



SCIENCE



CONNECTIONS



ACTION

Part V: Cost-Effectiveness Analysis

Outcomes in Natural Units: The Fifth of a Five-Part Series

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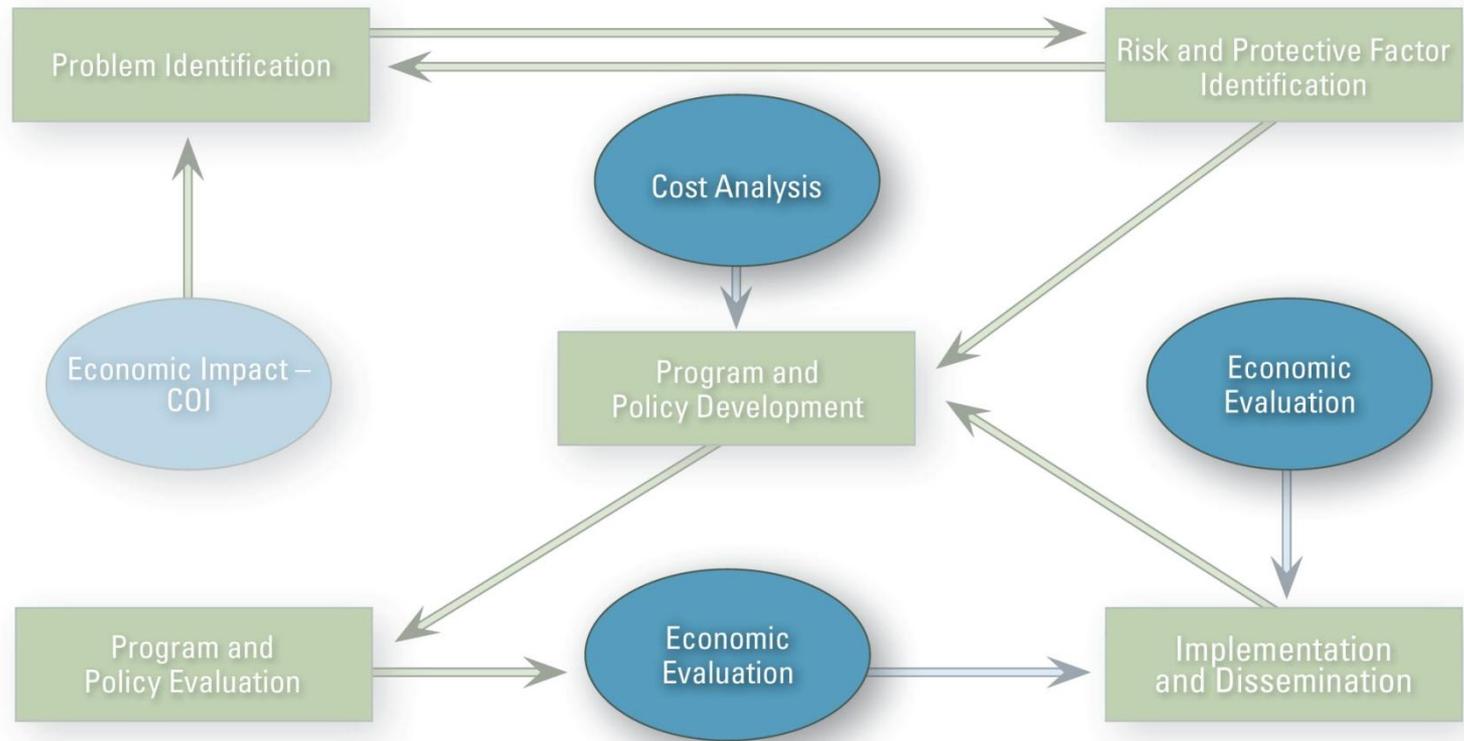


Heart Disease
& Stroke Prevention

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The last module discusses another type of economic evaluation: cost-effectiveness analysis.

Public Health Model for Prevention



As discussed in the benefit-cost analysis module, economic evaluations are best conducted once a program, policy, or intervention has proven effective but prior to widespread implementation and dissemination. In this way, economic evaluations are typically conducted retrospectively.

However, an economic evaluation is often conducted prospectively, alongside community or clinical trials. Either way, an economic evaluation conducted *before* implementation is the best way to ensure efficient allocation of scarce public health resources.

Cost-Effectiveness Analysis (CEA)

- Estimates costs and outcomes of interventions.
- Expresses outcomes in natural units.
 - e.g., cases prevented, lives saved.
- Compares results with other interventions affecting the same outcome.

