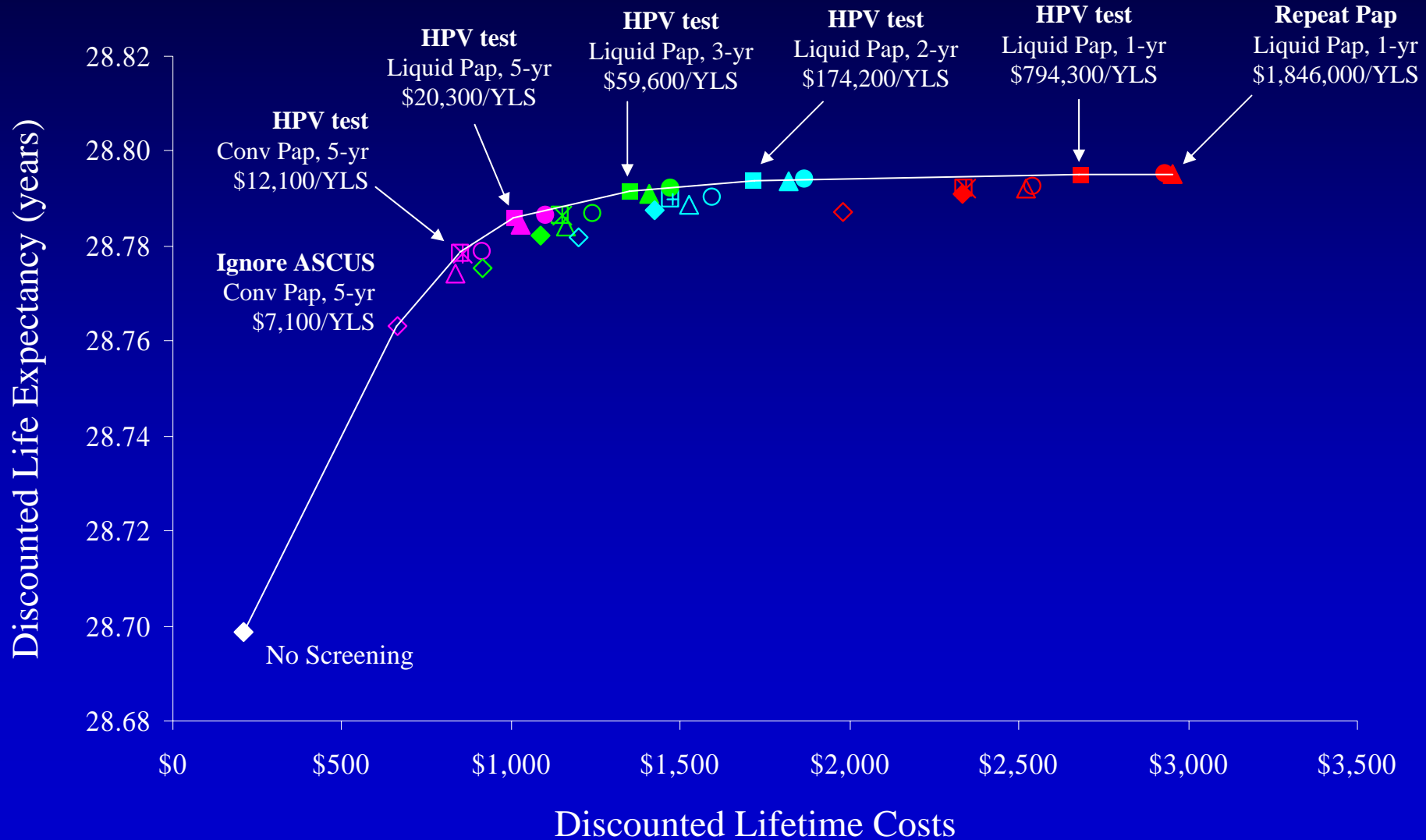
The Commission on Macroeconomics and Health recently defined interventions that have a cost-effectiveness ratio less than the GDP per capita as **very cost-effective**.

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Efficiency Frontier



Conclusions

- A strategy of repeat Pap (the most *common* strategy) is more costly and less effective than HPV testing.
- Immediate colposcopy (considered the most *effective* strategy) is more costly but provides only hours of life-expectancy benefit compared with HPV testing.
- Cost-effectiveness ratios associated with HPV testing for ASCUS in the context of every two- or three-year screening is attractive compared with other well-accepted public health interventions.

Example 2

Cost-Effectiveness of HPV DNA Testing in the UK, the Netherlands, France, and Italy*

Jane J. Kim, PhD; Thomas C. Wright, MD; Sue J. Goldie, MD, MPH

* *J Natl Cancer Inst* (2005)

Country-Specific Policies

	UK	Netherlands	France	Italy
Screening Interval	3, 5 years	5 years	3 years	3 years
Ages (years)	20-65	30-60	25-65	25-65
Coverage	84%	80%	60%	70%
Equivocal result	Repeat Pap	Repeat Pap	None	Colposcopy

Strategies

1. Pap smear throughout lifetime
HPV test *to triage women with equivocal results*
2. Pap smear until age 30
HPV test *instead of Pap smear* after 30
3. Pap smear until age 30
HPV test *in combination with Pap smear* after 30

Country-Specific Data

	Sensitivity	Specificity	Cost*
Pap	58 - 80%	93 - 98%	\$36 - 94
HPV Test	88 - 90%	91 - 95%	\$47 - 121
Pap + HPV Test	94 - 96%	88 - 93%	\$70 - 146

* All costs expressed in 2001 international dollars; includes lab, office visit, patient time, and transportation.

