The Clinical and Economic Impact of a Generic First-line Antiretroviral Regimen in the United States

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Conflicts of interest: None
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Background

- US HIV treatment guidelines recommend the branded once-daily, one-pill tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV) as a preferred first-line antiretroviral therapy (ART)

Background

- In Jan 2012, generic versions of lamivudine (3TC) became available; generic versions of efavirenz (EFV) are expected
- Possibility of a potent, largely generic first-line regimen in the US
  - Generic EFV, generic 3TC, branded tenofovir (TDF)

Background

Impact of a generic-based regimen

1) Though still once-daily, generic regimen will have increased pill burden (3 vs.1 pill) may result in poorer adherence, virologic outcomes
2) Replacement of FTC with 3TC *may*:
   - Diminish potency as a first-line regimen
   - Diminish potency of the second-line regimen associated with increased frequency M184V
3) Costs of generic regimen will be less

Objective

To assess the clinical impact, costs, and cost-effectiveness of the generic-based three-pill regimen compared to branded, co-formulated regimen

Methods
CEPAC-US Model

- Cost-effectiveness of Preventing AIDS Complications (CEPAC)-US Model
  - A mathematical simulation model of HIV infection
  - Populated with clinical/economic data from the US

Methods
CEPAC-US Model

- Model outcomes – US health systems perspective – are:
  - Clinical (quality-adjusted life years)
  - Economic (per-person lifetime costs)
  - Incremental cost-effectiveness ratios (ICER, 2009 $/QALY)
    - Willingness to pay threshold: <$100,000/QALY
- Project the national savings in the first-year of switching to a generic-based regimen

Methods
Strategies examined

1) ***No ART*** (for comparison)

2) ***Generic ART***

Generic 3TC, generic EFV, and branded TDF

3) ***Branded ART***

One-pill co-formulated TDF/FTC/EFV

Model input parameters

Cohort Characteristics

Variable	Base case value (SD)	Reference
Age, mean years	43 (9.5)	Althoff *CID* 2010
Initial CD4 count (cells/μl)	317 (283)	
Male (%)	84	

Regimen Efficacy

- **“Early suppression”**: the fraction of patients virologically suppressed after 24 weeks
- **“Late failure”**: the rate of virologic rebound after initial 24-week suppression
- More effective regimen: *high* early suppression, *low* late failure

Model input parameters

Regimen efficacy and costs

	Generic ART	***Branded ART***
Early Suppression (%, 24-wks)	78%[1]	85%[2]
Late failure (/100py, after 24 wks)	5.41[1]	2.52[2]
Regimen Costs (/yr)	$9,200[3]	$15,300[4]

[1]Gallant JAMA 2004
[2]Sax CROI 2012
[3]75% price reduction from Average Wholesale Price
[4]23% discount from Average Wholesale Price

Results

	Life expectancy (QALY)	Per-person lifetime cost* (USD 2010)	ICER ($/QALY)
No ART	4.05	131,200	--
Branded ART	12.45	342,800	25,200

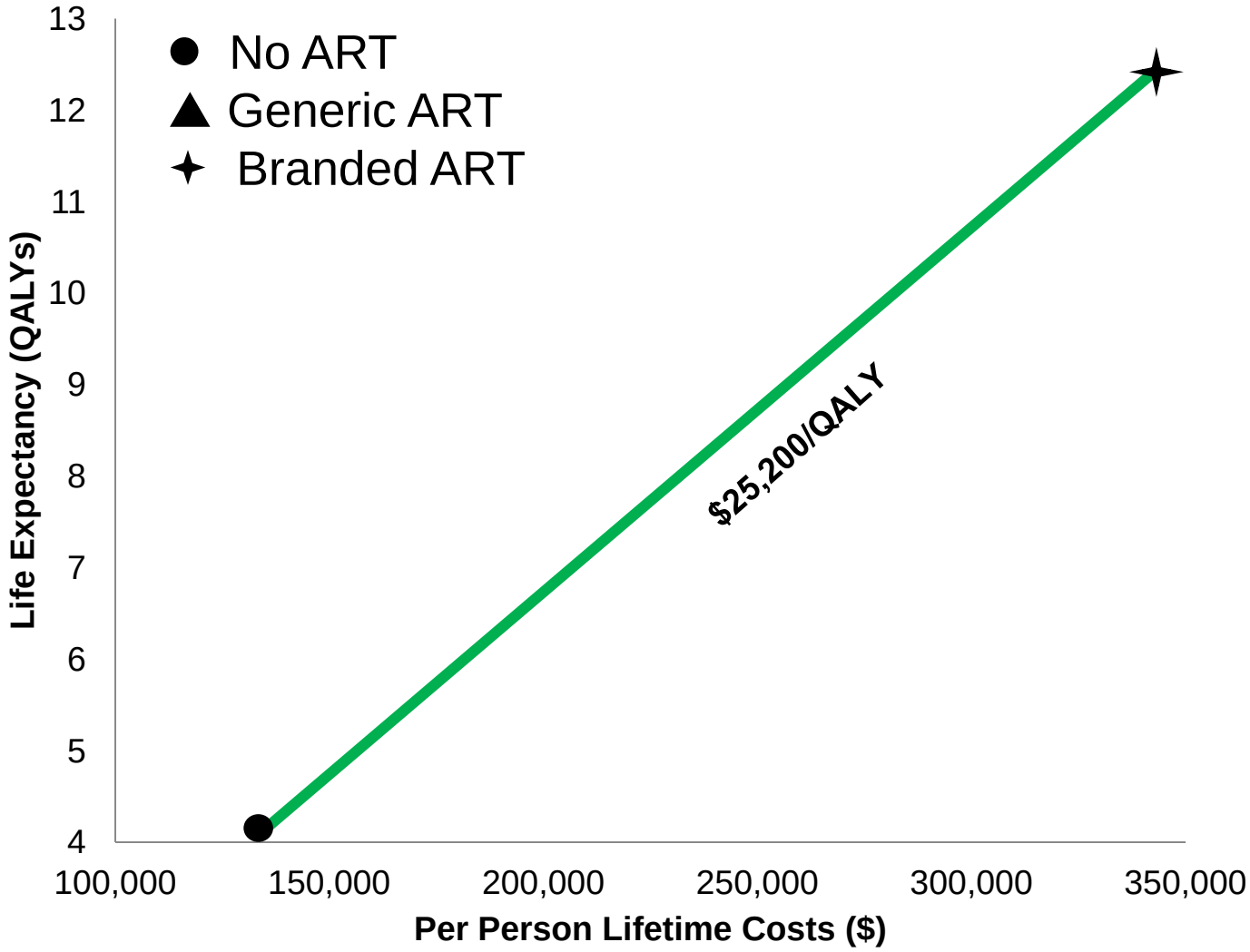
USD: United States Dollars; QALY: quality-adjusted life year; ART: antiretroviral therapy
*QALY and costs discounted at 3% annually

