Pharmacoeconomics and Management in Pharmacy XI

Further reading (ii)

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Pharmacoeconomics 101

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11 January

LtCol David Bennett, Capt Jill Dacus, Eugene Moore, PharmD

Pharmacoeconomics 101

- What is Pharmacoeconomics and how does it apply to formulary management?

Characteristics of Formulary Management

- Choosing drugs based on:
  - Clinical considerations
    - Efficacy
    - Safety
    - Tolerability
  - Humanistic considerations
    - Quality of Life (Is the gain worth the pain)
  - Cost considerations

Characteristics of a Pharmacoeconomic Evaluation

1. An evaluation that considers both the effects (consequences, outcomes) and costs of
2. Two or more alternative choices

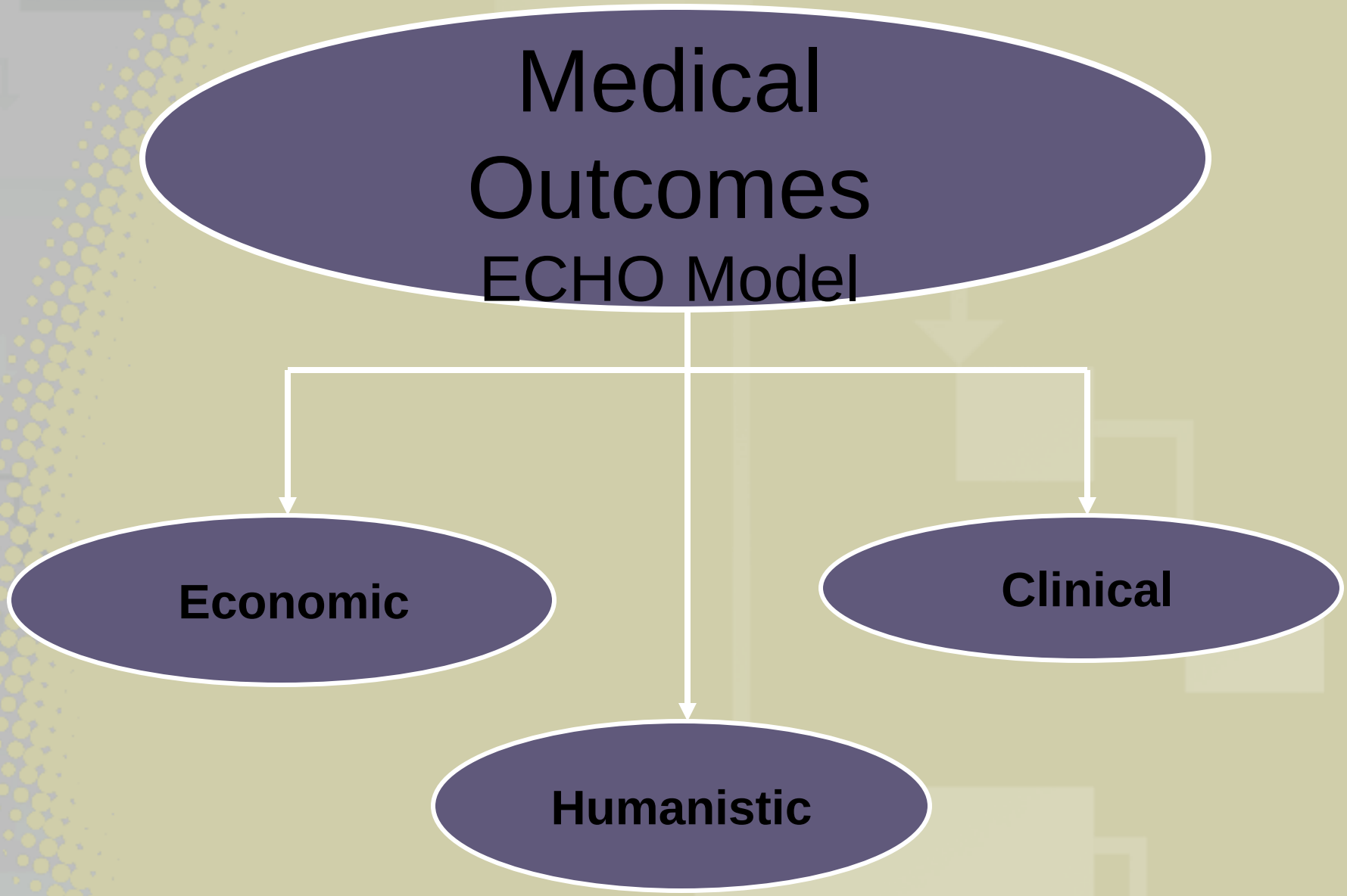
Defined as:

"the comparative analysis of alternative courses of action in terms of both their costs and consequences"

Drummond

Outcome Types

- **Medical Outcome = The end result of medical care**
  - **Could be positive**
    - **Using the right antibiotic to treat an infection**
  - **Could be negative**
    - **Using the wrong antibiotic to treat an infection**
- **Indicator (Surrogate marker)**
  - **A measurable unit that provides information regarding the outcome of interest**


Medical Outcomes
ECHO Model
Economic
Clinical
Humanistic

Clinical Outcomes

- Medical events that occur as a result of a disease or treatment
  - Cure
  - Comfort
  - Survival

Humanistic Outcomes

- Outcomes that incorporate patient satisfaction and/or quality of life (QOL) - results of care are expressed in terms of patient's perceptions
- QOL domains
  - Physical function
  - Emotional function
  - Social function
  - Role performance
  - Pain and other symptoms such as nausea/vomiting

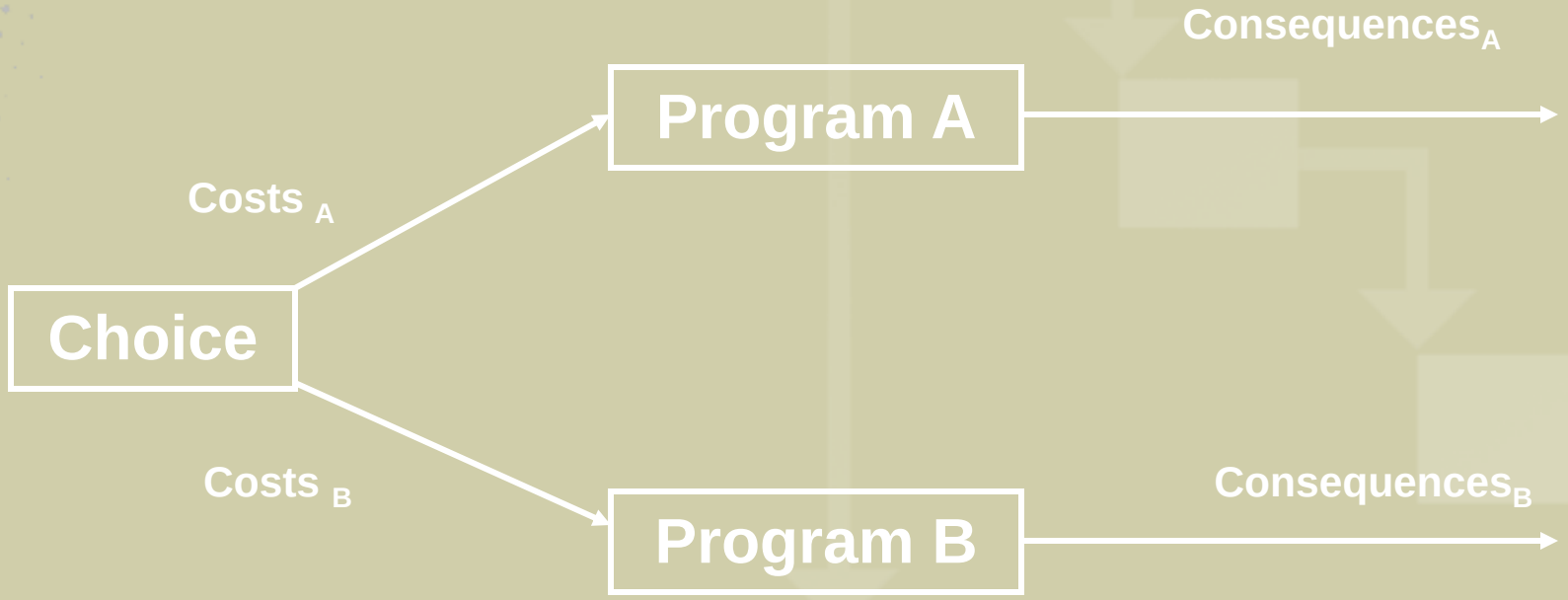
Economic

- **An outcome expressed in terms of the cost or value of delivering care**
  - **Expense**
  - **Savings**
  - **Cost Avoidance**

Outcome Measures

Disease	*Indicator*	*Clinical Outcome*	*Humanistic Outcome*	*Economic Outcome*
Hypertension	BP	Renal failure Stroke MI Death	QOL	Cost/↓ mmHg BP Cost/stroke avoided Cost/life year saved
Hyperlipidemia	LDL levels	Angina MI Death	QOL	Cost/MI avoided Cost/point ↓ in LDL
Diabetes	A1C BG levels	Retinopathy nephropathy Death	QOL	Cost/change in A1C Cost/kidney transplant avoided
Asthma	FEV, peak flow	Exacerbation event Death	QOL	Cost/symptom free day

Comparing the costs and consequences (outcomes) of two or more alternatives



Source: Methods for the Economic Evaluation of Health Care Programmes: Drummond 1997

Types of Evaluations

	Are both costs and consequences of alternatives examined		
Comparison of two or more alternatives	**No**		**Yes**
No	***Examines only consequences***	***Examines only costs***	**Cost-Outcome Description**
	Outcome Description	**Cost Description**	
Yes	**Clinical Trial**	**Cost Analysis**	**Full Economic Evaluation**

Adapted from Drummond: 1997

Full Economic Evaluations

Methodology Measured	*Units*	
	Cost	
Outcomes		
Cost-minimization	dollars	
equivalent		
Cost-effectiveness	dollars	natural units
Cost-Utility	dollars	QALY

Cost-Minimization Analysis

- Examines only the **COST** of competing technologies
- Assumes equivalent effectiveness
  - brand name vs. generic
  - two or more drugs in same therapeutic class
    - with similar side effect profiles
- Net result: (i.e., cost / patient treated)

Cost per Month of Selected Oral Antidiabetic Agents

Drug	Cost per Month
Glyburide (Diabeta)	$22.50
Glyburide (Mirconase)	$29.25
Glyburide (Glynase)	$24.75
Glipizide (Glucotrol)	$22.50
Glipizide (Glucotrol XL)	$20.40

Adapted from: Dagogo-Jack and Santiago, Arch Intern Med 1997;157:1802-

Cost-Effectiveness Analysis

- Costs are measured in physical units and valued in monetary units.
- Effectiveness is measured in natural units of health improvement - clinical outcome measure, years of added life, prevention of event.

