



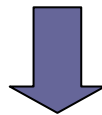
QALY

asist. dr. Marko Obradović

Katedra za socialno farmacijo
Fakulteta za farmacijo
Univerza v Ljubljani

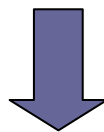
Kako se meri kakovost življenja?

- Z zdravjem povezana kakovost življenja



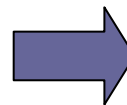
Opis zdr. stanja in vpliva
na delovanje in sposobnosti

- Splošni vprašalniki: SF-36
- Specifični vprašalniki: EORTC QLQ-C30 (rak)



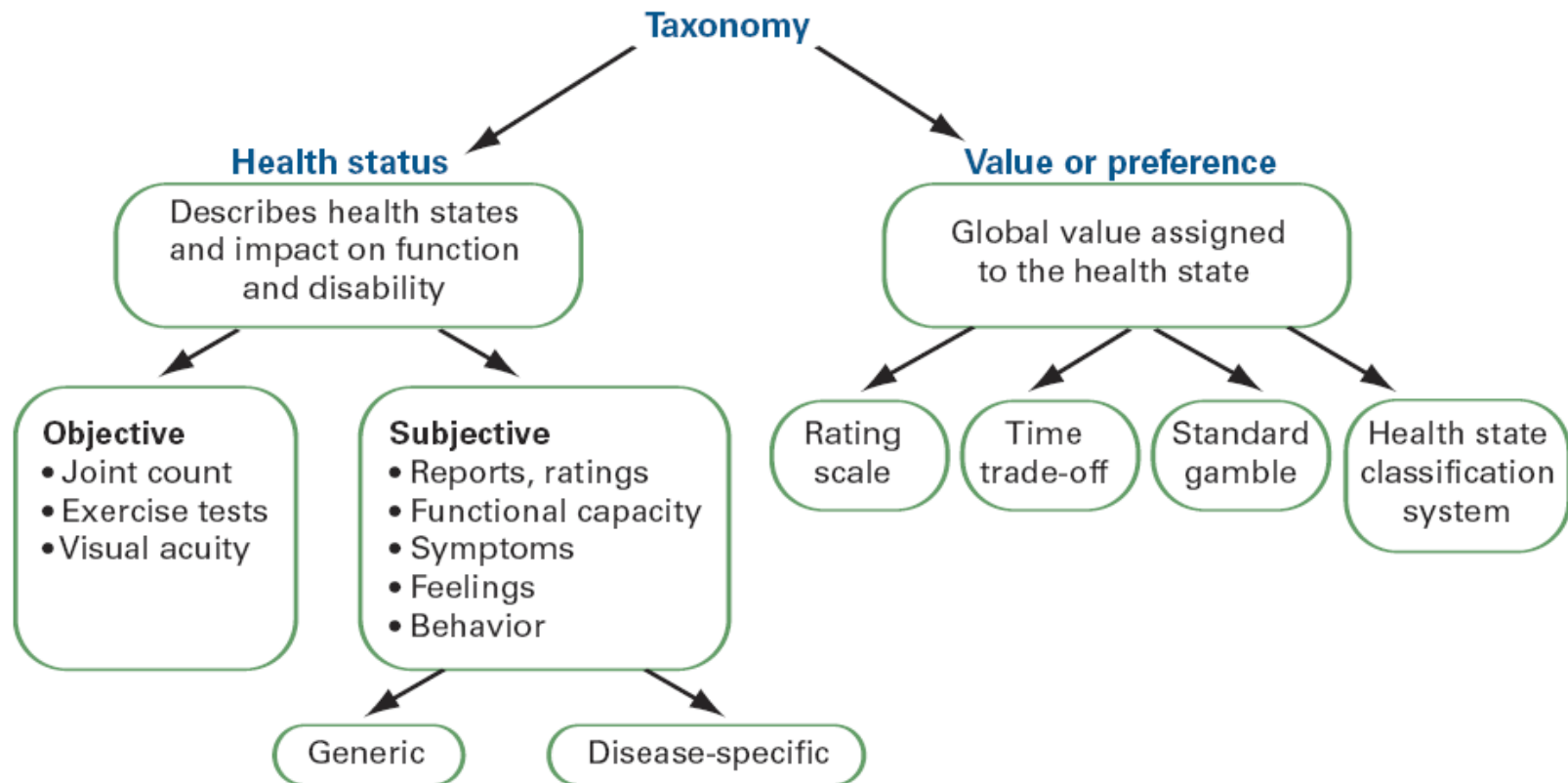
- V farmakoeekonomskih analizah se uporablja indeks “uporabnost” (ang. “utility”)

Preferenca do zdr. stanja



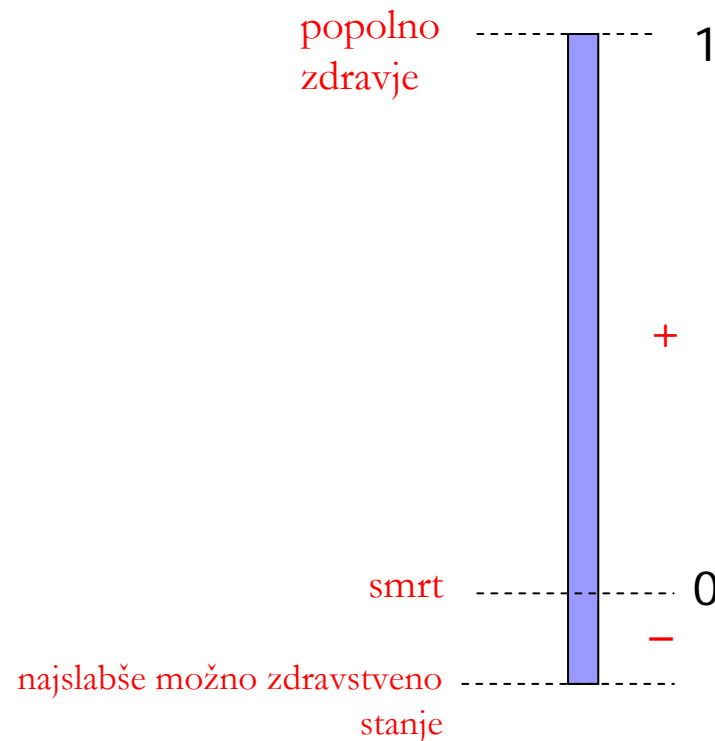
QALY

Merjenje kakovosti življenja – povzetek metod



Utility

- Kakovost je zajeta z QALY utežjo, ki se nahaja v intervalu od 0 do 1.
- Utež 1 predstavlja stanje popolnega zdravja, utež 0 pa smrt.





Utility

A hypothetical measure of the satisfaction from or desirability of consumption of goods or services

