Cost-utility Analysis



By: Dr. Paul Gerardo Yeh, DrPH
PH3915 Course
October 2023



Readings for 10/10 (left) and 10/12 (right)

- Drummond et al. 2015, Chap. 5
 - -Lairson, D., et al., (2014) Cost utility analysis of chemotherapy regimens in elderly patients with stage III colon cancer. Pharmaco-economics, Vol. 32 (10) pp. 1005-1013.
 - -Neumann PJ, Cohen, JT (2018) QALYs in 2018—Advantages and Concerns. JAMA Published Online May 24, 2018 doi:10.1001/jama.2018.6072.

- Sinno, Hani, et al. Utility outcome scores for unilateral facial paralysis (2012). Annals of Plastic Surgery. 69, (4) 435-438. (Review only)
- Blinman, P., et al. "Preferences for cancer treatments: an overview of methods and applications in oncology." Annals of oncology (2012): mdr559. (Review Only)
- Stewart ST, Lenert L, Bhatnagar V, Kaplan RM.
 Utilities for prostate cancer health states in men aged 60 and older. 2005; 43(4):347-55.
 (Review Only)
- Stiggelbout AM, deHaes JC. Patient preference for cancer therapy: an overview of measurement approaches. Journal of Clinical Oncology 2001; 19(1):220-30. (Review Only)



Topics

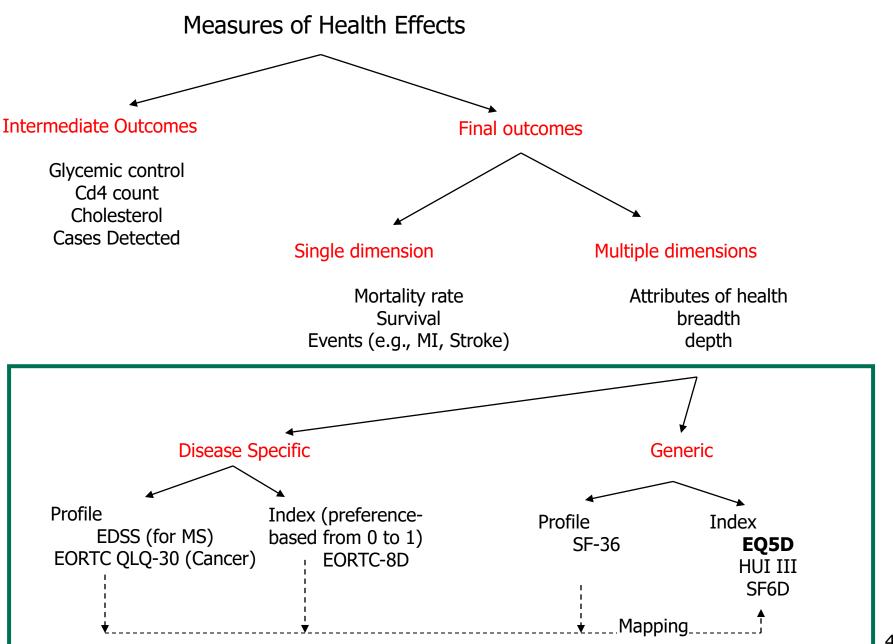
- Measures of health effects
- Definition of CUA
- Why, when, and when not to conduct CUA
- Types of Utility Measures
- von Neumann-Morgenstern (VN-M) Utility Theory
- CUA process
- Steps in utility measurement: Multi-attribute utility functions
- Methods for Measuring utility weights
 - Visual Analogue Scale (VAS)
 - Time Trade-off (TTO)
 - Standard Gamble (SG)