As with benefit-cost analysis, a cost-effectiveness analysis compares an intervention's costs to its outcomes.

Unlike a benefit-cost analysis, a cost-effectiveness analysis expresses outcomes in natural health units, such as the number of cardiovascular disease cases prevented or the number of lives saved, instead of converting outcomes to dollars.

Because of this major difference, cost-effectiveness analysis must be conducted with interventions or programs that impact the same health outcome. For example, you could compare two programs designed to prevent overweight or obesity, where one program focuses on physical activity and the other focuses on nutrition.

CEA — Summary Measures

Average Cost-Effectiveness Ratio	Incremental Cost-Effectiveness Ratio
$\frac{\text{Net Costs}_A}{\text{Net Effects}_A}$	$\frac{(\text{Net Costs}_B - \text{Net Costs}_A)}{(\text{Net Effects}_B - \text{Net Effects}_A)}$

Where Net Costs = Program Costs_A – COI Averted

The summary measure in cost-effectiveness analysis is the ratio of net programmatic costs divided by net program effects. Programmatic costs are program costs minus the cost of illness averted by the program.

Cost-effectiveness ratios can be an average. One intervention at a time is assessed in terms of net costs divided by net effects.

Two or more programs affecting the same health outcome can be compared in terms of incremental net costs of one program compared to another, divided by incremental net effects of one program compared to another.

Quantify Outcomes — CEA

- Intermediate outcomes:
 - Increased physical activity.
 - Decreased blood pressure.
- Final outcomes:
 - Heart disease cases prevented.
 - Lives or life years saved.

Outcomes or effects included in cost-effectiveness analysis can be narrowly or broadly defined, although for decisions bearing on public policy, broad definitions are preferred.

Narrowly defined effects include those that are intermediate in nature and that may be easier to capture, such as immediate increases in physical activity or decreases in blood pressure associated with a hypertension intervention.

However, more broadly defined effects are those that are more final and further removed, such as cases of heart disease prevented, lives saved, or life years saved.

These broad outcomes are more appealing in terms of effectiveness goals for a hypertension intervention. However, you may only have intermediate outcomes to work with unless you can follow intervention participants over time or find good epidemiologic evidence linking intermediate to final outcomes.

CEA Caveat

- Outcomes cannot be combined; they must be considered separately. Consider one or two of the most important measures.
- Number of summary measures depends on number of outcomes chosen.
 - If A and B are the most important, then:
 - Cost/outcome A.
 - Cost/outcome B.
- Translation for policy-makers can be difficult.

A major caveat in conducting cost-effectiveness analysis is that outcomes in natural units cannot be combined and must be considered separately.

For example, a physical activity program may have two intended effects: lowering blood pressure and decreasing body mass index. Because these two effects can't be combined in a cost-effectiveness analysis, the summary measure for the analysis would be cost per 1 percent reduction in blood pressure and cost per 1 percent decrease in body mass index. However, the cost in these two summary measures is the same, so the ratios are somewhat misleading. This makes cost-effectiveness ratios using natural units difficult for policy makers to translate.

Cost-Utility Analysis — CUA

- Compares costs and benefits, where benefits = # of life years saved *adjusted* for loss of quality.
- Combines length and quality of life.
- Compares disparate outcomes in terms of utility.
 - Quality-adjusted life years (QALYs).
 - Disability-adjusted life years (DALYs).
- Derives a ratio of cost per health outcome.
 - \$/QALY or \$/DALY

One method to deal with the problem of multiple outcomes, particularly if there are multiple health outcomes, is to conduct a cost-utility analysis. In this type of analysis, outcomes are expressed as a health index that combines all health outcomes associated with an intervention in terms of increases in length of life and quality of life.

Length of life adjusted by quality of life is known as a quality-adjusted life year, sometimes referred to as a disability-adjusted life year.

In a cost-utility analysis, you could compare interventions that affect different health outcomes with the use of a quality-adjusted life year. For example, comparing interventions that affect obesity, nutritional outcomes, and cardiovascular disease.

The summary measure in a cost-utility analysis is cost per quality-adjusted life year or cost per disability-adjusted life year.

When Is CUA Used?

- When quality of life is **the** important outcome.
- When the program affects both morbidity and mortality.
- When programs being compared have a wide range of outcomes.
- When one of the programs being compared has already been evaluated using CUA.

Cost-utility analysis is used when quality of life, rather than length of life, is the most important effect of the intervention.

