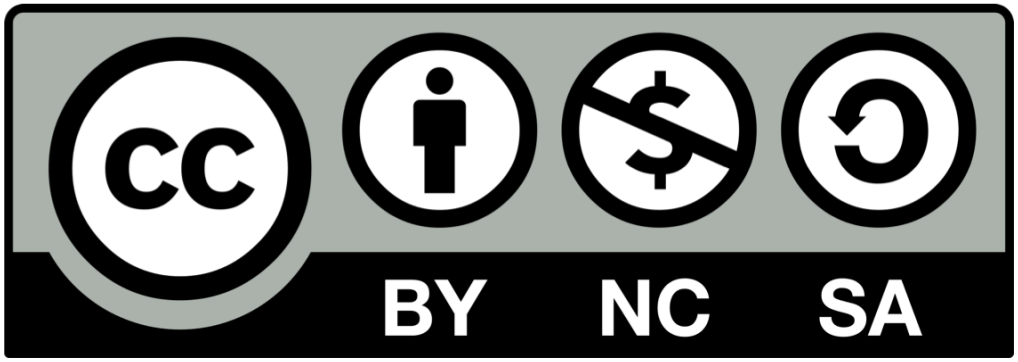
Economic Evaluation

Measuring and Valuing Health Outcomes

TVEE
TEACHING VACCINE ECONOMICS EVERYWHERE

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Objectives

- To describe Measurement of Health Gains in Terms of Health State Preference & Natural Units

Overview

- Defining Patient Preferences
- Instruments of Effectiveness Measurement
- Health Utility Measures
- Applying to Economic Evaluation
  - DALYs
  - QALYs

Patient Preferences

Measuring vs. Valuing Health

- Measuring Health
  - Count of deaths prevented, infections prevented, longevity, quality of life etc.
- Valuing Health
  - What is the value of avoiding an infection that is not fatal?
  - What is the value of surviving 10 years without infection instead of 5 years with infection
  - Preference based measures of health status or conditions (e.g. QALYs, DALYs) incorporate these concepts

Valuing Health

- Basic idea: ask people to express their preference for health states

- Use some method to value individual preference of different health states

Value tradeoffs in Health Care

- Vested interest in delivering Vaccine services that…
  - Improve length of life without infection
  - Improve quality of life without infection

- How can we construct a single numeric value that captures both attributes of vaccines that lead to prevention?

Patient Preference

- Rational decision making requires risk, uncertainty, and tradeoffs
- The "best" vaccine is in part subjective based on the person eligible to receive it, and what condition they avoid
  - Age
  - Race
  - Income
  - Gender
  - Other factors
- Need to quantify these tradeoffs in a way that facilitates decision making about vaccine use

Patient Preference Example

Rational decision making for patients requires tradeoffs like these:

- Hib influenza vaccine:
  - Short Term, common side effects
    - Pain, muscle aches
    - Fever in children
    - Costs of vaccine
  - Long Term
    - Avoid Hib, direct costs
    - May still contract another strain of influenza
    - Indirect consequences avoided
- Decision to proceed with Hib vaccine depends on tradeoff between short-term treatment of vaccine and flue symptoms and longer-term treatment risks

Patient Preferences

Assess a person's preference for length and quality of life based on vaccine usage with three types of measures:

- Value Preference:
  - How do you feel about one outcome for certain relative to another outcome for certain?
- Risk Preference:
  - How do you feel about one outcome for certain versus a gamble on other outcomes?
- Time Preference:
  - How do you feel about a certain outcome today versus the same outcome in the future?

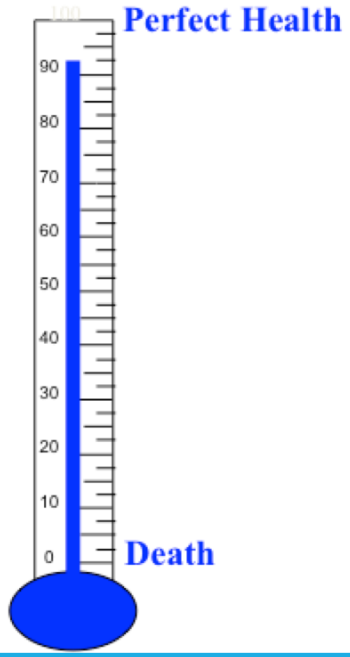
Instruments of Effectiveness Measurement

Method To Value Individual Preference

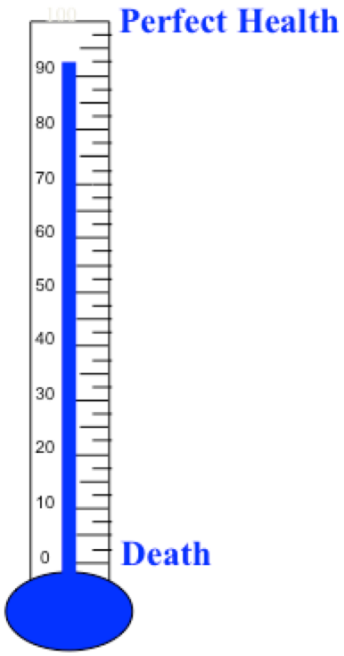
- Patient preferences (value, risk and time) are generated by a number of techniques, the most common are:
  - Visual Analog Scale (VAS)
  - Time Tradeoff (TTO)
  - Standard Gamble (SG)
- Imagine that you are at risk for polio, and of course there is a vaccine for it…
  - Polio => long-term onset paraplegia
  - No pain; paralysis from waist down
  - Wheel chair bound