$$U = f(H, T, P, W, X)$$

where

H = health

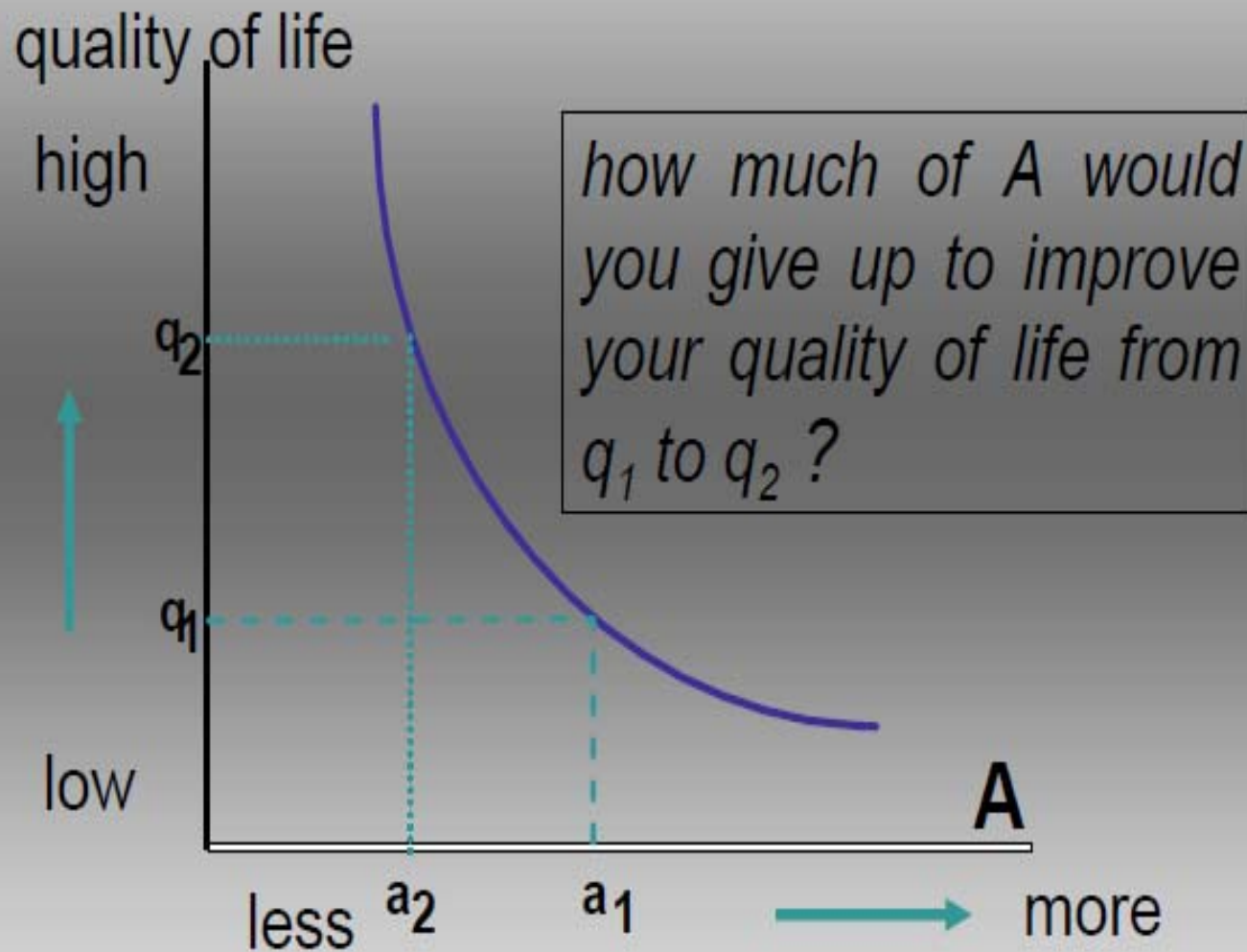
T = life expectancy

P = probability of survival

W = wealth

X = all other arguments

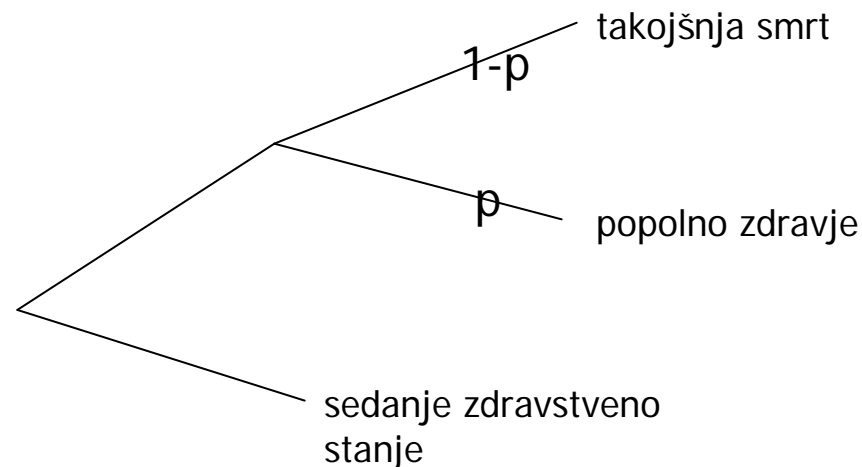
Measuring utility

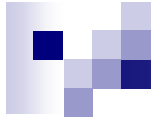


DIREKTNI NAČINI DOLOČANJA UTEŽI UPORABNOSTI (UTILITY WEIGHT)

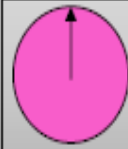
■ “Standard gamble”:

- klasična metoda merjenja uporabnosti v ekonomiji.
- izbira med gotovim preživetjem določen čas v nekem zdravstvenem stanju in tveganjem med preživetjem tega obdobja v popolnoma zdravem stanju na eni strani in takojšnjo smrtjo na drugi.
- spreminja se verjetnost za preživetje v popolnoma zdravem stanju, dokler posameznik nima preference do posamezne alternative.
- ta verjetnost določa vrednost uporabnosti (utility)






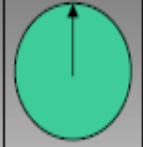
CHANCE BOARD

Life "A"	<div style="background-color: #ff69b4; padding: 5px; font-weight: bold; font-size: 24px;">100</div> <p>% CHANCE</p>		<div style="background-color: #add8e6; padding: 5px; font-weight: bold; font-size: 24px;">0</div> <p>% CHANCE</p>
<p style="text-align: center;">PERFECT HEALTH</p> <p>Able to see, hear and speak normally.</p> <p>Able to walk, bend, lift, jump, and run normally for age.</p> <p>Generally happy and free from worry.</p> <p>Able to learn and remember normally.</p> <p>Able to eat, bathe, dress, and use the toilet normally.</p> <p>Free of pain and discomfort.</p>		<p style="font-size: 24px; font-weight: bold;">IMMEDIATE DEATH</p>	
Life "B"	<div style="background-color: #32cd32; padding: 5px; font-weight: bold; font-size: 24px;">100</div> <p>% CHANCE</p>	<p style="text-align: center;">Health State "B"</p> <p>Able to see, hear and speak normally.</p> <p>Requires mechanical equipment (cane, crutches, braces, wheelchair) to walk or get around.</p> <p>Occasionally angry, irritable, anxious, or depressed.</p> <p>Able to learn and remember normally.</p> <p>Eats, bathes, dresses, or uses the toilet independently with difficulty.</p> <p>Free of pain and discomfort.</p>	