For example, a cost-utility analysis of a cardiac rehabilitation program might focus on improved quality of life versus the cardiac rehab's influence on the length of life.

Cost-utility analysis also is used when the program affects both morbidity and mortality outcomes. An example is emergency medical services pre-hospital stroke care, which has long-term effects on recovery and disability.

Cost-utility analysis can be used when comparing interventions that affect different health outcomes, like cancer versus cardiovascular disease prevention.

Finally, cost-utility analysis should be used when comparing results to other studies also employing cost-utility analysis as the economic evaluation methodology.

Quantify Benefits — CUA

- Utilities, or preference weights, are:
 - A quantitative approach for describing *preferences* for quality of life.
 - Typically based on a 0 to 1 scale, where:
 - 0 = death.
 - 1 = perfect health.

Utilities, or preference weights, are a way to quantitatively describe consumer preferences for a good quality of life and a subjective measure of the usefulness that results from being in different health states.

Because utilities are quantitative, they are measurable and analyzable. They're typically based on a 0 to 1 scale, where 0 is considered death and 1 is considered perfect health.

To quantify benefits in a cost-utility analysis—that is, to derive a quality-adjusted life year—you need to know the intervention's effect on length of life and quality of life. Data on length of life may be readily accessible from epidemiologic literature.

Effects on quality of life, however, are theoretically derived from individuals directly as their preference weights or utilities for the health state under consideration. For example, what is the preference for having a body mass index above 35 versus having one between 25 and 35?

Utilities: Direct Measurement

		Question Type	
		Certainty “value”	Uncertainty “utility”
Response Method	Scale	Rating Scale	
	Choice	Time Trade-Off	Standard Gamble

There are a number of ways to directly elicit utilities. There are methods that rely on a specific response method, such as scale versus choice, and methods that rely on a specific type of questioning format, such as asking about certain events versus uncertain events.

Theoretically, to be considered an economic “utility,” the response method must be a choice and the questioning format must include an uncertainty. Therefore, the only correct way to derive utilities for health states is the standard gamble approach, although other approaches are popular in the literature.

Standard Gamble Approach

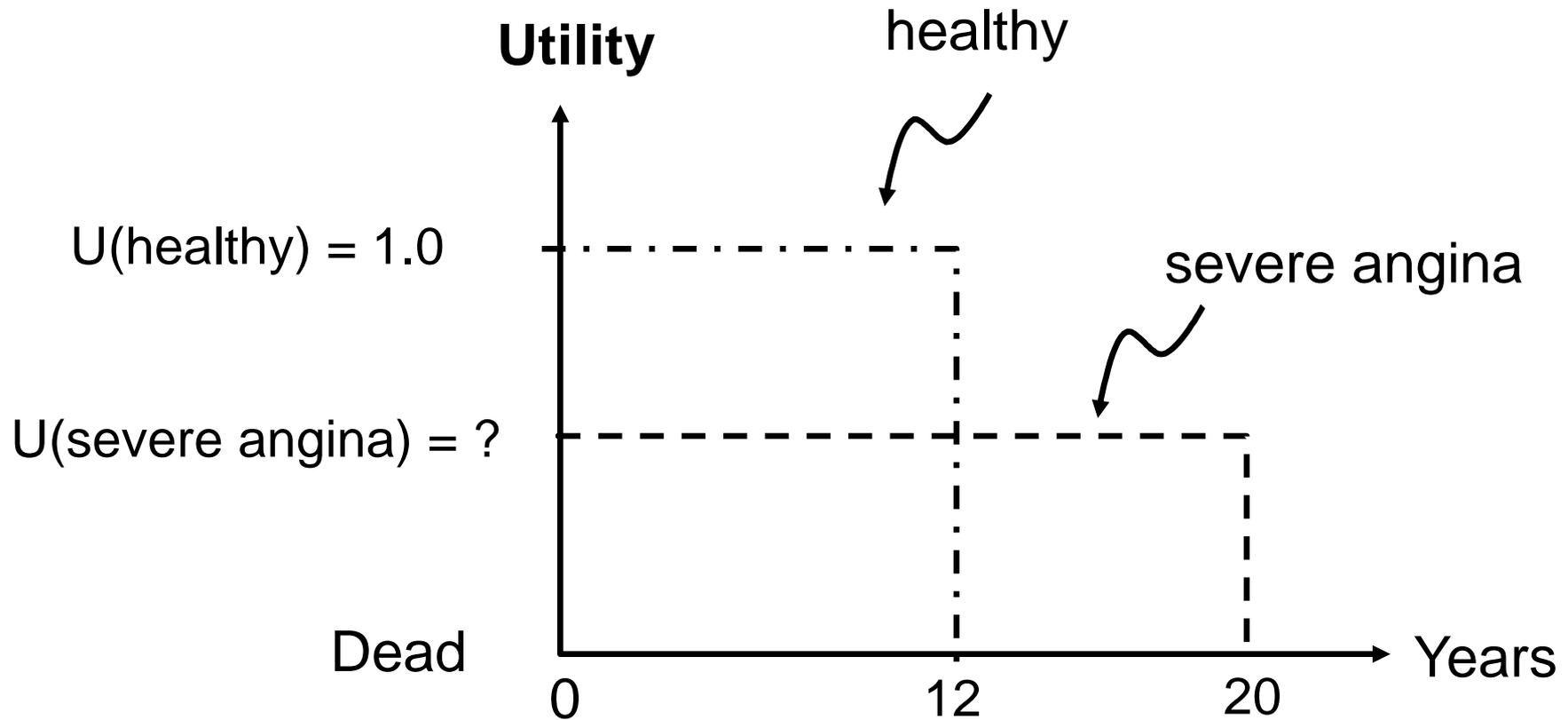
- The gold standard in utility elicitation.
 - Respondent must choose between two options:
 - Living with below-optimal health.
 - A lottery between two uncertain health states, for example:
 1. Good health with probability x .
 2. Bad outcome with probability $(1-x)$.
- Limitations
 - Time consuming.
 - Cognitively difficult for many people.