Visual Analog Scale

The VAS is a scale that asks you to rate exactly how you feel, typically on a 100-point scale (the feeling thermometer)



Visual Analog Scale for Polio



A. 100
B. 80
C. 60
D. 50
E. 40
F. 20
G. 0

Visual Analog Scale

- Calculating utility from a VAS score:
  - Directly translatable from the linear measuring scale
- Simple task, easy to use and interpret
- In actuality, results in ‘value’, not utility
- Not a true measure of utility
  - Not preference-based
  - Not compared to death or alternative health states
  - No cost or consequence for marking near ‘zero’
  - No time horizon specified… Do you have paralysis now or later?

Time Tradeoff

- Uses a time horizon
- Measures preference for remaining life years in current state (*Alt. 1*) compared to fewer years in a higher-quality state of being (*Alt. 2*)

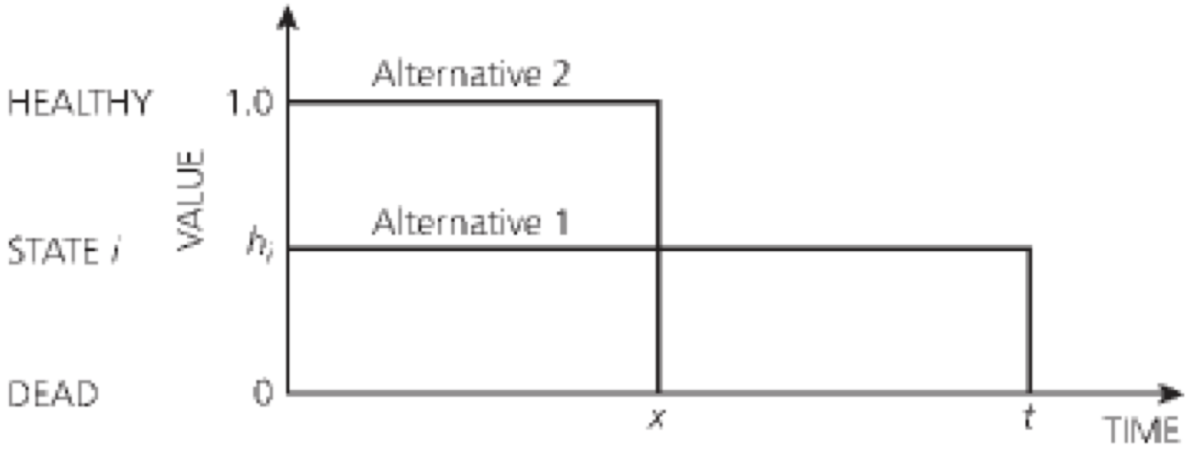


Fig. 5.6 Time trade-off for a chronic health state preferred to death.

Drummond et al, 2015

Time Tradeoff Example

- Imagine that you have early-onset polio
  - You can walk today, you are not paralyzed
  - You have occasional weakness in legs
  - Doctors say you have 10 years until complete paralysis

- But there is a potential cure…
  - Successful surgery would prevent symptoms indefinitely;
  - But there's a 50/50 chance that the polio onset is X years sooner

Time Tradeoff Example

- How many years (X) sooner would you be willing to risk for possibility of cure
  - 1 year
  - 2 years
  - 5 years
  - 7 years
  - 9 years

