Introduction to Pharmacoeconomics

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Why do we need Health Economics?

- Suppose you are comparing two drugs or services where one is more expensive than the other. In choosing the drug or service you want to consider
  - Efficacy of the drugs / services (eg, healthcare utilization cost related to the target disease)
  - Additional resources needed for use of the drug/ service (eg, administration, monitoring, follow-up care)
  - Healthcare cost associated with side effects of the drug / service
  - Time frame may change the cost associated with the drug / service
  - Perspective (patient, provider, payer) may alter the cost-benefit

Application of Economic Analyses

- ❑ Clinical Decision Making
  - ■ Making cost-effective choices when resources are limited (for provider, third party payer, or patient)
- ❑ Program Justification
  - ■ To justify investment in a clinical service or program
  - ■ To justify reimbursement of a clinical service or program

Application of Economic Analyses

- Formulary Management
  - Inclusion or exclusion of new drugs
- Drug Policy decisions, treatment guidelines
- Purchasing negotiation
- Pricing in the Pharmaceutical Industry

Establishment of Pharmacoeconomics

- ❑ In 1992 Australia started to require documented efficiency for FDA approval

- ❑ Canada, Finland, and Portugal now require similar documentation on efficiency

- ❑ Some HMOs in the US require proof of efficiency for formulary access

- ❑ NICE (National Institute for Clinical Excellence) in UK is now formal NHS entity that evaluate healthcare technology and makes recommendation for coverage

Is travel prophylaxis worthwhile? Economic appraisal of prophylactic measures against malaria, hepatitis A, and typhoid. Behrens BMJ 1994

	Typhoid	Hepatitis A	Malaria	
			Chloroquine & Proguanil	Mefloquine
No. of cases prevented	183	291	2,653	3,144
Cost of intervention (£)	30,247,947*	54,471,134**	3,607,308	12,822,263
Avoided expenditure on illness (£)	9,182	11,857	7,205	7,205
Prophylaxis per avoided case (£)	165,639	187,137	1,360	4,078
Cost benefit Ratio	18.1	15.8	0.19	0.57
* Typhoid Vi vaccine (one of three used - other vaccine details not shown because of lack of space on slide); ** Vaccine - immunoglobulin use had CB ratio of 5.8				

Perspectives

- ❏ 4 perspectives:
  - ■ Society
  - ■ Payer
  - ■ Provider
  - ■ Patient

- ❏ Determines cost components & time window

Patient's Perspective

❑ Patients: receive health care services

- **Costs**: Co-payments, Transportation, Loss of income
- **Consequences**: Relieve of symptoms, cure, quality of life
    - more subjective because it includes patient preferences
- less common in the empirical literature
- Example: Viagra/Sexual Dysfunction and Detrol/Overactive Bladder
- Becomes important when patients pay the majority of services

Provider's Perspective

- Providers: deliver health care services
    - **Costs**: Personnel, Supplies
    - **Consequences**: Length of stay, mortality, morbidity
    - Tend to be more concerned with evaluating treatment options based solely on reported efficacy
    - $$ perspective depends on capitation and managed care penetration
    - Example: Hospital formulary decisions

Payer's Perspective

- Payers: pay for health care services
- Tend to be the primary decision-makers for resource use
- Two categories:
  - Employers/Business Coalitions
  - Managed Care Plans

Employers' Perspective

- Employers: finance health care services
  - **Costs**: workers compensation, sick leave
  - **Consequences**: increased productivity, health insurance premiums
  - May have different time lines (lifetime vs. employment time)
  - Becoming more involved with quality improvement

Managed Care Plans′ Perspective

❑ Managed Care Plans: manage benefits for payers

- ▪ **Costs**: Healthcare utilization charges
- ▪ **Consequences**: decreased healthcare utilization
- ▪ Concerned with cost containment
- ▪ Long-term benefits may not be as important to certain plans/markets (Dis-enrollment rates)

Society's Perspective

- Costs: all costs
- Consequences: all consequences including quality of life
- Usually does not make health care decisions (in USA)
- Takes into consideration ALL costs
- Some think it is the "best" perspective
- Example: Immunization requirements