Dr. Sun will cover on 10/12

Defining CUA CUA Scope Utility Types Utility Theory

CUA Evaluation Process

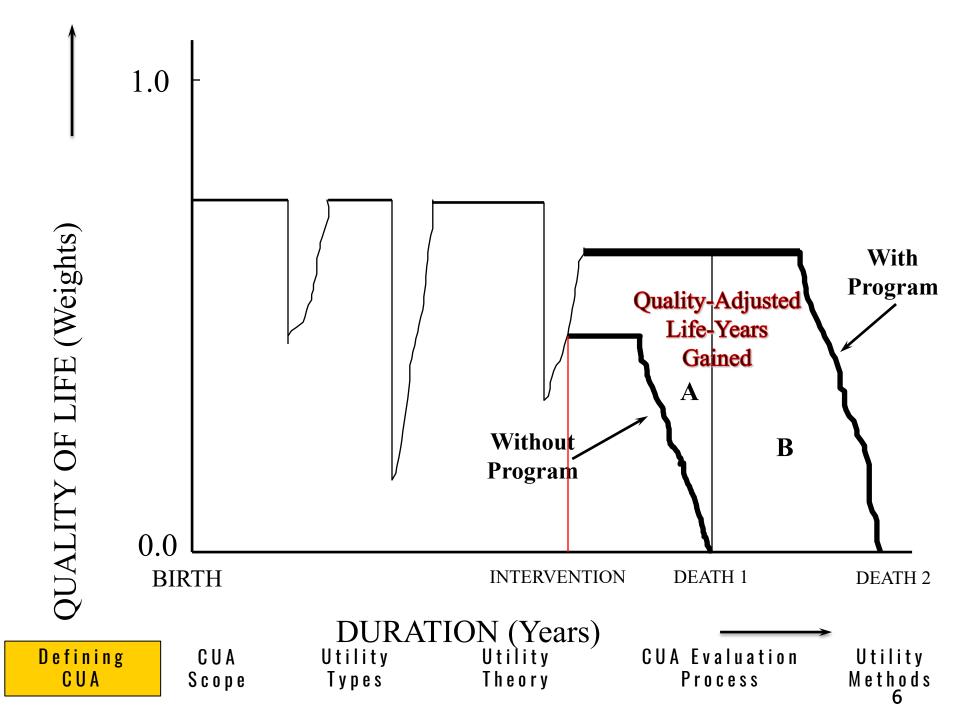
Fig. 5.1 Taxonomy of measures of health effects