- At point of indifference, your value of polio cure is (10-X)/10

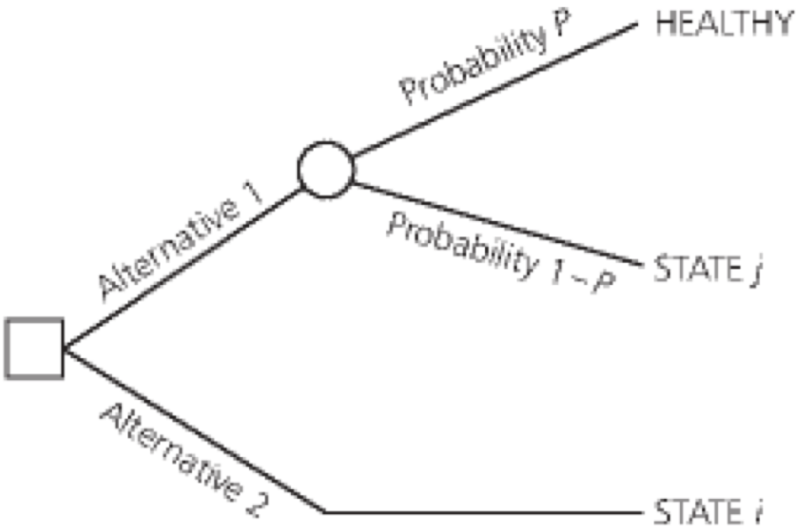
Time Tradeoff

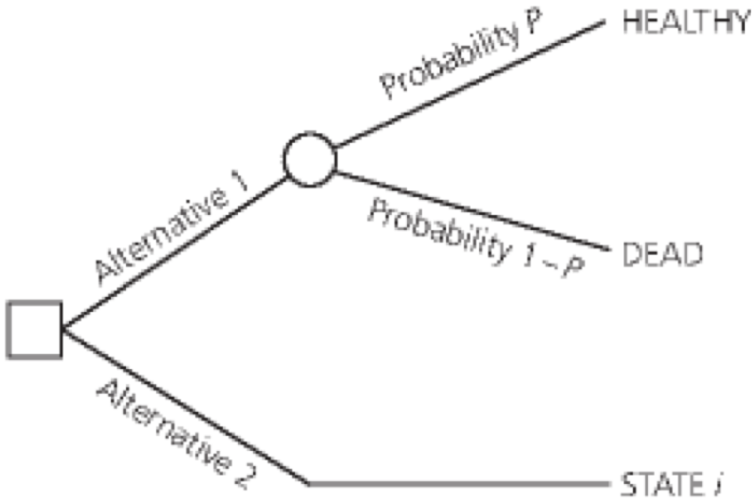
- Used in the DALYs valuation exercise
  - Explicitly addressing trade-offs between life and HRQL for people with different diseases
- Used in QALYs
  - Health state preference weights are elicited using the EQ-5D survey instrument
  - in the US and UK

*Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Medical care. 2005 Mar 1:203-20

Standard Gamble

- Requires one to choose between…
  - a 'sure thing'(*state i*)
  - a gamble between the best (*healthy*) and worst outcome (e.g. *death* or *state j)*…





Drummond et al, 2015

Standard Gamble Example

- Imagine that you have early-onset polio
  - You can walk today, you are not paralyzed
  - You have occasional weakness in legs
  - Doctors say you will become paralyzed in next year

- But there is a potential cure…
  - Successful surgery would prevent symptoms indefinitely;
  - But there's an X% chance that you die from the surgery

Standard Gamble Example

- What X% chance of death would you be willing to risk for possibility of cure
  - 10%
  - 25%
  - 50%
  - 75%
  - 90%

- At point of indifference, your value of polio cure is 1.0 - X

Standard Gamble

- Both SG and TTO are preferred by many economists—hold that eliciting preferences in this manner is consistent with utility theory (a model for how people make decision under conditions of uncertainty*)

* Gold MR, et al (2002)

Hierarchy Of Utility Measures

- SG > TTO > VAS
  - SG is the only true measure of utility
    - Involves choice and uncertainty
    - Compare current state to death without vaccine
  - TTO measures an element of preference not available in SG or VAS – time
  - VAS is the most straight forward

Utility Measures

What is health utility?

- When quality valuations reflect preferences then they are referred to **utility weights**
- A quantifiable index of health
- Captured on a scale of 0.0 to 1.0, representing the extremes of death and full health
  - 0.84 ~ average American
  - Possible to have a negative score (e.g. -0.05) for a 'worse than death' state, such as debilitating end-of-life with polio
  - Have scale properties, i.e. a change from 0.4 to 0.6 is numerically equivalent to a change from 0.7 to 0.9

Summary Measures of Population Health

- Common measures of population health with vaccines
  - Quality-adjusted life years (QALYs)
  - Disability-adjusted life years (DALYs)

- Incorporate both survival and the impact of morbidity associated with different health states **into a single utility index**
  - This feature makes these measures useful for comparisons across a range of infections, vaccine interventions, and populations
  - Commonly used to compare vaccine interventions in cost-effectiveness analysis (CEA)/cost-utility analysis (CUA)

* Gold, MR., Stevenson D, and Fryback DG. "HALYS and QALYS and DALYS, Oh My: similarities and differences in summary measures of population Health." Annual Review of Public Health 23.1 (2002): 115-134.

Summary Measures of Population Health

- Health-related quality of life (HRQL)
  - The morbidity (in DALYs) or quality of life (in QALYs) components of an infectious disease contracted without the presence of a vaccine are referred to as “HRQL units”
  - Use **utility weights** that reflect population preferences for different conditions of health and disease

    (i.e. infection disease, injury, and disability)
  - Are multiplied by life expectancy and through different methodologies produce QALYs or DALYs associated with different levels of health benefited by vaccines

* Gold, MR., Stevenson D, and Fryback DG. "HALYS and QALYS and DALYS, Oh My: similarities and differences in summary measures of population Health." Annual Review of Public Health 23.1 (2002): 115-134.

Quality-Adjusted Life Years (QALYs)

- QALYs are the Gold* standard in measuring health utility for cost-effectiveness analysis
  - Developed in the 1960s by economists, operations researchers, and psychologists primarily for use in CEA
  - Utility weights are attached to individual experiences of health for either their own health state (patient weights) or the health states of others that are described to them (community weights)
  - QALYs are a measure of health expectancy - a “good” to be maximized