Results

	Life expectancy (QALY)		Per-person lifetime cost* (USD 2010)		ICER ($/QALY)
No ART	4.05		131,200		--
Generic ART	12.08	Δ 0.37	300,300	Δ $42,500	21,100
Branded ART	12.45		342,800		114,800

USD: United States Dollars; QALY: quality-adjusted life year; ART: antiretroviral therapy
*QALY and costs discounted at 3% annually

Results
Cost-effectiveness Plane



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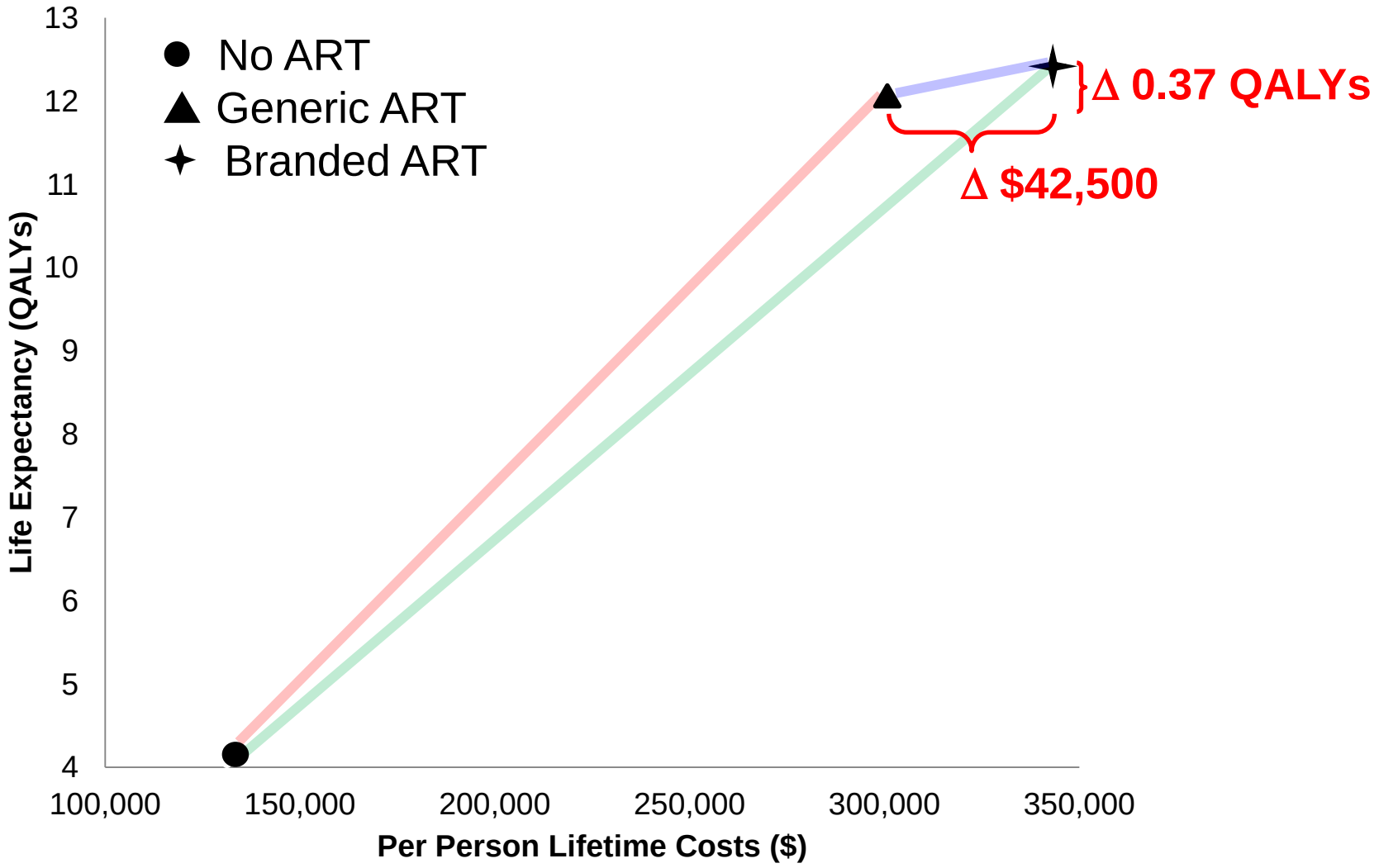
Cost-effectiveness Plane



