Cost Effectiveness Analysis for Diagnostic Testing

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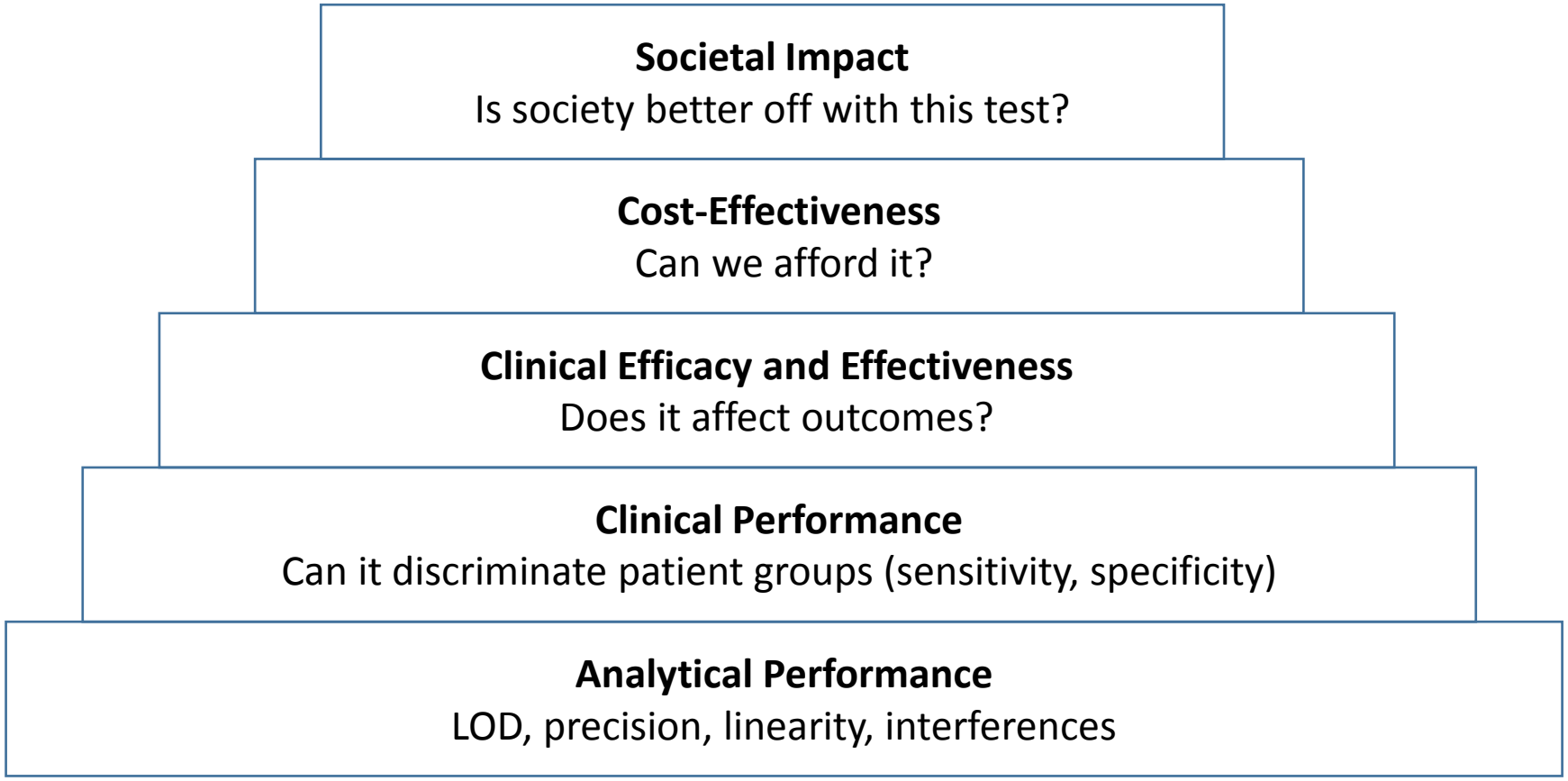
Objectives

- Review the basic types of analyses that support cost-effectiveness analysis
- Describe the opportunities and challenges in applying cost-effectiveness analysis to diagnostic tests
- Examples of how lab data is being used to determine if certain lab testing strategies are cost effective

Hierarchy of Effectiveness



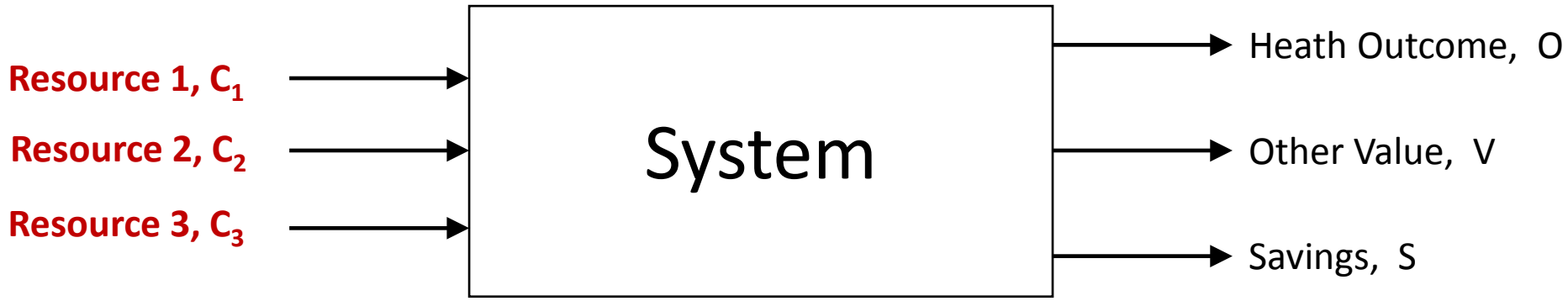
Horvath R, et al. 2014

What is the goal of cost effectiveness analysis?

- Economic Perspective: Maximize overall welfare of society
  - education vs roads vs healthcare

- Clinical Perspective: Maximize welfare of an individual patient

Cost Evaluation Basics

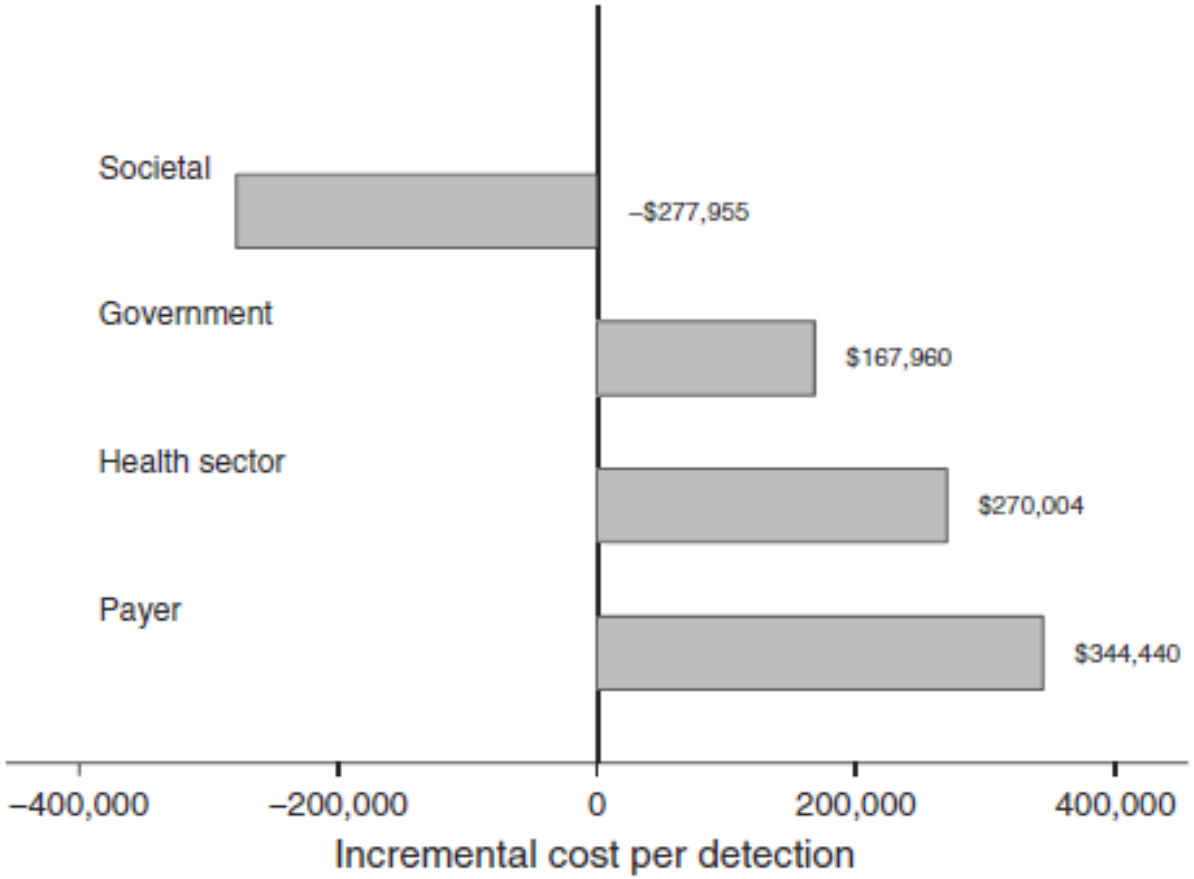


Evaluating Costs: Choice of Perspective

Item	Perspective		
	Societal	Healthcare Agency	Provider
Productivity losses	x		
Patient time	x		
Family time	x		
Medications	x	x	
Physician Time	x	x	x