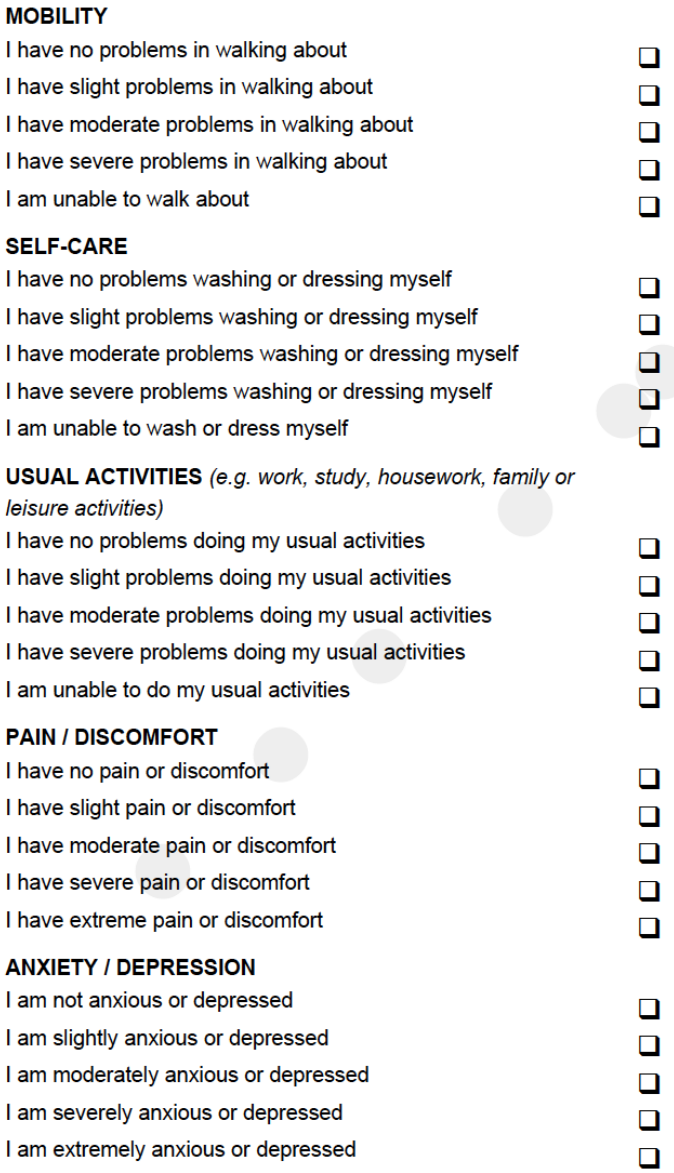
* Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.

Quality-Adjusted Life Years (QALYs)

- In 1993, the Panel on Cost-effectiveness in Health and Medicine (PCEHM) recommended the use of community-based nationally representative preferences for use in CEA
  - Several generic health status description and valuation survey instruments are available to measure health care outcomes
  - Most prominent survey instruments are:
    - the Quality of Well-Being Scale
    - the Health Utilities Index
    - the EuroQol Group's EQ-5D*

*Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Medical care. 2005 Mar 1:203-20

- Various countries (e.g. U.S. and U.K.) have estimated country-specific preference weights using the EQ-5D survey instruments
  - Initially developed simultaneously in Dutch, English, Finnish, Norwegian and Swedish.
  - Widely used in many countries around the world
  - Translated into most major languages
- New version
  - EQ-5D-5L
  - 3,125 health states



MOBILITY
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 unable to walk about ❑

SELF-CARE
I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*
I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION
I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

Herdman, Michael, et al. "Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L)." *Quality of life research* 20.10 (2011): 1727-1736. Or see https://euroqol.org/

Sources of QALY weights

- Link to U.S. repository of “off-the-shelf” access to a wide number of disease and condition-specific preference weights
  - The US repository is maintained by Center for the Evaluation of Value and Risk in Health Value Databases http://healtheconomics.tuftsmedicalcenter.org/cear4/Home.aspx
- Examples
  - Perfect health = 1.0
  - Pneumonia = 0.954
  - Hypertension = 0.789
  - Symptomatic HIV: >500 cells/ml = 0.75
  - Stroke (CVA) = 0.650
  - Senility = 0.545
  - Pneumococcal pneumonia = 0.5
  - Death = 0

*Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Medical care. 2005 Mar 1:203-20

Disability Adjusted Life Year (DALY)

- Developed in 1993 by a World Bank and WHO collaboration
  - Quantify the global burden of premature death, disease, and injury
  - Make recommendations that would improve health, particularly in developing nations
  - Concerned with self-assessment of health –viewed as potentially misleading, particularly for cross-cultural comparison

- DALYs measure health gaps so it is a “bad” to be minimized

Disability Adjusted Life Year (DALY)

- Rather than creating a classification scheme of generic health states (done in all other HRQLs), DALYs focus on the impact of a disease or condition on the preference of an individual
  - Drawn from the International Classification of Impairments, Disabilities, and Handicaps (ICIDH)
  - The value of undesirable ICIDH disabilities specific to diseases and conditions are generated by health professionals
  - Developed by a panel of health care workers who met in Geneva
- The preferred measure of vaccine outcomes

Disability Adjusted Life Year (DALY)

DALYs = YLL+YLD

- YLL: years of life lost due to death
- YLD: years of life lost due to disability
  - YLDs depend on the weight factor that reflects the severity of the disease on a scale from:
    - 0 (perfect health) to 1 (equivalent to death)
  - Weight factors are attached to specific diseases, rather than to health states
- Apart from the disability weights, DALYs also included time-discounting and age weights

Sources of DALY weights

- Global Burden Of Disease 2004 Update: Disability Weights For Diseases And Conditions
  - http://www.who.int/healthinfo/global_burden_disease/GBD2004_DisabilityWeights.pdf
  - Revised disability weighting: Salomon el al (2010)

- Examples for female 0-4 years old
  - Perfect health = 0.0
  - Measles = 0.152
  - Congestive heart failure = 0.201
  - Otitis media Deafness = 0.229
  - AIDS cases not on ART = 0.505
  - Meningitis from Haemophilus influenzae= 0.616
  - First-ever stroke cases = 0.920
  - Death= 1.0

- DALY Country profiles are maintained by the Institute for Health Metrics and Evaluation
  - http://www.healthdata.org/results/country-profiles

Salomon, J.A., et al., *Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010.* The Lancet, 2012. **380**(9859): p. 2129-2143.