Cost-Effectiveness Analysis

- **Outcomes must be measured in the same units to compare interventions**
  - **Can't compare cost/ reduction in Hem A_1C with cost/ reduction in systolic Blood pressure**

- **Results expressed as cost / effect**
  - **$100 per 1% reduction in Hem A_1C**
  - **$50 per 10 mg reduction in LDL**
  - **$5 per symptom-free day gained**

Incremental Cost-Effectiveness Ratio

$$ICER = \frac{TC_1 - TC_2}{E_1 - E_2}$$

TC_1 = total cost of treatment for drug 1

TC_2 = total cost of treatment for drug 2

E_1 = effectiveness of drug 1

E_2 = effectiveness of drug 2

CEA Example: Prevention of Stroke

- **Drug A**
  - **Total cost for 100 patients = $10,000**
  - **Effectiveness = 10 strokes prevented**
- **Drug B**
  - **Total cost for 100 patients = $60,000**
  - **Effectiveness = 50 strokes prevented**

Stroke Prevention Example: Average CE

Agent	Total Cost for 100 pts	Strokes Prevented	Cost/ Stroke Prevented
Drug A	$10,000	10	$1000
Drug B	$60,000	50	$1200

Incremental Analysis

- **“The additional costs that one service or program imposes over another, compared with the additional effects, benefits, or utilities it delivers.”**

Drummond – Methods for the Economic Evaluation of Health Care Programs

Incremental Cost-Effectiveness Analysis

$$= \frac{\$60{,}000 - \$10{,}000}{50\text{-}10}$$

$$= \frac{\$50{,}000}{40}$$

= $1250 per additional stroke prevented

Cost-Benefit Analysis

- Resources consumed and health outcomes measured in monetary units
- Decision Rule: Choose the treatment with the highest net benefit
- Controversy – assigning value to health

Cost-Benefit Analysis

- **Results expressed in two ways:**
  - **Benefits – Costs = Net Benefit or Net Cost**
  - **Benefit / Costs = Ratio**

- **Decision Rule: Accept programs with net benefit or benefit:cost > 1.0 When comparing alternatives, choose the treatment with the highest net benefit ratio**

Cost-Benefit Ratio

$$\text{Benefit per Cost} = \frac{\text{Net Benefits}}{\text{Net Costs}}$$

Accept those programs (drugs) where ratio > 1.0

Cost-Utility Analysis

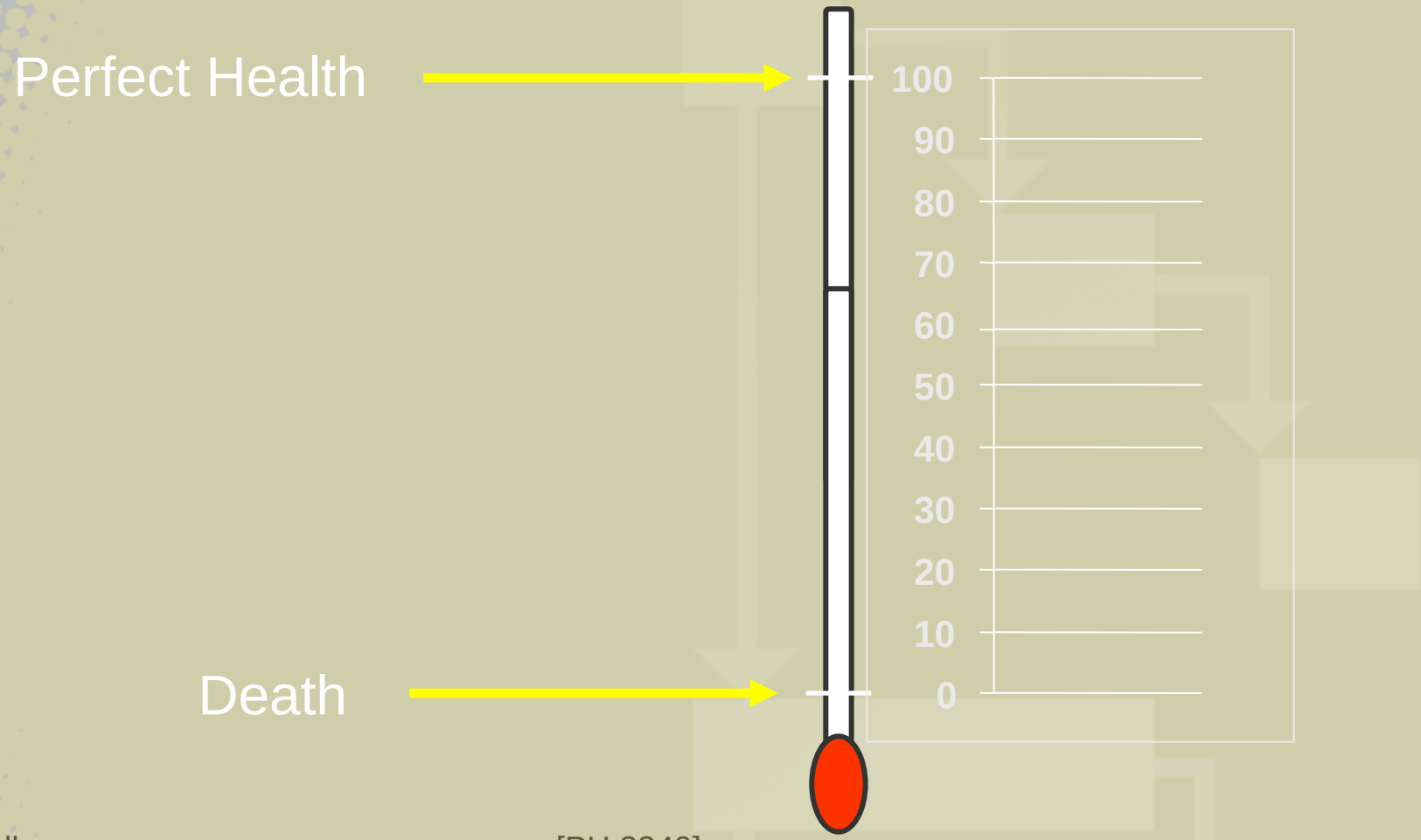
- Resource consumed measured in monetary units
- Health outcomes/consequences adjusted for quality
  - Quality adjusted life year (QALY)
- QALYs based upon utility (patient preference)

Cost-Utility Analysis

- **Utility – the value or worth placed on a level of health status, or improvement in health status, as measured by the preferences of individuals or society.**