Cost-Effectiveness Ratios*

Strategy**	UK	Netherlands	France	Italy
Status Quo (by country)	-	-	-	-
HPV Test as Triage	6,300	3,400	8,100	10,100
HPV Test Alone (>30)	19,800	21,800	24,200	38,100
HPV Test + Pap (>30)	49,300	25,300	38,900	45,800

* CE-ratios expressed in I\$ per QALY-gained.

** All strategies assume same frequency as status quo policy.

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GDP per capita	30,200	31,700	29,100	25,600

Conclusions

- Policies incorporating HPV testing (either for triage of equivocal results or for primary screening in women >30) will provide greater benefit than the status quo.
- At current screening frequencies of every 3 to 5 years, the use of HPV testing as a primary screening test (alone or combined with a Pap smear) has an attractive cost-effectiveness ratio.

Example 3

Cost-Effectiveness of Cervical Cancer Screening in Kenya, India, Peru, South Africa, Thailand*

S. Goldie, L. Gaffikin, J. Goldhaber-Fiebert, A. Gordilla,
C. Levin, C. Mahe, T. Wright

Engender Health, International Agency for Research on Cancer, JHPIEGO Corporation, Pan
American Health Organization, Program for Appropriate Technology in Health

Sponsored by the Bill & Melinda Gates Foundation

* *NEJM* (2005)

Proposed Alternatives

- **Simplify Pap Strategy**
 - eliminate diagnostic confirmation step (2nd visit)
- **Visual Inspection Methods (VIA)**
 - acetic acid applied to cervix, inspected by naked eye
 - no lab services required, provides immediate result
- **HPV DNA testing**
 - test for high-risk HPV types in cervical smear
 - minimal training and quality control constraints, self-collected specimens are possible