Impact of perspective

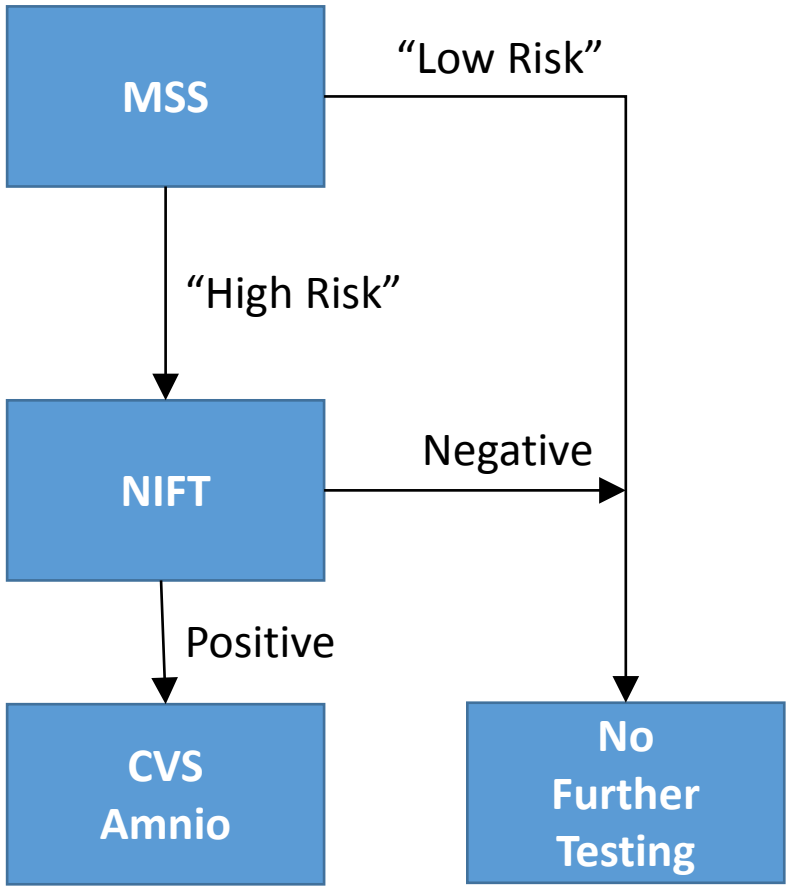
MSS vs NIFT for Down Syndrome

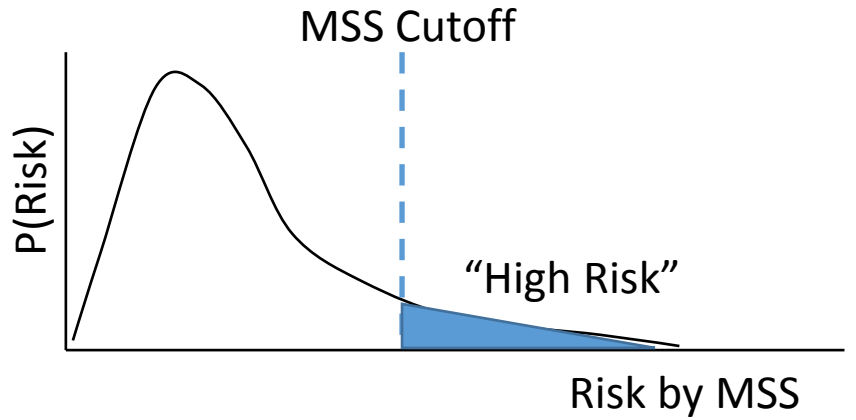


Walker BS, et al. 2014
PMID: 25273838

Impact of perspective on decision limits

Contingent use of NIPT for Down Syndrome



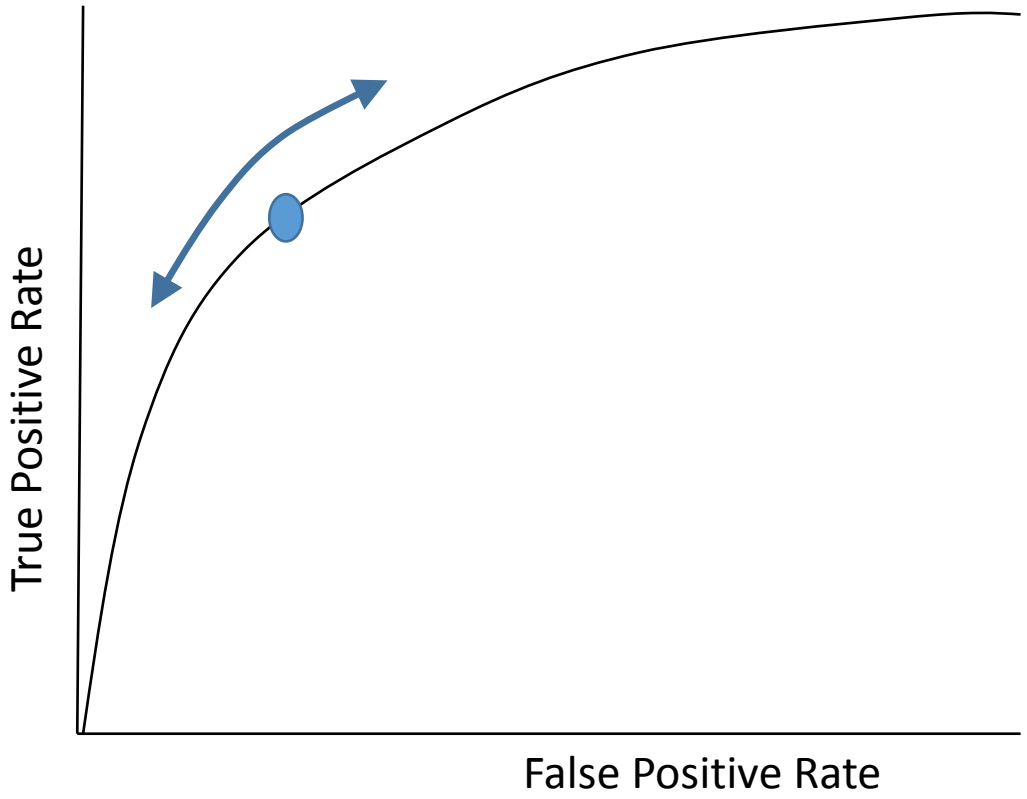


Perspective	Optimal Cutoff	NIFT Referral rate
Societal	1:1515	24%
Government	1:420	9%
Payer	1:350	7%

Walker BS, et al. 2015

Threshold optimization

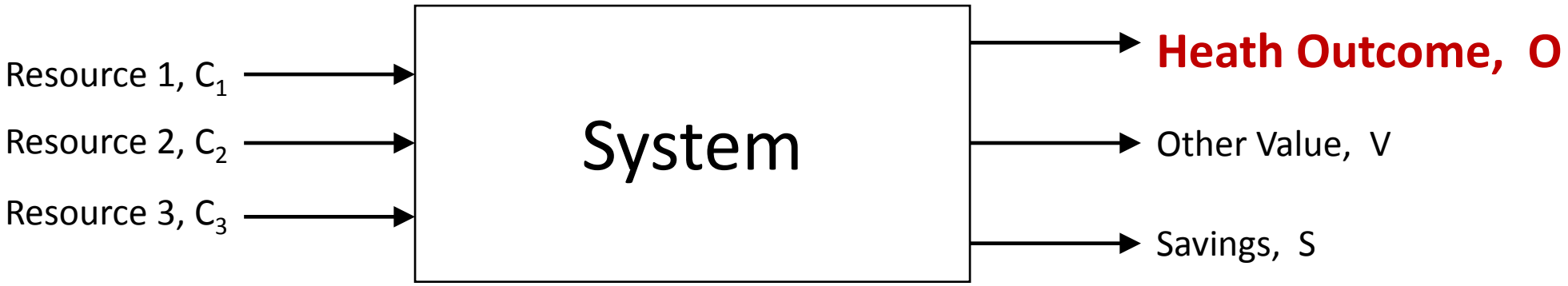
Optimal decision limit = f(FPR, TPR, FNR, TNR)