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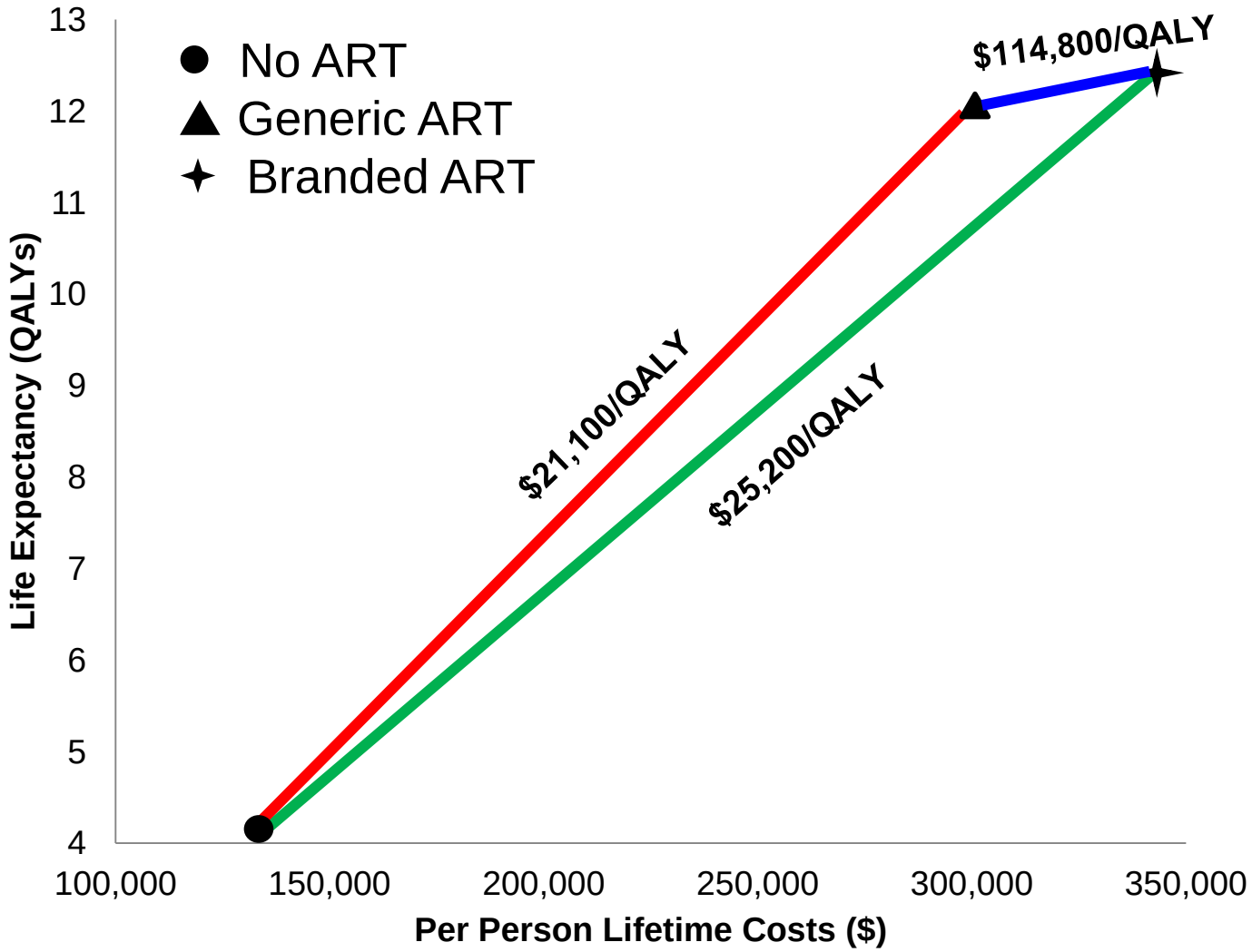
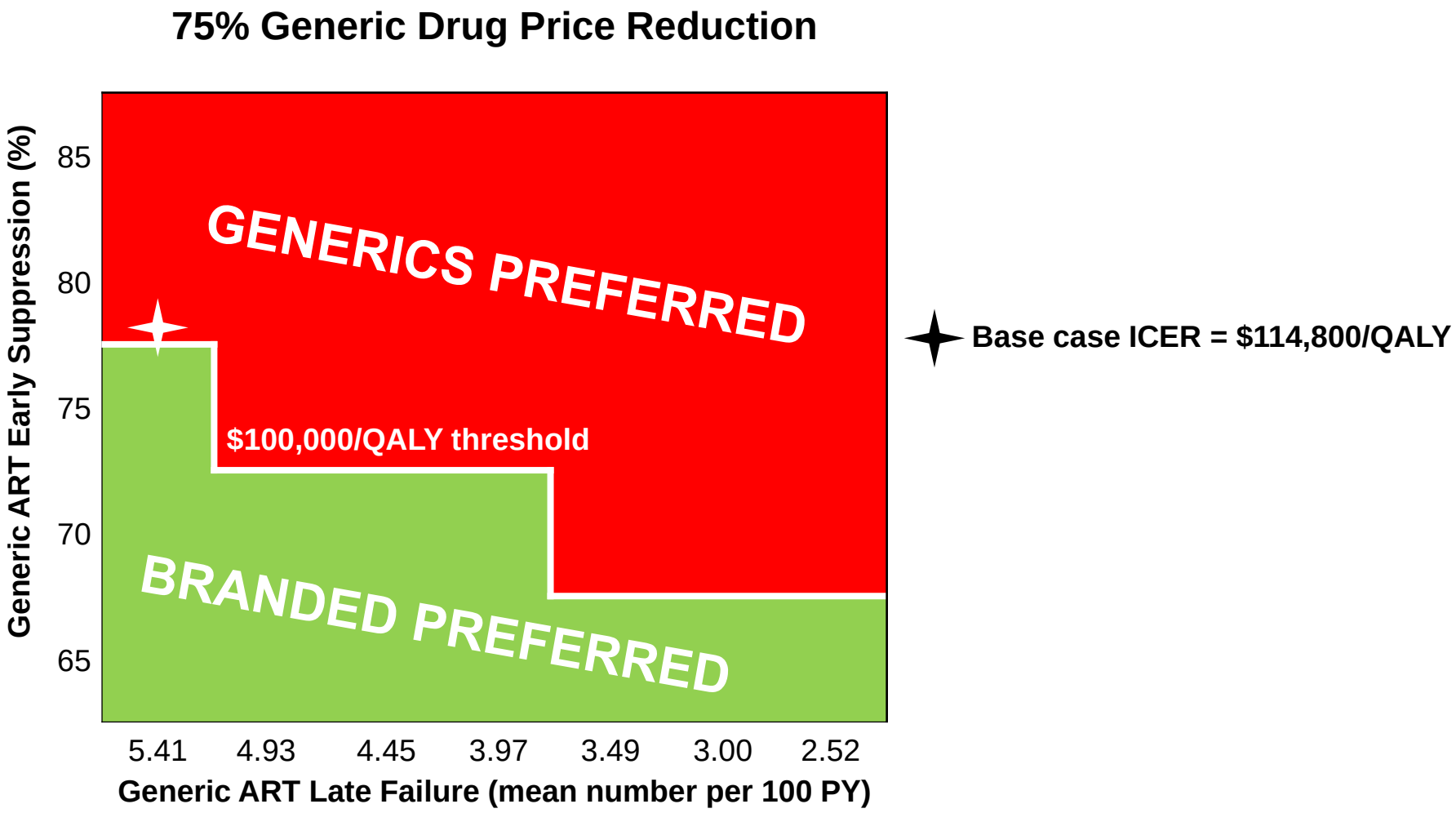
Cost-effectiveness Plane