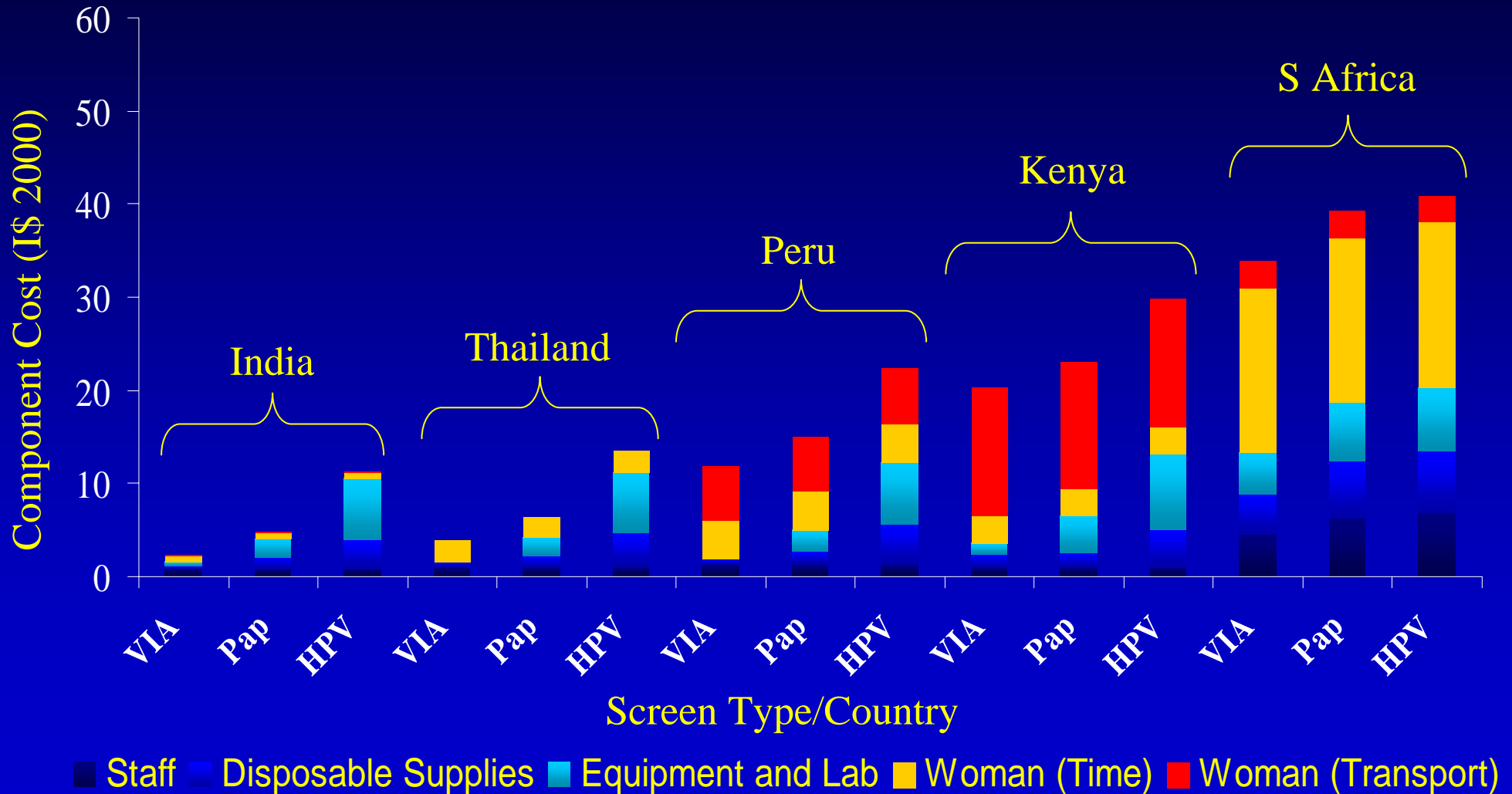
Strategies

- Screening test: Pap, VIA, or HPV
- Number of clinical contacts: 1-visit, 2-visit, 3-visit
- Frequency: 1x, 2x, 3x, 5-year
- Optimal target age: 20 – 50 (5 year intervals)

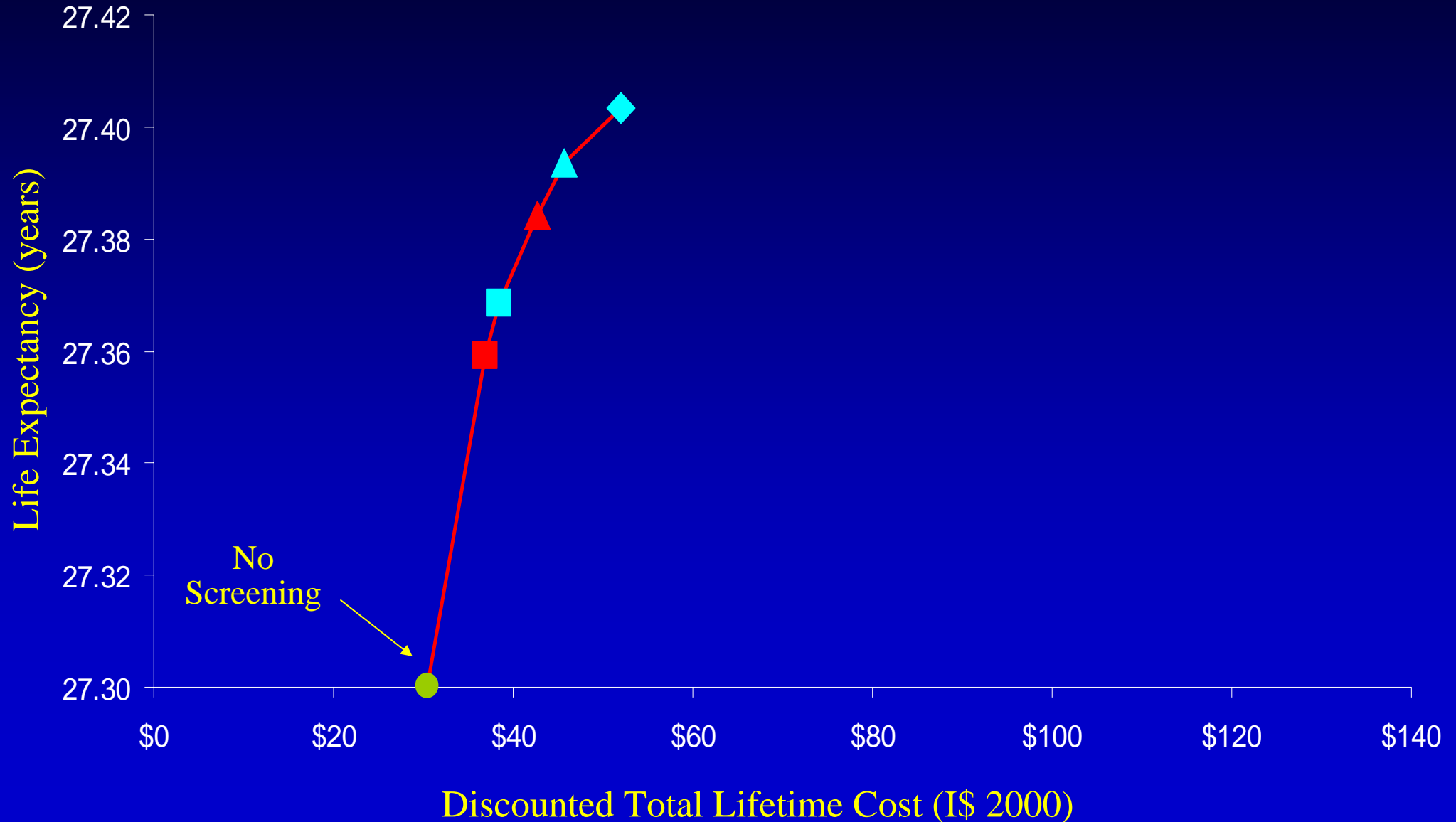
Screening Test Performance

Screening Test	Sensitivity	Specificity
Pap smear	63% (33-90)	94% (75-98)
Visual inspection (VIA)	76% (56-90)	84% (64-98)
HPV DNA test	88% (58-95)	93% (77-97)