Other costing issues

- Costs vs charges
- Discounting
- Capital charges
- Overhead allocation

Valuing Outcomes



How to Handle Outcomes

- Three Choices

    1. Ignore outcomes (cost minimization)

    2. Don’t value outcomes, use natural units (cost-effectiveness analysis)

    3. Value outcomes
        a) Utility (cost-utility analysis)
        b) Money value (cost-benefit analysis)

Ignore outcomes (cost minimization)

Example: Rapid onsite-evaluation (ROSE) for fine needle aspiration biopsy

	FNA + ROSE	FNA without ROSE
Description	Pathologist inspects each biopsy for adequacy. Procedure is stopped when adequate sample is obtained	Clinician takes n samples. Repeat procedure if no sample is adequate
Outcome	Adequate sample of solid pancreatic lesion	Adequate sample of solid pancreatic lesion
Procedure time	45 min	30 min
Risk of repeat	1%	10-20%
Pathologist cost	$100	0
Total cost per adequate sample	**$1700**	**$2000**

Schmidt RL, et al. 2015
PMID 26317785

Don’t value outcomes (cost effectiveness analysis)

	Alternative 1	Alternative 2
Costs	C_1	C_2
Savings	S_1	S_2
Value	V_1	V_2
Outcome	O_1	O_2

Incremental Cost Effectiveness Ratio (ICER) = $\frac{\Delta Cost}{\Delta Effectiveness} = \frac{(C_2 - S_2 - V_2) - (C_1 - S_1 - V_1)}{(O_2 - O_1)}$

Examples:

- Cost per life saved
- Cost per episode prevented
- Cost per correct diagnosis

Cost-effectiveness analysis

- Comparisons are limited to alternatives that affect the same outcome
  - Hospital infections due to a *specific* organism
  - Readmission prevented for CHF
  - Death averted
  - Diagnosis of a *specific* disease
  - Days in ICU

$$Incremental\ Cost\ Effectiveness = \frac{\$}{Outcome\ measure} = \frac{\$}{death\ averted}$$

Example: Traditional Maternal Serum Screening (integrated test) vs Noninvasive Fetal Testing (cfDNA)

	Integrated	cfDNA
Outcomes		
Cases detected	1474	1915[a]
Cases diagnosed	1047	1360[a]
Down syndrome live births	1221	1039
Unnecessary invasive testing	11 972	687
Unaffected procedure-related miscarriages	91	5
Costs		
Screening costs	$160 544 211	$324 298 422
Diagnostic testing costs	$14 411 432	$3 053 516
Termination cost	$1 294 473	$796 064
Lifetime medical costs	$220 832 869	$188 006 605
Lifetime educational costs	$301 942 088	$256 940 831
Lifetime indirect costs	$1 324 181 252	$1 127 532 667
Total costs	$2 023 206 325	$1 900 628 105

Walker BS, et al. 2015
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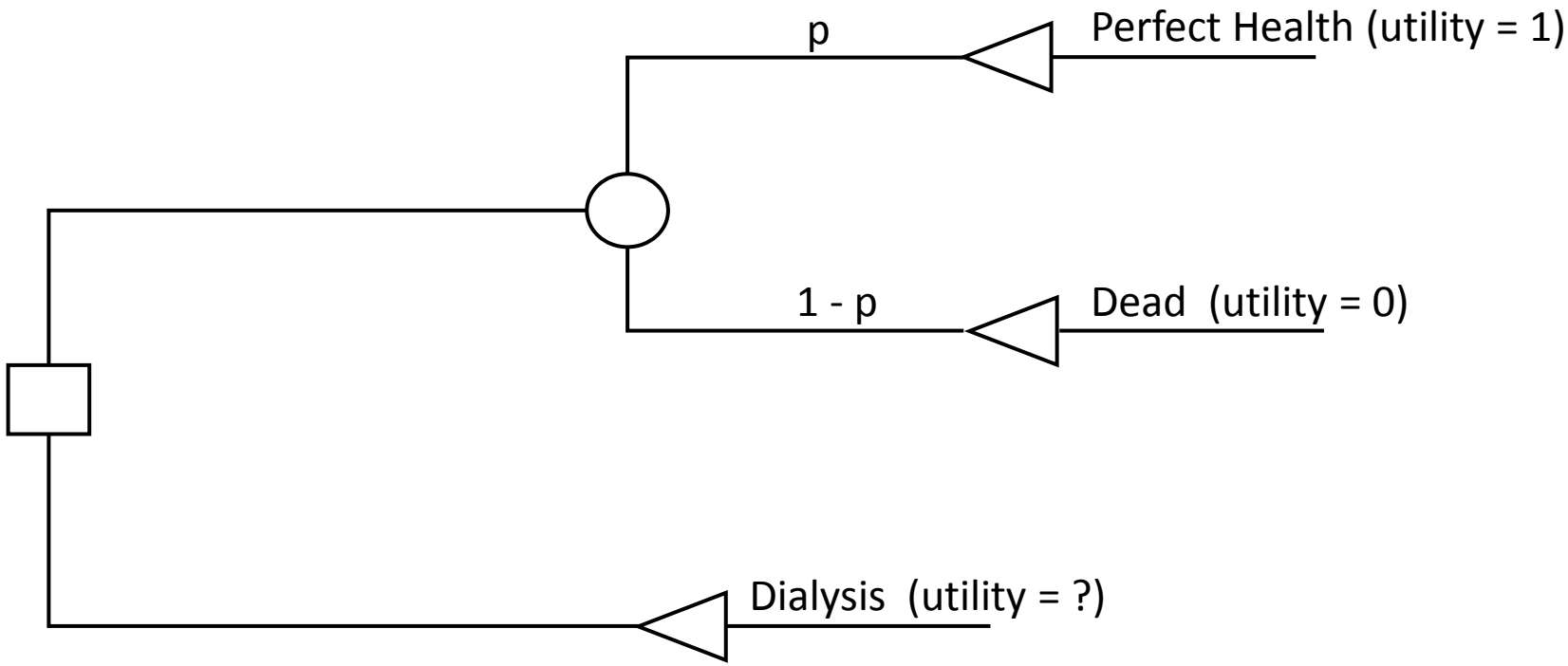
Valuing Health Outcomes

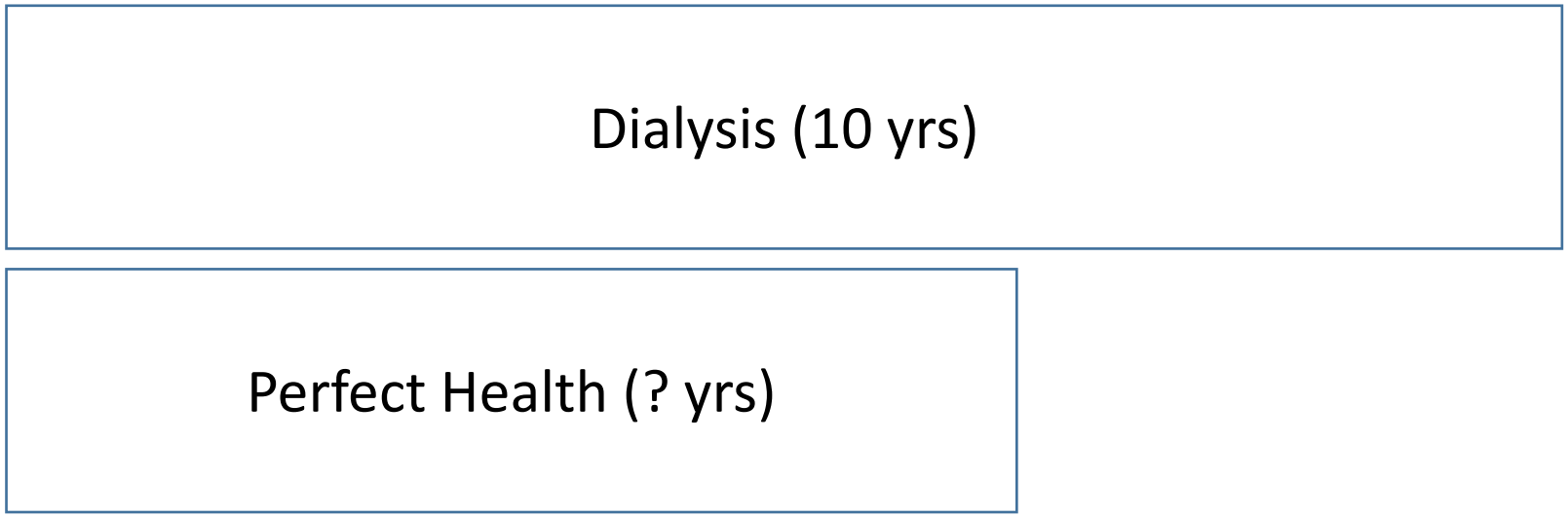
Health Dimension	Outcome 1	Outcome 2
Pain	No Problem	Problem
Mobility	Problem	Major Problem
Self-care	Major Problem	Major Problem
Usual Activities	Problem	Some Problem
Anxiety/Depression	Some Problem	No Problem