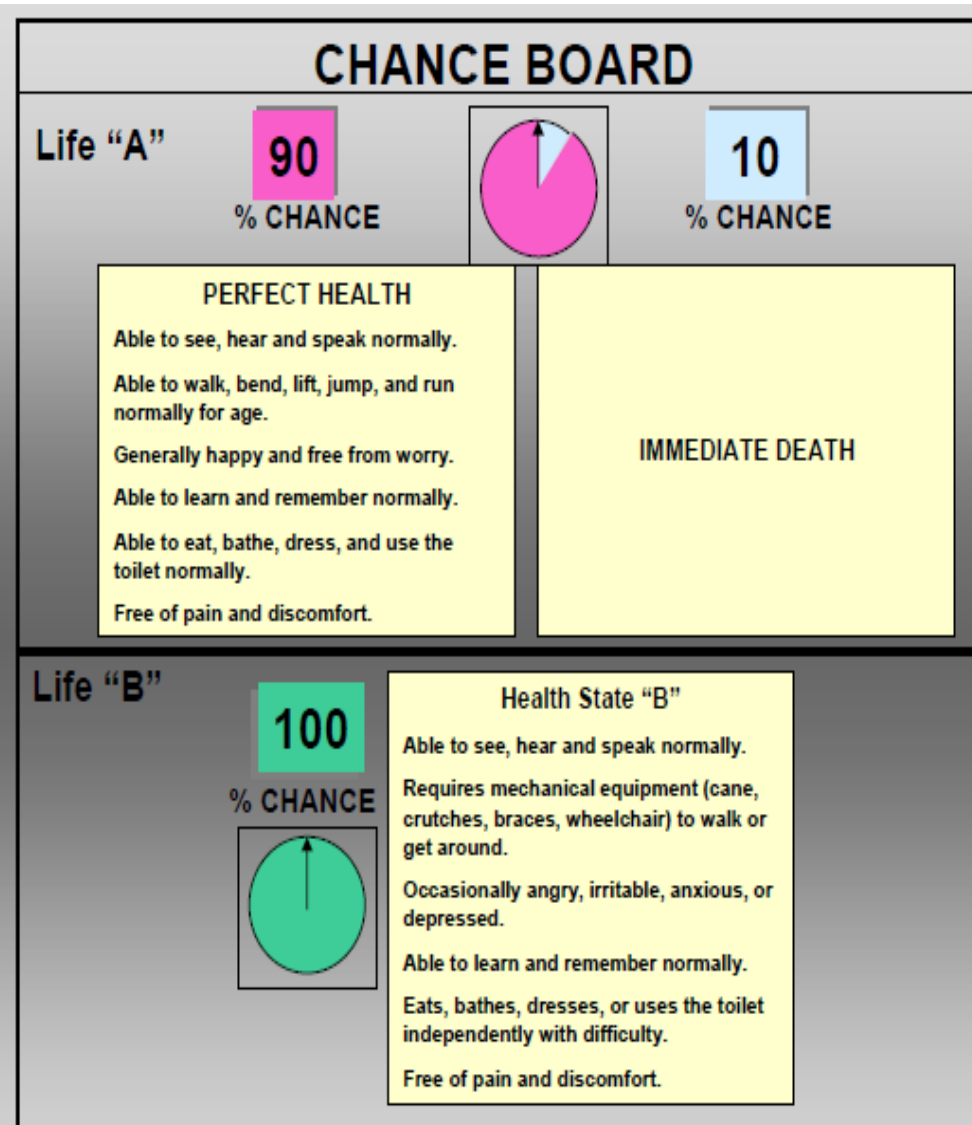
Standard Gamble Chance Board
Select Life "A" or Life "B" or are they 'equal'



CHANCE BOARD

Life "A"	<div style="background-color: #ff69b4; color: white; padding: 5px; font-weight: bold; font-size: 24px;">10</div> <p>% CHANCE</p>		<div style="background-color: #add8e6; color: black; padding: 5px; font-weight: bold; font-size: 24px;">90</div> <p>% CHANCE</p>	
<p style="text-align: center;">PERFECT HEALTH</p> <p>Able to see, hear and speak normally.</p> <p>Able to walk, bend, lift, jump, and run normally for age.</p> <p>Generally happy and free from worry.</p> <p>Able to learn and remember normally.</p> <p>Able to eat, bathe, dress, and use the toilet normally.</p> <p>Free of pain and discomfort.</p>		<div style="background-color: #ffff00; padding: 20px; border: 1px solid black;">IMMEDIATE DEATH</div>		
Life "B"	<div style="background-color: #00ff00; color: white; padding: 5px; font-weight: bold; font-size: 24px;">100</div> <p>% CHANCE</p>		<p style="text-align: center;">Health State "B"</p> <p>Able to see, hear and speak normally.</p> <p>Requires mechanical equipment (cane, crutches, braces, wheelchair) to walk or get around.</p> <p>Occasionally angry, irritable, anxious, or depressed.</p> <p>Able to learn and remember normally.</p> <p>Eats, bathes, dresses, or uses the toilet independently with difficulty.</p> <p>Free of pain and discomfort.</p>	

Standard Gamble Chance Board
Select Life "A" or Life "B" or are they 'equal'

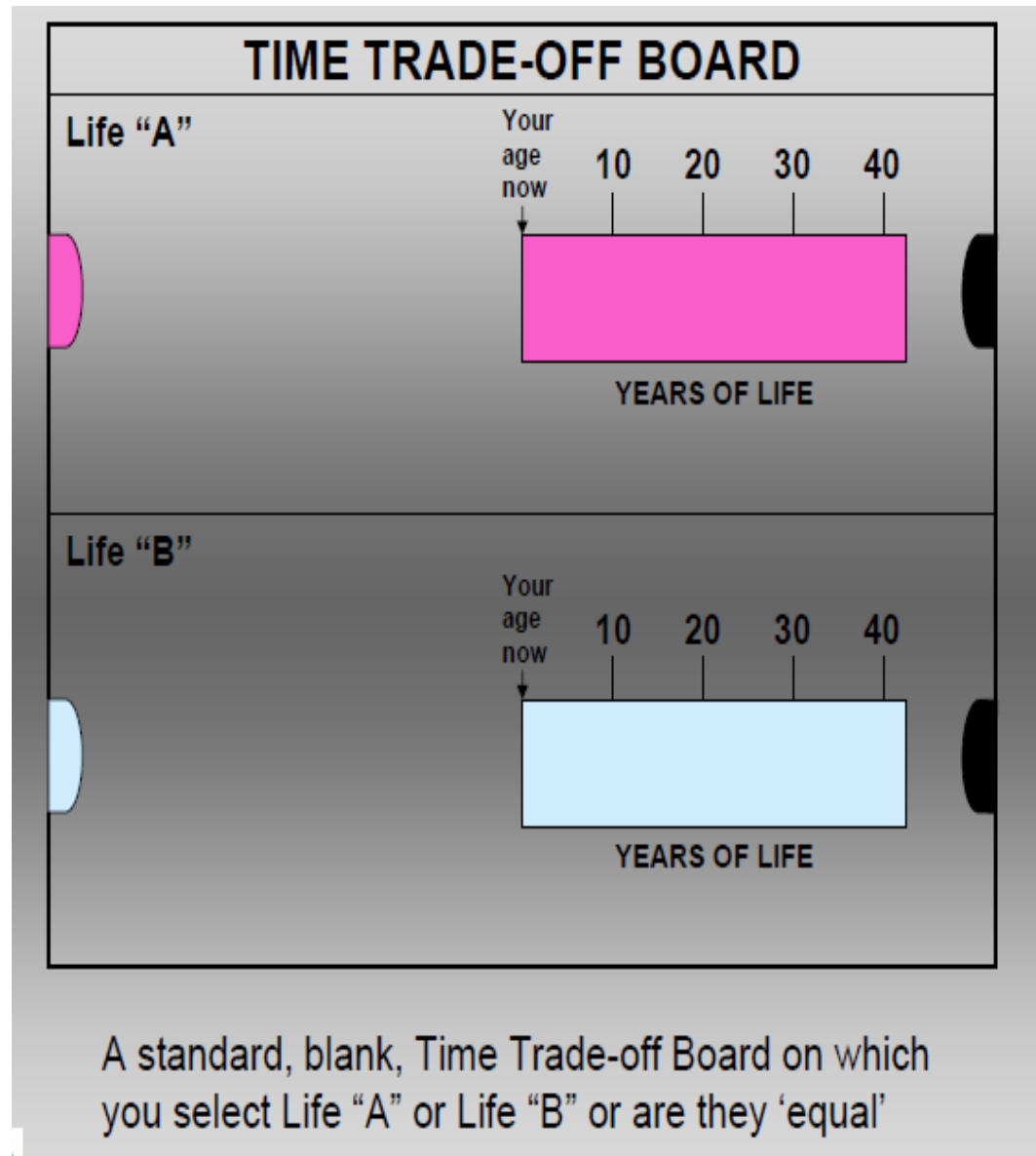
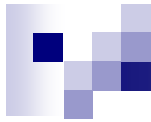


Standard Gamble Chance Board
Select Life "A" or Life "B" or are they 'equal'



■ “time trade-off”

- domnevno enostavnejša alternativa “standard gamble” metodi.
- posameznik izbira med alternativo, da preživi določen čas v sedanjem zdravstvenem stanju, ali pa izbere alternativo s krajšim časom preživetja v popolno zdravem stanju.
- spreminja se trajanje časom preživetja v popolno zdravem stanju, dokler posameznik nima preference do katere od alternativ.