The standard gamble approach is based on the conceptual framework for examining decisions under uncertainty. The respondent is given a choice between a less than optimal health state, for example, having a body mass index above 35, and a lottery between two uncertain health states. The two uncertain health states are often perfect health and death and can be valued as 1 and 0, respectively. The two uncertain health states don't have to include perfect health and death. The only requirement is that the certain health state be in between the two outcomes associated with the gamble.

In this setup, the respondent is asked something like this: Imagine you have a body mass index above 35, with no other adverse health outcomes. Now suppose there's a surgery available to you that would reduce your body mass index to a perfect level, thus giving you perfect health. However, there's a probability of death associated with the surgery. How low does the probability of death have to be for you to be indifferent between your certain health, with a body mass index above 35, and the gamble of taking the surgery, which could lead to death or perfect health?

The probability, or p value, derived from this scenario reflects the utility for the certain health state under consideration, in this case body mass index above 35.

Time Trade-Off



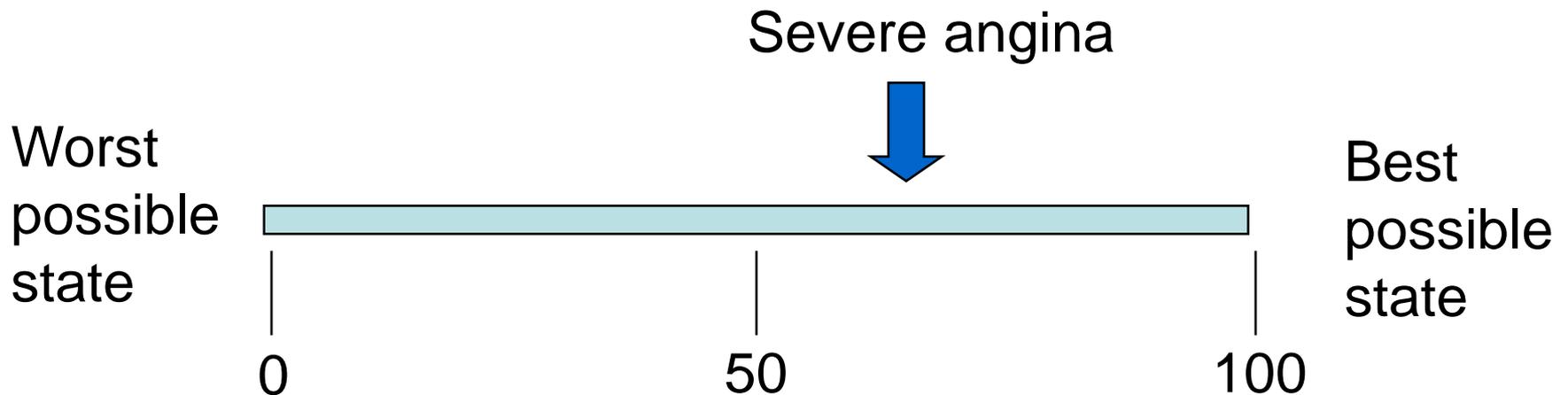
Another way to directly elicit utilities is the time trade-off method, which was developed as an alternative to the standard gamble. This method is used primarily in health research. The respondent is offered a choice between two alternatives of certainty. The goal is to find the point where the person becomes indifferent between the two alternatives.