Example of Perspectives :
LMWH used in DVT Outpatient Treatment

- ❑ Patient
  - ▪ Discharge from Hospital Earlier
  - ▪ Less income loss, less or more copays
- ❑ Physician Practice Group
  - ▪ Is patient at greater risk from earlier discharge?
  - ▪ Capitation agreements
- ❑ Hospital
  - ▪ Per Diem vs. Capitation
- ❑ Managed Care Plan
  - ▪ Outpatient vs. Hospitalization Stay

Cost

- Total Costs - sum off all costs defined by research design (perspective)
- Direct Medical Costs - what is paid for specified health resources and services
  - physician visit
  - medications
  - labs
  - hospitalization

Cost II

❑ Direct Non-Medical Costs - costs necessary to enable an individual to receive medical care

  ❑ lodging, special diet, transportation

  ❑ lost work time (important to employers)

    ❑ Example: Acute Otitis Media in Pediatric Patients with Professional Parents

Costs III

- Indirect Costs - lost productivity in society
  - unpaid caregivers, lost wages
  - expenses borne by patients, relatives, friends, employers and government
- Intangible Costs - patient's pain and suffering
  - effect on quality of life/health perceptions
  - Example: Incontinence, Severe CHF

Cost of Illness Analysis (COI)

- **Descriptive** study: sums all costs of a disease
- Uses data on epidemiology of the disease, its treatments and outcomes and sums everything in costs
- Used to identify and set priorities for policy making

Steps in Economic Evaluation

Analytic studies:

Step 1: Quantify the costs of the intervention/drug (input)

Step 2: Quantify the outcomes / consequences (output)

Step 3: Compare magnitude of differences in costs and evaluate "value for money" (e.g., by reporting a cost-effectiveness ratio)

Step 4: Evaluate the precision of these comparison (sensitivity analysis)

Cost Minimization Analysis (CMA)

- Compares all the relevant costs of two or more drugs
- Drugs must have identical efficacy (VERY IMPORTANT!!)
- Distinguished from other analytic studies in that consequences are shown to be equivalent
- Objective is to identify less costly alternative
- Formulary committees do this all the time!!

Cost Minimization Analysis

- Output: identical (not considered)
- Input:
  - Drug #1 costs $300
  - Drug #2 costs $500
  - Drug #3 costs $200
    plus $150 lab costs for monitoring

WICH DRUG WOULD YOU ADD TO YOUR FORMULARY?

Cost Benefit Analysis (CBA)

- ❑ Economic analysis in which dollar values are assigned to implementation of the service / drug (input) and consequences (benefits) in order to determine the net cost of that intervention or program

- ❑ Input and output is summarized in monetary units so that different drugs / services can be compared

- ❑ Input: cost for tx

- ❑ Output: cost for consequences of tx

Cost-Benefit Analysis

- ❑ **Scenario Drug #1**
  - ■ New Drug: Clot-away (thrombolytic)
  - ■ Drug will cost $300/patient
  - ■ Standard therapy – no savings

- ❑ **Scenario Drug #2**
  - ■ New Drug: Clot-Buster (thrombolytic)
  - ■ Drug will cost $1000/patient
  - ■ Drug will save $1500 in total hospital costs

- ❑ **Scenario Drug #3**
  - ■ New Drug: Recombinant Human Clot-Away (thrombolytic)
  - ■ Drug will cost $5000/patient
  - ■ Drug will save $3500 in total hospital cost

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Cost-Benefit Results

Drug	Cost ($)	Benefit ($)	Benefit-Cost-ratio (B/C)	Net present value (B-C)	ROI (B-C)/C
A	1.000	1.500	1,5:1	500	50%
B	10.000	14.000	1,4:1	4000	40%

Advantages Cost-Benefit Analysis

❑ Multiple outcomes can be combined or different outcomes can be compared

❑ Maximizes benefit of investment

❑ Problems: How do you value pain and suffering or QOL?