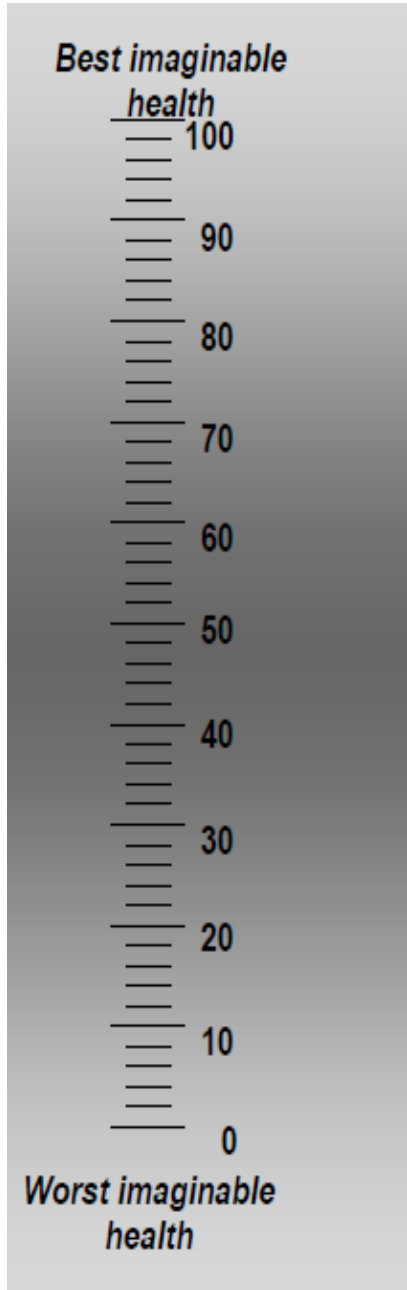


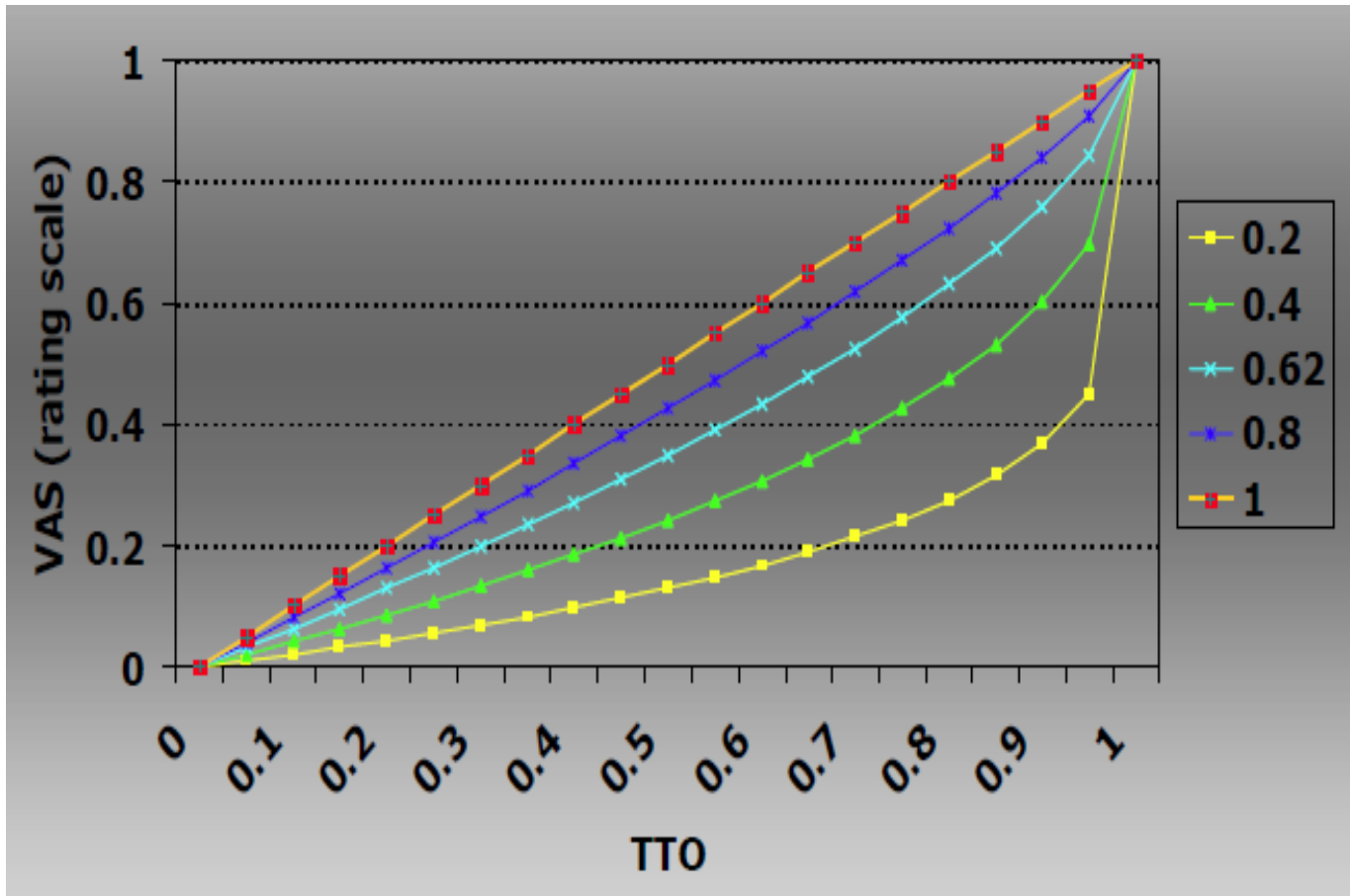


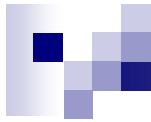
■ “rating scale”

- na skali od 0 do 100 posameznik označi položaj določenega zdravstvenega stanja.
- položaj 70 pomeni uporabnost 0,7.
- ne vključuje negotovosti
- študije pokazale, da isti posamezniki s to metodo dodelijo različne vrednosti istemu zdravstvenemu stanju.