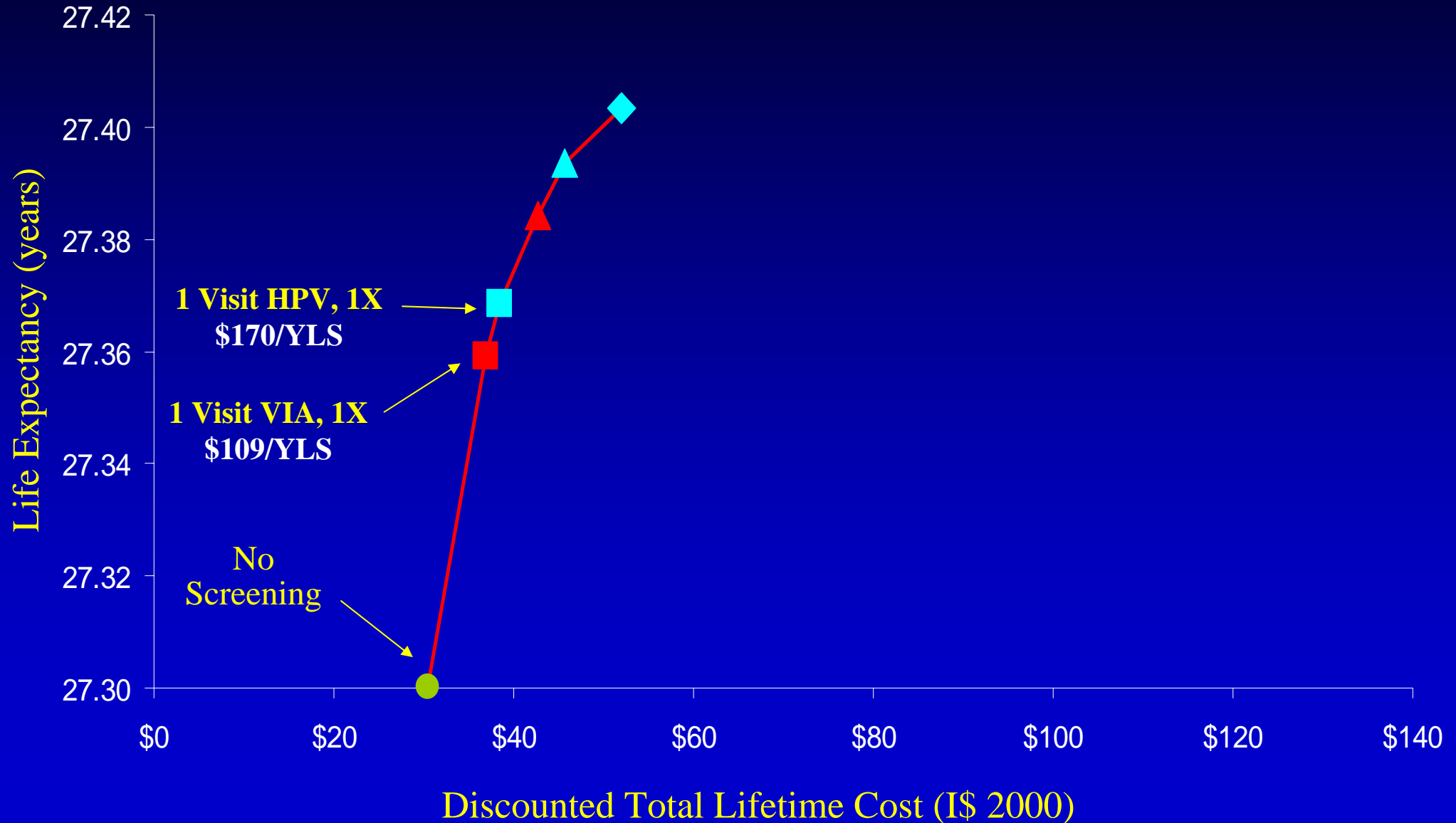
Screening Cost Components



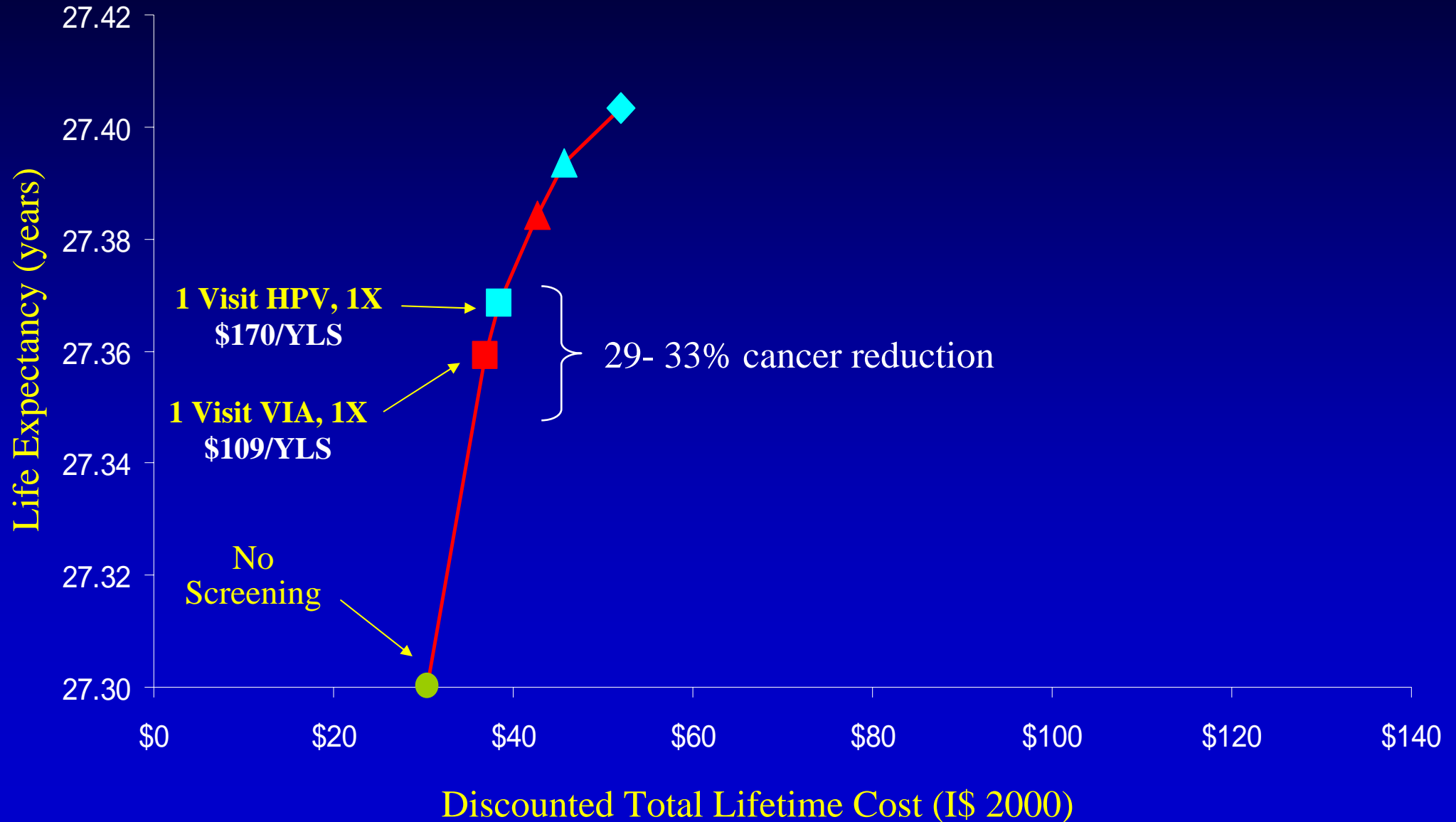