Standard Gamble



Expected Utility = U(Dialysis) = p*U(perfect health) + (1-p)*U(dead) = p

Time Tradeoff



Utility = yrs perfect health / yrs dialysis

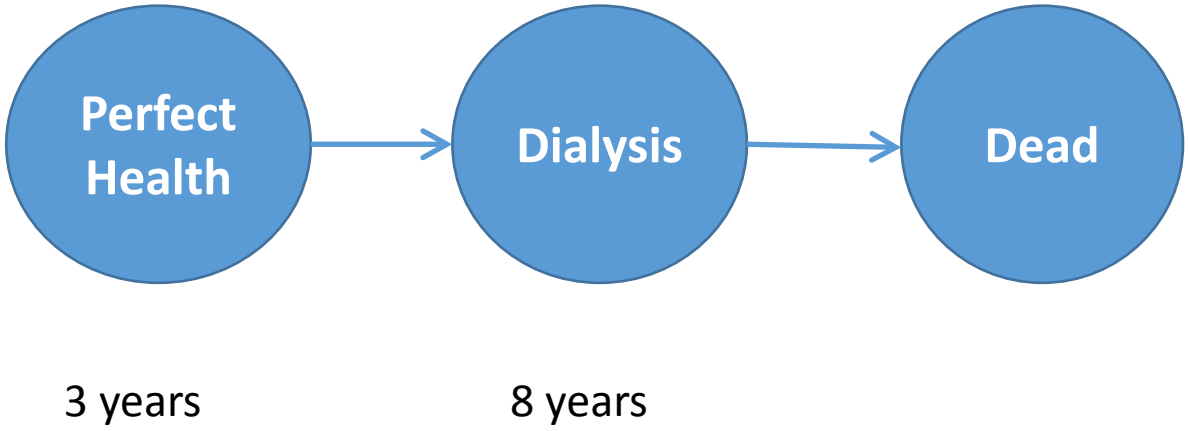
Utility

- Measure of relative preference for health states
- Preference for whom?

Quality Adjusted Life Years

1 yr of perfect health = 1 QALY

1 yr on dialysis = 0.7 QALY



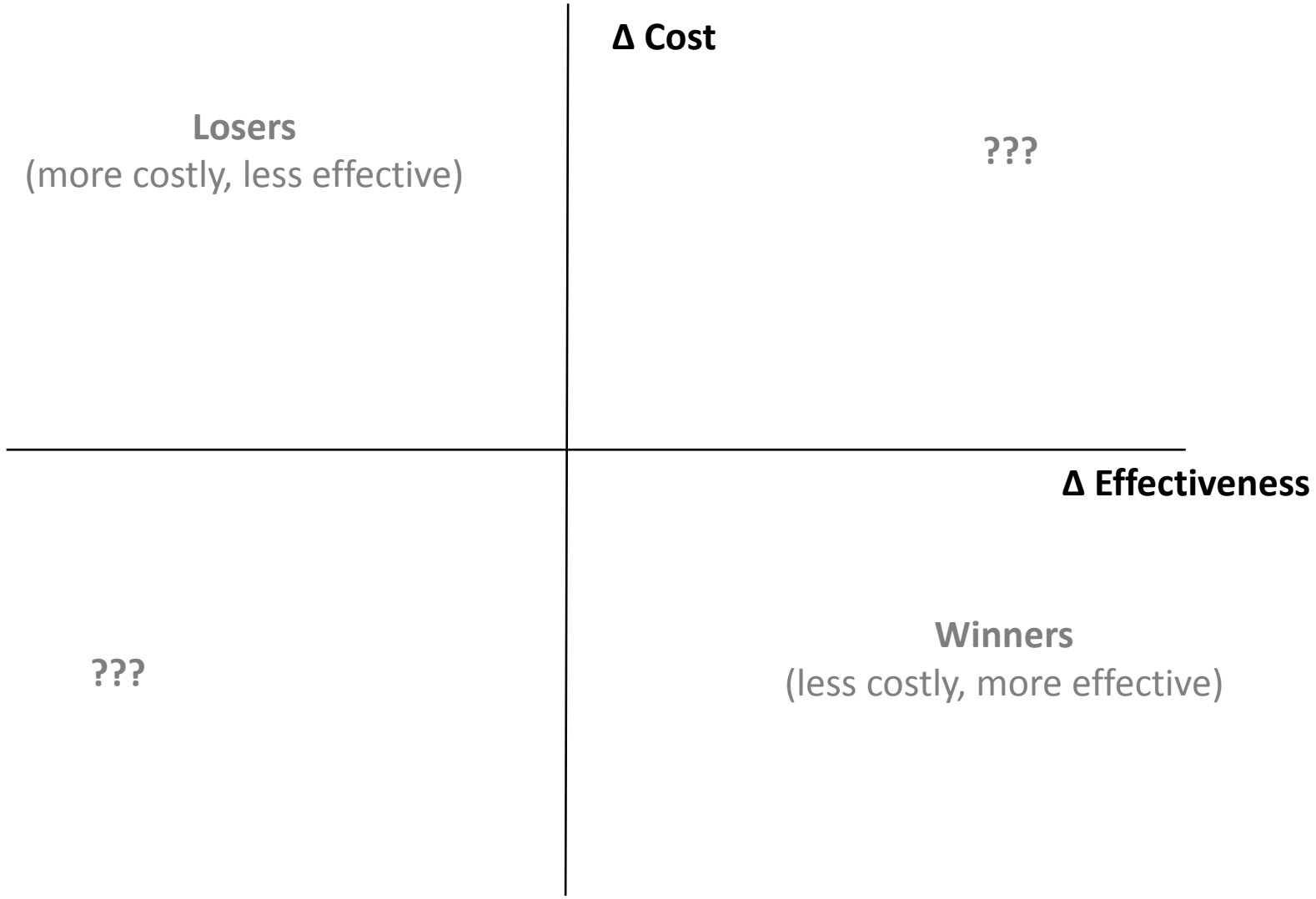
Total = 3 + 5.6 = 8.6 QALY

Cost utility analysis

Item	Alternative 1	Alternative 2
Resource Consumption	C_1	C_2
Resource Savings	S_1	S_2
Other Value	V_1	V_2
Health Outcomes (Utility)	$U(O_1)$	$U(O_2)$

$$ICER = \frac{(C_2 - S_2 - V_2) - (C_1 - S_1 - V_1)}{U(O_2) - U(O_1)} = \frac{\$}{QALY}$$