Cost Effectiveness Analysis (CEA)

❏ Economic analysis in which cost for different treatment options are compared with non-monetary outcomes

❏ Measured in dollars per outcome
(dollars per life saved, per patient cured)

❏ Output: health outcomes

❏ Input: cost for tx

Cost-Effectiveness Based on Cure Rates ($)

Flu-away: Cost = 75.07+47.68   = 122.75
                     Cure Rate = 35/43   = 81.4%
                     CER=122.75/81.4   = $1.50

No-flu :   Cost = 47.70+23.59   = 71.29
                     Cure Rate = 86/98   = 87.8%
                     CER=71.29/87.8   = $0.81

Fluquil: Cost = 58.16+5.95   = 64.11
                     Cure Rate = 249/268   = 92.9%
                     CER=64.11/92.9   = $0.69

Cost: Medical cost and drug cost
CER: Cost-Effectiveness Ratio (cost per patient cured)

Cost Effectiveness Ratios

| Drug	Cost	Survival	Cost-Effectiveness ratio
Drug A	100	85	100/85 = $1.18 / surviving patient
Drug B	70	50	70/50 = $1.4 / surviving patient
	Net cost	*Net effectiveness*	*Incremental cost-effectiveness ratio*
Change to drug A	30	35	30/35 = 0.86 $ / surviving patient

Cost-Effectiveness Analysis

- Used when effectiveness levels of two different tx are not the same
- Only compares programs/drugs with the same clinical endpoints
- Measures the differences in effectiveness
- Measures the <u>incremental cost</u> between alternative therapies

Cost Utility Analysis (CUA)

- Compares the costs of a program or therapies in monetary terms and its effects or outcomes in quality-adjusted life years (QALYs).
  - Special form of CEA
- Utility is a measure of Health-related Quality of Life
- Measures cost per incremental change in patient preference.
- Input: cost
- Output: health outcomes adjusted for HrQoL (e.g., QALY)
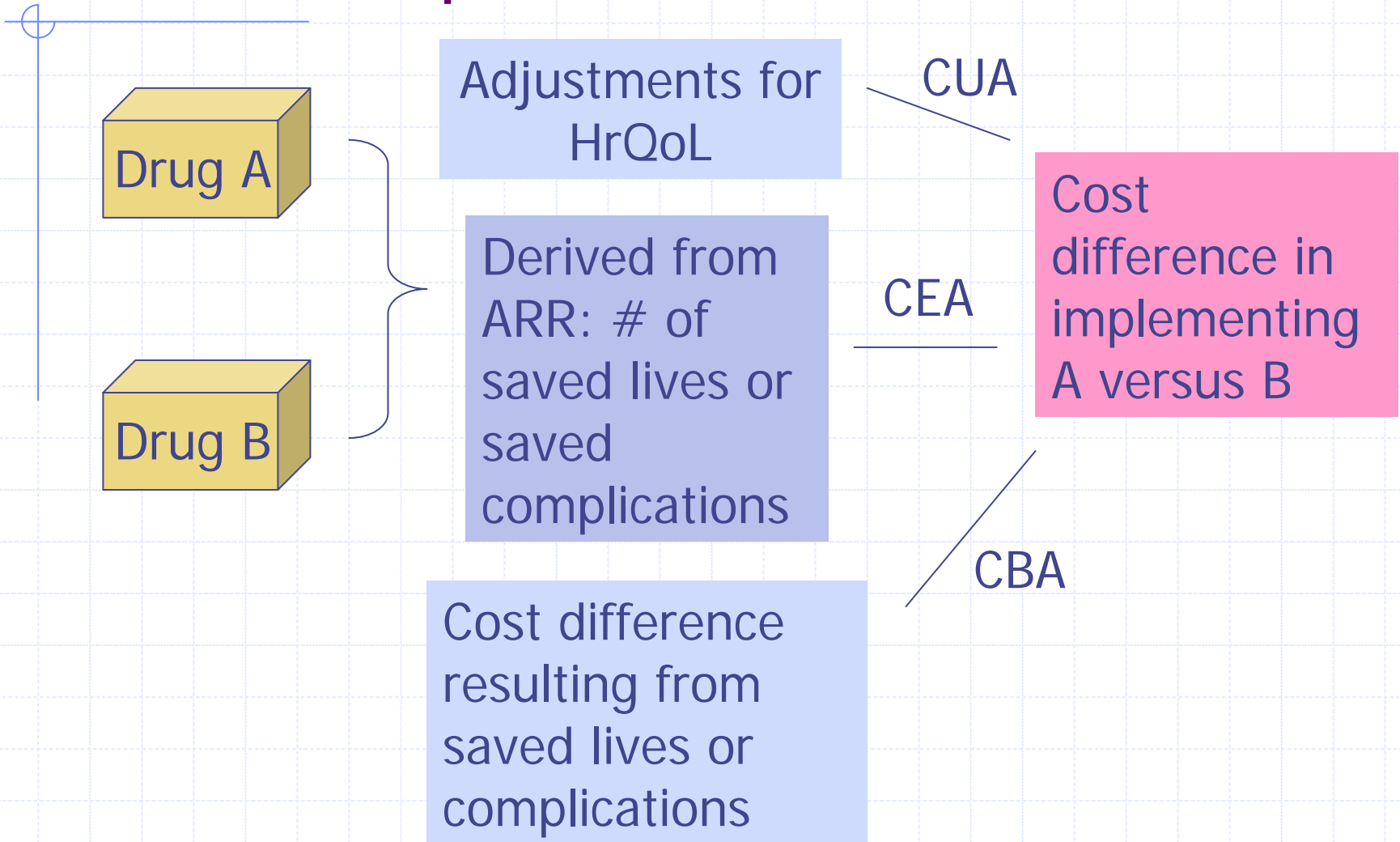
Quality Adjusted Life Years (QALY's)