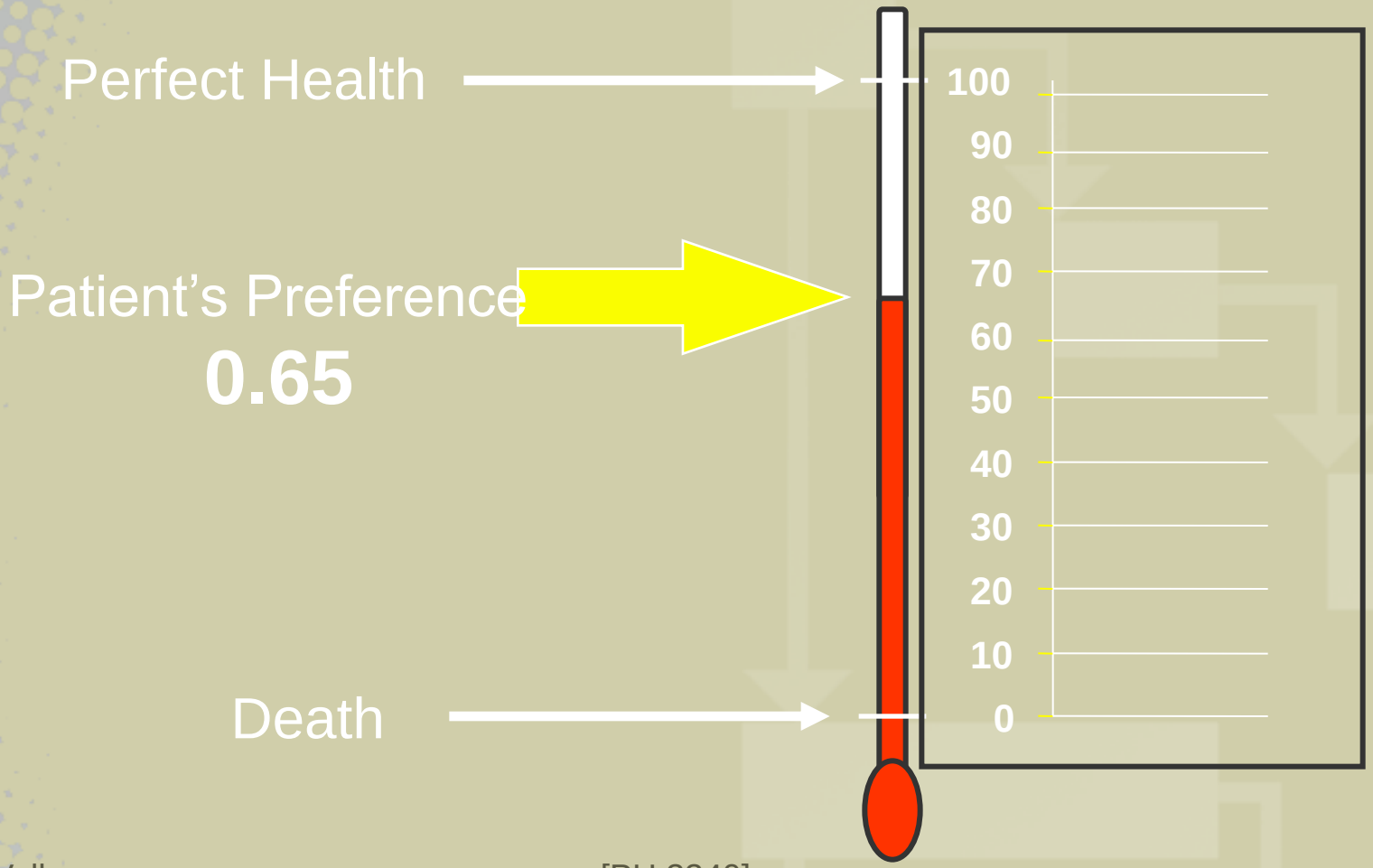
Rating Scale

Feeling Thermometer



Rating Scale

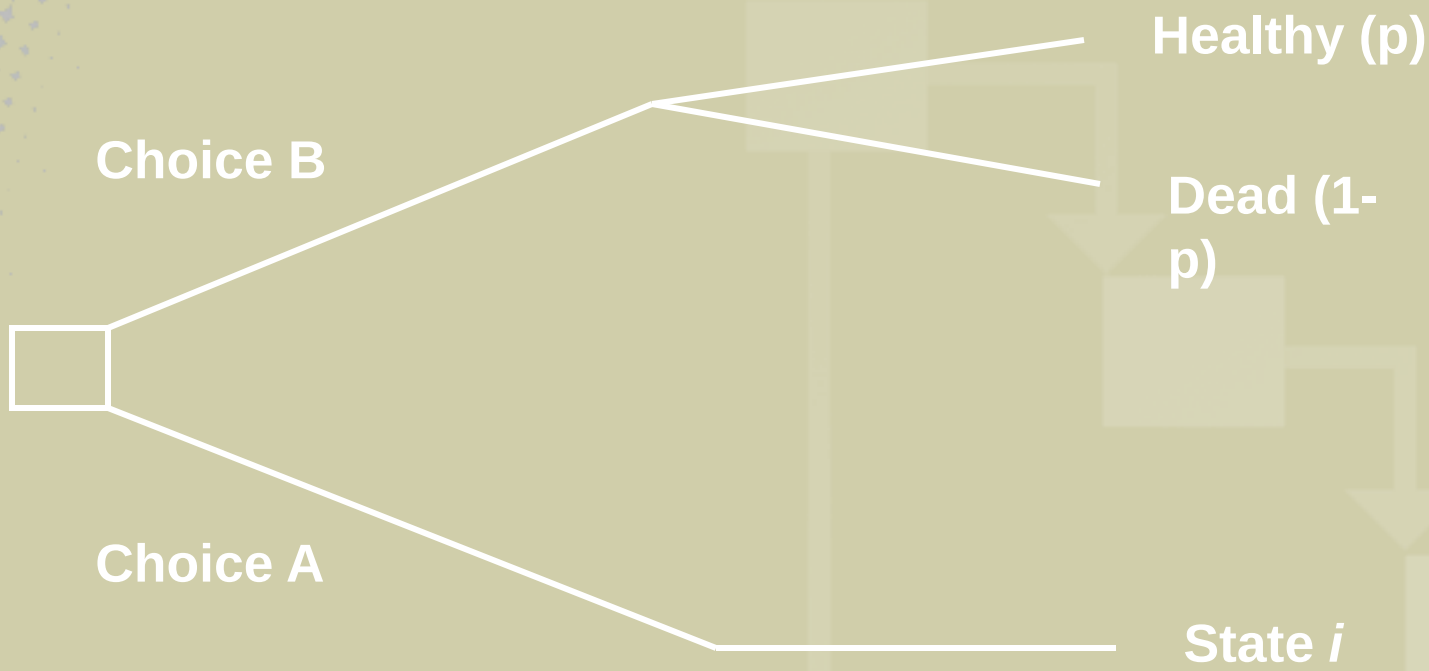
Feeling Thermometer



The Standard Gamble

- “True” utility instrument
- Requires choices between alternatives under conditions of uncertainty
- Respondents asked to select one of the two alternatives
- Captures the subject’s risk attitude

The Standard Gamble



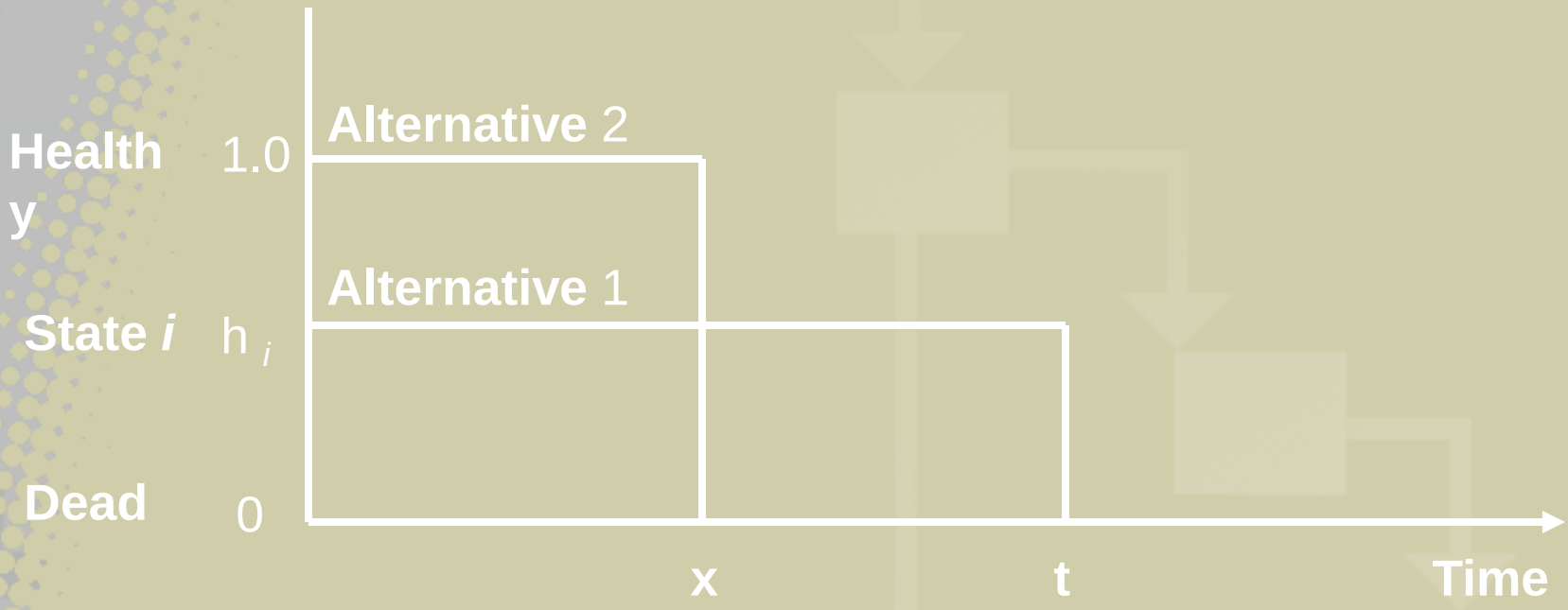
Standard gamble for a chronic health state. *i* = chronic health state; p = probability of achieving perfect health

von Neuman and Morgenstern, 1944

Time-Trade Off

- Utility measure developed specifically for health care
- Involves respondents selecting between known choices (no uncertainty)
- Scale is anchored by death and perfect health
- Not a true utility instrument