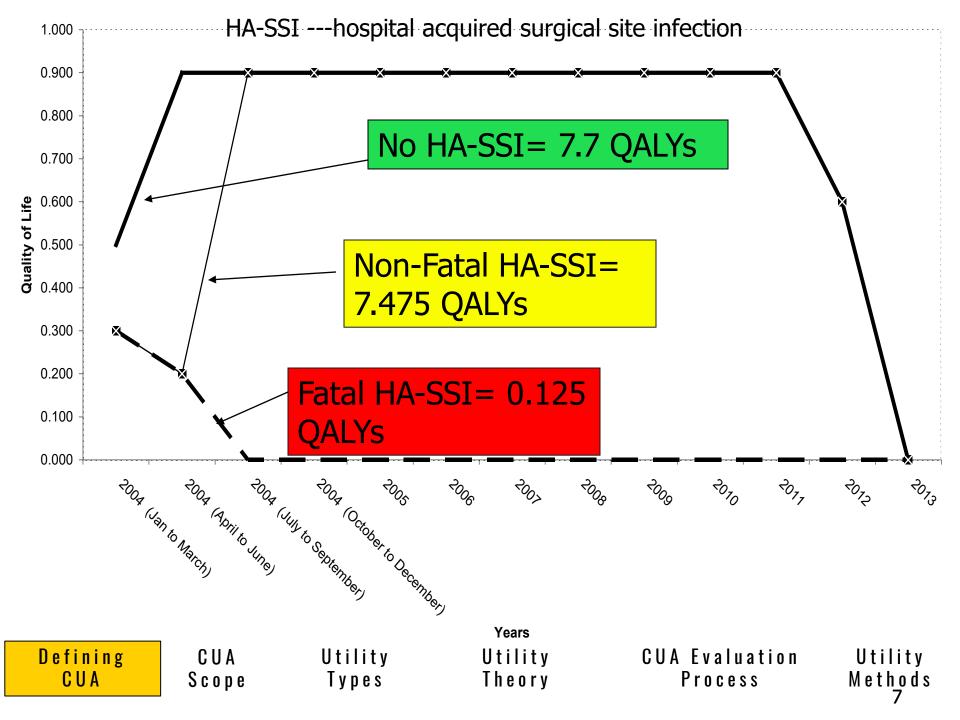


Definition of CUA

- Utility= measure of preference with future uncertainty
- Type of analysis that measures benefits in utility units or utility-weighted life-years (QALYs); Computes a cost per utility-measure ratio for comparison among programs.
- QALYs combine <u>changes in quantity and quality</u> of life (mortality and morbidity) into one <u>composite measure</u> which is independent of program or disease.

Canadian Guidelines, 1994







Why Conduct a CUA

- CEA ---cannot make <u>comparisons across</u> broad set of interventions.
- Often there is more than one outcome of interest.
 - For example, incidence of strokes, retinopathy, nephropathy in diabetes?
- Some <u>outcomes are more important</u> than others.





Utility Types Utility Theory

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When to Use CUA?

- When there are multiple objectives attained differentially, and one program does not "win" on all.
- When quality of life is the important outcome. E.G..... Arthritis.



When to Use CUA?

- When quality of life and quantity of life are both important outcomes.
 E.G..... Neonatal Intensive Care
- When there is a wide variety of disparate programs that must be compared. e.g...... Typical health planner's problem.







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When Should CUA Not Be Used?

- Only intermediate outcome data are available
- Effectiveness data show new program is dominant (less costly and more effective)
- Extra cost of doing CUA are not costeffective
 - results of CEA highly likely to be reinforced by CUA





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Early Example of CUA

- Treatment: Neonatal intensive care for small babies
- Costs: incremental costs of:
 - Neonatal period (hospitalization & physician)
 - Follow-up (re-hosp., Physician visits, appliances, Rx, special services, special education).
- Effects: incremental changes in QALYs.
 - Community assessment of quality of life in alternative health states.

Source: Boyle, Torrance, Sinclair et al (1983), NEJM, p. 1330.

Defining CUA CUA Scope Utility Types Utility Theory CUA Evaluation Process

Ways To Obtain Utility Values

- Use pre-scored multi-attribute health status classification system
 - Quality of well-being (QWB)
 - Health utilities index (HUI)



- **EuroQol** (EQ-5D)
 - SF-6D classification system
 - Tufts CEA Registry
- Values from own MEASUREMENT
- Judgment of EXPERTS (not recommended)

Defining CUA

CUA Scope



Utility Theory

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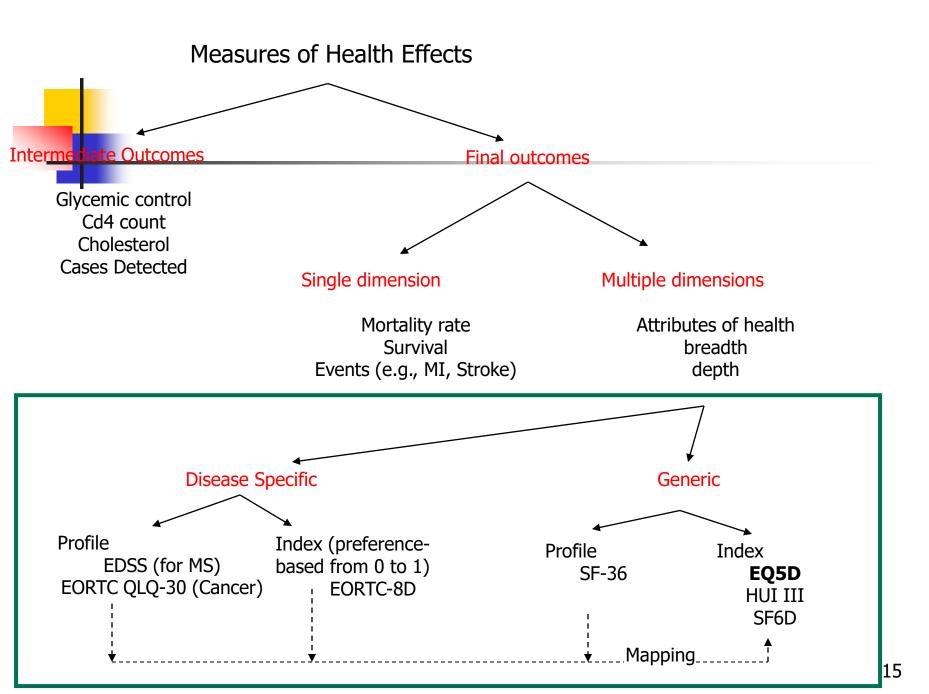