Cost-effectiveness plane



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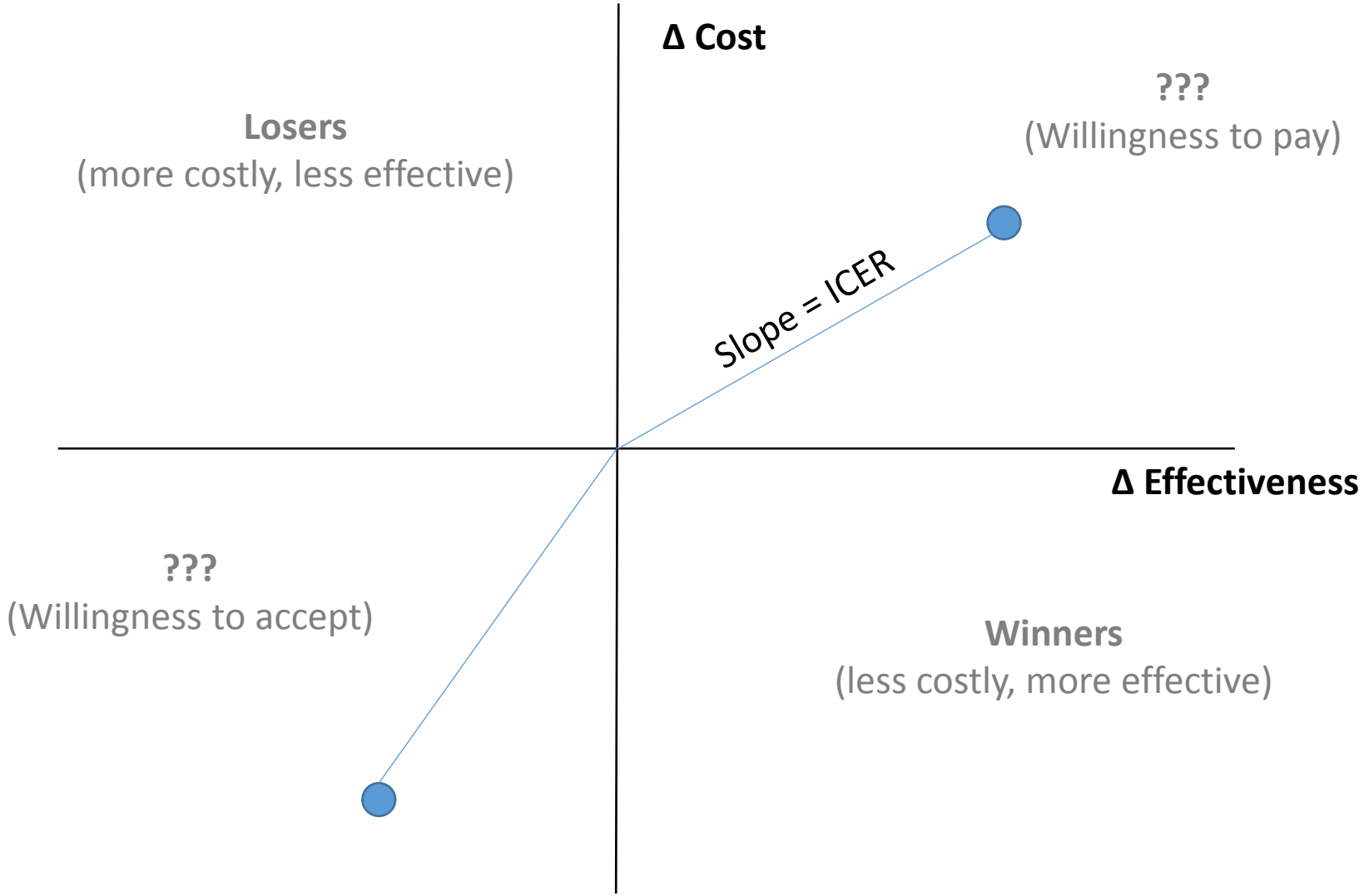
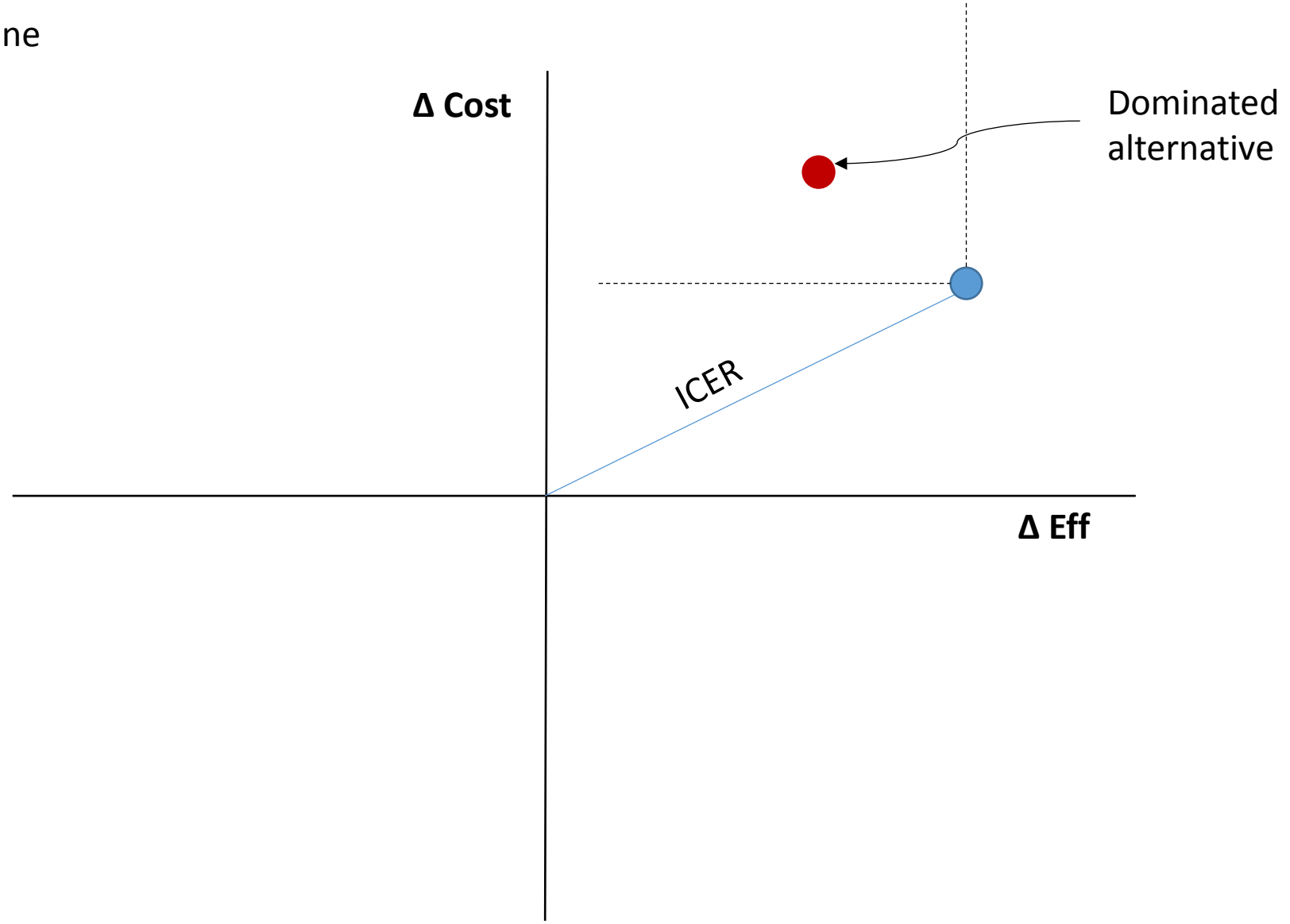
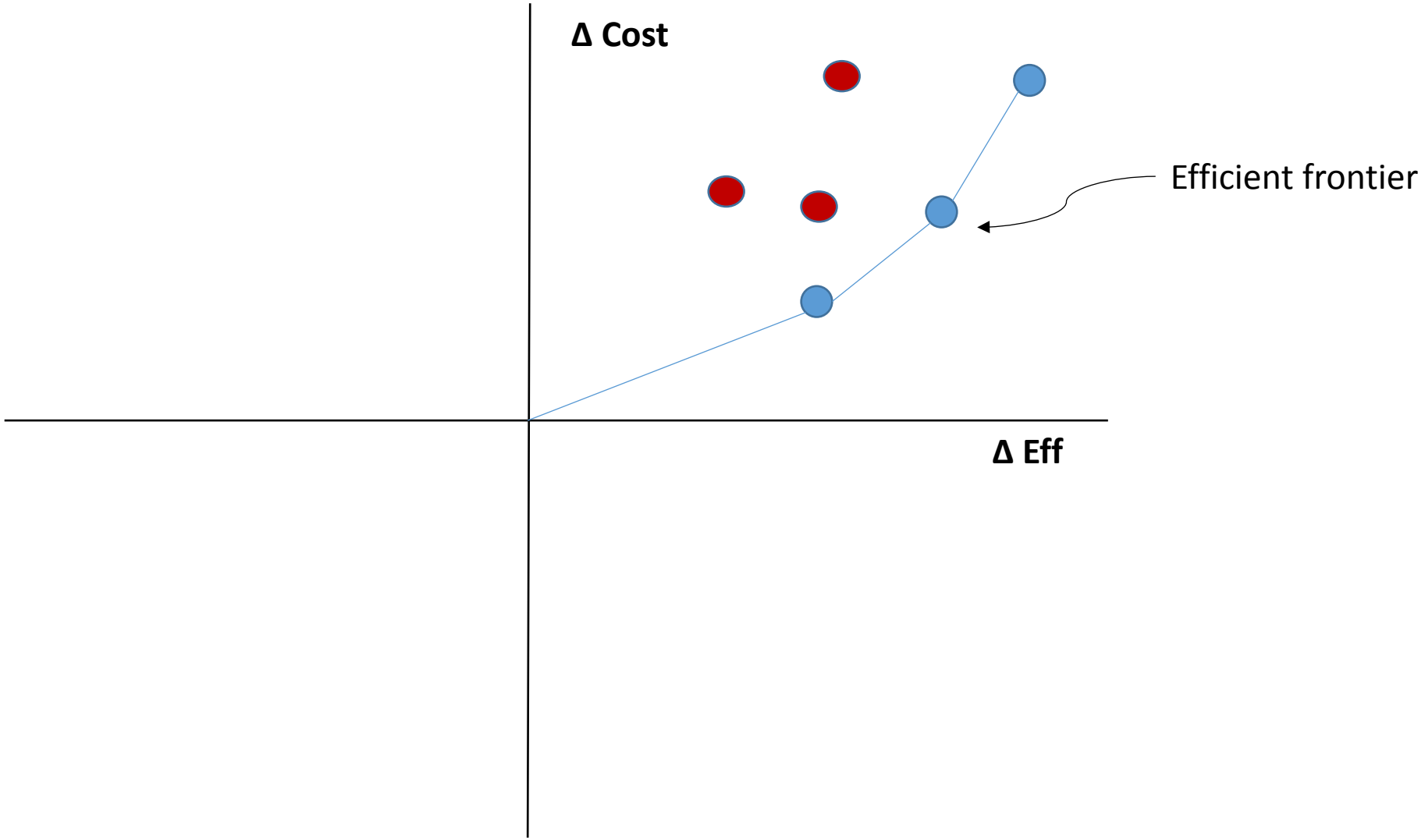