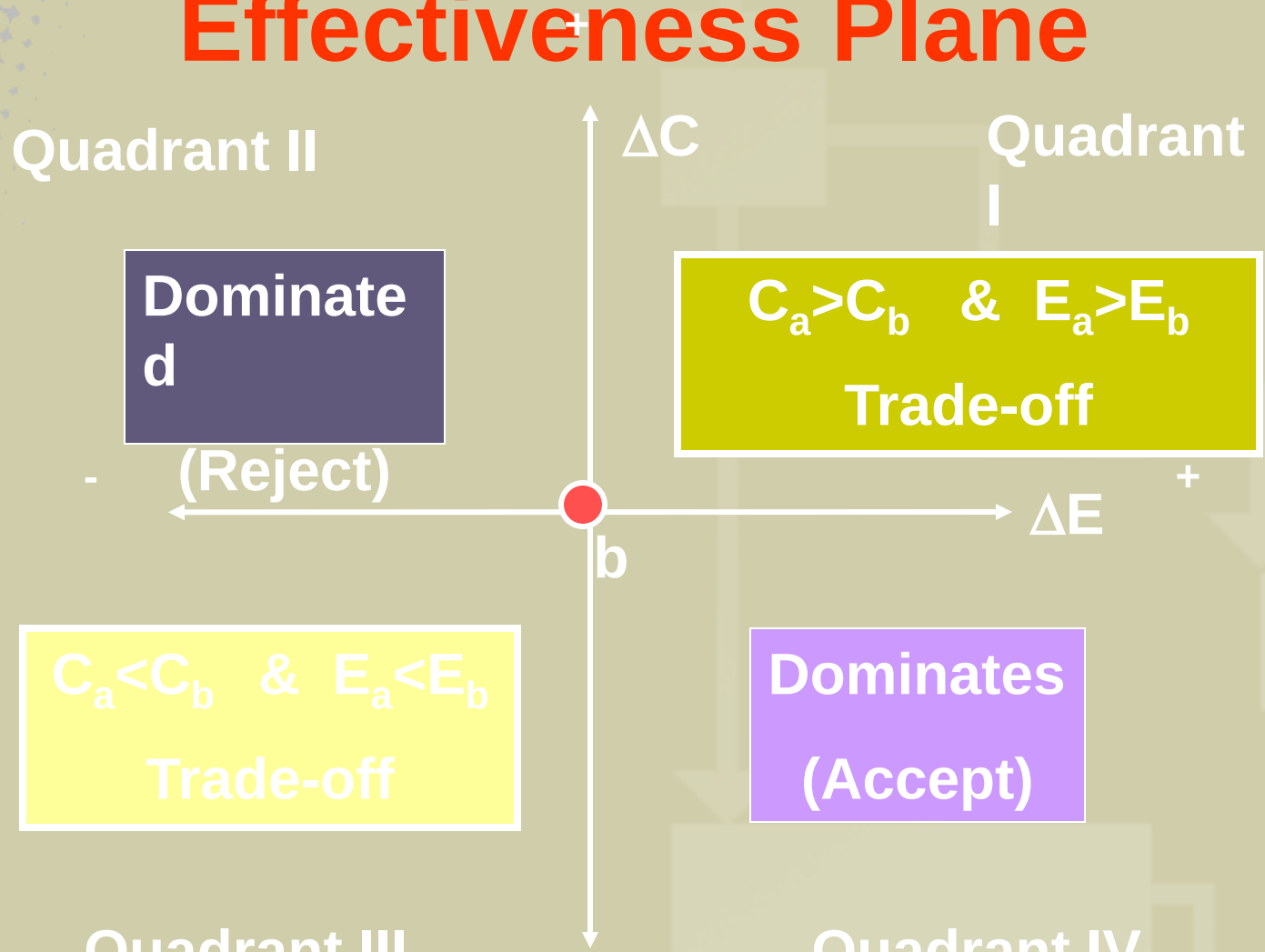
Time-Trade Off



Time trade-off for a chronic health state. $h_i = x/t$, where h_i = preference value for state *i*; state *i* = chronic health state; t = life expectancy for an individual with chronic health state *i*; and x = time at which respondent is indifferent between alternatives 1 and 2.

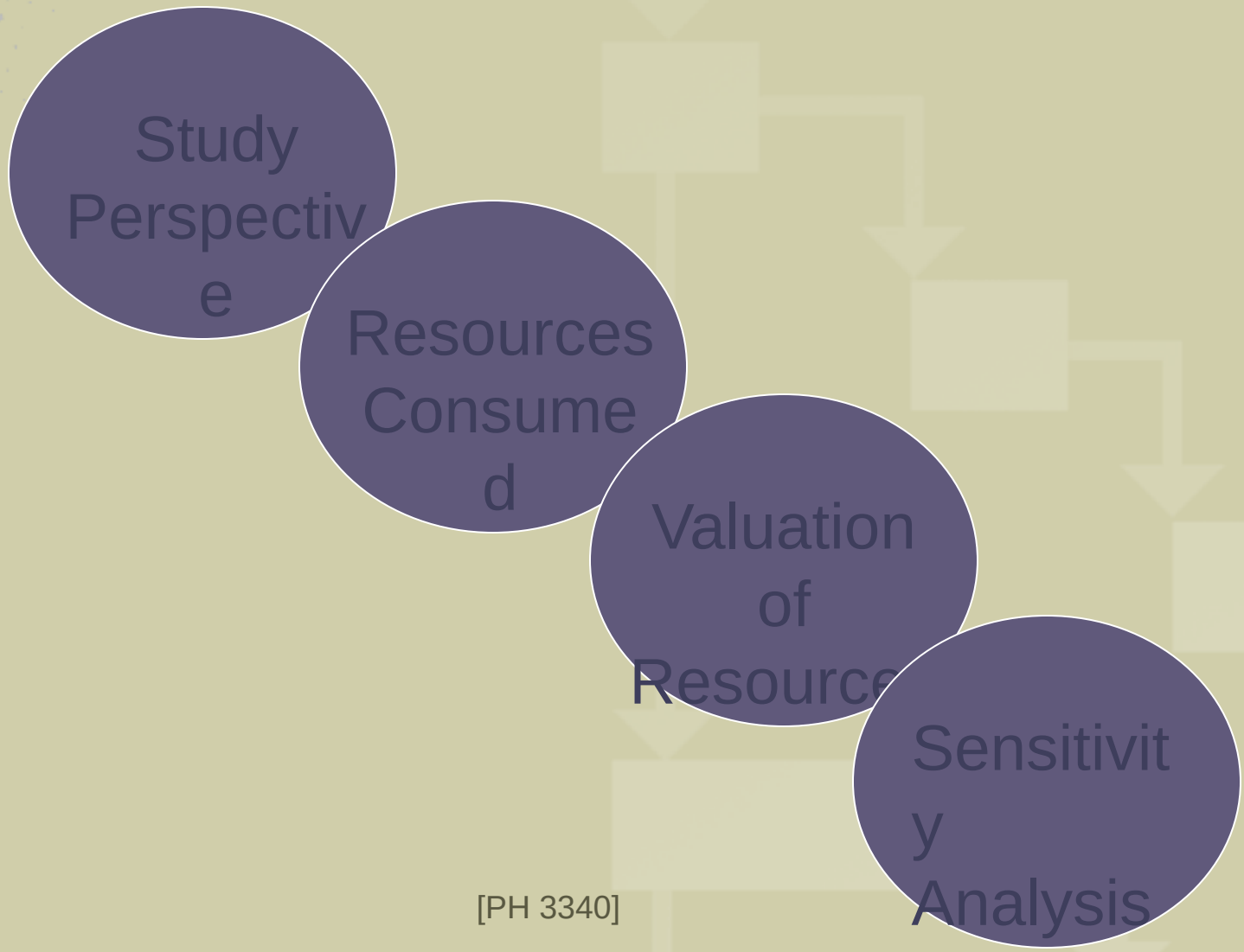
Torrance *et al*. (1972)

When to conduct a CE analysis The Cost-Effectiveness Plane



Adapted from Black (1990)

Cost Analysis Framework



Study Perspective

- Determines which costs are relevant to the analysis
  - Societal
  - Payer
  - Hospital
  - Patient
  - DoD
  - Hospital Pharmacy Department

Resources Consumed

- Specify the ingredients
- Count the units

Valuation of Resources:

- Types of Costs
  - Direct Medical
  - Direct Non-medical
  - Indirect
  - Intangible

Valuation of Resources:
Types of Costs

- **Direct Medical**
  - **Resources spent on medical services or products as a direct consequence of a disease or illness**

Valuation of Resources:
Types of Costs

- **Direct Nonmedical**
  - **Expenses related to the provision of medical care, but incurred outside the medical sector**
    - **Transportation to a medical care facility**
    - **Childcare**
    - **Lodging**

Valuation of Resources:
Types of Costs

- **Indirect Costs:**
  - **Amounts spent or lost as an indirect consequence of illness or consumption of medical costs**
    - **Lost wages due to sickness**
    - **Lost production**

Valuation of Resources:
Types of Costs

- **Intangible Costs**
  - **Pain and suffering**
  - **Social and emotional stress**

Decision Analytic Modeling

- A technique used to evaluate competing decisions
- Can focus on cost, outcomes or both
- Uses a “decision tree” to help determine the best selection

Elements of a Decision Tree

- Event branches
- Nodes
  - Decision □
  - Chance (event) ○
  - Terminal ◄
- Probabilities
- Rollback values

Decision Tree Branches

- Represent alternative paths and events (either chosen or based on probabilities) that may occur

Decision Tree Nodes

- Decision – represents a point where a choice of alternatives can be made
- Chance – represents a point where potential events can occur (based on probabilities)
- Terminal – represents a point where the end results (payoffs) of a particular pathway are calculated

Building a Decision Tree Model*

- Identify the problem
- Structure the tree
- Gather data to populate the tree
- Analyze the tree
- Conduct sensitivity analysis

*Adapted from: Veenstra D, Sullivan S. Modeling Methods – Decision Analysis. Presented at the 4th Annual Pharmacoeconomic Principles and Applications Conference, July 2004

Identify The Problem

- What is the question you are trying to answer?
  - Which long-acting insulin is most cost-effective in the DoD MHS?
- What decision must be made?
  - Treat with NPH or Insulin glargine
- What events follow the decision?
  - Glucose control
  - Adverse events
  - Adjust or change drug

Clinical Scenario

- Type 1 Diabetes Mellitus
  - New diagnosis
    - Begin basal insulin therapy
- Type 2 Diabetes Mellitus
  - Pt is not well-controlled on oral antidiabetic agents.
    - Option 1: Stop oral meds and begin insulin
    - Option 2: Cont oral meds and begin insulin

How do you define well-controlled?