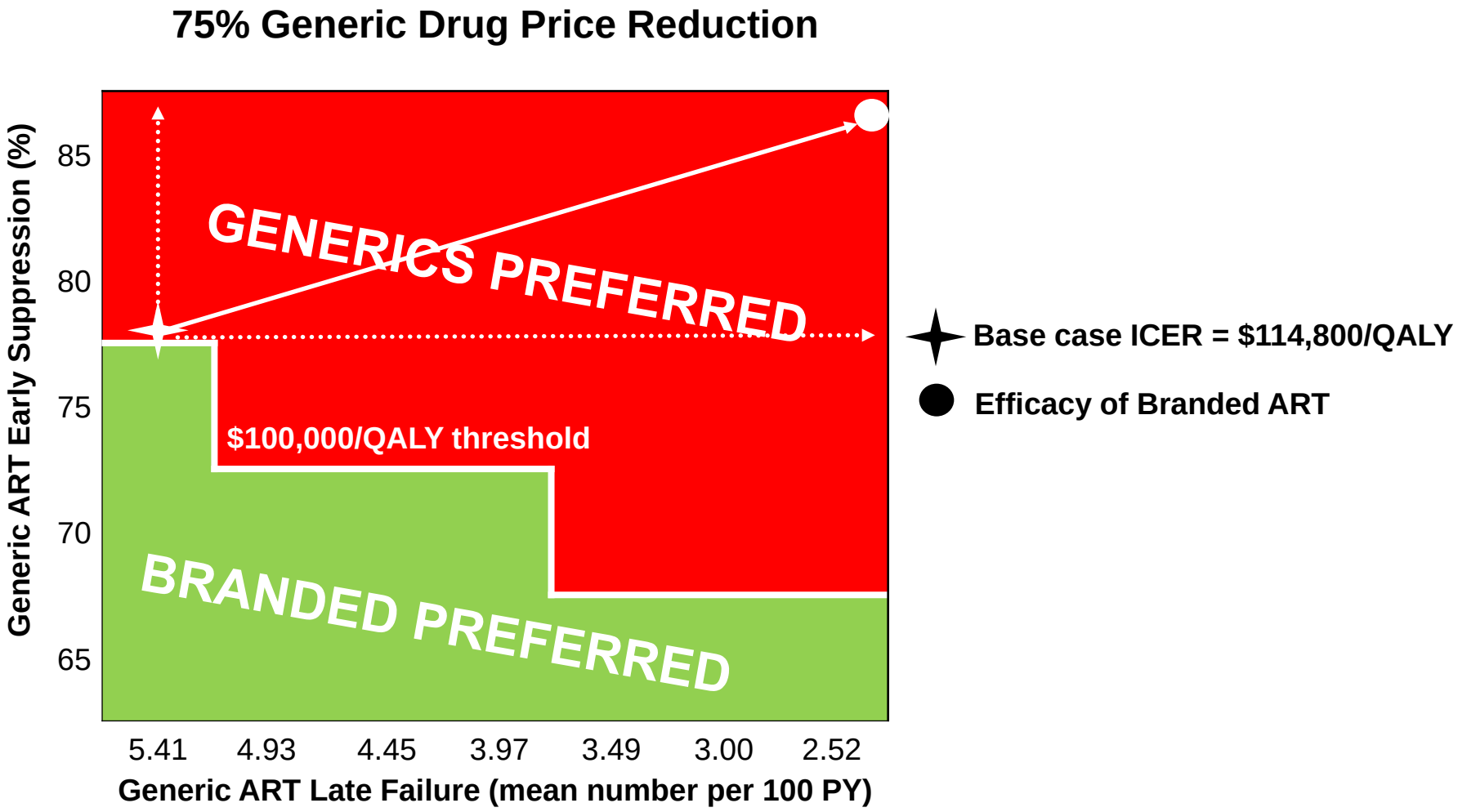


Sensitivity Analysis

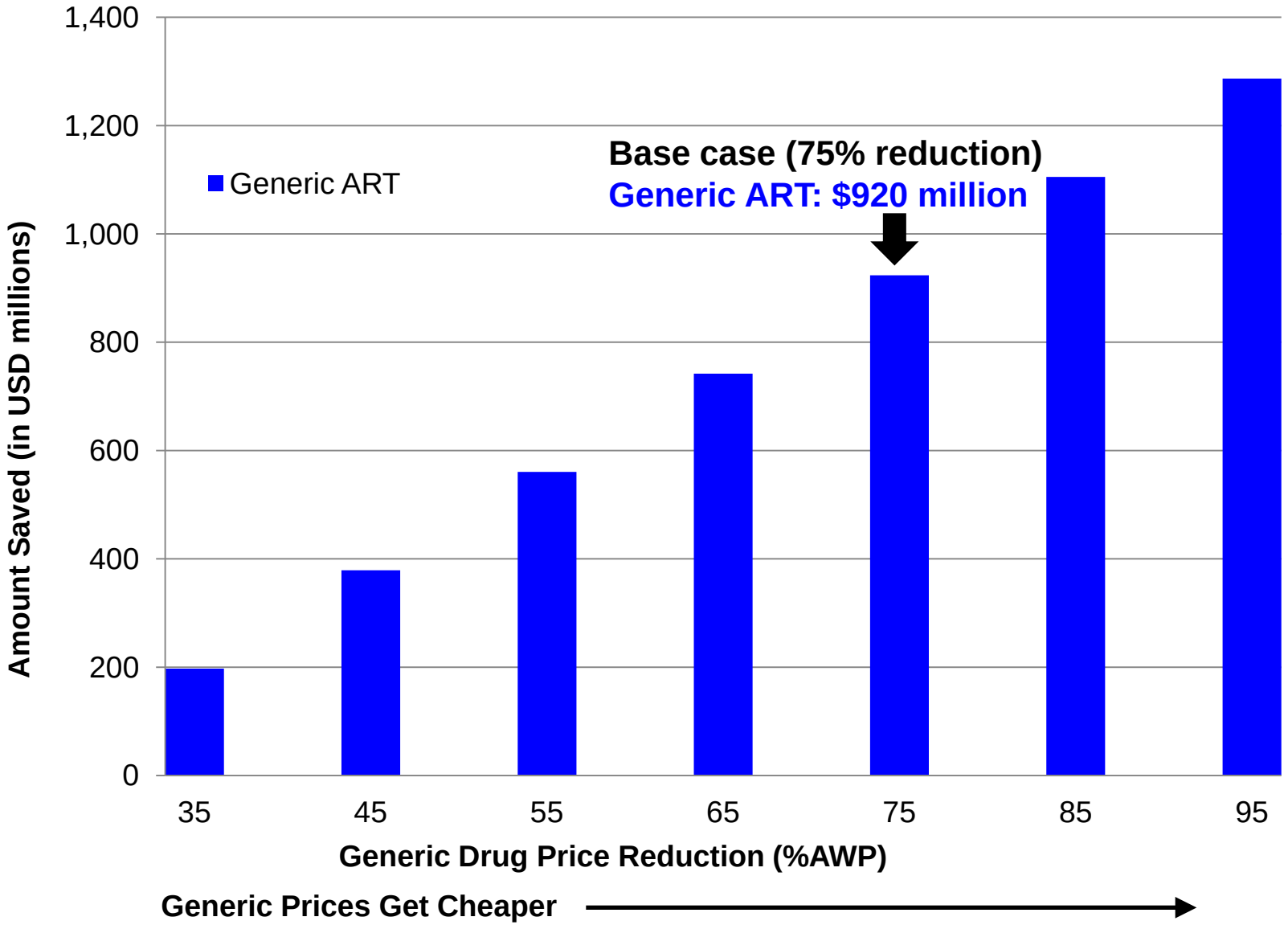


Sensitivity Analysis

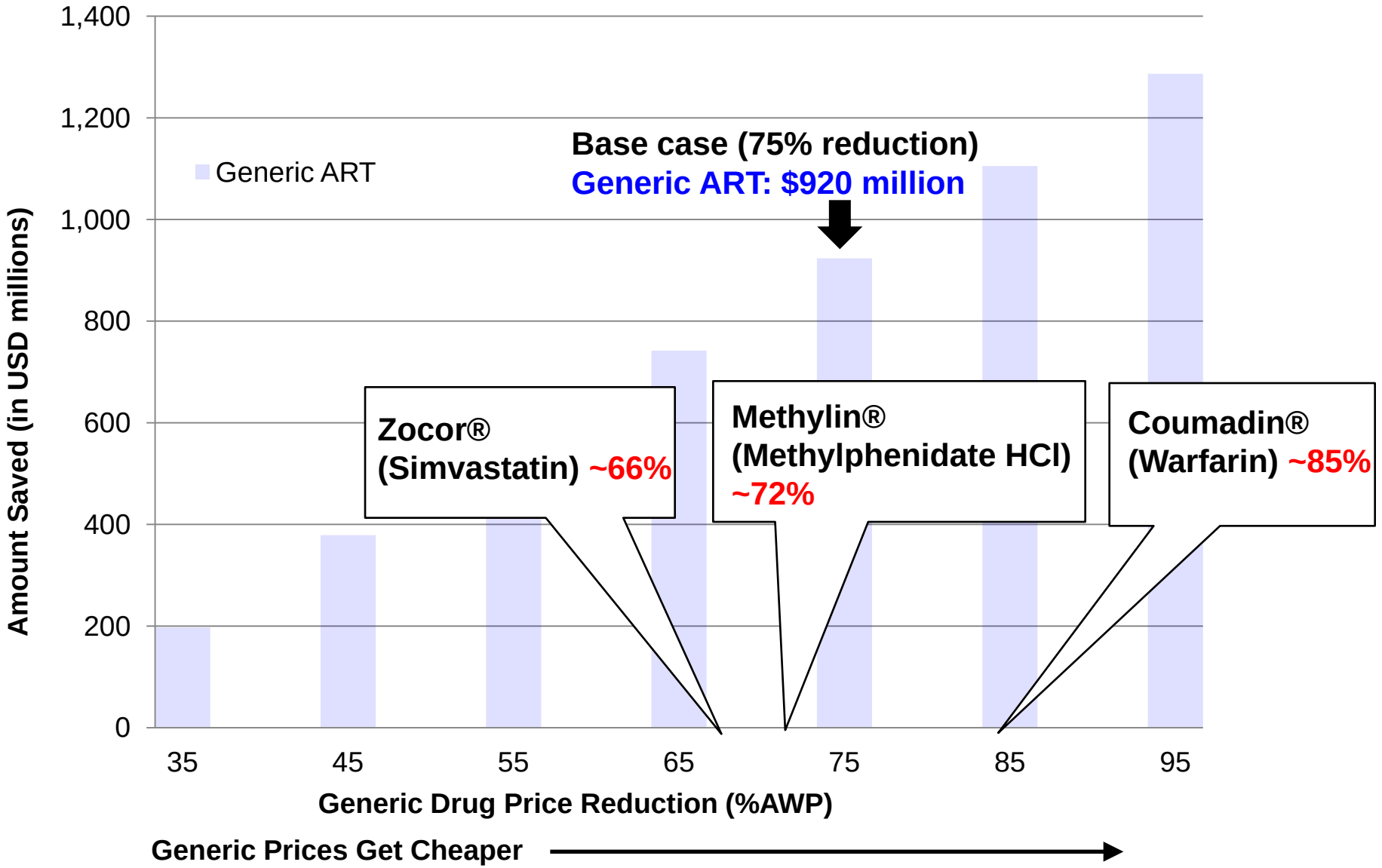
ICER of Branded Compared to Generic ART



Potential Savings in the First-Year



Potential Savings in the First-Year



Limitations

- Efficacy and price reduction associated with generics are unknown
  - Assumptions are intended to be conservative for generics
  - Better performance of generic drugs would render the branded regimen even less attractive
- The $100,000/QALY willingness-to-pay threshold, while frequently cited, may be debated

Economic Savings vs. Health Losses

- Are we, as a society, ready to forgo small individual survival benefits for large national savings?
- Do we recognize that economic savings will vary among payers?
  - e.g. State ADAPs vs. state Medicaid programs vs. US Veterans Administration
- Are we prepared for the fact there is no guarantee that money saved will be reinvested in HIV care?

Opportunities for Reinvestment

- President Obama's 2010 National HIV/AIDS Strategy is explicitly financed by "re-purposed" rather than new funds
- If investment in the national HIV mission requires "redirected" financing, $1 billion saved from use of generic drugs might be an attractive source for this national reinvestment