Quality of Life (vertical axis, from 0.0 to 1.0)

Birth · QALYS (Years) · Death
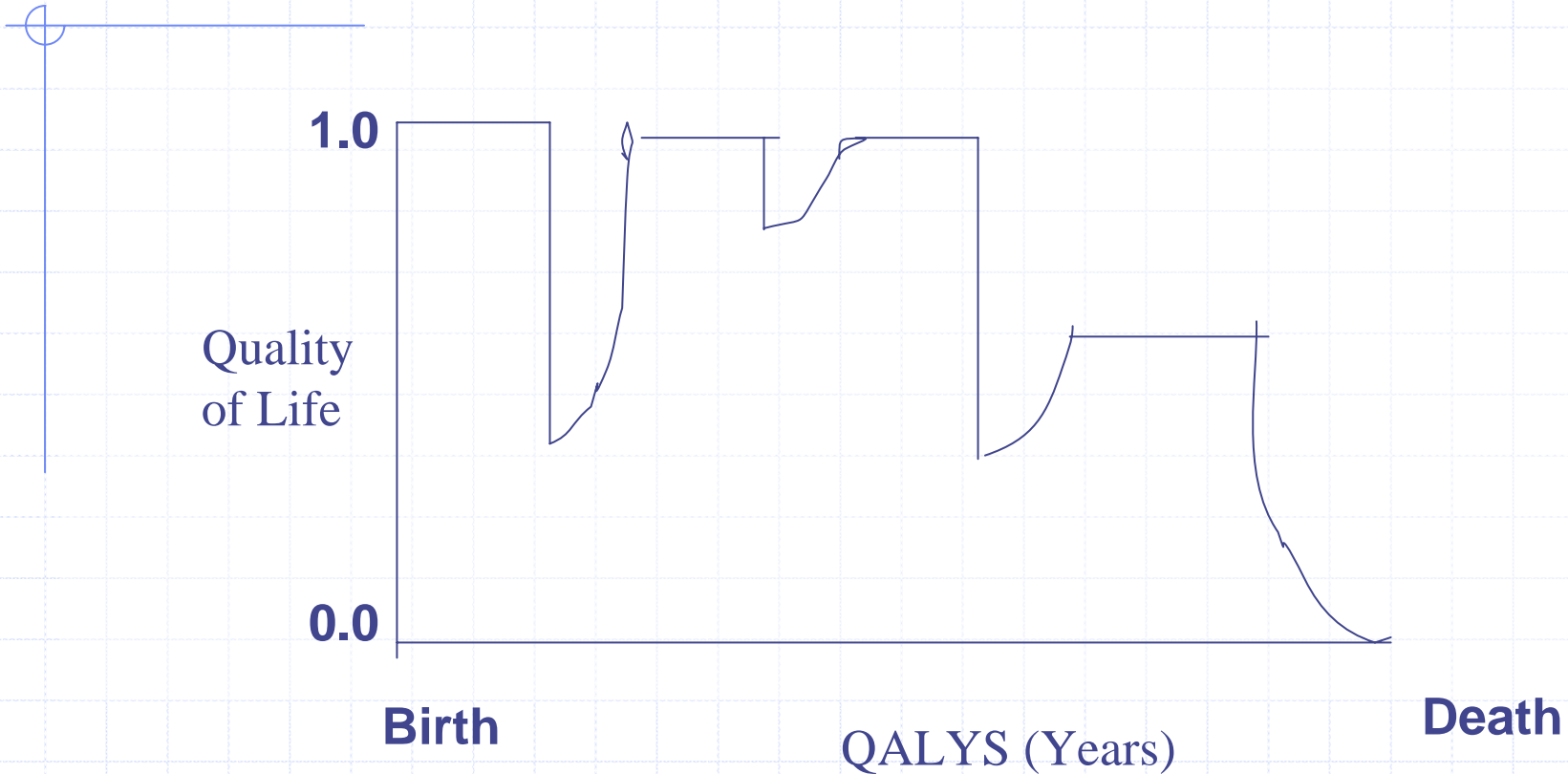
Life years are weighted by QoL = QALYs
Alternatives: Healthy Year Equivalents, Well Years