- **The American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus**
  - Hemoglobin A1c ≤ 6.5
  - Fasting Serum Glucose ≤ 110
  - Post-prandial Serum Glucose ≤ 140

The American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus: The AACE System of Intensive Diabetes Self-Management-2002 Update

Long acting insulin alternatives

- NPH (neutral protamine Hagedorn)
  - Novolin*
  - Humulin
- Mixed NPH and regular/short acting
- Glargine (Lantus)

*National Contract with VA, DoD, IHS, BOP, and Option 2 State Veteran Homes

NPH insulin

- Advantages
  - Least expensive
  - Pre-filled devices available
- Disadvantages
  - Greater frequency of nocturnal hypoglycemia
  - Increased immunogenicity
  - More weight gain
  - Lower glycemic control
  - Reduced patient satisfaction
  - Duration of action 18-24 hours

Glargine insulin

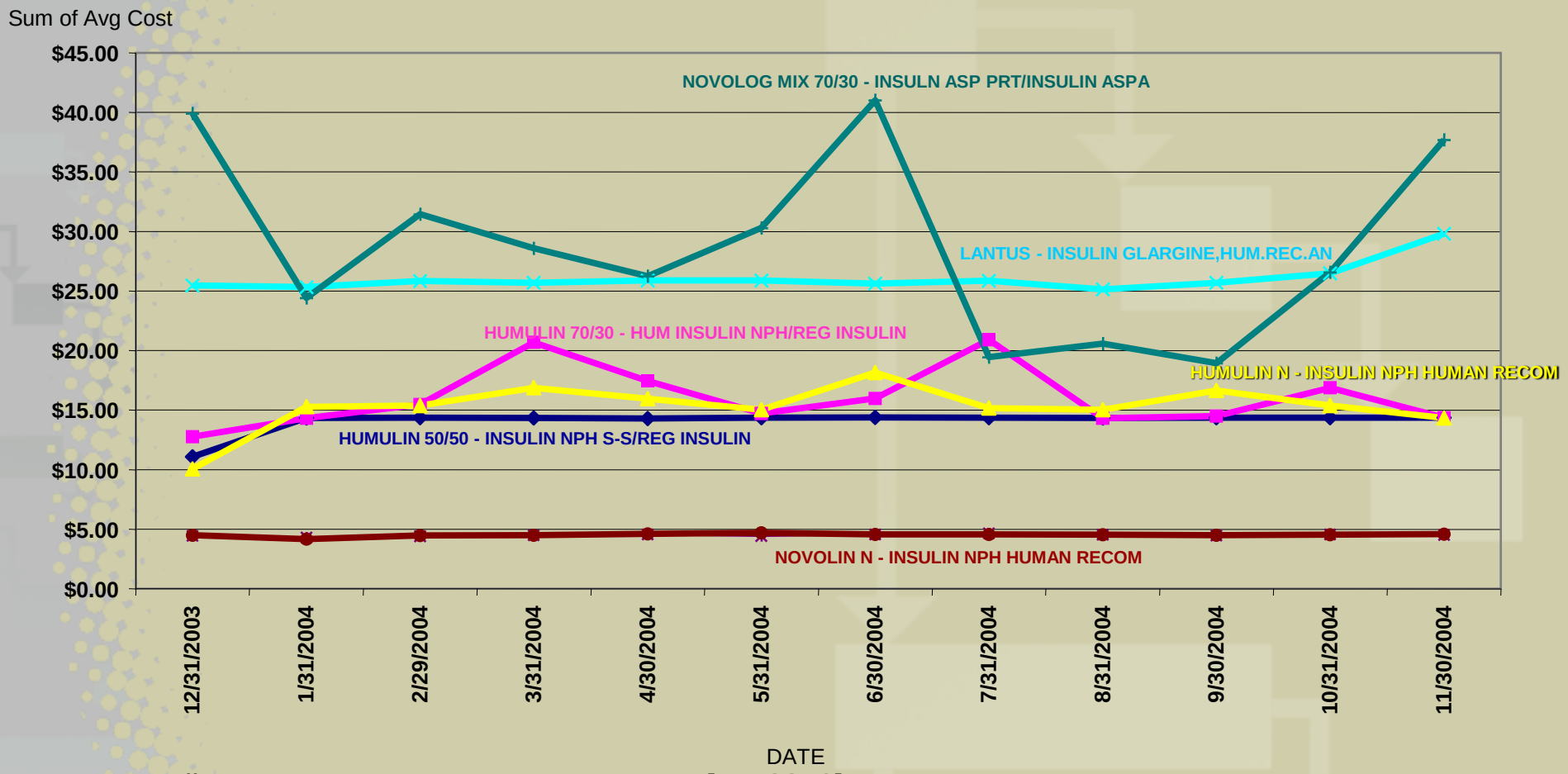
- Advantages
  - Duration of action 24 hours, so no peak effect
  - Once daily dosing
  - Reduced frequency of nocturnal hypoglycemia
  - Type I
    - Greater reduction in fasting blood or plasma glucose levels
    - Improved patient satisfaction
  - Type 2
    - Improved HgA1c values
- Disadvantages
  - Most expensive

Avg Cost (10mL vial) in DoD* Dec 03 – Nov 04

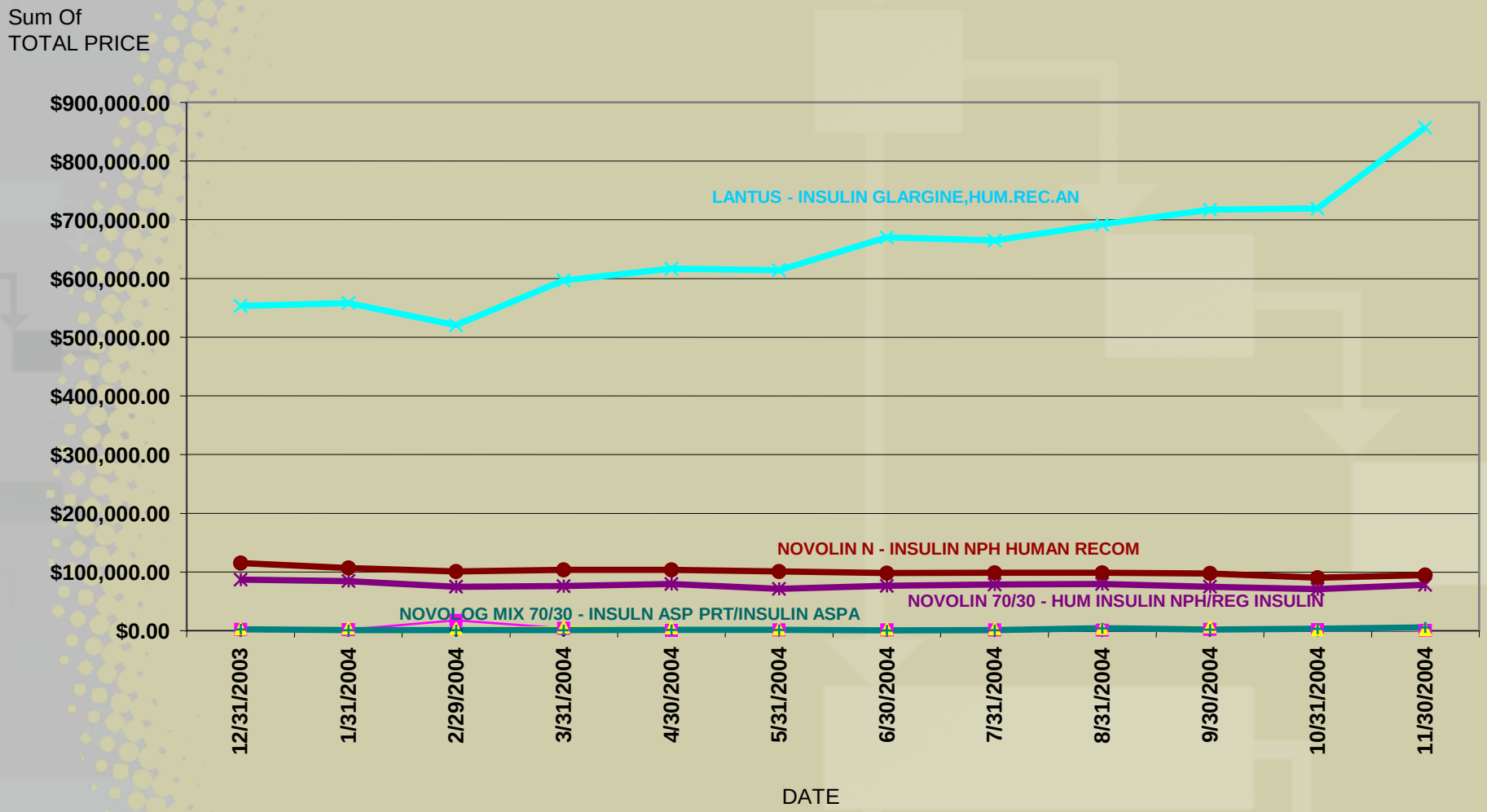
- NPH (neutral protamine Hagedorn)
  - Novolin $4.50
  - Humulin
- Mixed NPH and regular/short acting
  - Approximately $15.00
- Glargine (Lantus)
  - $26.11