- Treatment for HCV co-infection:
  - Fewer than 50% of AIDS Drugs Assistance Programs currently cover protease-inhibitor based HCV treatment

Conclusions

- A switch from first-line Branded to Generic ART will result in a lifetime average savings of $42,500 and a modest survival loss (0.37 QALYs)
- Aggregate annual savings in the first year would amount to nearly $1 billion
- Compared to a slightly less effective generic-based regimen, the cost-effectiveness of the branded regimen likely exceeds $100,000/QALY

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Methods: Potential Savings in the First Year

- N=2,500 Newly diagnosed and eligible to start ART in next year:
  - 8,300 new diagnoses/year
  - 36% on ART
  - 85% on EFV-based regimen

- Eligible to switch from EFV-based brand name to generic-based: n=**147,300**
  - 1.2M with HIV in US
  - 36% on ART
  - 34% on EFV-based regimen

Model input parameters

Regimen efficacy and costs

	24-wk virologic suppression	Virologic rebound after 24 wks (/mo)	Annual regimen cost	Reference
Branded ART	85%	0.21%	$15,300	Sax CROI 2012
Two-pill Generic ART	84%	0.43%	$11,600	Lennox *Lancet* 2009
Three-pill Generic ART	78%	0.45%	$9,200	Gallant *JAMA* 2004