Cost-effectiveness plane



Cost-effectiveness plane



Cost benefit analysis (value outcomes in dollars)

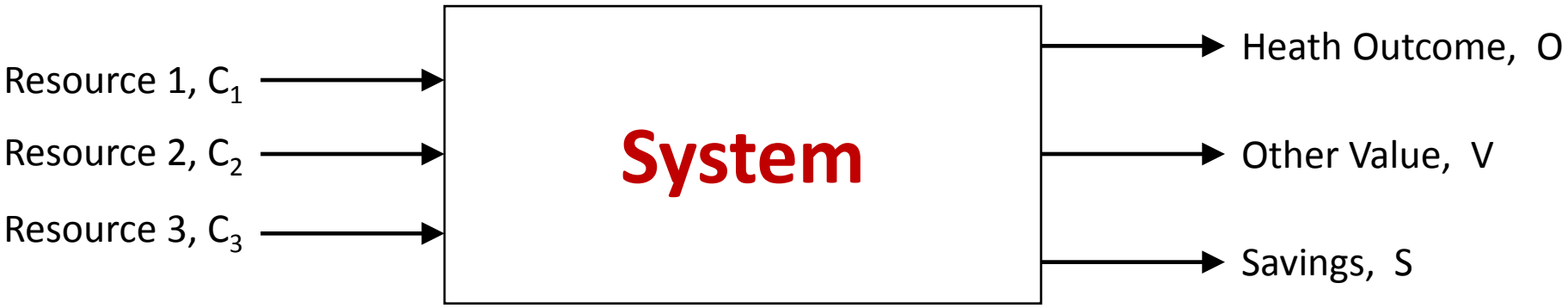
Item	Alternative 1	Alternative 2
Resource Consumption	C_1	C_2
Resource Savings	S_1	S_2
Other Value	V_1	V_2
Health Outcomes (Willingness to pay)	$W(O_1)$	$W(O_2)$

$$Net\ Benefit = W[O_2 - O_1] - [(C_2 - S_2 - V_2) - (C_1 - S_1 - V_1)] = \$$$

Comparison of outcome evaluation methods

Method	Characteristics of Outcomes			Example Evaluation (outcomes)
	More than One?	Different Types?	Different Magnitude?	
Cost Minimization	No	No	No	**FNA sampling protocols** (adequate biopsy sample for solid pancreatic lesion)
Cost Effectiveness	No	No	Yes	**Diagnostic tests for TB** (cases of TB detected)
Cost Utility	Yes	Yes (restricted)	Yes	**Diagnostic test for kidney failure vs infection** (mobility, self care, anxiety/depression, pain)
Cost Benefit	Yes	Yes (unrestricted)	Yes	**Education vs healthcare (diagnostic test)** (net benefit in dollars)