Source for Pre-scored Utility Weights

- Tufts New England Medical Center Web Site (comprehensive list of cost-utility ratios in health and medicine) CEA Registry
- Global Health CEA Registry(DALYS) GH CEA Registry
- Health Utility Indexes Canada http://www.healthutilities.com/



Fig. 5.1 Taxonomy of measures of health effects





Alternative Health Related Quality of Life (HRQL) Measures

- Generic vs. Disease specific instruments
 - HRQL Profile
 - Non preference based measure may be used for CEA.
 - HRQL Index:
 - Preference measurement of HRQL on 0 death to 1 perfect health scale is preferred

for economic evaluations*



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Disease Specific Profile: Not Preference Based

- Designed to detect those aspects of HRQL in the disease or condition of interest.
- Expected to have <u>higher responsiveness</u> to change in health
- May not be relevant to other conditions.
 - Example: EORTC QLQ-30 for cancer.
 - Modified Rankin Score for Stroke.



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Generic Profile: Not Preference Based

- Allow <u>comparisons across</u> programs and conditions
- Not responsive to fine but important differences between conditions for some treatments
- May pick up <u>unexpected beneficial or adverse</u> <u>effects</u> missed by disease specific questionnaire.
- Examples: SF-36, Sickness Impact Profile, Nottingham Health Profile, <u>PROMIS</u>.







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- Provide a single summary score of HRQL
- Scaled from 0 (death) to 1 (perfect health)
- Encompasses how respondents feel about one health state vs. other health states.*
- Examples:
 - Health Utilities Indexes (HUI), EuroQol (EQ-5D), SF-6D.

What is a health state?

EQ-5D-5L



 $5^5 = 3,125$ different possible health states

1 = no problem

2 = slight problem

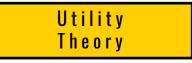
3 = moderate problem

4 = severe problem

5 = unable to/extreme

A unique health state is defined by combining 1 level from each of the 5 dimensions

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Euro qual (EQ-5D-3L)



5 domains with **3 levels (less variance)** each domain; 243 possible health states (3x3x3x3x3)

Mobility:

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Self-Care:

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Values are generated from TTO (USA) or VAS methods; may suffer from "ceiling effects"; inability to detect small changes in health status **for people** with mild conditions.

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- **Usual Activities** (e.g., work, study, housework, family, or leisure activities):
- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

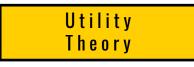
Pain/Discomfort:

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/Depression:

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

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Euro qual (EQ-5D-5L)



5 domains with 5 levels each domain; 3,125 possible health states (5x5x5x5x5)

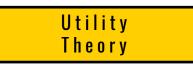
Each of the 5 Health States has 5 levels

Mobility Example:

- I have **no** problems in walking about
- I have slight problems in walking about
- I have moderate problems in walking about
- I have severe problems in walking about
- I am confined to bed

Values are generated from Time Trade Off (TTO) and Visual Analog Scale (VAS) methods

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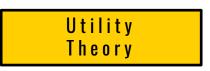


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Utility Theories: basis of preference concept

- 19th century economists: cardinal utility measurement (give choice A, B a value)
- 20th century economists: ordinal utility measurement (we prefer B to A but no magnitude is given)
- 1940s von Neumann & Morganstern (vN-M)
 - Individual choice under uncertainty
 - Normative theory with 3 axioms

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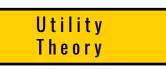


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Normative Approach

- VN-M decision theory does not describe how individuals actually make decisions in the face of uncertainty, but how they <u>ought to</u> <u>make</u> such decisions if they wish to act rationally, as defined by the basic axioms.
- Aids judgment for complex and important decision problems.