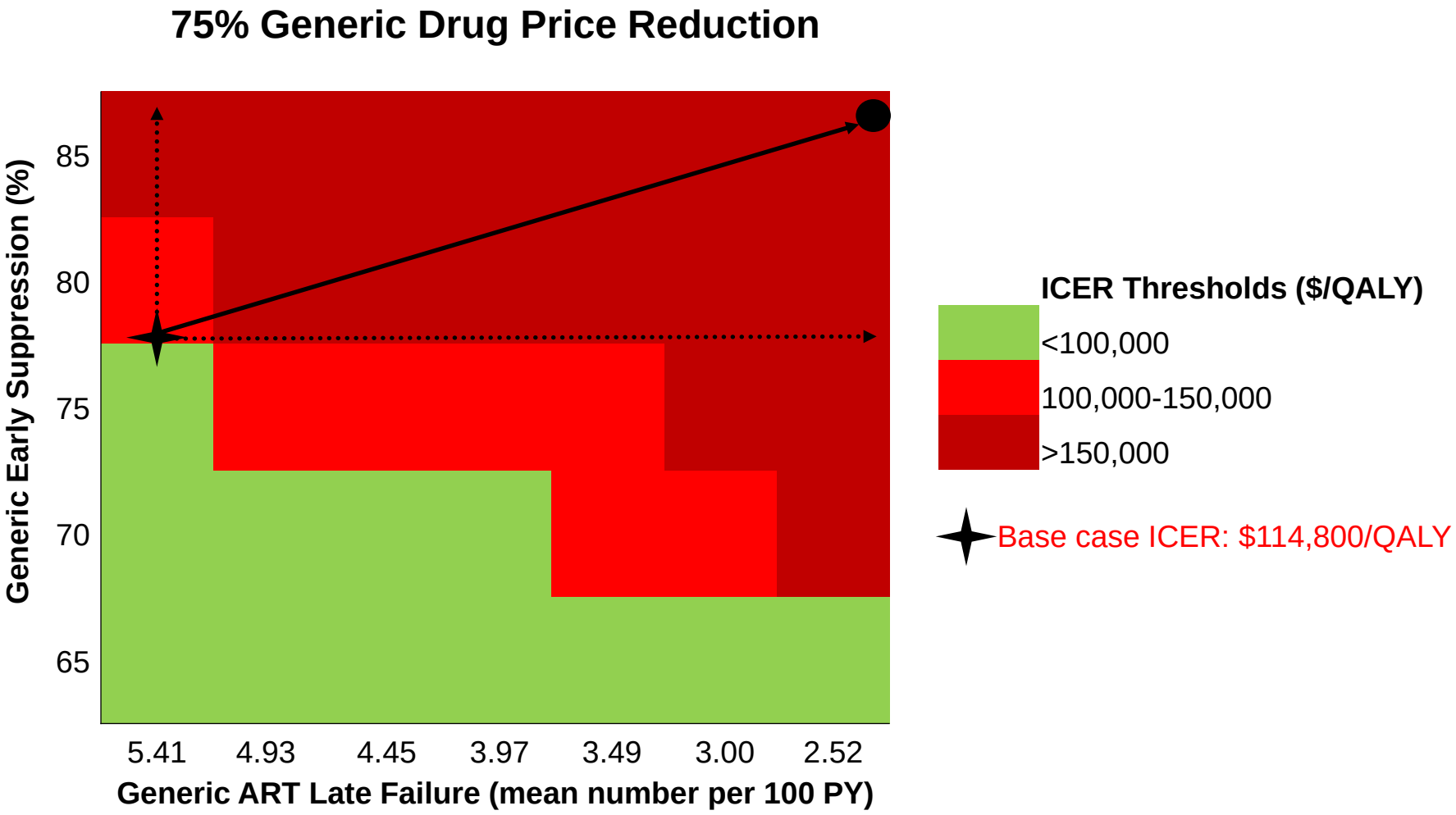
Results

	Life expectancy (QALY)	Per-person lifetime cost* (USD 2010)	ICER ($/QALY)
No ART	4.05	131,300	--
Three-pill Generic ART	12.09	305,100	21,100
Two-pill Generic ART	12.25	323,300	95,400
Branded ART	12.45	349,100	130,600

USD: United States Dollars; QALY: quality-adjusted life year; ART: antiretroviral therapy
*QALY and costs discounted at 3% annually

Sensitivity Analysis

ICER of Branded Compared to Generic ART



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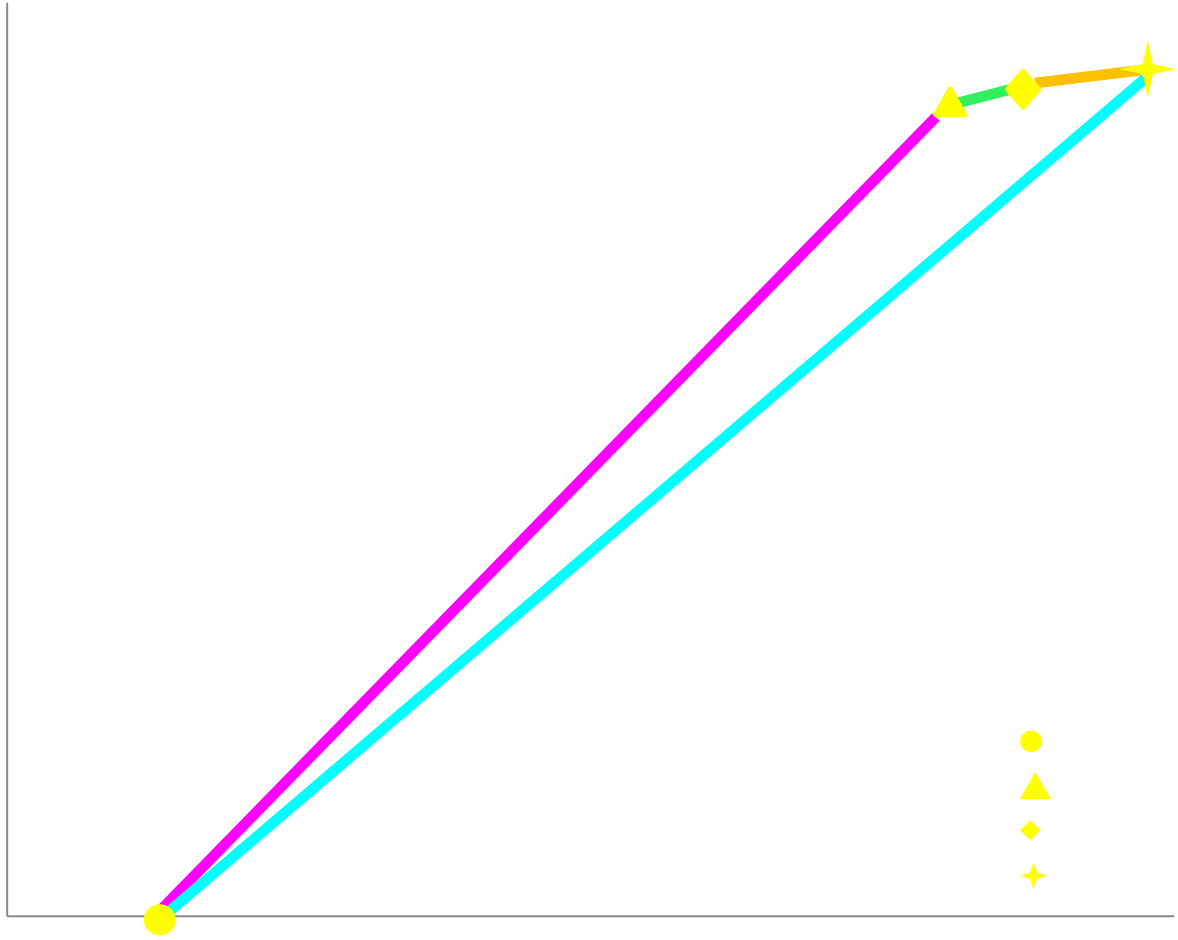
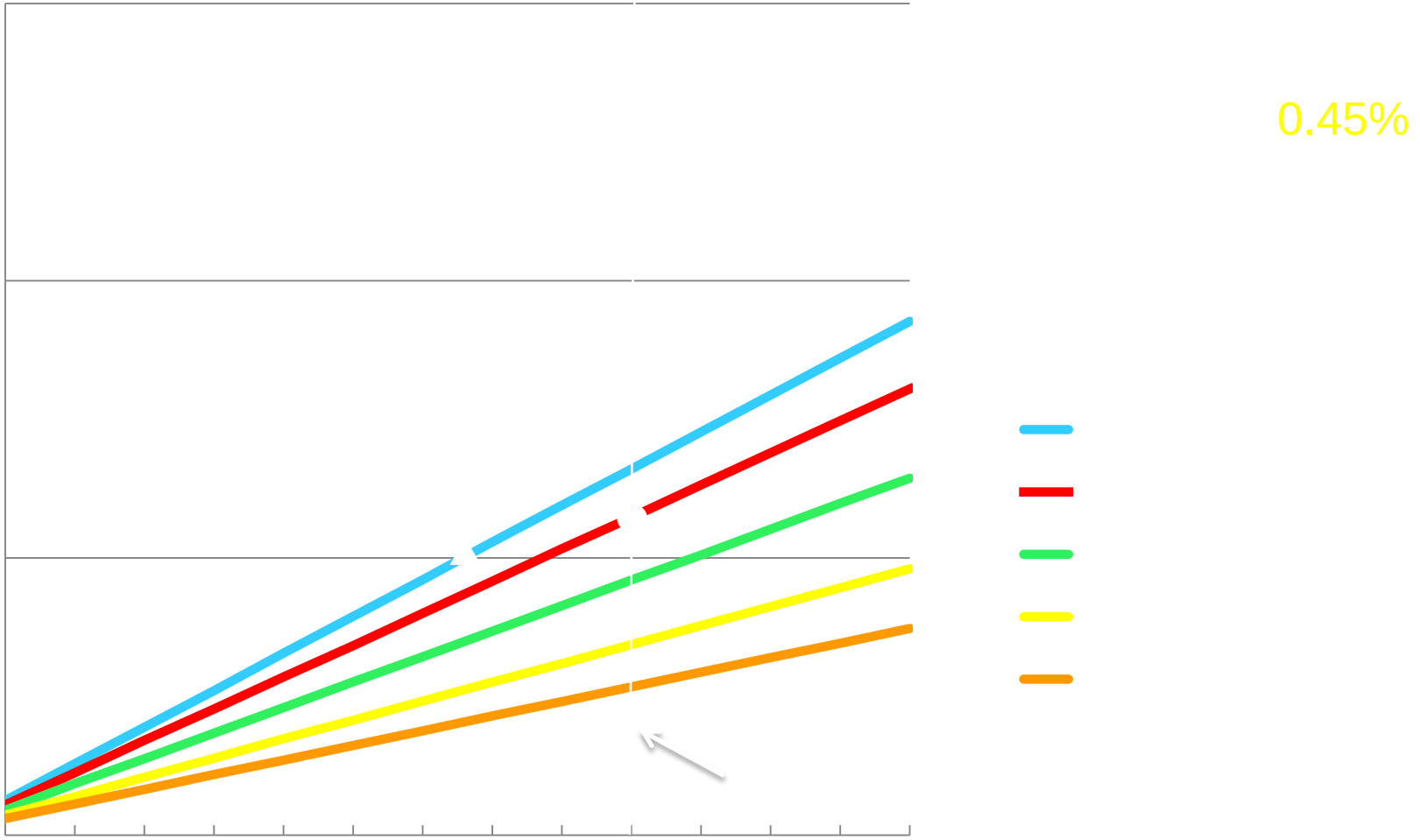