Using DALYs

- Can answer “How bad is disease X?” by counting up deaths or DALYs due to X

- Can answer “How good is intervention Y?” by counting up deaths prevented or DALYs **averted** by doing Y

10 Leading Causes of DALYs

Lower Income Countries

1. Pneumonia
2. Diarrhea
3. Perinatal Conditions
4. Major Depression
5. Tuberculosis
6. Measles
7. Malaria
8. Ischemic Heart Disease
9. Congenital Anomalies
10. Cerebrovascular Disease

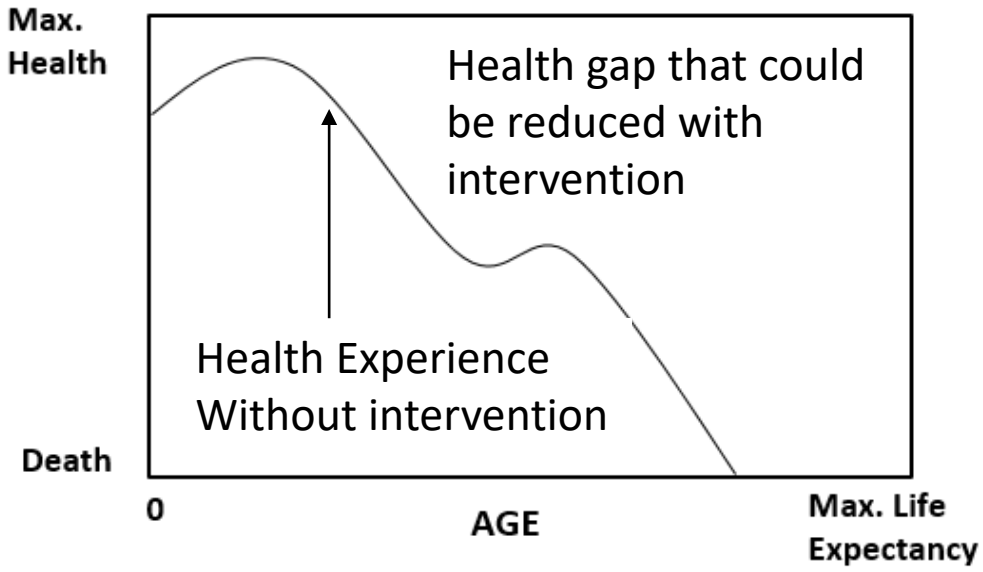
Cheap Ways to Reduce Population DALYs

- Immunization
- Nutrient Supplementation
- ORT
- Vector Control
- Enforcing traffic laws
- Tobacco Control
- Sanitation
- Safe Sex
- Antibiotics
- Antidepressants

Applying to Economic Evaluation - DALYs

Applying DALYs to Vaccine Economic Evaluation

- Measure of health gap
  - Disability scale is 0.0 (no disability) to 1.0 (death)
  - Compared to a life with no disability during the maximum life expectancy
    - LE is defined using Life tables (separate for female and male)
- For CEA, interested in comparison of burden of disease (health gap) with and without a new intervention



Revised disability weighting (2010)

	Estimate (95% uncertainty interval)
Infectious disease	
Infectious disease: acute episode, mild	0·005 (0·002–0·011)
Infectious disease: acute episode, moderate	0·053 (0·033–0·081)
Infectious disease: acute episode, severe	0·210 (0·139–0·298)
Infectious disease: post-acute consequences (fatigue, emotional lability, insomnia)	0·254 (0·170–0·355)
Diarrhoea: mild	0·061 (0·036–0·093)
Diarrhoea: moderate	0·202 (0·133–0·299)
Diarrhoea: severe	0·281 (0·184–0·399)
Epididymo-orchitis	0·097 (0·063–0·137)
Herpes zoster	0·061 (0·039–0·094)
HIV: symptomatic, pre-AIDS	0·221 (0·146–0·310)
HIV/AIDS: receiving antiretroviral treatment	0·053 (0·034–0·079)
AIDS: not receiving antiretroviral treatment	0·547 (0·382–0·715)
Intestinal nematode infections: symptomatic	0·030 (0·016–0·048)
Lymphatic filariasis: symptomatic	0·110 (0·073–0·157)
Ear pain	0·018 (0·009–0·031)
Tuberculosis: without HIV infection	0·331 (0·222– 0·450)
Tuberculosis: with HIV infection	0·399 (0·267–0·547)
Cancer	
Cancer: diagnosis and primary therapy	0·294 (0·199–0·411)

Salomon, J.A., et al., *Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010.* The Lancet, 2012. **380**(9859): p. 2129-2143.

Sample Calculation Of DALYs Tuberculosis (TB)

Suppose out of a million, people 100 get TB at age 20

- 10 die of TB right away
- 90 survive but they are sick for 1 year

Suppose without TB, those who died would have lived to 70

- 1 year with TB is equal to 0.67 years
- The “Disutility” of TB 0.33 years.