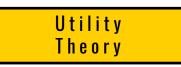
vN-M Axiom 1

Preferences exist:

 For any pair of risky prospects a and b, either a is preferred to b, b is preferred to a, or the individual is indifferent between a and b.

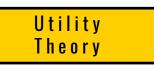
Preferences are transitive:

- For any three risky prospects, a, b, and c, if a is preferred to b, and b is preferred to c, then a is preferred to c.
- Similarly, if a is indifferent to b, and b is indifferent to c, then a is indifferent to c.



Axiom 2: Independence

- An individual should be <u>indifferent between a two stage risky prospect and its</u> <u>probabilistically equivalent one stage</u> <u>counterpart</u> derived using the ordinary laws of probability.
- a \rightarrow x1 with prob. p1 and b \rightarrow x2 with prob. p2 is equal to a \rightarrow x2 with prob. p1*p2





- If there are three outcomes such that x₁ is preferred to x₂, which is preferred to x₃, there is some probability p at which the individual is indifferent between
 - 1. 100% probability of outcome x₂ or
 - 2. Receiving the risky prospect made up of outcome x₁ with probability p and outcome x₃ with probability (1 -p).





Utility Types





Reliability & Validity of Utility Measures

Reliability - Consistency

By taking average values from large groups of raters, consistent results have been obtained for measuring health state utilities. **Individual raters are not highly reliable.**

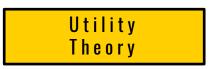
Validity - Does the measure accurately reflect the concept or phenomenon that it claims to measure?

Do results correlate with other indicators of health status, e.g. how do nephrologist's assessment of patients quality of life compare with those obtained by utility measurement?

Face Validity: Are conditions described as worse rated worse?

 Sensitivity Analysis — assess how results change with alternate measures of utility.

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Summary Measures of Test Retest Reliability

VAS: correlations of 0.62 to 0.95

TTO: correlations of 0.63 to 0.81

SG: correlations of 0.53 to 0.83

EQ-5D: correlations of 0.63 to 0.80

HUI: correlations of 0.71 to 0.80

SF-36: correlations of 0.60 to 0.81

Feeney et al. 6th World Congress of International Health Economics Association not by International Society for Pharmacoeconomics and Outcomes Research, Lund Sweden 2007.

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Does choice of reference population affect scores?

- Preference scores do not systematically vary by:
 - race, income, and gender (this conclusion was not supported by Nyman et al 2007 for EQ-5d)
 - Prior experience with rated health state
 - Populations in different countries and places within countries

Drummond et al. pp. 172

 "Differences that exist from the geographic factor are small compared to the differences that exist among instruments".

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HOW TO CONDUCT A CUA

- Define Problem/ Question (similar to CBA & CEA).
- Determine health states and corresponding utility weights.
- Determine health state of each study subject at baseline and during discrete periods of time during the follow-up period (e.g. every 3 months).

Utility Theory



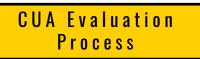
STEPS IN UTILITY MEASUREMENT Multi-attribute Utility Function

- Identify health states for each study subject for each discrete time period during the follow-up period.
- Calculate QALYs for each subject during the follow-up period by combining time and utility weights, e.g. if a subject lives 3.5 years in a health state with util. of .7, assign (3.5*0.7) or 2.45 QALYs.
- Conduct sensitivity analysis based on variance (confidence limits) on utility measures.



CUA Process

- Multiply utility values by time in each health state for each subject and sum across individuals & divide by N to obtain average QALY's.
- Collect cost data independent of the ratings.
- Compute incremental Cost Utility ratios
- Apply Decision Rule
 - select those alternatives that will provide the highest level of utility for any total cost constraint.