Summary: Variables in PE Studies

|	Input/investment	Output/benefit	Aim
Cost-minimization	Cost	Therapeutic equivalence	Efficiency
Cost-effectiveness	Cost	Health outcomes ("effectiveness units")	Cost-minimization given adequate resources
Cost-benefit	Cost	Cost for health outcomes	Optimized benefit given limited resources
Cost-utility	Cost	Health outcomes adjusted for HrQoL	HrQoL gains

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Basic Principle

Drug A

Drug B

Adjustments for HrQoL

CUA

Derived from ARR: # of saved lives or saved complications

CEA

Cost difference in implementing A versus B

CBA

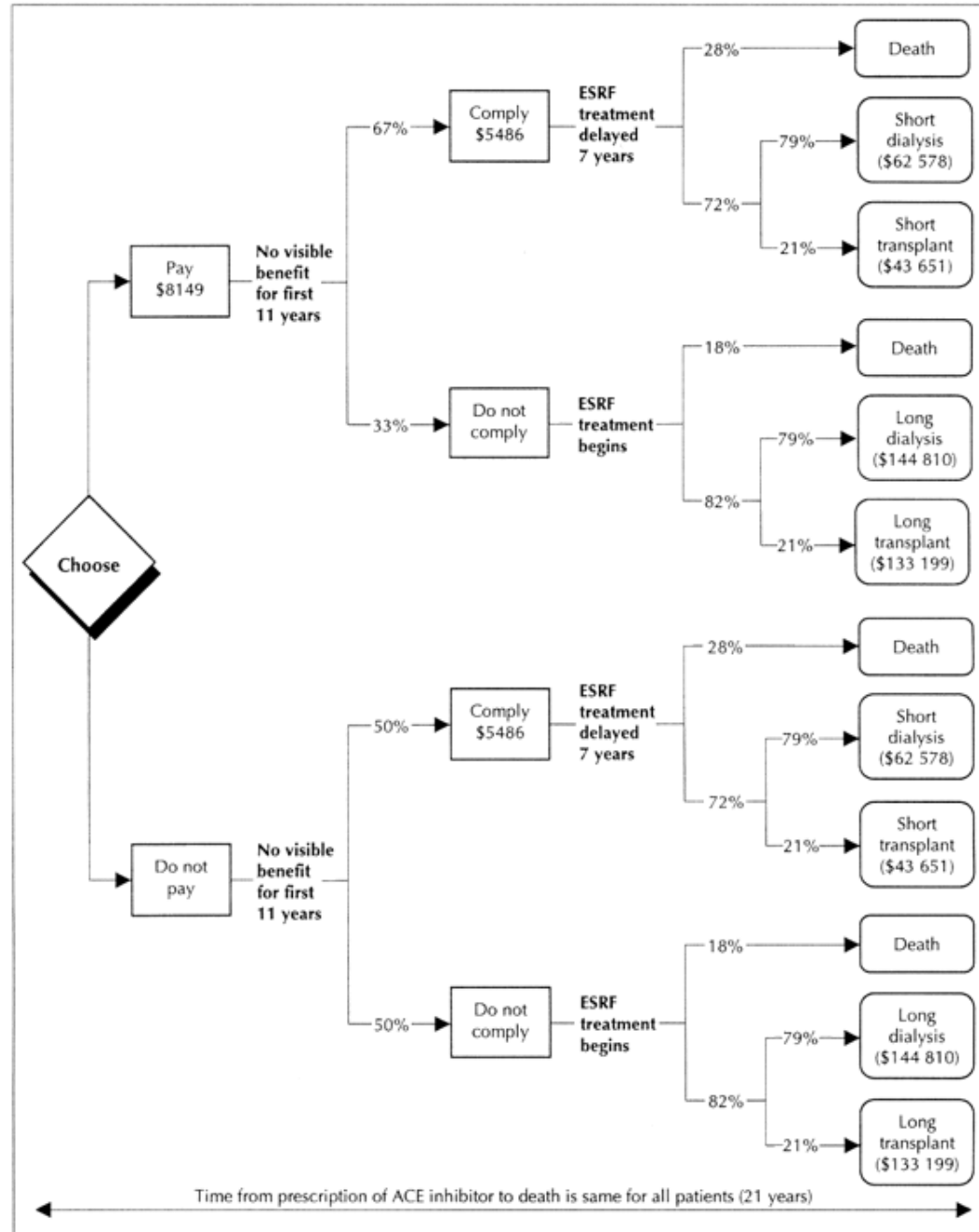Cost difference resulting from saved lives or complications