Converting Resources to Outcomes



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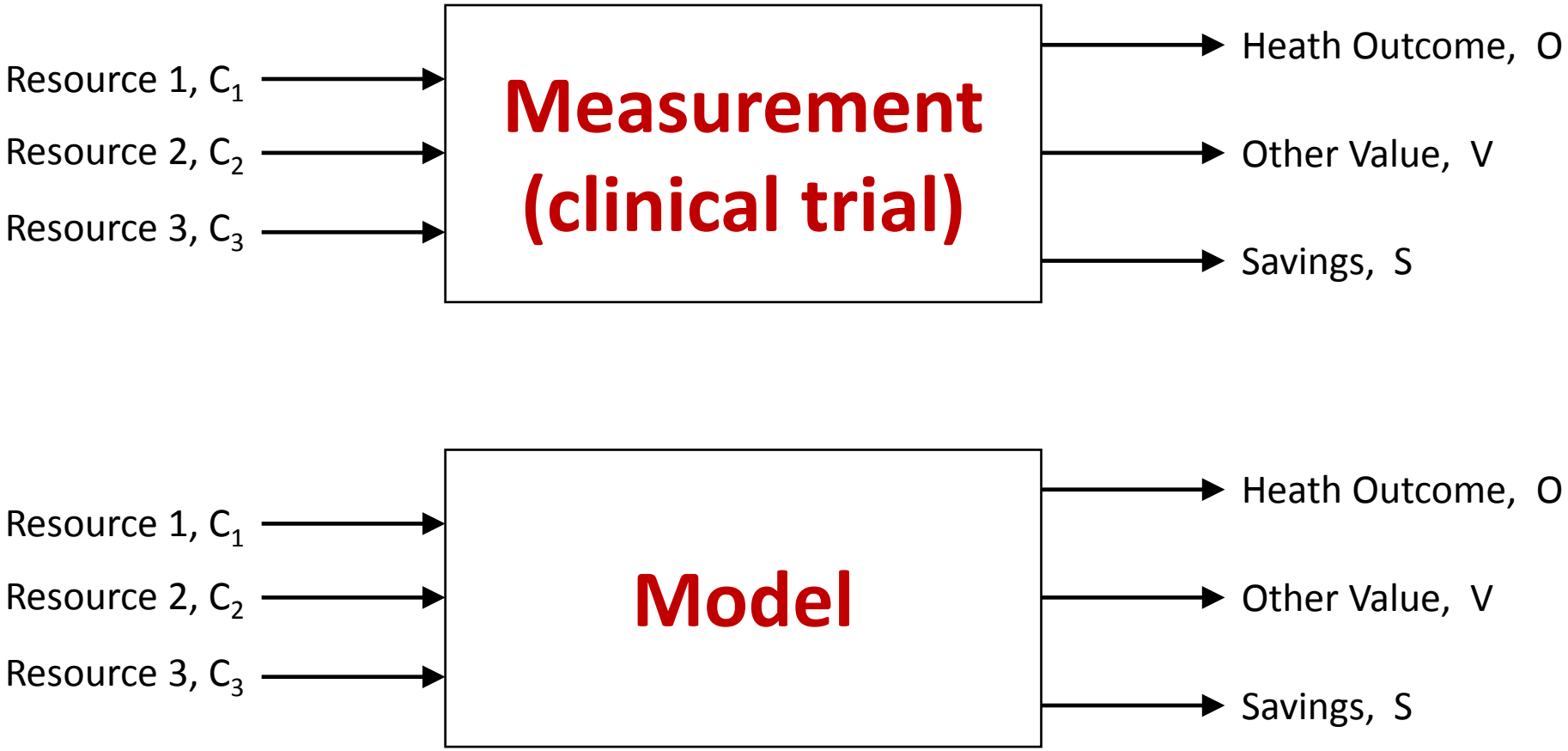
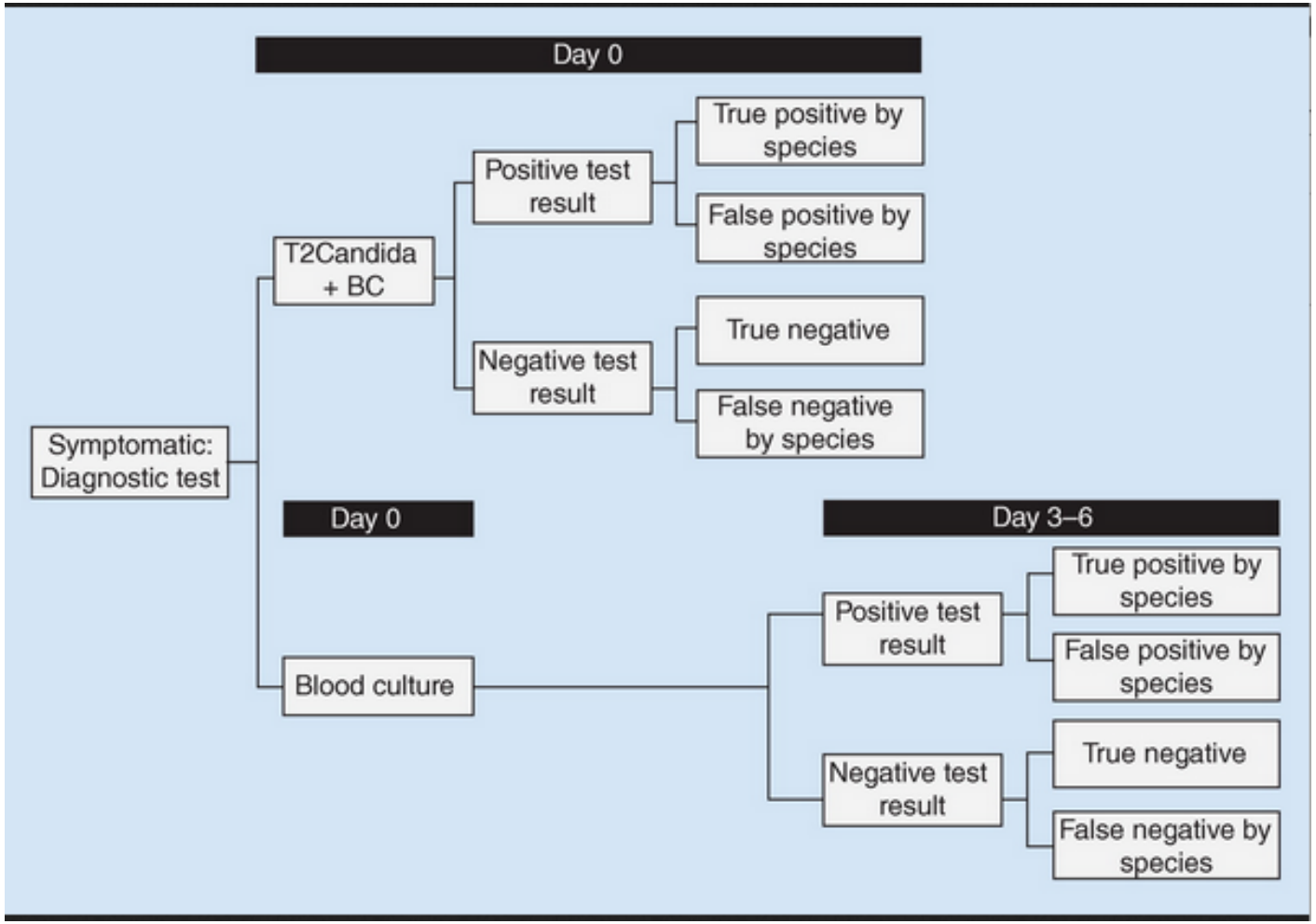
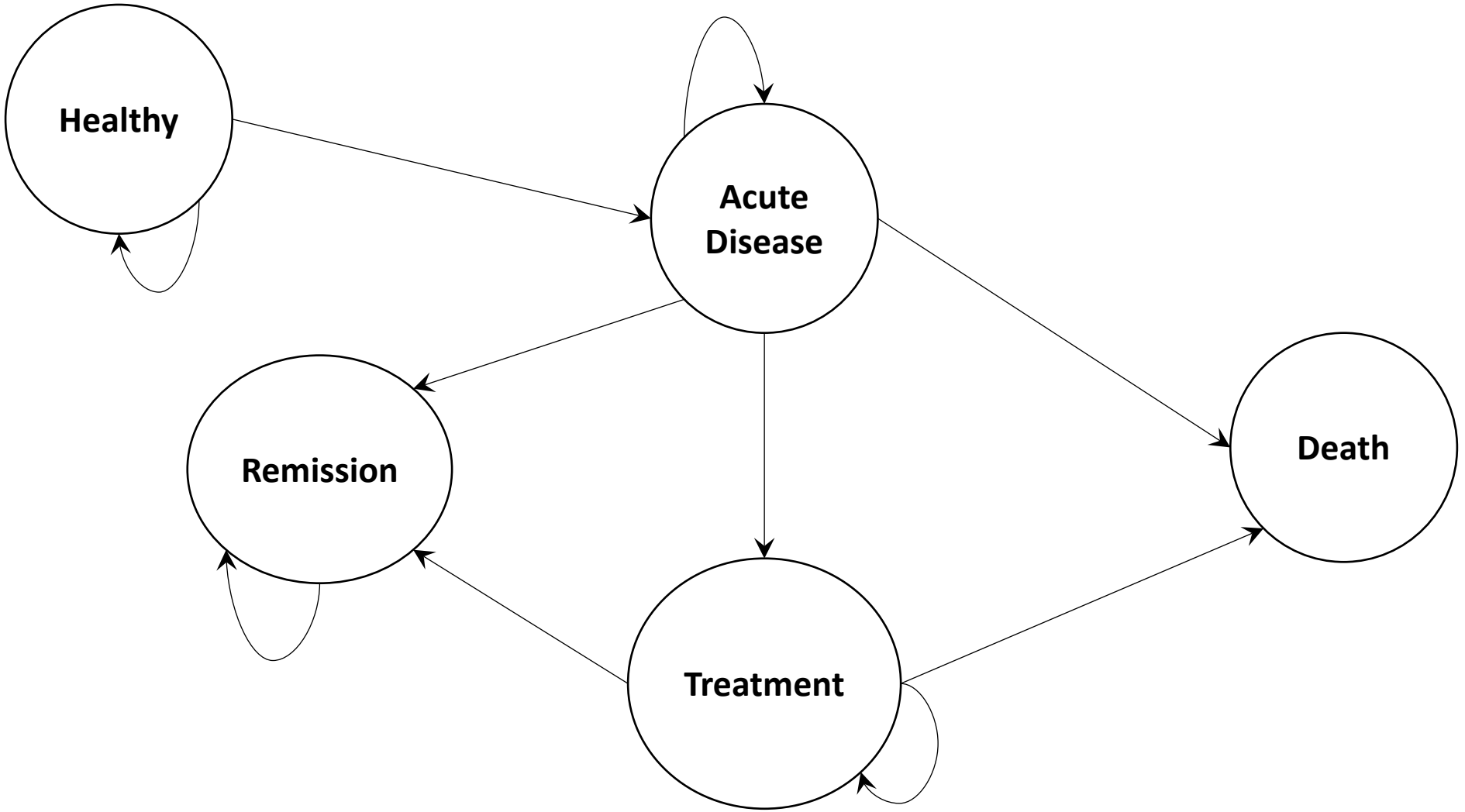


Decision Analytic Model



Bilir SP, et al. 2015

Disease model (Markov chain)



Models require many inputs

- Costs
- Probabilities
  - Test performance
  - Disease model (transition probabilities)
- Outcomes

Table 1. Model probabilities and costs.

Probabilities	Mean	95th% CI
MSS uptake, U_{MSS}	69%	64%-74%
Increase in contingent NIPT uptake over MSS, ΔU_{cNIPT}	8.2%	4.6%-12.6%
Increase in universal NIPT uptake over MSS, ΔU_{uNIPT}	13.5%	7.6%-20.8%
Diagnostic testing uptake	66%	61%-71%
Procedure-related fetal loss	0.22%	0%-1.16%
Termination rate of trisomy 21	80%	74%-86%
Termination rate of trisomy 18	80%	73%-87%
Termination rate of trisomy 13	92%	85%-97%
NIPT detection rate of trisomy 21	99%	98.3%-99.5%
NIPT detection rate of trisomy 18	96.8%	95%-98.2%
NIPT detection rate of trisomy 13	92.1%	86.9%-96.1%
NIPT false positive rate	0.41%	0.29%-0.55%
NIPT failure rate due to low fetal fraction	2.8%	1.2%-5.1%
Costs	Mean	95th% CI
Combined screen	$166	$95-$257
Cost of NIPT	$400	$229-$619
Cost of CVS	$1,010	$577-$1,562
Cost of genetic counseling	$160	$91-$247
Termination of pregnancy	$581	$332-$898
Direct lifetime costs of trisomy 21	$427,577	$244,397-$661,147
Indirect lifetime costs of trisomy 21	$1,069,195	$611,137-$1,653,257
Direct lifetime costs of trisomies 13 and 18	$37,971	$21,704-$58,713
Indirect lifetime costs of trisomies 13 and 18	$1,363,877	$779,574-$2,108,913,