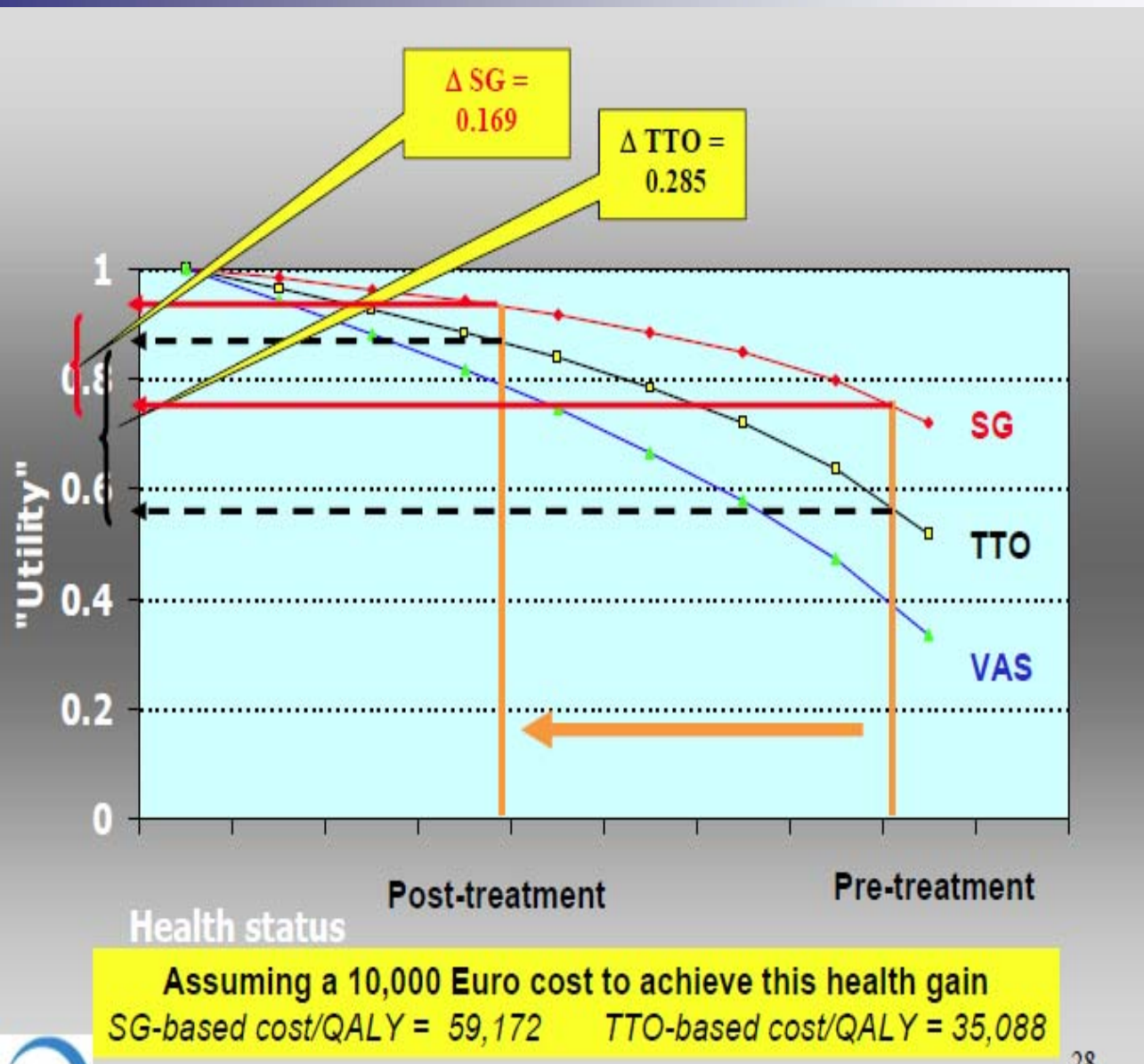
$$RS = 1 - (1 - TTO)^{power}$$

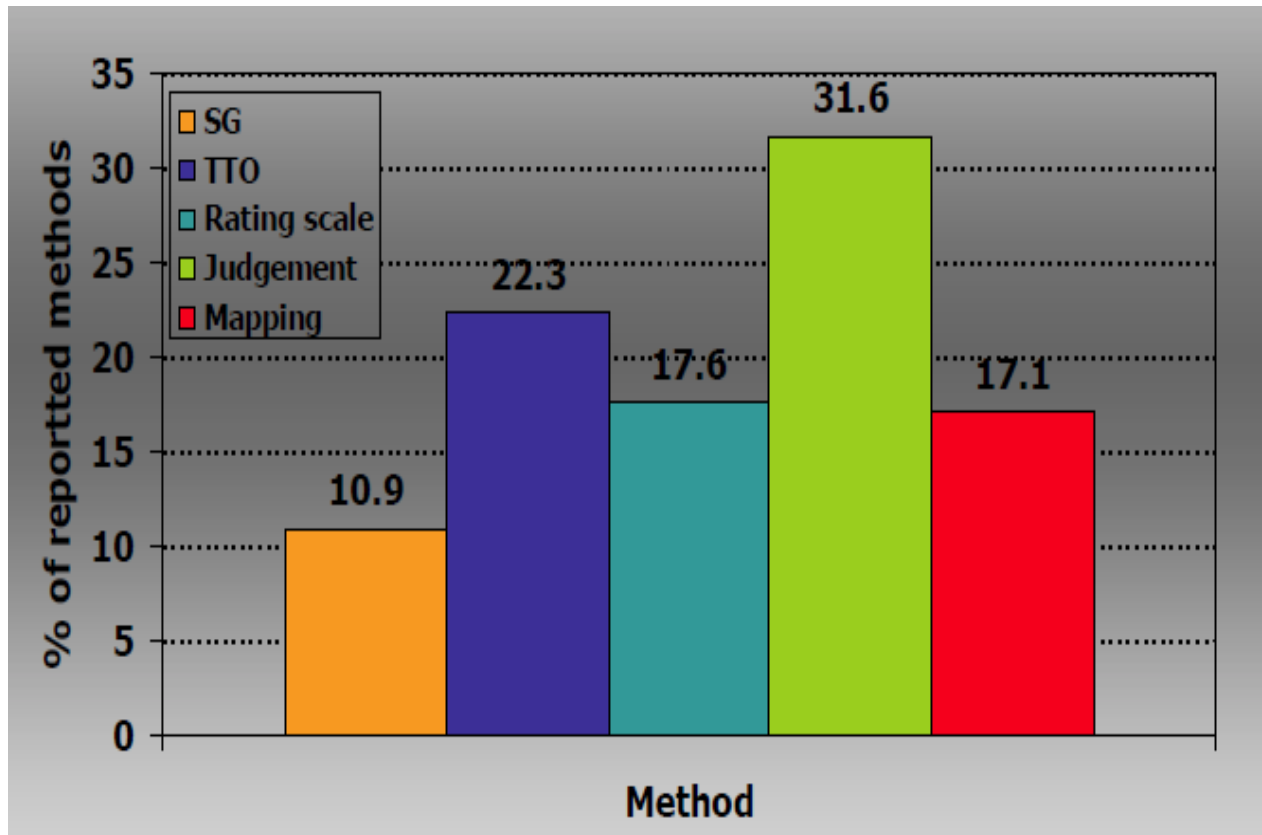
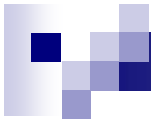






$U = 1 - (1-V)^{1.6}$	Torrance et al (1976)
$U = 1 - (1-V)^{2.2}$	Wolfson et al (1982)
$U = 1 - (1-V)^{2.3}$	Torrance et al (1996)
$U = 1 - (1-V)^{2.4}$	Feeny et al (2000)
$U = 1 - (1-V)^{2.7}$	Krabbe et al (1997)
$U = 1 - (1-V)^{2.9}$	Feeny et al (2000)
$U = V^{0.56}$	Furlong et al
$U = V^{0.47}$	Furlong et al / Le Gales et al (2001)








DOLOČANJE UPORABNOSTI S VPRAŠALNIKI

- Vprašalniki Euro-Qol 5-D, SF-6D, Health Utility Index (HUI 2,3), QWB
- Prednosti: hiter in enostaven zajem podatkov
- EQ-5D:
 - 5 dimenzij (pokretnost, bolečina/neugodje, skrb zase, tesnoba/depresija, vsakdanje aktivnosti)
 - vsaka dimenzija ima 3 nivoje (brez težav, nekaj težav, velike težave)
 - 243 stanj + stanje smrti in nezavesti (skupaj 245 stanj)



EQ-5D

POKRETNOST

- Pri hoji nimam nobenih težav.
- Pri hoji imam nekaj težav.
- Priklenjen-a sem na posteljo.

SKRB ZASE

- Zase poskrbim brez težav.
- Pri umivanju ali oblačenju imam nekaj težav.
- Ne morem se sam-a umivati ali oblačiti.

VSAKDANJE AKTIVNOSTI (*npr. delo, študij, gospodinjska dela, družina, prosti čas*)

- Vsakdanje aktivnosti mi ne povzročajo težav.
- Vsakdanje aktivnosti opravljam z nekaj težavami.
- Vsakdanjih aktivnosti nisem zmožen-na opravljati.