How many DALYs were lost?

- Deaths
- YLL years of life lost (due to death)
- YLD years of life lost due to disability
- DALYS disability adjusted life years

= 10

= 50yr x 10ppl = 500 years

= 0.33du x 90ppl = 30 years

= YLL + YLD

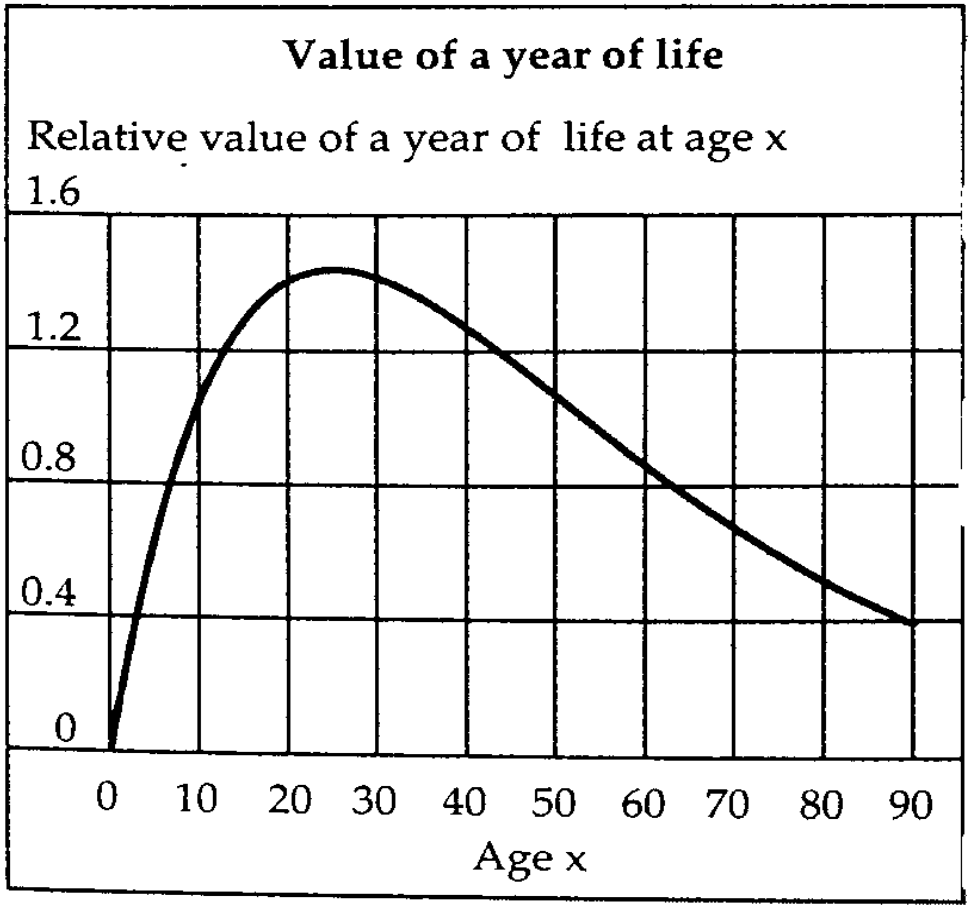
= 500+30 = 530

“Correct” DALY Calculation: Parameters

YLDs and YLLs are functions of various parameters

Symbol	Parameter Description	Standard Values
r	Discount rate (0 = no discounting)	0.03
a	(YLL) age at death (YLD) age at onset of disability	-
L	(YLL) Life expectancy at age of death (YLD) Duration of disability	-
β	Age weighting constant	0.04
C	Adjustment constant for age weights	0.1658
K	Age weighting factor (yes/no) (No age weighting = 0 Yes age weighting = 1)	1
D	Disability weight	-

Age-weighted DALY



Source: World Bank data.