Walker BS, et al. 2015

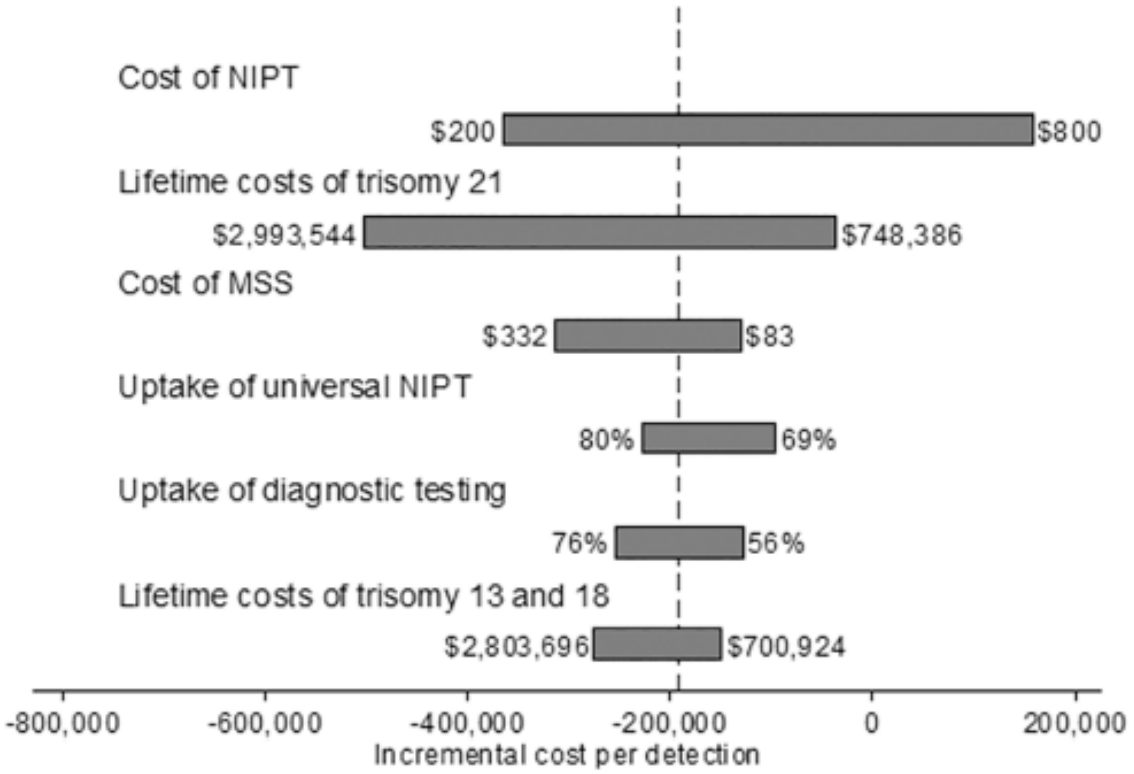
All models are wrong, but some are useful

- Examples of wrong but useful models
  - Ideal gases
  - Point masses
  - Competitive market
  - Newtonian fluid
  - First order kinetics
  - Fickian diffusion

Box GP, 1987

One way sensitivity analysis

Cost of NIPT	ICER
200	-398,000
300	-300,000
400	-200,000
500	-100,000
600	125,000
700	150,000
800	175,000

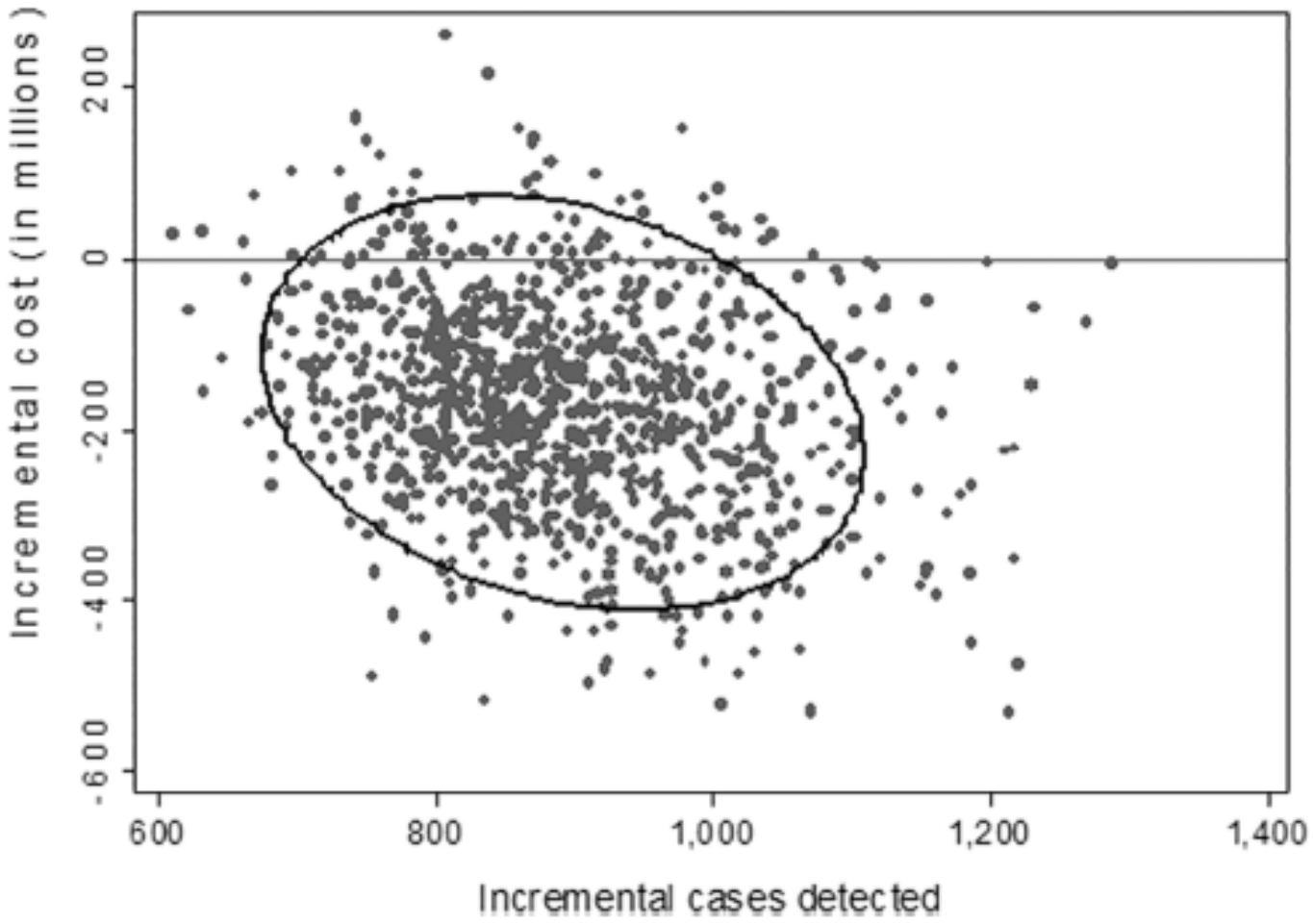


Probabilistic Sensitivity Analysis

trial	NIPT Cost	Lifetime Cost	Uptake of NIPT	Uptake of Diagnostic Testing	ICER
1	642	1200000	72	75	-1074
2	660	1900000	75	76	-1395
3	567	1200000	69	68	-1660
4	212	1800000	78	56	-1563
…	649	1000000	71	76	-1594
…	691	2100000	79	66	-1790
…	687	2900000	79	64	-2000
1,000,000	293	2700000	80	59	-1289

Probabilistic Sensitivity Analysis

MSS (integrated test) vs NIFT



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Opportunities

- CEA is theoretically correct way to evaluate tests
- Modeling provides insight

Barriers

- Clinical trials are expensive
- Modeling
  - Data collection is time consuming
    - Provide evidence for distribution of each input
    - Meta analysis
    - Evidence base is poor (reporting, bias, few studies on patient outcomes)
  - Requires many skills
    - Clinical knowledge
    - Modeling/analysis
    - Laboratory
  - Review process
    - Many targets

Conclusions

- CEA is time consuming
- CEA can provide insight into important questions about lab testing
- CEA can be cost-effective for *selected* problems
  - Not all problems required CEA
- There is a gap between what is needed and what is being produced

Objectives

- Review the basic types of analyses that support cost-effectiveness analysis
- Describe the opportunities and challenges in applying cost-effectiveness analysis to diagnostic tests
- Real-world examples of how lab data is being used to determine if certain lab testing strategies are cost effective

References

- Horvath AR, et al. From biomarkers to medical tests: the changing landscape of test evaluation. Clin Chim Acta 2014;427:49-57.
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