*Prime Vendor Data

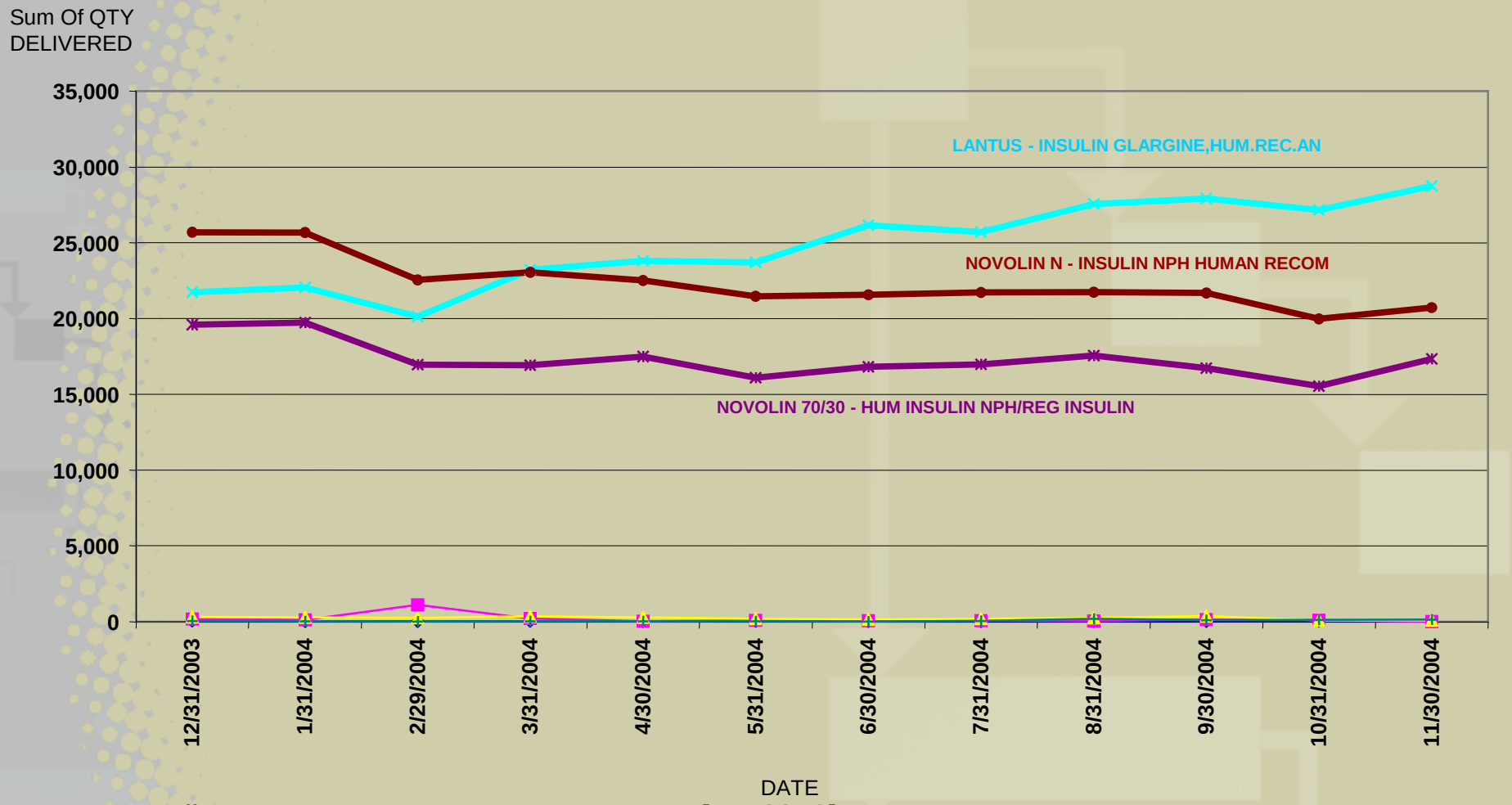
Average Cost ($) of Insulin in DoD
Dec 03 – Nov 04



Dollars Spent in DoD on Insulin
Dec 03 – Nov 04



Number of Insulin Vials Dispensed in DoD Dec 03 – Nov 04

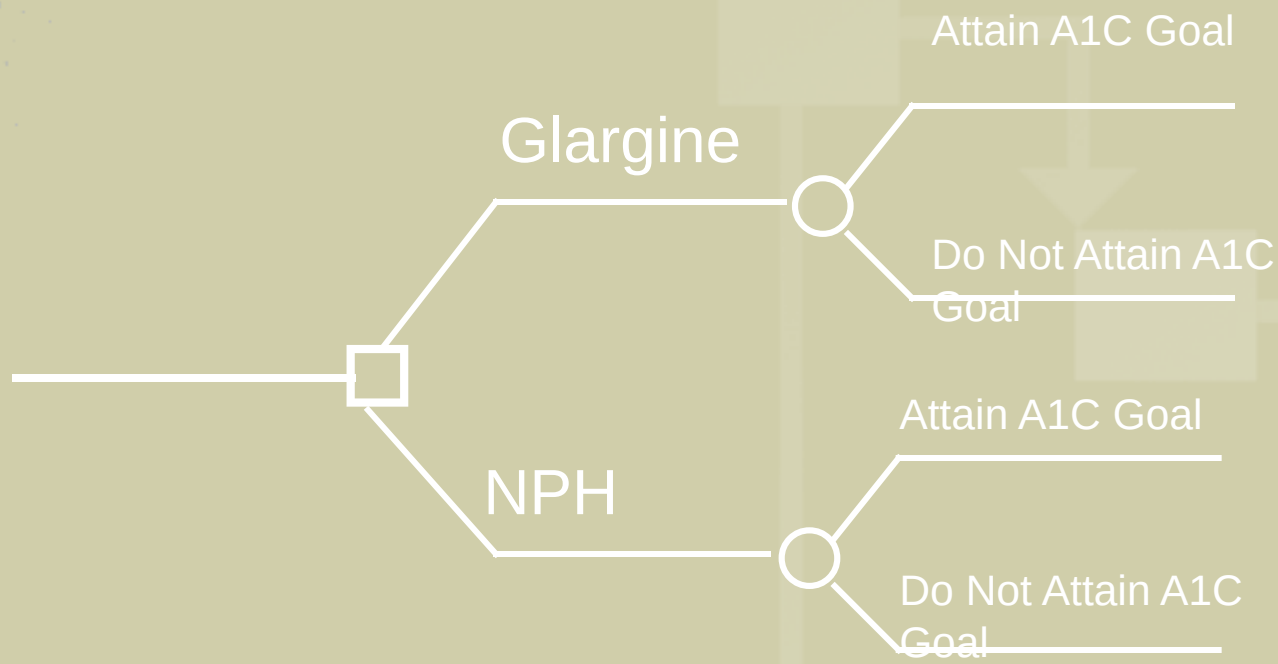


Structure the Decision Tree

- Depicts the components of the problem graphically
- Build tree left to right
  - Nodes and branches

What Are Our Choices

What Events Will Follow Our Choices



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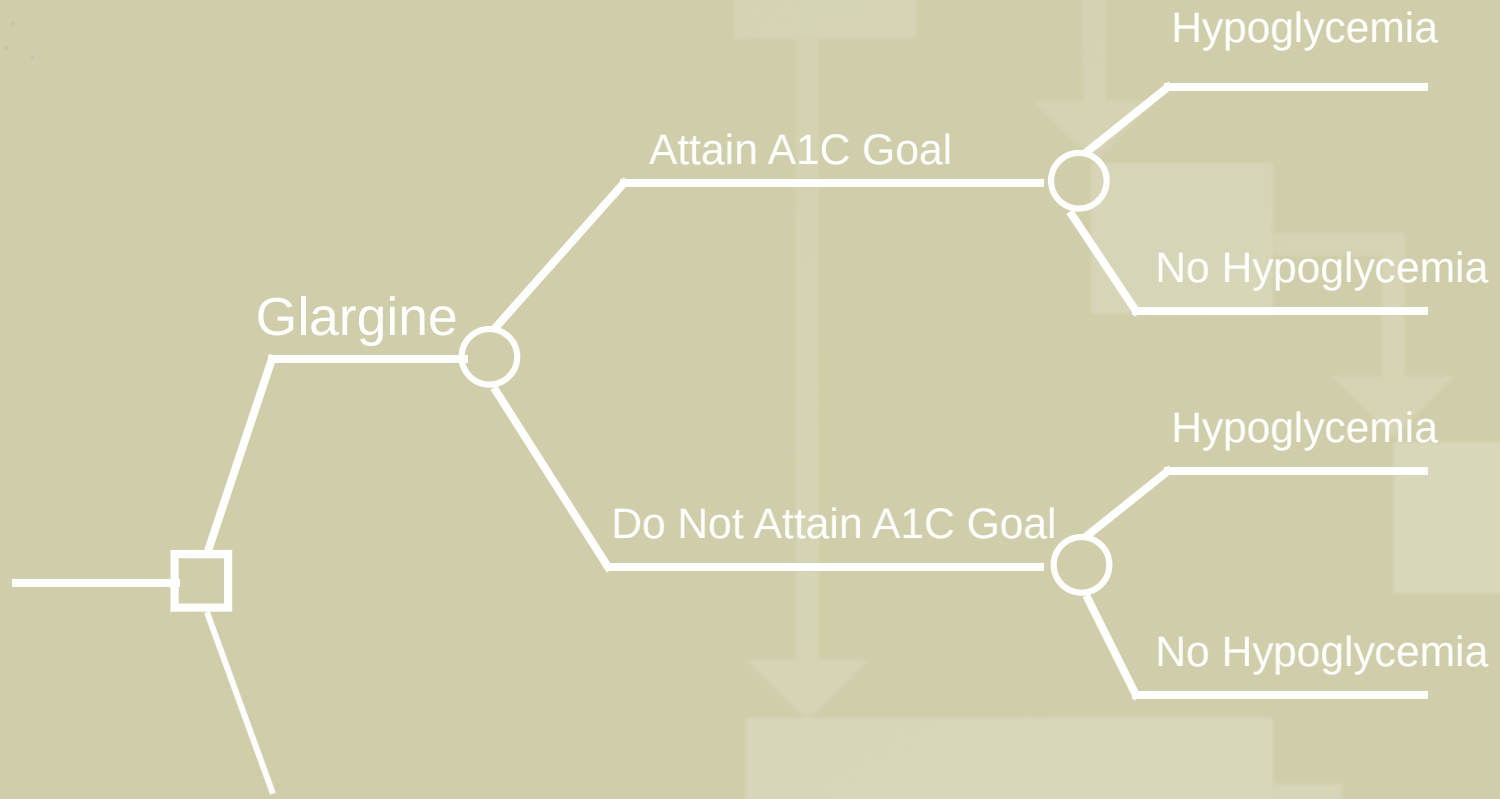