Results: Thailand



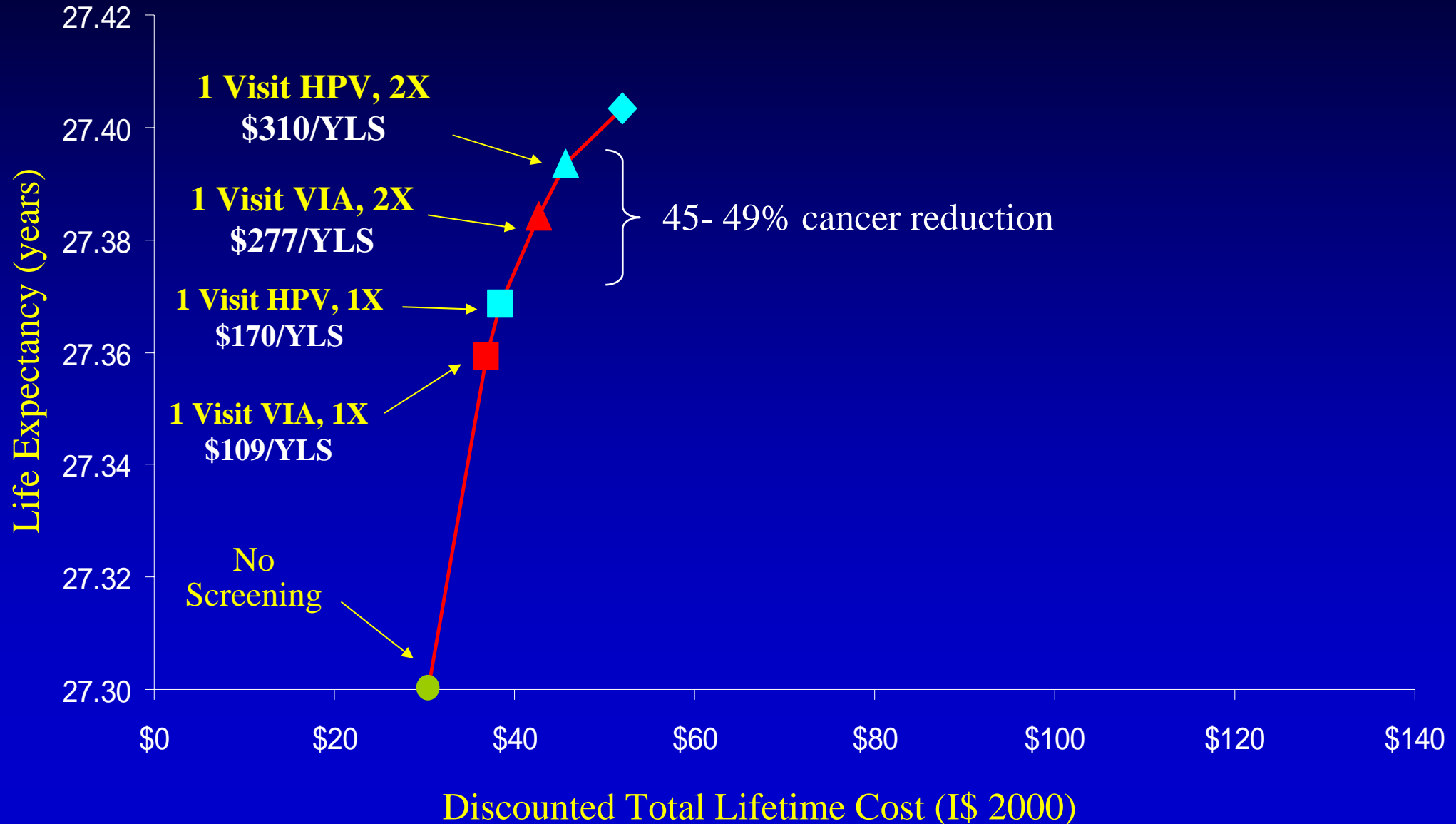