BOLEČINA/NEUGODJE

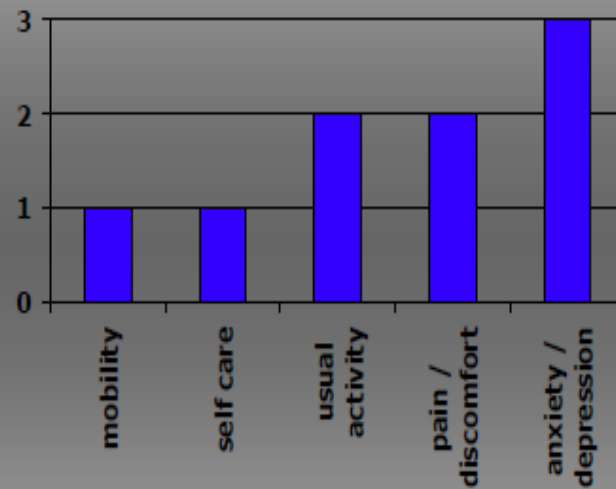
- Ne čutim bolečin oz. nimam občutka neugodja.
- Pestijo me zmerne bolečine ali občutki neugodja.
- Čutim nevzdržne bolečine ali skrajno neugodje.

TESNOBA/DEPRESIJA

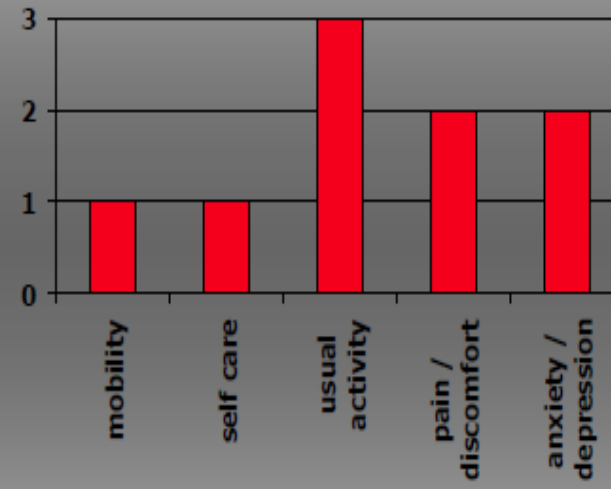
- Nisem tesnoben-na ali depresiven-na.
- Sem zmerno tesnoben-na ali depresiven-na.
- Sem skrajno tesnoben-na ali depresiven-na.

Does moving from A to B benefit a patient?

If so, then by how much?



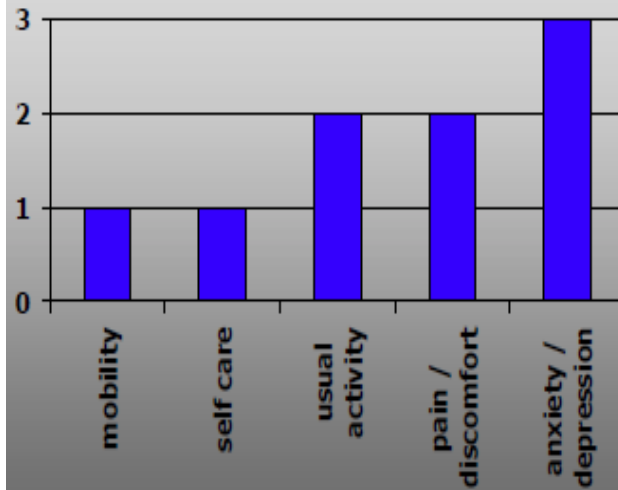
Profile A : 1 1 2 2 3



Profile B : 1 1 3 2 2

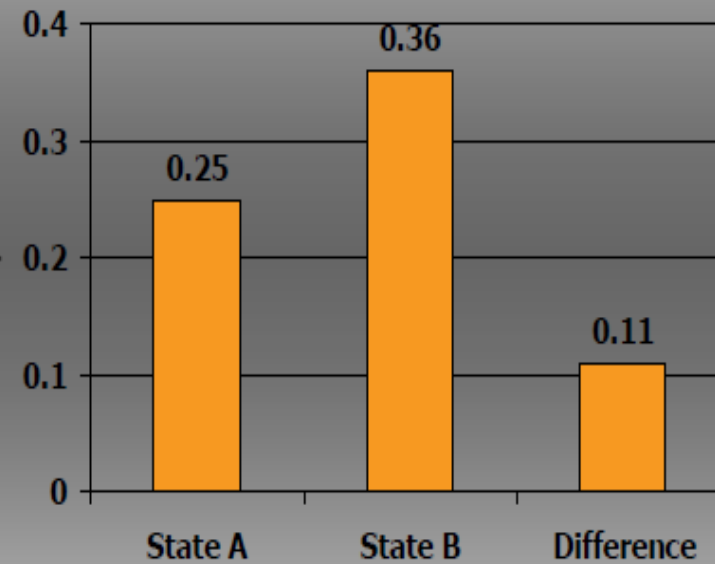
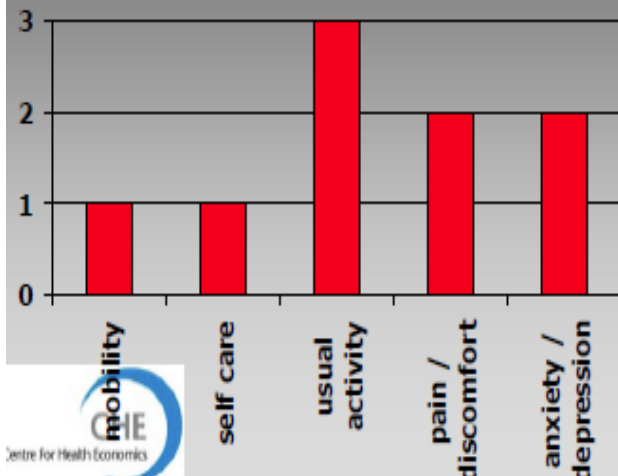