Applying to Economic Evaluation - QALYs

Applying QALYs to Economic Evaluation

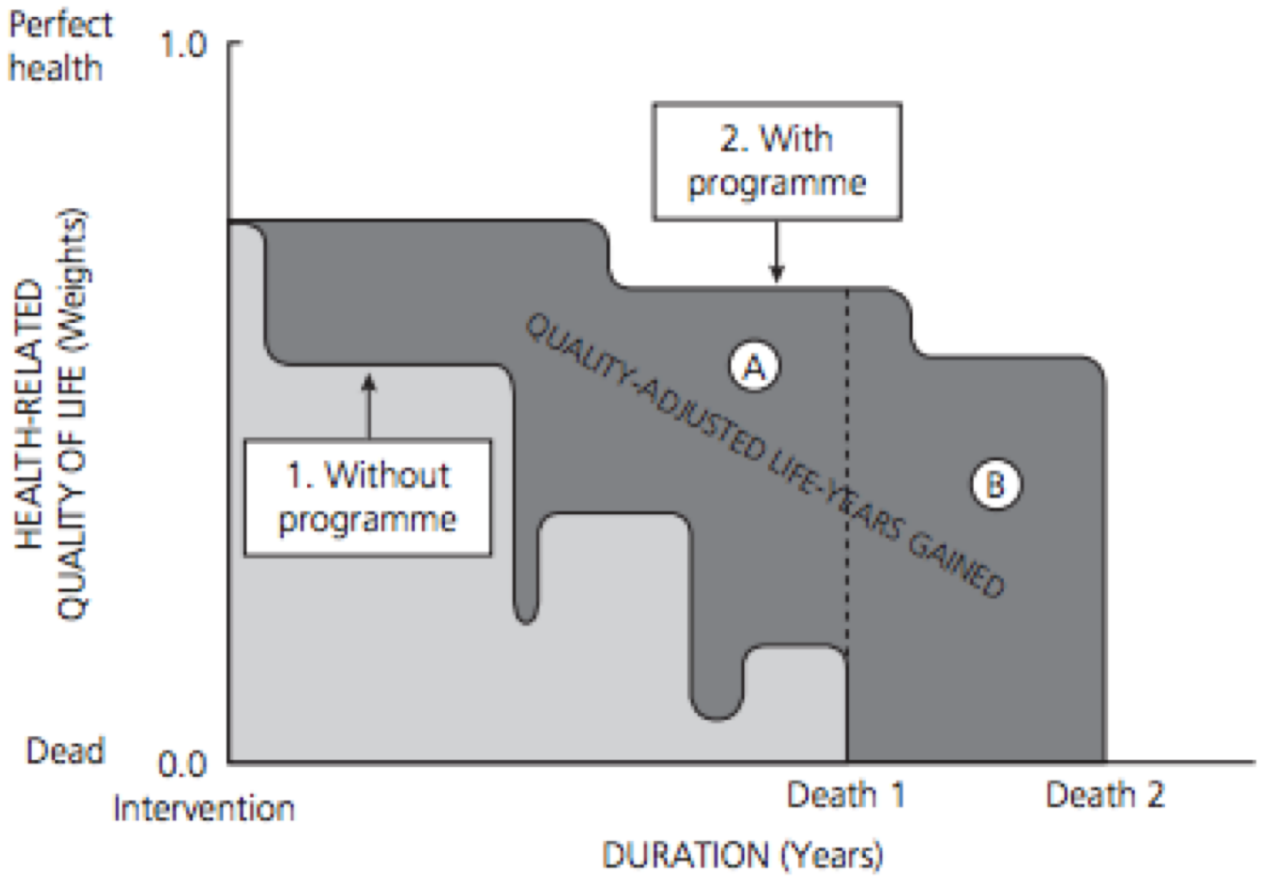


Fig. 5.2 Quality-adjusted life-years gained from an intervention.