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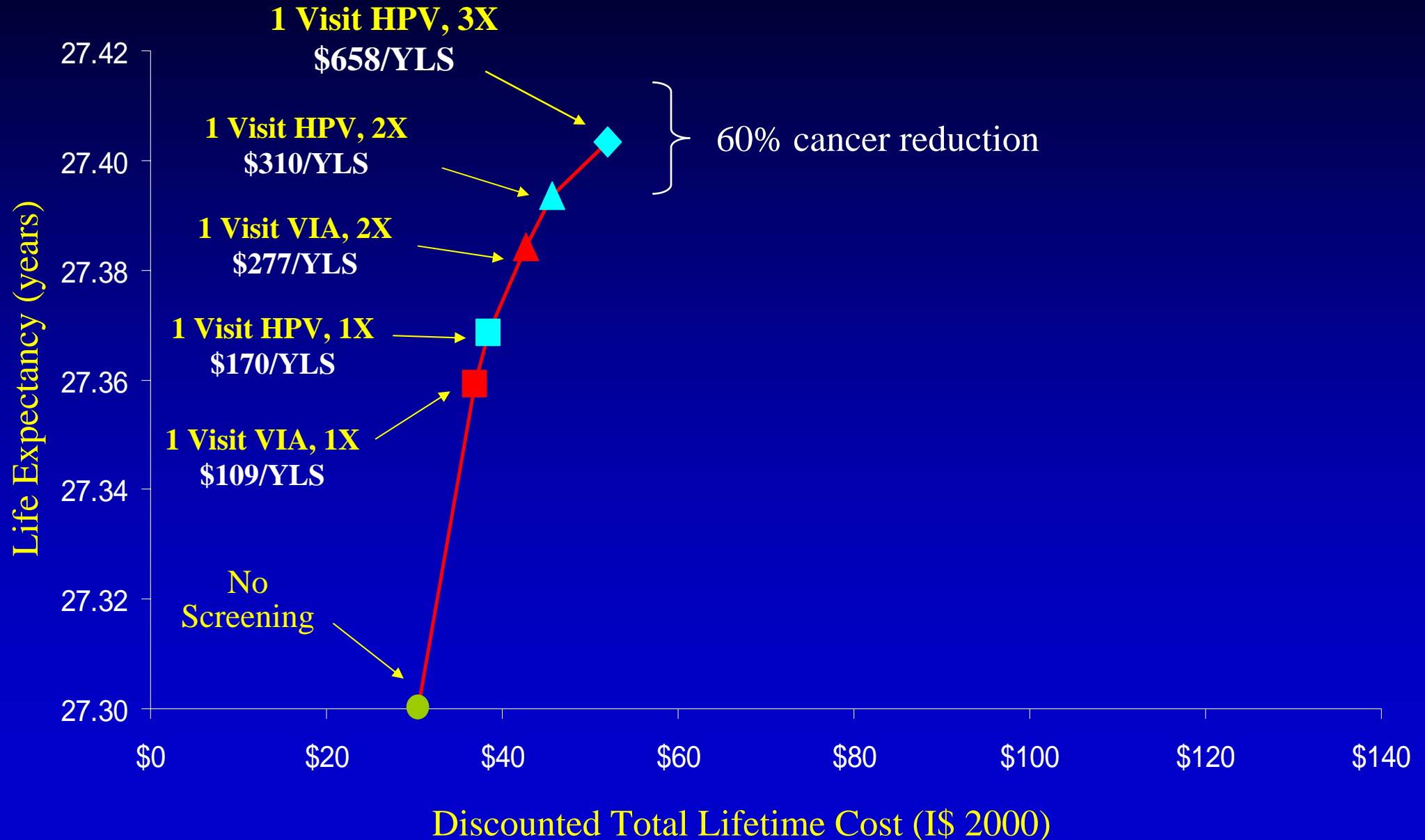