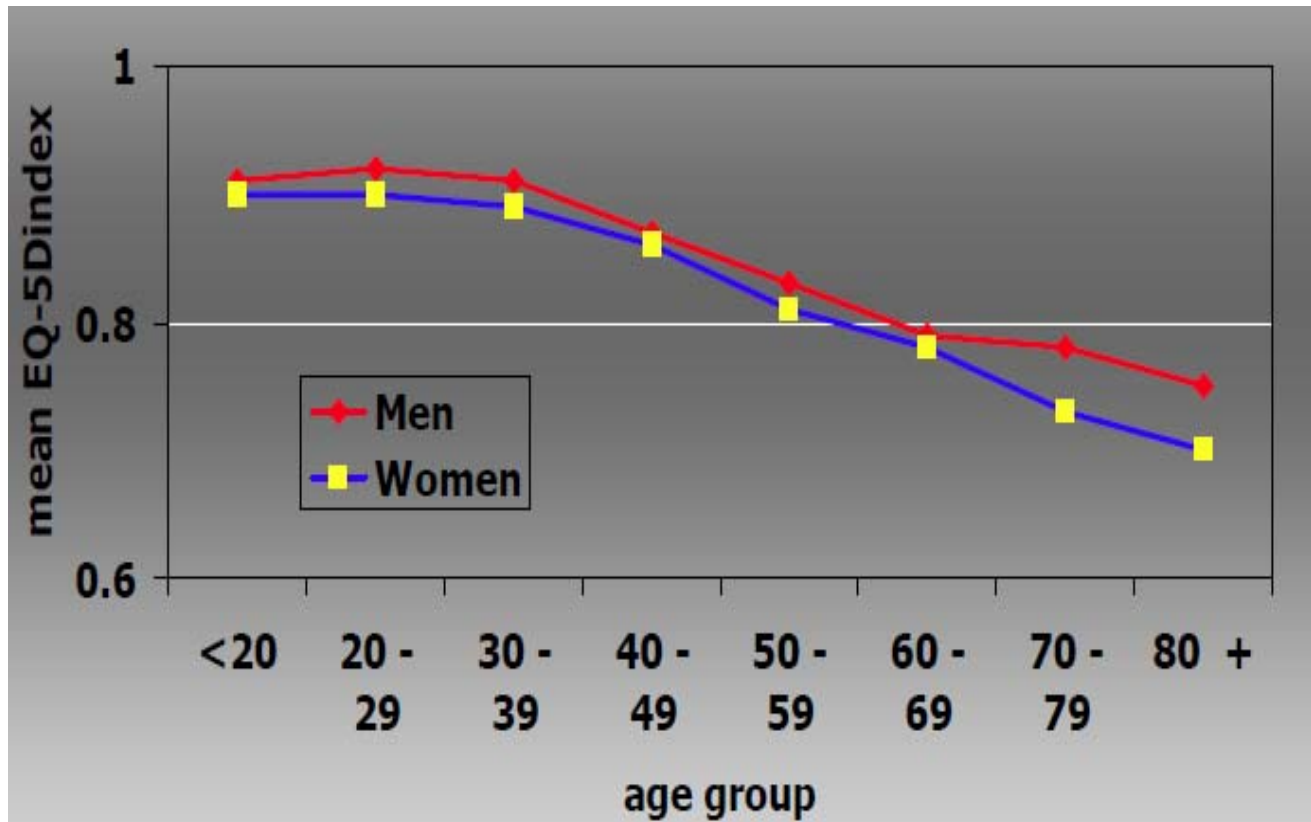
Profile A : 1 1 2 2 3

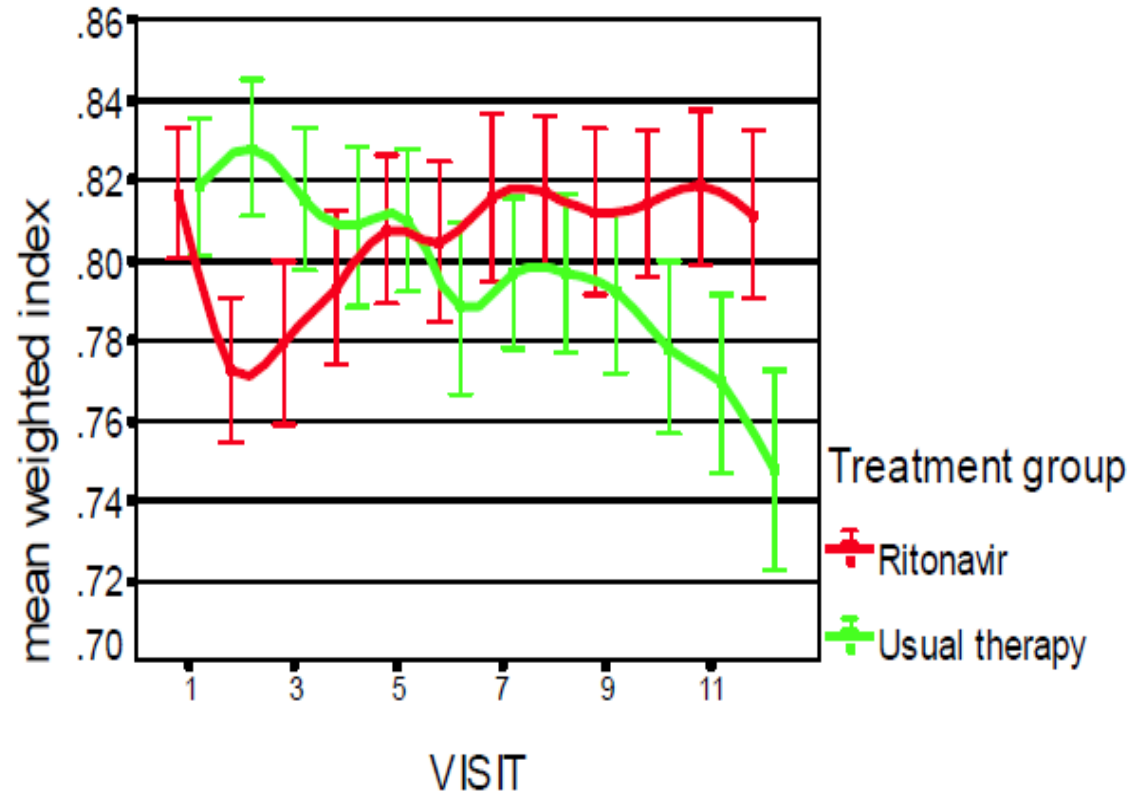
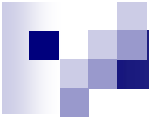


Population preference weights

Profile B : 1 1 3 2 2








Acne	Dyspepsia	Low back pain	Population health surveys
Acupuncture	Dystonia	Lung cancer	Primary care
Alcohol dependency	Elderly (QOL)	Lung embolism	Prostatic hypertrophy
Angioplasty	Endometriosis	Lung transplantation	Prostate cancer
Angina (treatment options)	Enteral nutrition	Lymphoedema	Psoriasis
Anorectal reconstruction	Epilepsy	Magnetic Resonance Imaging	Psychiatric problems in GP practice
Asthma	Erectile dysfunction	Melanoma (stage III)	Redundancy (impact of)
Blood transfusion	Fabry's disease	Menorrhagia	Rehabilitation (effects of)
Bone marrow transplant	Gastro-enteritis	Migraine	Renal disease (end-stage)
Breast cancer	General practice	Multiple Sclerosis	Renal oncology
Breast cancer screening	Geriatrics	Myeloid Leukaemia	Renal (kidney stone disease)
Bronchitis	Gilles de la Tourette	Myocardial infarction	Respiratory illness
Cardiac surgery	Graves eye disease	Neonatal surgery	Rheumatoid arthritis
Cardiology	Growth Hormone	Neural tube defects	Rhinitis
Cardiovascular disease	Haemophilia	Neurosurgery	Road accidents (non-fatal)
Cataract surgery	Hip fracture/replacement	Non-Hodgkin's disease	Schizophrenia
Chemotherapy (impact)	HIV infection	Lupus	Sepsis
Chronic fatigue	Hodgkin's dis.	Lymphoma	Sinusitis
Chronic illness	Homeopathy	Nutrition	Smoking (impact of)
Cochlear implantation	Hormone replacement therapy	Obstructive sleep apnoea	Stent
Colles fracture	Hospital waiting lists	Orthopaedic medicine	Stroke
Colorectal carcinoma	Hysterectomy	Osteoarthritis	Trauma
Congestive heart failure	Imperforate anus	Pain	Tuberculosis (prevention in HIV)
Conservation work (benefits of)	Inguinal hernia	Pancreatic cancer	Turner's syndrome
Cosmetic surgery	Incontinence	Parenteral nutrition	Urology
Cystic fibrosis	Intensive care	Peripheral arterial disease	Vascular surgery
Dementia	Intestinal failure	Peripheral vascular disease	Venous leg ulcers
Detoxification	Ischaemic heart disease	Physiotherapy	Visual impairment
Diabetes	Joint replacement	Picture archiving and Communication systems (PACS)	Weight loss (treatment for)
Drug monitoring (nursing home residents)	Leg ulcer clinics		Women's surgery
	Liver disease		
	Liver transplantation		



Izračun QALY

- QALY upošteva tako **kvantiteto** kot **kvaliteto** življenja.
- Je zmnožek med pričakovano življenjsko dobo in kakovostjo preostalega življenja.