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Time Horizon

❑ Time horizon refers to the time between the beginning and the final end-point of the study

❑ Studies may model long-term costs and benefits appropriate to the disease even when RCTs were shorter and only included surrogate outcomes

Drug A

Drug B

Difference in surrogate outcome

— · — · →

Difference in mortality or complication
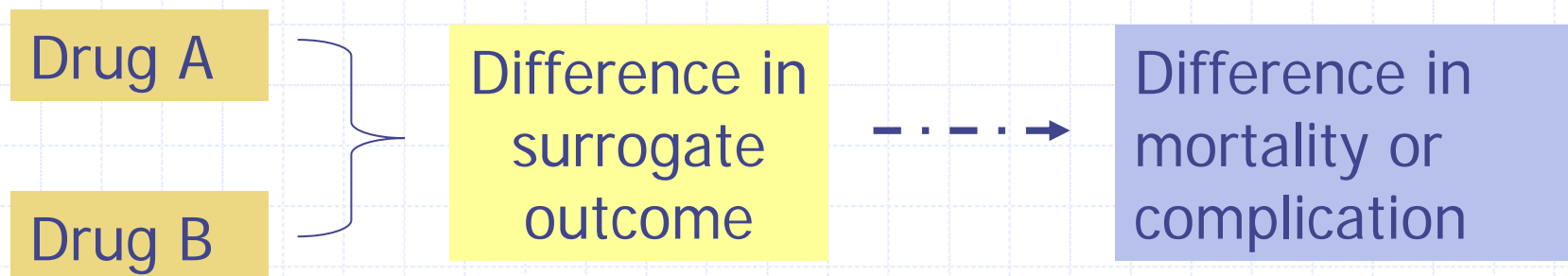
Models..

"To pay or not to pay"
ACE-I therapy for diabetic nephropathy

(Clark CMAJ 2000)

Model continued

❑ A decision analysis tree was created to demonstrate the progression of type I diabetes with macroproteinuria from the point of prescription of ACE inhibitor therapy through to ESRD management, with a 21-year follow-up. Drug compliance, cost of ESRD treatment, utilities and survival data were taken from Canadian sources and used in the cost-utility analysis

❑ Compared with a no-payment strategy, provincial payment of ACE inhibitor therapy was found to be highly cost-effective: it resulted in an annual cost savings of $849 per patient.

❑ The sensitivity analyses indicated that the cost-effectiveness depends on compliance, effect of benefit and the cost of drug therapy.

Model contd. (outcomes)

❑ On the basis of the Collaborative Study Group report we assumed

- (a) a baseline creatinine clearance of 1.37 mL/s and a decline at an annual rate of 11% in patients who comply with the ACE inhibitor therapy and of 17% in those who do not comply;

- (b) that patients reach ESRD when their creatinine clearance is 0.17 mL/s, which will occur in 18 years for compliers and 11 years for noncompliers; and

- (c) that, at an annualized death rate of 1.8%, 28% of the compliers will die over the 18 years and 72% will go on to ESRD treatment, and 18% of the noncompliers will die over the 11 years and 82% will progress to ESRD treatment.