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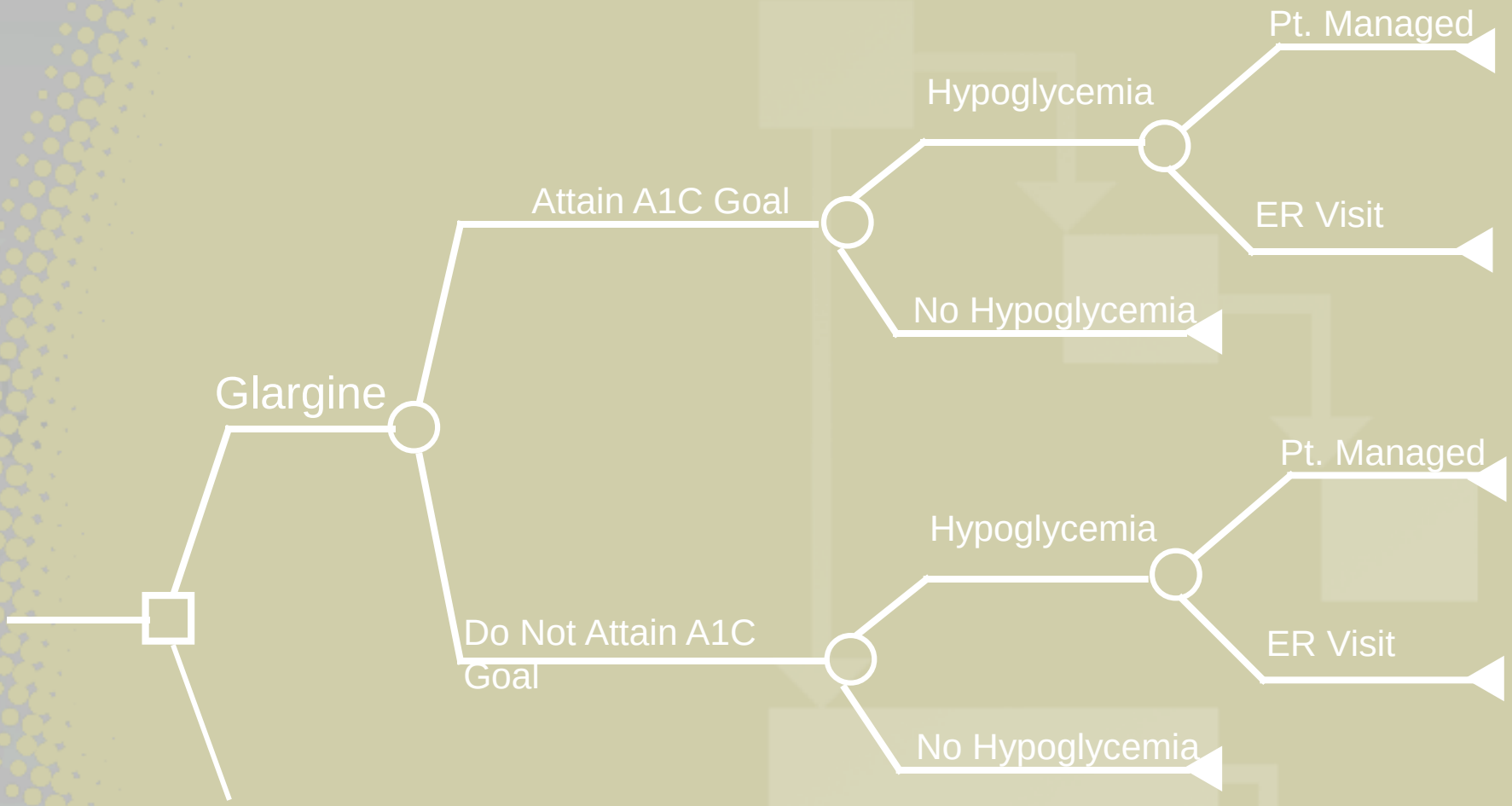
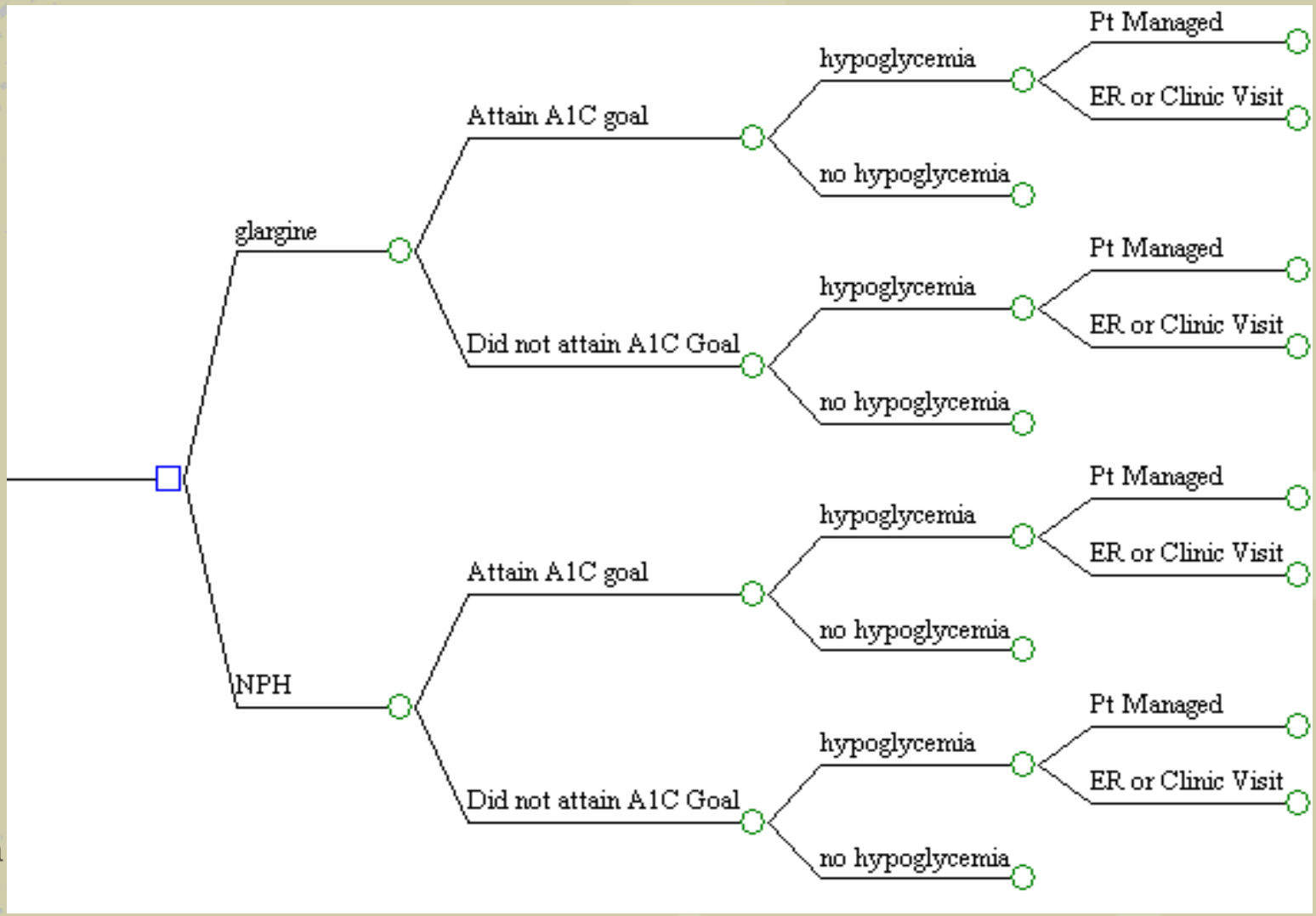


The Complete Decision Tree



Gather Data to Populate the Tree

- Literature review
  - Estimates from clinical trials (e.g. efficacy, adverse events)
- Expert Opinion
  - Good where no clinical trial data exists or for specifics like system costs
- Database studies
  - Good for “real-world” event probabilities, cost identification

Data Needed for This Model

- Probabilities
  - Probability of attaining A1C target
  - Probability of having hypoglycemic event
  - Probability that patient manages hypoglycemia
  - Probability that hypoglycemia requires medical intervention
- Payoffs
  - Cost of treatment with NPH
  - Cost of treatment with glargine
  - Cost of complications if A1C goal not reached
  - Cost of medical intervention if hypoglycemia severe

Data Estimates for Model

Variable	Point Estimates	
	NPH	Glargine
Probability of attaining A1C goal*	0.439	0.579
Probability of hypoglycemia*	0.382	0.165
Probability hypoglycemia managed by patient†	0.95	0.95
Cost of 3 years insulin treatment	$162	$564
Cost of complications if A1C goal not attained	$1565	$1565
Cost of medical intervention if hypoglycemic requiring treatment †	$125	$125