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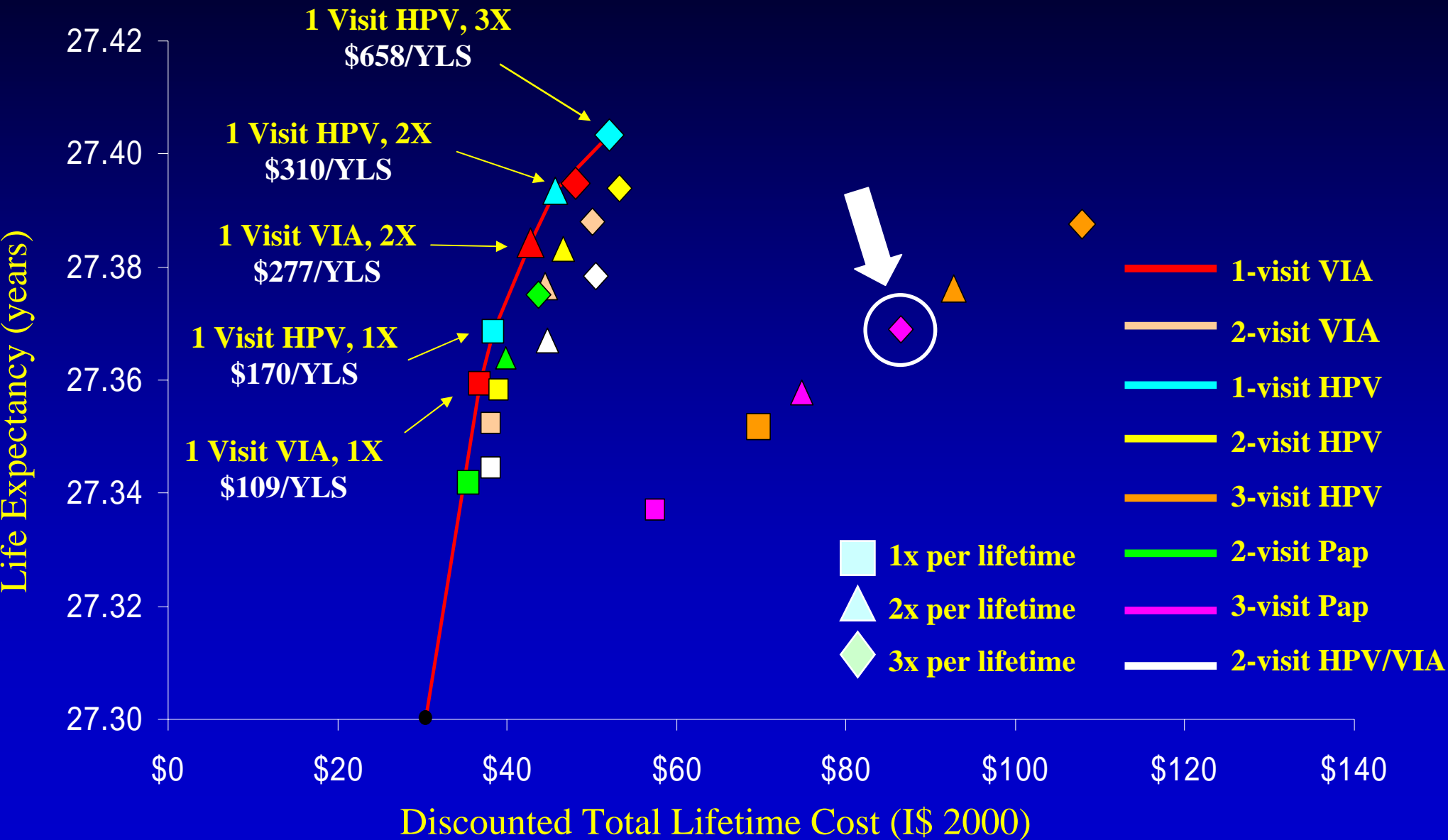
Results: Thailand