Here's the setup: Imagine that your remaining life expectancy is 20 years. How much of your remaining life expectancy would you give up to eliminate your severe angina so that you have perfect health?

The number of years you would give up, divided by the remaining life expectancy and subtracted from 1, represents the utility associated with severe angina.

Rating Scale

- Does not involve trade-offs, not a valid measure of utilities.
- Simple, easy to administer.



Finally, the rating scale is the most common approach to directly eliciting utilities.

This involves ranking alternatives and then placing them on an ordinal scale. For example, alternatives might include perfect health, mild angina, severe angina, and death. This example uses a visual analog scale, which is typically horizontal.

There are a couple of advantages of this approach. The cognitive burden is less than with other techniques, and people are familiar with the technique.

There are several disadvantages, however. First is the anchoring effect. What is set as the best possible state and the worst possible state is subjective, creating an indexing problem.

In addition, we can't make any interpretations about the numbers themselves, such as 88 versus 60, because of the ordinal scale.

Furthermore, people have an aversion to the end of the scale. Therefore, they treat the middle of the scale as one scale and the ends of the scale as another scale.

There are also context effects. Ranking and scoring depend not just on the states themselves, but also on the states being compared.

Finally, this approach is based on conditions of certainty and not really tied to utilities or the theoretical foundation cost-effectiveness analysis is based on.

Where to Get QALY Weights?

Source	Examples	Disadvantages
Literature	<ul style="list-style-type: none">• Individual studies• CUA databases	<ul style="list-style-type: none">• Lack of comparability
Indirect measures	<ul style="list-style-type: none">• Beaver Dam study, QWB• Joint US-Canadian health survey included HUI• MEPS included EQ-5D US	<ul style="list-style-type: none">• Only common diseases• No severity levels
Direct measures	<ul style="list-style-type: none">• Expert panel• Special sample survey	<ul style="list-style-type: none">• Expense• Time• Representation

In addition to directly eliciting utilities, there are published preference weights in the literature from individual studies. Compendia of weights are available online at the Tufts Medical Center Web site.

The disadvantage of using weights derived from other studies is comparability. It could be that weights are derived from different populations, for slightly different health outcomes, etcetera.

As an alternative, there are widely available, indirect elicitation tools that involve people classifying their health states based on a number of domains of health, such as physical functioning, role, social, and emotional, then applying directly elicited preference weights. Many such tools are available, sometimes for a small fee.

The disadvantages of these tools are that their weights may be derived from dissimilar populations, they may not have included the same health outcome you are considering, and they may not have included the same severity levels.

The direct measures we discussed should be elicited from general populations, but expert panels or special disease-specific samples are often used. Major disadvantages are costs, time to collect, and representativeness outside your study.

QALY Weights for Chronic Diseases

- Data from MEPS, 2000–2002.
- Regression methods used to estimate disutility for 95 ICD-9 codes, controlling for:
 - Age, gender, comorbidity, race/ethnicity, income, education.
- Results—Marginal disutilities:

– 389	Hypertension	-0.0250
– 410	Acute MI	-0.0409
– 427	Dysrhythmia	-0.0190
– 428	Heart failure	-0.0635