Sensitivity Analysis

Incremental Cost-effectiveness Ratio of Branded ART

Efficacy and costs



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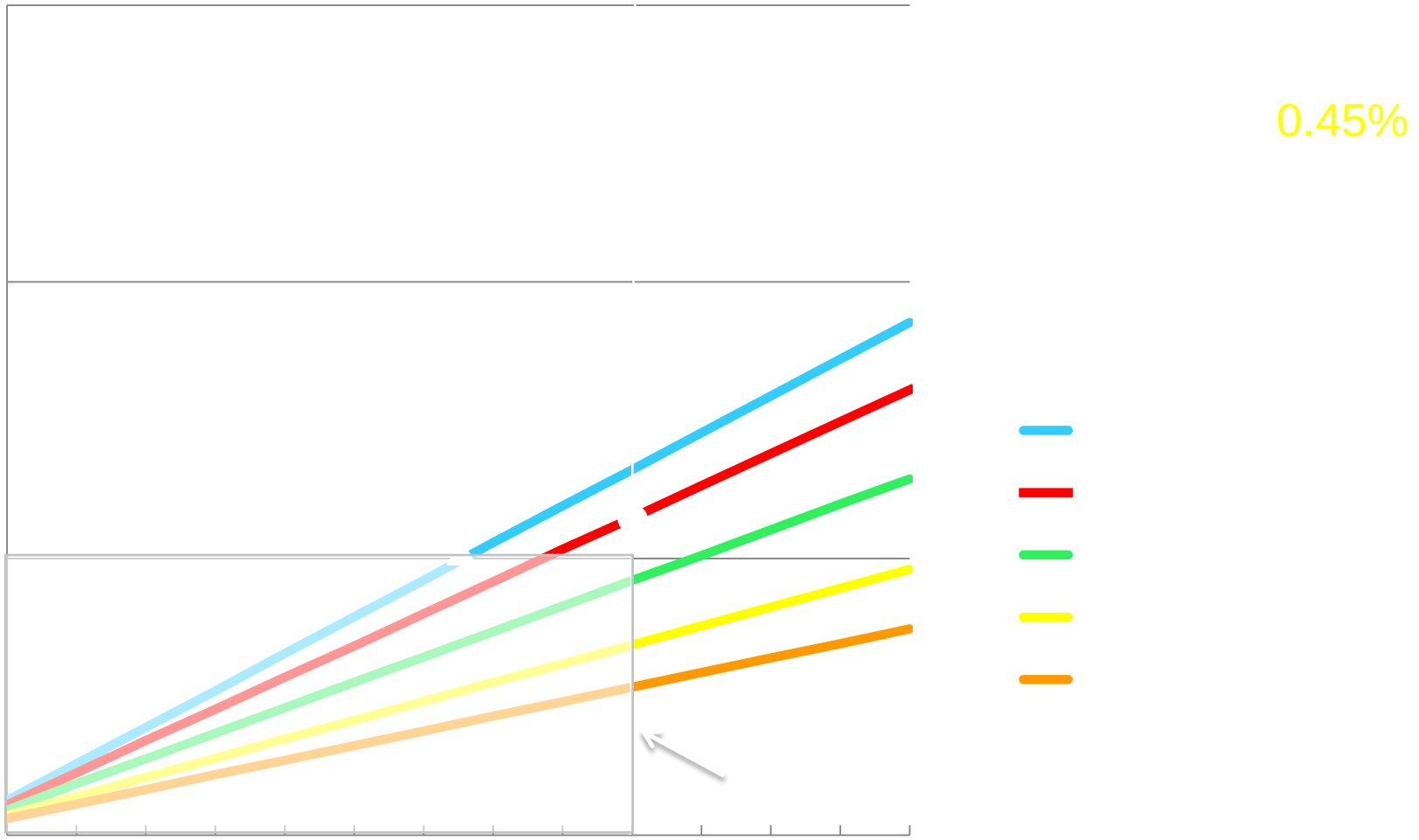