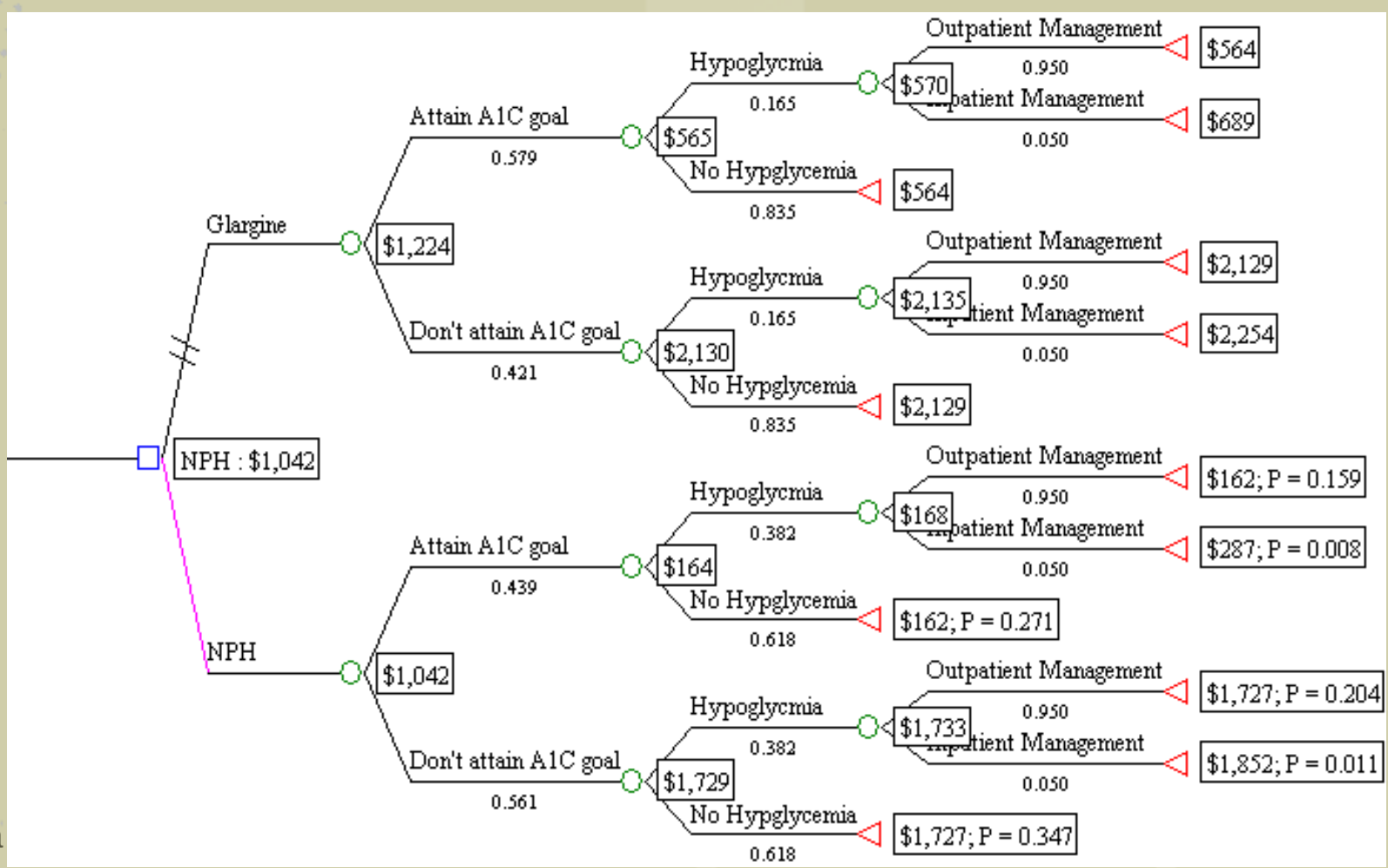
•Fritsche, et al 2003 Ann Int Med 138(12):952-9; †Expert opinion; Gilmer, et al. 1997 Diabetes Care 20(12):1847-53

Analyze the Tree

- Done by “rolling back” the tree to get “expected values”
- Start at terminal node and multiply probabilities as you trace tree to origin to get probability of outcome
- Sum weighted outcomes for each potential path

*Adapted from: Veenstra D, Sullivan S. Modeling Methods – Decision Analysis. Presented at the 4th Annual Pharmacoeconomic Principles and Applications Conference, July 2004

Rolled-Back Decision Tree



Conduct Sensitivity Analysis

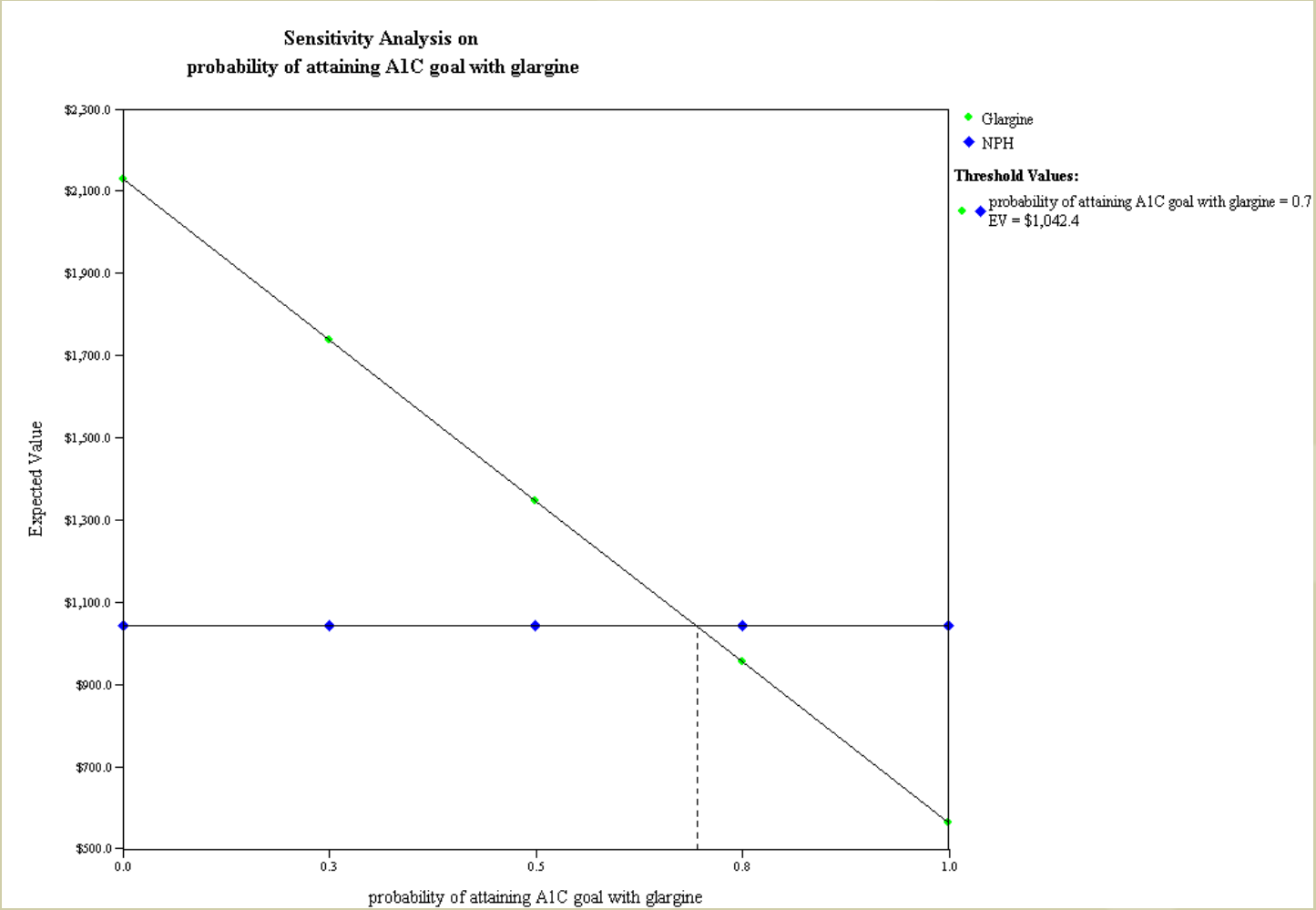
- Done to “debug” the tree
- Done to check whether changes in parameters influence model’s results

Sensitivity Analysis

- Perform one-way sensitivity analyses on all parameters to debug tree
- Vary probabilities from 0 to 1; response to changes should be logical
- Set all cost/outcomes equal to zero; strategies should have same expected value

*Adapted from: Veenstra D, Sullivan S. Modeling Methods – Decision Analysis. Presented at the 4th Annual Pharmacoeconomic Principles and Applications Conference, July 2004

Sensitivity Analysis: Varying the probability of attaining A1C Goal with Glargine



J. Vella

Conclusions

- Pharmacoeconomic analysis
  - Valuable tool to answer a clinical question
    - Cost effectiveness – efficacy, safety, tolerability, other & cost
    - QOL
  - Limitations of modeling
    - Sensitivity analysis
    - Applicability of study data to individual patient
    - Physician factors

A final thought…

- Individual patient issues weigh into the decision
  - Compliance
  - Patient preference
  - Patient satisfaction* in DM 1
  - Values of the individual and society

*Dunn et al. Insulin glargine: an updated review of its use in the management of diabetes mellitus. *Drugs* 2003; 63 (16): 1743-1778.

A final thought…

- What factors influence a physician to prescribe a new drug?*
  - Pharmaceutical company prescribing loyalty
  - Prescribing volume – high volume
  - Age – more experience, more caution
  - Pharmaceutical marketing
  - Practice type – office > hospital based
  - Clinical investigator experience
  - Specialty - endocrine

*Glass, H; Rosenthal, B. Demographics, Practices, and Prescribing Characteistics of Physicians Who Are Early Adopters of New Drugs. *P&T* 2004;Vol 29:699-708.