Summary Statistics for HUI® Reference Scores of Health-Related Quality of Life

HUI3: USA

Females and Males in General Population

Age 18 years and older

Ages (yrs)	n	Mean	Error	Bound	Bound	Median
18-44	2377	0.858	0.0064	0.845	0.871	0.93
45-64	1060	0.781	0.0120	0.757	0.805	0.86
65+	470	0.697	0.0157	0.666	0.729	0.78
All ages	3907	0.812	0.0065	0.799	0.825	0.91

From "HUI Reference Scores" section of www.healthutilities.com. © Health Utilities Incorporated, Dundas ON, Canada. All rights reserved.

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Preference Weighted Generic Instruments (Index): EQ-5D-5L

Gender	Age	Mean	SD	95% CI	Median
Male	<25	0.906	0.157	0.86-0.95	0.94
Female	<25	0.931	0.085	0.91-0.96	0.94
Male	25-34	0.907	0.114	0.89-0.93	0.93
Female	25-34	0.916	0.107	0.90-0.93	0.93

Jiang R, Bas Janssen MF, Pickard AS. US population norms for the EQ-5D-5L and comparison of norms from face-to-face and online samples. Quality of Lifes Research. 2021;30:803-816

Gordon H. Guyatt, C. et al. for the Evidence Based Medicine Working Group **How to Use Articles About Health-Related Quality of Life Measurements** JAMA. (1997;277(15):1232-1237)

Muennig, P (2008) <u>Designing and Conducting Cost-effectiveness analyses</u>. Josey-Bass, San

Francisco, CA.Chapter 8. Defining CUA

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CUA Evaluation Process



Table 5.1 Methods of Measuring Preferences

Response Method	Question Framing	
	Certainty (values)	Uncertainty (utilities)
Scaling	Rating Scale Category Scaling VAS, Ratio Scaling	2
Choice	Time trade-off Paired comparison Equivalence Person trade-off	Standard gamble

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Most Common methods for measurement of QALY weights

Methods

- Rating scale/VAS
- Time trade-off
- Standard gamble

Raters

- Patients
- General public

Rating Scale



Subjects are asked to identify best and worst health states. She is then asked to locate other health states on a rating scale relative to each other such that distances between locations are proportional to her preference differences.

1-----0.

Perfect health

death

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If death is worst case (0).

The preference value of a state is scaled according to its placement.

■ If death is not the worst case and is placed at some value say d = .05, the preference values for other state, xi, is given by:

Vi =
$$(xi - d) / (1 - d)$$
; If $x = .75$.
Then vi = $(.75 - .05) / (1 - .05)$.
Vi = .736.

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- Does not capture subject's <u>risk attitude</u>
- Scaling, unlike choice is NOT a natural human task
- Measurement biases
 - Subjects refrain from using ends of the scale
 - Tend to space out outcomes over scale regardless of the outcome

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Advantages of Scaling

- Simpler to administer compared to choice measures.
- May convert scale values to standard gamble or time-trade-off scores with a power curve.
 - Utility = 1-(1-value) r , where r=1.6 to 2.3 Torrance (1996)

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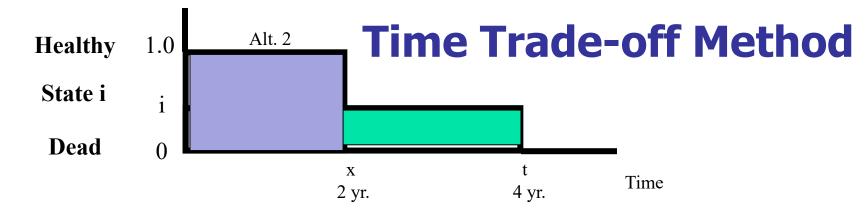
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Choice: Time Trade-off (TTO)

- A method of measuring value by finding the point at which the respondent is indifferent between two health states for different lengths of time.
- There is choice but no uncertainty
- Limitation:
 - TTO scores are not vN-m utilities.