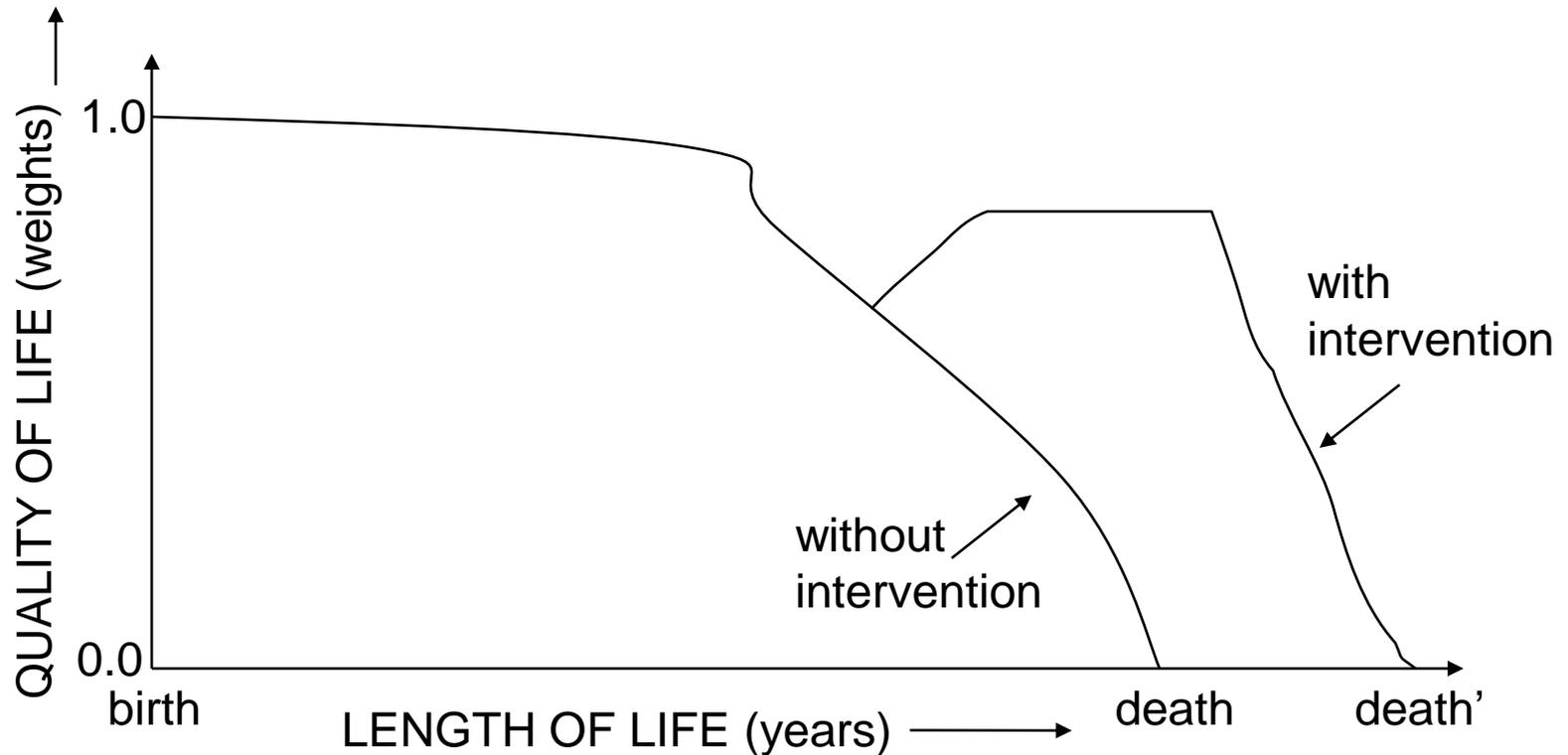
Sullivan & Ghushchyan, *Medical Decision Making* 2006.

Here's an example of an indirect utility elicitation tool using the EuroQol 5 dimension scale included in the medical expenditure panel survey for a few years in the early 2000s. Examples of decreases in utilities, or disutilities, are shown for a number of chronic diseases.

Here's how you can interpret these results: Imagine a person with chronic hypertension with a remaining life expectancy of 20 years. You could say that the person has a quality-adjusted life expectancy of 19 years and 6 months—or a loss of 6 months in quality-adjusted life expectancy. This is derived by multiplying .025 by life expectancy to get .5 years, or 6 months.

Valuation of Benefits in a CEA

Combining Length of Life with Quality of Life



Once the utilities are determined for the effects of the intervention, the difference in quality of life and length of life between the intervention and no intervention in this example can be compared.

Cost-Effectiveness of a Health Promotion Program

- Evaluation of WISEWOMAN program:
 - Program cost \$440 per 1% reduction in cardiovascular disease risk.
 - Cost-effectiveness ratio estimates:
 - \$4,400/life year with optimistic assumptions.
 - \$15,300/life year with more realistic, long-term outcomes.
 - \$133,500/life year if changes assumed to last only 1 year and only for those with follow-up.
 - Conclusion: Cost-effectiveness depends on long-term outcomes, which are not known.



Here's an example of a cost-effectiveness analysis of the WISEWOMAN program. The unit of effectiveness was reduction in cardiovascular disease risk, which was then translated, based on epidemiologic evidence in the literature, to life years gained. The uncertainty in the analysis was how long the changes in the cardiovascular disease risk were assumed to last, thus affecting life years saved and costs per life years saved.