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Results: Thailand



CE Ratios* for Strategies on Efficient Frontier

Screening and treatment in a single visit

Strategy	India	Kenya	Peru	S.Africa	Thailand
VIA, 1x lifetime	10	134	124	-	109
HPV, 1x lifetime	-	-	152	467	170
VIA, 2x lifetime	91	319	-	-	277
HPV, 2x lifetime	-	705	453	1,093	310
VIA, 3x lifetime	268	-	-	-	-
HPV, 3x lifetime	591	1,119	1,145	2,458	658

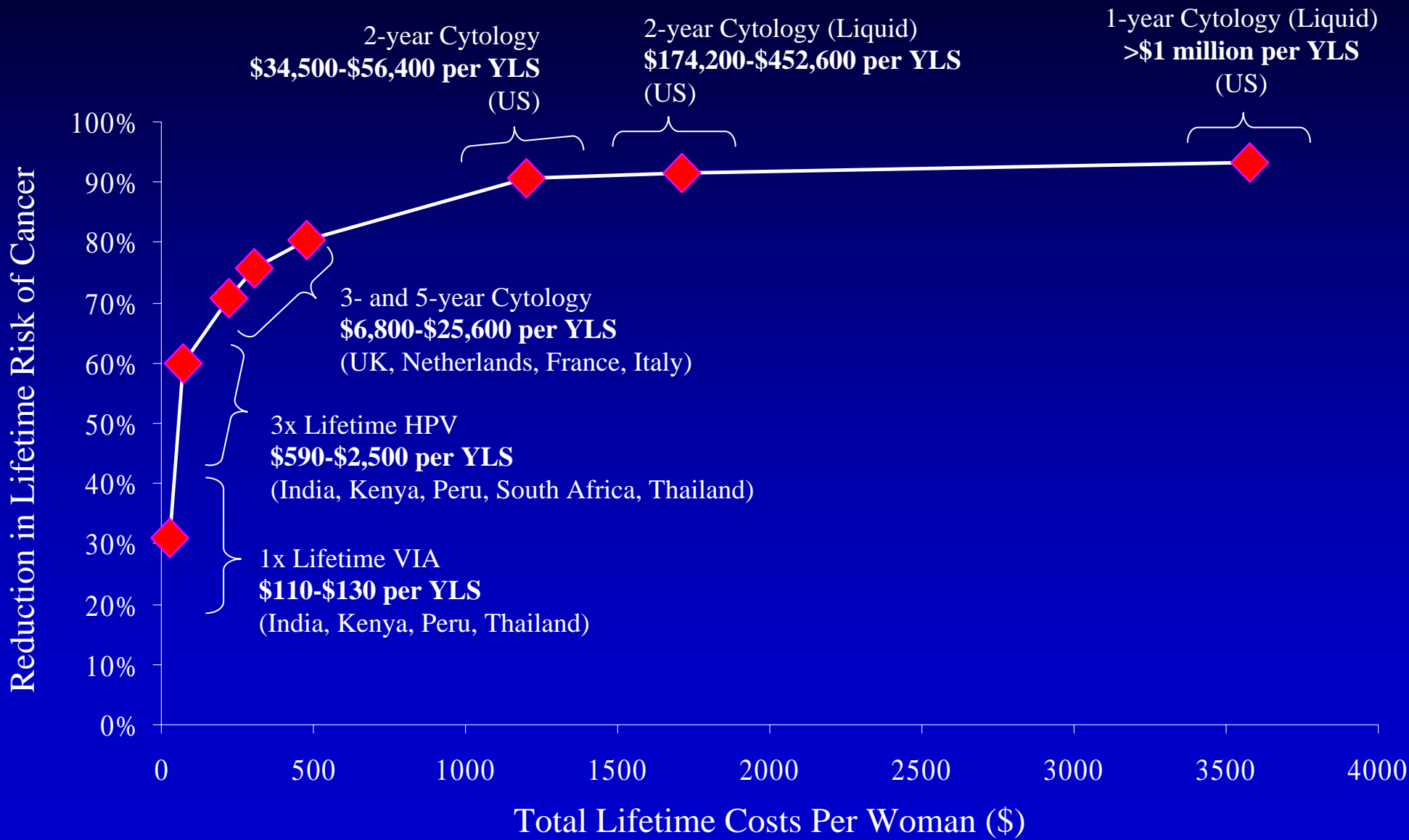
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HPV, 3x lifetime	591	1,119	1,145	2,458	658
GDP per capita	462	371	2,051	2,620	1,874

Summary of Results

- Previous recommendations: Pap smear 3x per lifetime at ten year intervals (e.g., age 20, 30, 40)
- Pap smears are consistently both less effective and less cost-effective than VIA and HPV testing.
- Optimal age to screen is between 35-45 years of age; optimal interval is every 5 years, not every 10 years.
- Cervical cancer incidence could decrease up to ~30-50% with 1 or 2 screenings.



Key Themes

- For countries with existing screening programs, substitution of annual Pap smears with more sensitive tests (i.e., HPV test or liquid-based Pap) without modification of the screening interval will not be cost-effective;
- These options in the context of every 2-3 year screening, would provide comparable or better cancer protection than the status quo *and* would be reasonably cost-effective.
- For countries with limited resources, screening efforts should target women age 35 or older, and efforts should focus on attaining high coverage of single lifetime screening before increasing the frequency of screening.