A. Chronic health state.

The subject is again offered two alternatives.

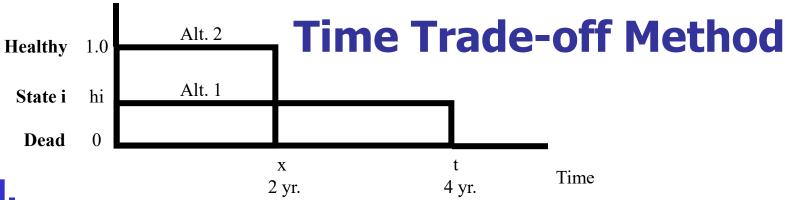
Alt. 1 is *state i for time t* (life expectancy of an individual with the chronic condition) followed by death;

Alt. 2 is healthy for time x < t followed by death.

You prefer adding additional year of life now versus later

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Method.

Time x is varied <u>until the respondent is *indifferent between*</u> the two alternatives, at which point the preference value for state i is given by:

$$H_i = x / t$$
.

Thus, as x increases h_i increases ------ as x approaches t you are willing to give up less and less time in order to avoid the chronic state of health i. This implies the chronic state i is not much worse than being "healthy".

As x approaches 0 you are willing to give up most of the rest of your life to avoid health state i.

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Standard Gamble (SG): choice with uncertainty to measure utility

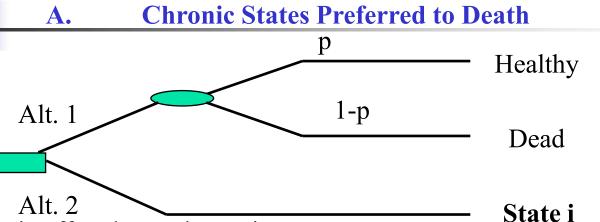
- A method of directly measuring utility, founded directly on the fundamental von Neumann-Morgenstern axioms of expected utility theory.
- A utility score is revealed by finding the probabilities in the gamble for which the respondent is indifferent between an uncertain alternative (the gamble) and a definitive alternative.

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Standard Gamble

Classical method for measuring cardinal preferences, based on the fundamental axioms of utility under uncertainty (von-Nueman and Morgenstern (1953))



The subject is offered two alternatives.

Alt. 1 is treatment with two possible outcomes

- Return to normal health and live t years with a p% prob.
- Immediate death with a probability of (1-p)

Alt. 2 is certain outcome of chronic state i for t years.

Gamble (Alt 1) a 0.50 probability (p) of living healthy for 10 years (life expectancy) and a 0.50 probability (1-p) of immediate death, to avoid a 100% chance of stroke for 10 years (state i), the utility of stroke is 0.5 (p)

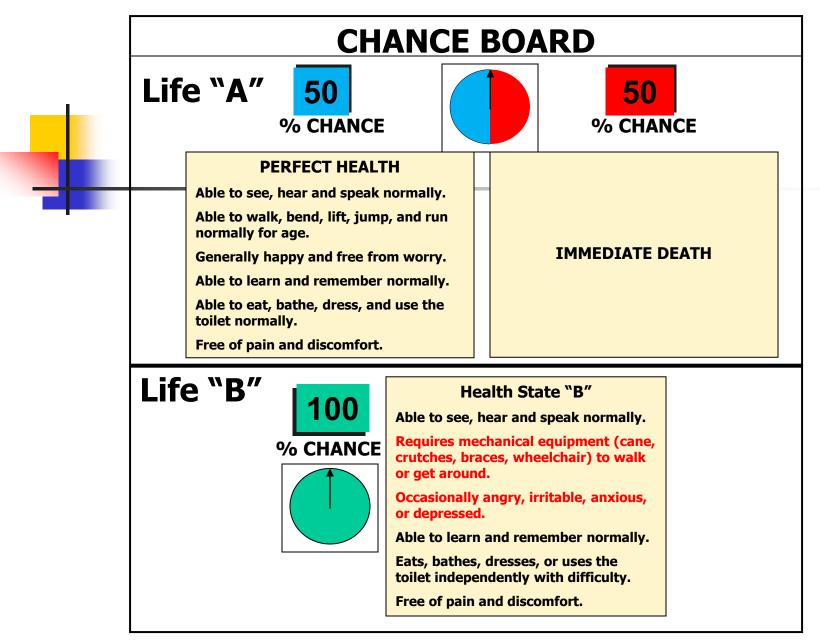
Probability p is varied until the person is indifferent between two

alternatives, at which point **the preference value of chronic state i is p**.