The program was assessed in relation to itself, not compared to other interventions, which produced an assessment of the average cost-effectiveness ratio. As a result, the authors found that the program cost 440 dollars per life year under the most optimal assumptions, which would be changes in cardiovascular disease risk assumed to last a lifetime.

But when more realistic, longer-term outcomes were evaluated, the costs increased to 15,300 dollars per life year saved. These changes in cardiovascular disease risk were assumed to last for the lifetime of only 24 percent of the participants.

Costs were more than 133,000 dollars per life year saved when the cardiovascular disease risk changes were assumed to last only 1 year and not longer.

This study shows the importance of having longer-term, final outcomes in the cost-effectiveness analysis.

Interpreting Cost-Effectiveness Ratios

- Some assume that only interventions with ratios $< \$50,000$ or $< \$100,000$ are “cost-effective.”
 - UK uses a threshold of £30,000 per QALY.
- These are arbitrary thresholds.
 - Round numbers.
 - Not adjusted for inflation.

Unlike in benefit-cost analysis, where the summary measures are objective, cost-effectiveness analysis results in a *subjective* summary measure. The policy maker must still determine the threshold below which an intervention is considered cost-effective and above which an intervention is not considered cost-effective.

Some arbitrary thresholds have been set both in the United States and the United Kingdom, but there is still some controversy about these thresholds, particularly because the cost-effectiveness ratios haven't been adjusted for inflation.

Decision Rules and League Tables

\$14,000/QALY ≤ CE Ratio < \$35,000/QALY		
Hypertension Screening	Hypertension, Screening, Counseling, and Treatment	Measure blood pressure routinely in all adults and treat with antihypertensive medication to prevent incidence of cardiovascular disease.
Cervical Cancer Screening	Cervical Cancer, Screening	Screen women who have been sexually active and have a cervix within 3 years of onset of sexual activity or age 21 routinely with cervical cytology (Pap smears).

Adapted from Maciosek et al., *American Journal of Preventive Medicine* 2006.

One way to determine threshold values is to compare cost-effectiveness ratios to ratios published in the literature or to ratios for interventions commonly accepted as good practice.

Here are a few examples of cost-effectiveness ratios in chronic diseases and the ranges they fall within.

Lessons from Research

- Paper by Grosse, Teutsch, and Haddix covered:
 - Birth defects prevention.
 - Newborn screening.
 - Cervical cancer screening.
 - Childhood immunization.
 - Blood product safety.
- Conclusions:
 - Economic evaluation not consistently informing policy.
 - Missed opportunities.
 - No evidence of consistent threshold for cost effectiveness.

The Grosse and colleagues 2008 paper specifically discussed the use of economic evaluations to inform public policy. The authors found no consistent use of economic evaluations to inform public policy in the United States. The same cannot be said in the United Kingdom, where economic evaluations are part of how the National Health Service determines which benefits are covered.

The authors also found many missed opportunities and no clear thresholds for cost-effectiveness analysis in whatever policies were informed by economic evaluations.

More on Cost-Effectiveness Ratios

- A continuum, not a decision rule.
- Low ratios, $< \$30,000/\text{QALY}$, are a good value.
- High ratios, $> \$300,000/\text{QALY}$, seldom good value.
- Intermediate ratios are difficult to assess.
- Different standards for prevention vs. treatment and clinical vs. population-based interventions.



We might think of the cost-effectiveness ratio on a continuum but without an actual rule for policy making. There are some ranges within which an intervention is clearly a good value, and other ranges within which an intervention is clearly not. It's the intermediate cost-effectiveness ratios that require some subjectivity on the part of policy makers.

Furthermore, a different set of standards seems to apply to policy making in the treatment or clinical world compared to the prevention or population-based health world.

But this discrepancy is due in part to the newness of economic evaluations to prevention and public health. Much of the acceptance of economic evaluations for informing policy making and standardizing practices comes from education modules like this that introduce the concepts to the field. Much has been done in public health since the early 1990s, but there's still a ways to go.

Lessons of Cost-Effectiveness Research for Cardiovascular Disease Prevention

- Preventive strategies with lowest CE ratios:
 - Secondary prevention with statins in hyperlipidemia.
 - Smoking cessation programs.
 - Primary prevention in treatment of high blood pressure with diuretics and beta-blockers.
 - Primary prevention with regular exercise programs.
 - Secondary prevention with cardiac rehabilitation.
 - Postinfarction treatment with beta-blockers and angiotensin-converting enzyme (ACE) inhibitors.