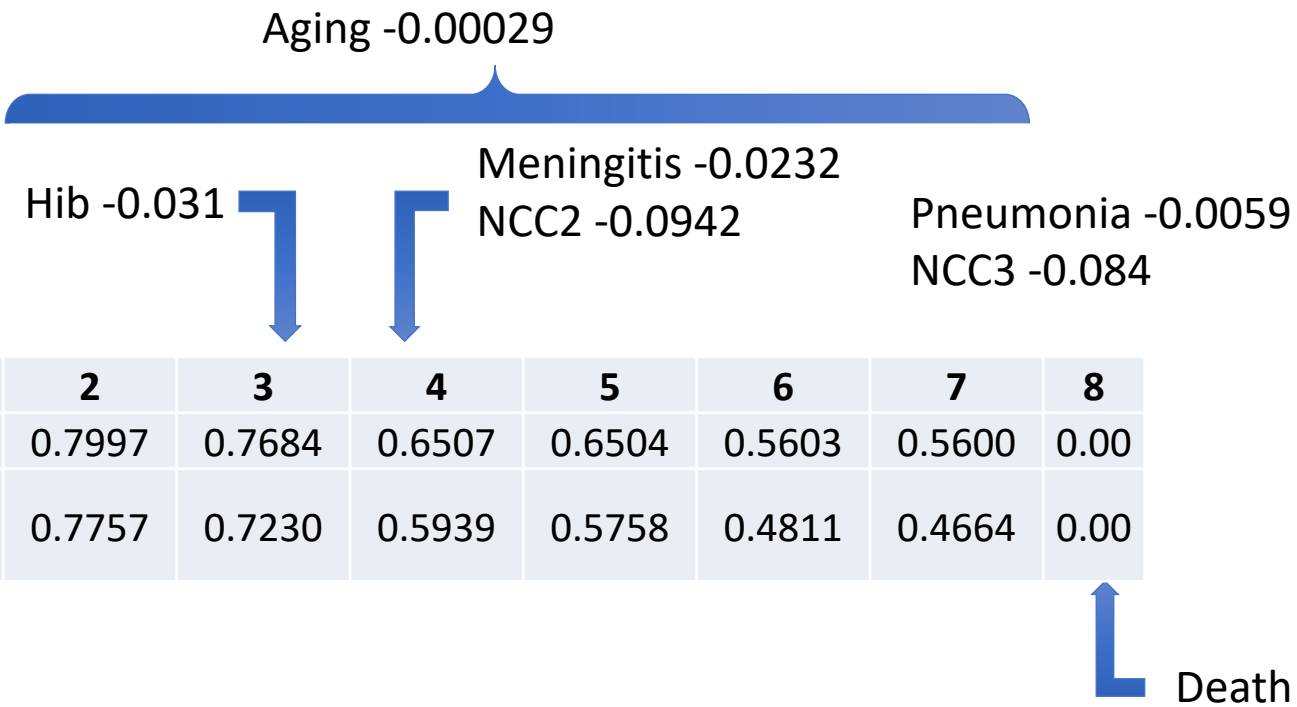
Drummond et al, 2015

Sullivan & Ghushchyan *MDM* 2006

ICD-9 Classification	n	Mean Age	NCC[b] 25%	NCC[b] 50%	NCC[b] 75%	Unadjusted Mean EQ-5D	Unadjusted EQ-5D 25%	Unadjusted EQ-5D 50%	Unadjusted EQ-5D 75%	Regression Results[a] Disutility of Condition[a]	Regression Results[a] Condition[a] Standard Error	Regression Results[a] Statistical Significance (Condition)
ICD-9 436 CVA	340	68	3	5	7	0.650	0.463	0.768	0.816	–0.0524	0.0001	*
ICD-9 444 Arterial Embolism	201	66	3	5	7	0.734	0.708	0.778	0.827	–0.0198	0.0002	*
ICD-9 453 Oth Venous Thrombosis	100	65	3	5	7	0.727	0.597	0.778	0.827	–0.0380	0.0002	*
ICD-9 455 Hemorrhoids	246	51	2	3	6	0.826	0.800	0.827	1.000	–0.0008	0.0002	*
ICD-9 459 Oth Circulatory Disease	367	64	3	5	7	0.732	0.708	0.778	0.827	–0.0376	0.0001	*
ICD-9 473 Chronic Sinusitis	2047	45	2	3	5	0.853	0.800	0.827	1.000	–0.0022	0.0001	*
ICD-9 477 Allergic Rhinitis	3326	46	2	3	5	0.853	0.800	0.827	1.000	–0.0009	0.0001	*
ICD-9 492 Emphysema	296	68	3	5	7	0.663	0.508	0.708	0.810	–0.0667	0.0001	*
ICD-9 493 Asthma	1604	46	2	3	5	0.797	0.761	0.827	1.000	–0.0213	0.0001	*
ICD-9 518 Other Lung Diseases	167	59	3	5	7	0.714	0.597	0.778	0.827	–0.0428	0.0002	*
ICD-9 519 Oth Resp System Diseases	284	52	2	3	5	0.816	0.768	0.827	1.000	–0.0277	0.0001	*
NCC = 2	5704	48	—	—	—	0.853	0.800	0.827	1.000	–0.0942	0.0001	*
NCC = 3	3800	53	—	—	—	0.815	0.778	0.827	1.000	–0.0876	0.0001	*
NCC = 4	2514	57	—	—	—	0.788	0.768	0.810	0.844	–0.0711	0.0001	*
NCC = 5	1657	61	—	—	—	0.755	0.708	0.800	0.827	–0.0547	0.0001	*
NCC = 6	1079	63	—	—	—	0.721	0.708	0.778	0.827	–0.0419	0.0002	*
NCC = 7	688	63	—	—	—	0.684	0.573	0.768	0.816	–0.0350	0.0002	*
NCC = 8	397	63	—	—	—	0.661	0.508	0.768	0.810	–0.0344	0.0002	*
NCC = 9	256	65	—	—	—	0.661	0.467	0.708	0.800	0.0026	0.0003	*
NCC ≥ 10	362	66	—	—	—	0.585	0.397	0.708	0.778	0.0097	0.0003	*

QALY Example – Hib/Meningitis

- Adult patient with Asthma = 0.800 QALYs -> mean EQ5D index score (Sullivan *MDM* 2006)
- Hib Influenza in year 3 = -0.031 QALYs -> mean disutility (Hollman *Plos One* 2013)
- Meningitis in year 4 = -0.0232 QALYs -> mean disutility (Hollman *Plos One* 2013)
- Pneumonia in year 6 = -0.0059 -> mean disutility (Maurer *Vaccine* 2016)
- Death in year 8



Year (t)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Control	0.8000	0.7997	0.7684	0.6507	0.6504	0.5603	0.5600	0.00
Discounted*	0.8000	0.7757	0.7230	0.5939	0.5758	0.4811	0.4664	0.00

Future years discounted at 3% per year = QALY[(1-0.03)^t-1]

Intervention Effectiveness

Year (t)	1	2	3	4	5	6	7	8	Total
Control	0.8000	0.7997	0.7684	0.6507	0.6504	0.5603	0.5600	0.00	**4.7895**
Discounted*	0.8000	0.7757	0.7230	0.5939	0.5758	0.4811	0.4664	0.00	**4.4160**
No Health Problem	0.8000	0.7757	0.7522	0.7293	0.7072	0.6857	0.6648	0.6446	**5.7594**

- Same process
  - Live longer, avoid onset of Hib (discount 0.800 for 8 years)
  - Total discounted QALYs = 5.76

- Incremental QALYs gained by national public health intervention:
  - 5.76 – 4.42 = 1.34 QALYs gained per person
  - 500,000 children = 675,000 QALYs

Exercise: Measuring and Valuing Health Outcomes

- Review questions in groups
- Discuss potential responses
- Respond to questions online

Discussion Questions (Quiz)

1. What is a true measure of health utility?
   a. Visual Analog
   b. Time Tradeoff
   c. Standard Gamble

2. Which measure of utility is better suited for vaccine economic evaluation?
   a. QALYs
   b. DALYs
   c. Value preference
   d. Time preference

3. What are the potential risks associated with vaccines use that we should be concerned about?

4. Do vaccines always result in improved quality and length of life?