Model contd. (costs)

- The cost of ACE inhibitor therapy was derived from a 1-year cost analysis of initial antihypertensive therapy in patients with newly diagnosed moderate hypertension.[16] We included the cost of supplemental drugs, laboratory monitoring, clinic visits and treatment because of side effects.[17]

- The costs for hospital hemodialysis and continuous ambulatory peritoneal dialysis[18] were derived from fully allocated cost analysis in 1993 Canadian dollars for patients treated by the same dialysis modality for a full year. This measurement included in-patient and out-patient costs, over-head costs, personnel, supplies, medication costs and physician fees.[19]

- The costs of ACE inhibitor therapy and ESRD treatments were converted to 1996 Canadian dollars using the Consumer Price Index for Canada.[17,19]

- …

Discounting

- *The passage of time* has an impact on costs and outcomes because waiting carries an opportunity cost (ie, you could spend the money elsewhere if you had it).

- Since decisions have to be made in the present, we need a way to compare costs and benefits that occur at different points in time.

- Different from inflation adjustments
  - Done when cost values generated at different points in time are compared; e.g., to update your Canadian study from 1996 to 2003 values
  - Done with the medical consumer price index (published by department of labor and statistics)

# Discounting

- Formula for 3% discount rate:

  *cost value (\$) * 1/(1+0.03)^n*

  n=# years the annual discount rate is applied to

- E.g.,
  - \$5000 in first year (not discounted)
  - \$1000 in second year (3% discount) = 1000 * 1/(1+0.03) = \$970
  - \$1000 in third year (3% discount) = 1000 * 1/(1+0.03)^2 = \$943

Discounting Approaches

- Determine when you like to start discounting
  - Typically any study >1 year is discounted
- Determine when cost occur
- Costs are "centered" for patients who die or who experience an event (mid-cycle correction)

Jan ---------- Dec01 Jan ----------- Dec02 Jan -------------- Dec03

10 strokes   10 strokes   10 strokes
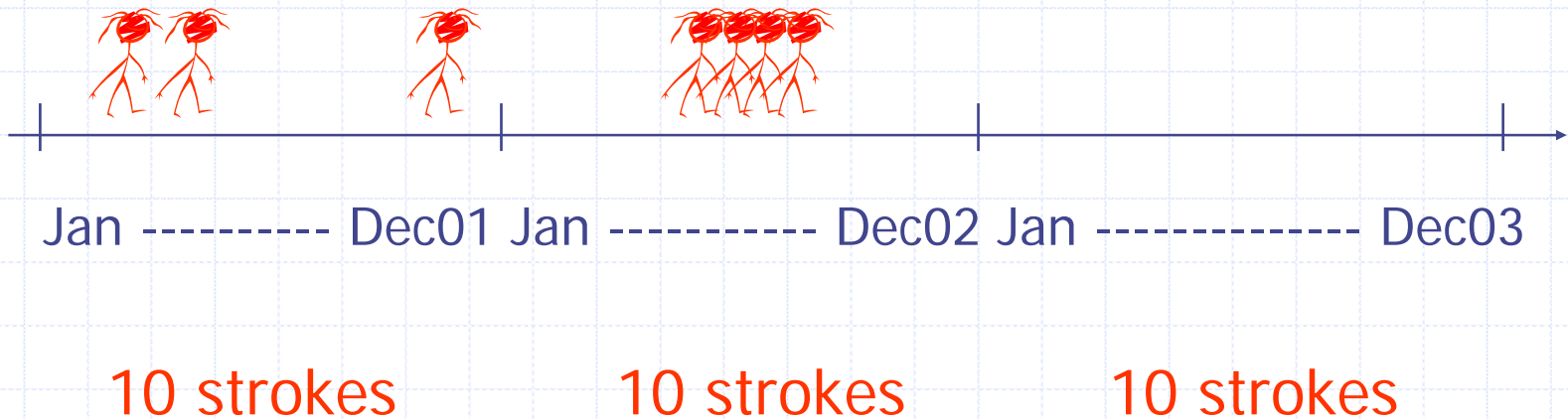
Sensitivity analysis

❑ Used to see if study conclusion change as assumptions are altered.

❑ Necessary whenever there is uncertainty about key variables.

  ▪ Parameter uncertainty

  ▪ Methodological uncertainty

  ▪ Structural uncertainty

  ▪ Heterogeneity / Bias

Sensitivity Analysis

❑ Deterministic analysis

❑ Probabilistic analysis (e.g. Monte Carlo)