Defining CUA

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Standard Gamble Chance Board Utility of Health State B=?

0.5

CHANCE BOARD Life "A" 80 20 % CHANCE % CHANCE PERFECT HEALTH Able to see, hear and speak normally. Able to walk, bend, lift, jump, and run normally for age. **IMMEDIATE DEATH Generally happy and free from worry.** Able to learn and remember normally. Able to eat, bathe, dress, and use the toilet normally. Free of pain and discomfort. Life "B" Health State "B" Able to see, hear and speak normally. Requires mechanical equipment (cane, % CHANCE crutches, braces, wheelchair) to walk or get around. Occasionally angry, irritable, anxious, or depressed. Able to learn and remember normally. Eats, bathes, dresses, or uses the toilet independently with difficulty. Free of pain and discomfort.

Standard Gamble Chance Board Utility of Health State B=?

8.0

CHANCE BOARD Life "A" 90 % CHANCE % CHANCE PERFECT HEALTH Able to see, hear and speak normally. Able to walk, bend, lift, jump, and run normally for age. **IMMEDIATE DEATH Generally happy and free from worry.** Able to learn and remember normally. Able to eat, bathe, dress, and use the toilet normally. Free of pain and discomfort. Life "B" Health State "B" Able to see, hear and speak normally. Requires mechanical equipment (cane, % CHANCE crutches, braces, wheelchair) to walk or get around. Occasionally angry, irritable, anxious, or depressed. Able to learn and remember normally. Eats, bathes, dresses, or uses the toilet independently with difficulty. Free of pain and discomfort.

Standard Gamble Chance Board



Advantages of Standard Gamble

- Strong normative foundation based on theory of choice under uncertainty.
- Applicable to situations involving either certainty or uncertainty.
- Choice based methods are natural tasks with which individuals have experience.







Disadvantage of SG Method

- More difficult to administer than visual analogue scales.
- vN-m theory <u>only directly applies to</u> <u>individual</u> decision-making
 - To apply to society, must assume "that society is a single individual with utilities equal to the mean utilities of the community" (Drummond et al., 2005; Pp. 146-47).

CUA Evaluation Process

Well established utility indexes

(E.G.... Health Utilities Index, Quality of Well-being, EuroQol)

- Factors to Consider in selecting an index:
 - No head to head comparisons of these methods are available
 - Select in advance one that best suits the study objectives
 - Justify the selection in the study protocol
 - SG incorporates choice & uncertainty

Canadian Guidelines, 1994

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Additional issues in instrument selection

- Is the instrument creditable (demonstrated feasibility, reliability, validity, and responsiveness in studies)?
- Does the health status classification system cover the attributes and levels of attributes important to the study?
- Is the instrument likely to be responsive to changes expected?
- Does the intended audience for the study have any preference or guidance in selection of the instrument?
- Is the instrument based on sound theory?
- How much time is required to complete the questionnaire and is the questionnaire clear and easy to follow?

Summary

- Utility measurement is important for economic evaluation of health programs.
- Measurement of utility is highly complex.
- Utility and quality of life assessments are being <u>increasingly applied</u> in health economic evaluations.
- Different methods (e.g., TTO vs. VAS vs. SG) may result in varying scores for the same health state.
- Groups with different clinical conditions may have varying scores for the same health state
- Dr. Sun to demonstrate how utility assessment is clinically used in the oncology/research setting on Oct. 12

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Utility Theory CUA Evaluation Process