In the cardiovascular disease field, Probstfield and colleagues noted that prevention strategies with the lowest cost-effectiveness ratios included secondary prevention with statins in high cholesterol, smoking cessation programs, primary prevention in treatment of high blood pressure with diuretics and beta-blockers, primary prevention with regular exercise programs, secondary prevention with cardiac rehabilitation, and post-infarction treatment with beta-blockers and angiotensin-converting enzyme inhibitors.

DALYs

- Developed to quantify burden of disease and disability.
- Applications:
 - Used primarily for burden of disease and injury estimates.
 - Most CUAs in US; Europe uses QALYs.
 - CUAs in resource-poor countries use DALYs due to World Bank and WHO guidance.
- DALY weights:
 - Inverted scale: 0 = health, 1 = death.
 - Estimated for diseases or injuries and disabling sequelae.
 - Based on preferences of experts, not individuals.

Disability-adjusted life years are another outcome measure that can be used in cost-utility analysis.

Disability-adjusted life years were developed in the international community primarily to measure disease and injury burden and to be able to make comparable estimates of these burden measures across countries.

The disability-adjusted life year weights are slightly different than the quality-adjusted life year weights, with an inverted scale of 0 referring to perfect health, or no disabilities, and 1 referring to death, or 100 percent disabled.

DALY Methods

- Combination of:
 - Years of life lost (YLL).
 - Years of life lived with disability (YLD).
- DALY weights
 - Person trade-off (PTO) exercises:
 - Experts asked to trade off numbers of people to keep alive with different conditions.
 - Measures relative desirability of conditions, *not* disability (activity limitations).

Disability-adjusted life years are derived from the estimates of years of life lost, which is a common metric to measure burden of disease internationally, and years of life lived with a disability. It's essentially the same thing as quality-adjusted life years in that life expectancy, in life years, is adjusted for the number of years living with a disability.

Disability-adjusted life year weights are derived differently than quality-adjusted life year weights. Instead of using the standard gamble, time trade-off, or rating scale approaches with a general population sample, experts are asked to trade off numbers of people to keep alive with certain conditions.

U.S. Burden of Disease and Injury Study

Table 27: Top 16 leading causes of Disability Adjusted Life Years (DALY), Years Lost to Disability (YLD), Years of Life Lost (YLL) and Deaths for Males – US 1996

Rank	Cause	DALY (%)	YLD (%)	YLL (%)	Death (%)
1	Ischemic heart disease	1,958 (11.0)	152 (2.1)	1,806 (17.2)	287 (24.7)
2	Road traffic accidents	934 (5.2)	233 (3.2)	701 (6.7)	29 (2.5)
3	Lung trachea or bronchial cancer	813 (4.6)	35 (0.5)	778 (7.4)	103 (8.8)
4	HIV/AIDS	764 (4.3)	189 (2.6)	575 (5.5)	25 (2.2)
5	Alcohol use	732 (4.1)	651 (8.9)	81 (0.8)	5 (0.4)
...					
16	Asthma	303 (1.7)	273 (3.7)	30 (0.3)	2 (0.2)

In a list of the top 16 leading causes of disability-adjusted life years for males in the United States in 1996, ischemic heart disease is ranked first in disability-adjusted life years and years of life lost. But if you look at years of life lived with a disability, 12 other causes rank higher, with alcohol use and osteoarthritis coming in at the top.

Use of DALYs in Setting Priorities

- Comparisons of DALYs with funding allocations by disease or risk factor.
 - DALYs best predictor of funding by disease category.
 - Heart disease and stroke 1st and 4th in DALYs but 4th and 11th in NIH research funding.
- Comparison of burden measure rankings by disease.



A study by Grosse and colleagues compared disability-adjusted life year rankings to National Institutes of Health funding and found that heart disease and stroke should receive more funding if such funding were linked to disability-adjusted life years.

Conclusions

- Economic evaluation is valuable to decision-making and in setting health policy.
- Economic evaluation is both art and science.
- Economic evaluation can help prioritize resources.
- For researchers in public health and prevention, this is an important component of program evaluation.
- Demand for these analyses is growing.

In conclusion, economic evaluation is valuable to decision making and in setting health policy.

Economic evaluation is both art and science, and it can be used to help prioritize resources for the most effective strategies. It assumes evidence and evidence-based decisions. For researchers in public health and prevention, this is an important component of program evaluation that should be considered because the demand for these evaluations is growing.

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