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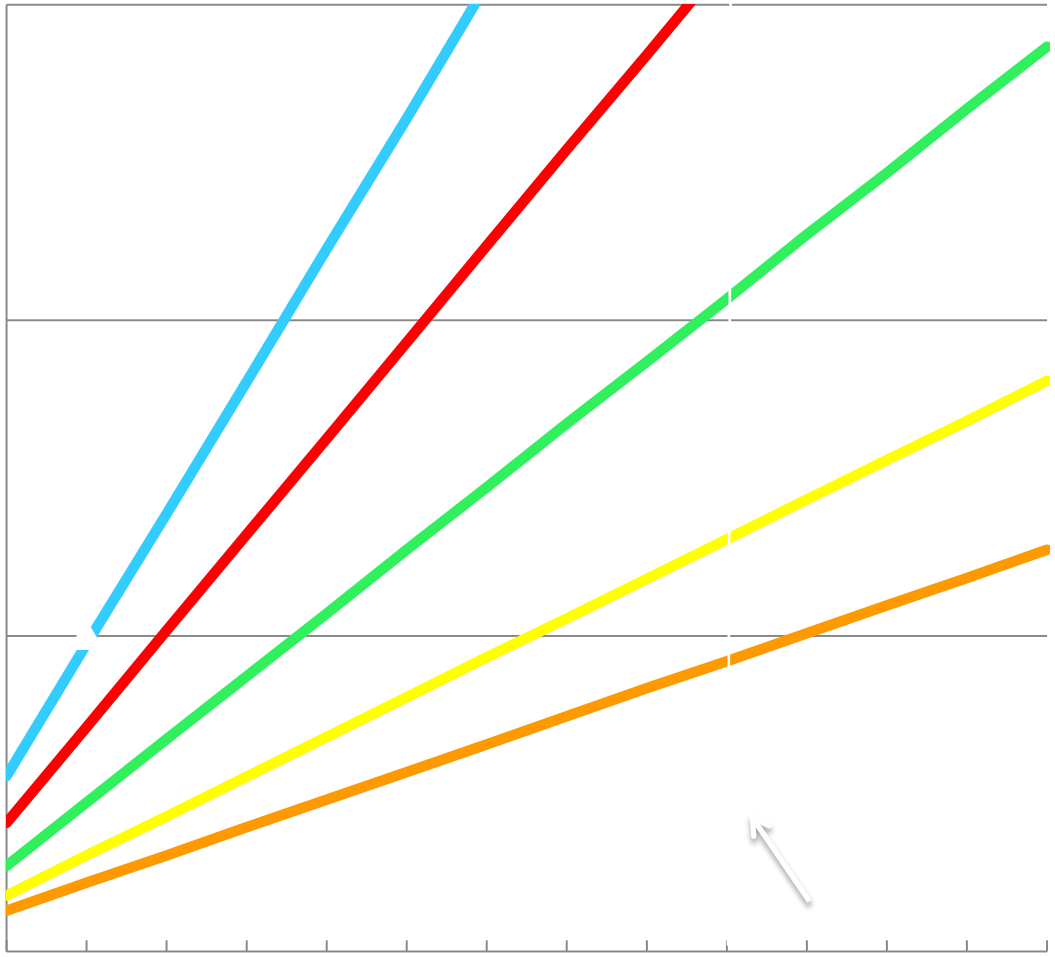


0.21%

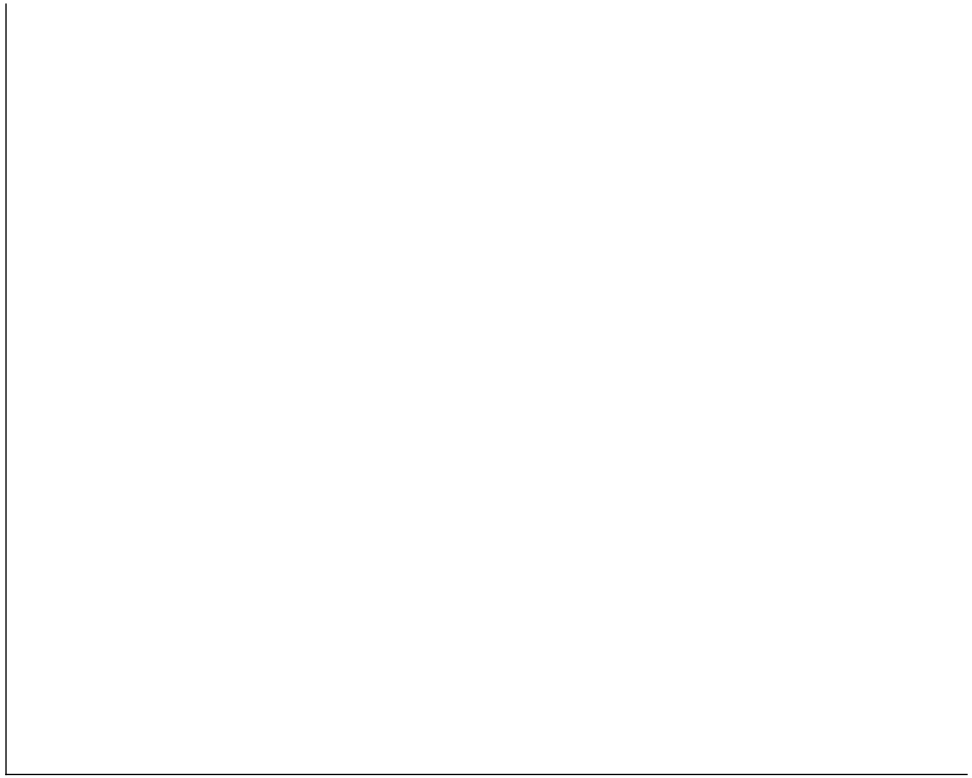
Model input parameters

Regimen efficacy and costs

Conclusions

Sensitivity Analysis

Incremental Cost-effectiveness Ratio of Branded to Generic ART



Base case ICER =

Methods
Potential Savings in the First Year

- 2,500 newly diagnosed and eligible to start ART in next year

- 147,300 eligible to switch from EFV-based branded ART to generic ART

Other Sensitivity Analyses

- Results demonstrate the ICER of *Branded ART* vs. *Generic ART* remain >$100,000/QALY under assumptions of:
  - Changes in the efficacy of the second-line regimen
  - Mean CD4 of the cohort
  - Alter background mortality rates by risk group