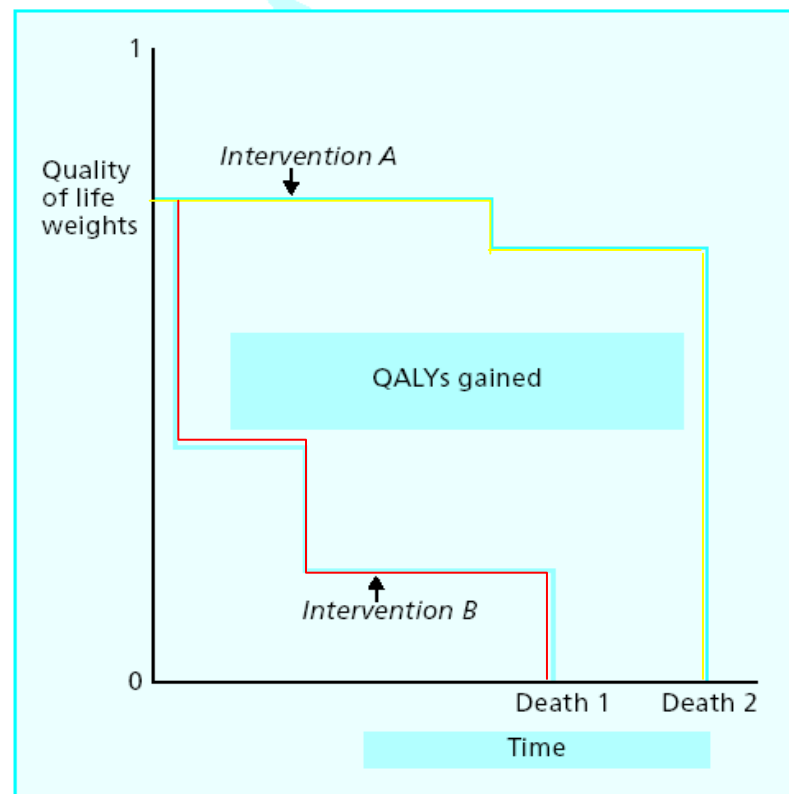
Relacija uporabnosti in z zdravjem povezane kakovosti življenja (HR-QOL)

- Z zdravjem povezano kakovost življenja ima več dimenzij (npr. fizična, mentalna, kognitivna, družbena funkcionalnost, bolečina itd.) in instrumenti za merjenje kakovosti življenja imajo v splošnem večje število domen, ki predstavljajo posamezne dimenzije (SF-36 ima 9 domen).
- Uporabnost skuša zajeti z zdravjem povezano kakovost življenja v en indeks, ki **naj bi** predstavljal preferenco do vseh dimenzij v celoti.



- Vprašalniki **Euro-Qol 5-D, Health Utility Index 2,3, SF-6D, QWB** imajo povezavo z uporabnostjo in jih zato lahko uporabimo v ekonomskih analizah
- Občutljivost pri specifičnih boleznih in razlikah med posameznimi zdravili
- Specifični vprašalniki – mapiranje

Izračun razlik pridobljenih QALY-jev med dvema posegoma:





Dejstva

- Razvoj QALY za namen pomoči pri relokaciji sredstev
- Predpostavimo, da je namen maksimizacija zdravstvenih koristi
- pravičnost, enakopravnost, politični vidiki?
 - konvencionalni QALY: NICE, US Panel on CE in Health and Medicine
 - “equity-weighted” QALY
- koncept QALY temelji na teoriji pričakovane uporabnosti oz. koristnosti (EUT)
 - predvideva nevtralnost ljudi do tveganja



Kaj je vrednost?

- Vrednost= preferenca do zdr. stanja, zaželjenost
- meri se preferenca zdr. stanja in NE spremembe zdr. stanja
 - čigava?
 - merjena na kakšen način?
 - vrednost posameznikovega zdr. stanja vs. vrednost zdr. stanja skupnosti (PTO)

Kako se lahko QALY uporablja?

Table 1 Matrix characterizing uses and definitions of QALYs

Question:	Personal clinical decision or insurance decision	Societal audit: evaluation of ongoing activities or programs	Societal resource allocation: priority setting across proposed programs and program changes	
Value concept: whose health outcome and whose preferences	Individual's health: ex ante desirability as seen by the individual	Individuals' health: experienced utility, then aggregated	Individuals' health: ex ante desirability as seen by each individual, then aggregated	Community health: the health of others,* as seen by each individual, then aggregated
Whom to ask:	The individual, informed by patients/disabled people [†]	Those affected by the activity; e.g., patients/disabled people, those "prevented" from a disease, etc.	Representative sample of population	Representative sample of population
Valuation technique:	SG, [‡] TTO, [§] RS	SG, [‡] TTO, [§] RS, or MAU instrument	SG, [‡] TTO, [§] RS, or MAU instrument	PTO, or transformation of MAU values
Health outcomes:	Complete health profiles over time [¶] Health states and durations	Complete health profiles over time [¶] Health states and durations	Health states and durations (conventional QALY application)	Health states and durations
Additional assumptions needed:	None, if SG used Risk neutrality on longevity, additivity across time	Aggregation across individuals Risk neutrality on longevity, additivity across time, aggregation across individuals	Risk neutrality on longevity, additivity across time, aggregation across individuals	Risk neutrality on longevity, additivity across time, aggregation across individuals
Additional considerations needed:		Equity of actual outcomes Equity of actual outcomes	Equity of potential outcomes	Equity/fairness built in to some extent?

SG, standard gamble; TTO, time trade-off; RS, rating scale; MAU, multiattribute utility; PTO, person trade-off.

*In valuing health changes for others, respondents may include concerns for equity and fairness.

[†]Patients/disabled people can provide valuable information about the magnitude of the gain from adaptation, where such occurs, to temper the disutility as seen ex ante including the disutility from the loss of opportunity.

[‡]SG may be preferred because it alone has been shown to have interval scale properties with respect to preferences, i.e., a change from 0.2 to 0.4 is equally preferred to a change from 0.6



■ Uporaba:

- razporejanje sredstev oz. določevanje priorit^{et}
 - merjenje preferenc posameznikov splošne populacije (zdr. stanja, ki se tiče posameznika oz. ki se tiče ostalih članov skupnosti)
 - informiranje posameznikov o zdr. stanjih (ex-ante)
- odločitve za zdr. obravnavo posameznika:
 - določuje se preference posameznika, ki ima bolezen (ex-post)
- merjenje zdravja oz. bremena boleznⁱ v družbi:
 - merjenje preferenc določene populacije bolnikov



■ Načini merjenja

- klinične odločitve: SG; TTO, RS

- družbene odločitve:

- zdr. stanja, ki se tičejo posameznika: SG, TTO, RS, vprašalniki

- zdr. stanja, ki se tičejo ostalih članov skupnosti: PTO



- Kako so definirana zdr. stanja?
 - konvecionalni QALY: zdr. stanje nima časovne dimezije
 - preference do zdr. profilov

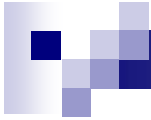
- Diskontiranje QALY-jev



Pomankljivosti QALY

- Pomanjkanje občutljivosti
- Vrednosti ekvivalentnih zdravstvenih koristi so različne v različnih kontekstih (starost, zdr. stanje, itd.)
- Ne zajame breme skrbnika in ostalih članov družine
- Čigave preference meriti – splošna populacija, bolniki
- Različni načini merjenja QALY uteži lahko privedejo do različnih zaključkov o stroškovni učinkovitosti*

* McDonough et al. *Pharmacoeconomics* 2007, 25 (2): 93-106.



■ Kljub pomankljivostim:

- je QALY indeks, ki omogoča primerjavo strategij zdravljenja med različnimi področji zdravstva in tudi izven zdravstva
- ga je smiselno uporabljati kot enega od kriterijev za odločitve o financiranju zdravstvenih strategij in na ta način povečati racionalnejšo uporabo sredstev



Naloga:

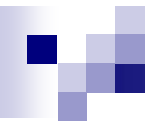
- Skupina 1: Kaj so DALY-ji?

- Skupina 2: Bolniki z rakom
 - Katere načine določevanja U so uporabljale raziskave?
 - Kakšne so vrednosti uteži uporabnosti?

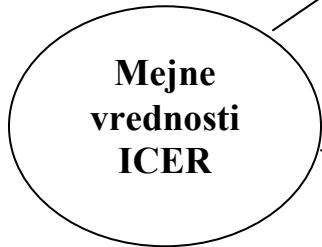
- Skupina 3: Bolniki z osteoartritisom
 - Katere načine določevanja U so uporabljale raziskave?
 - Kakšne so vrednosti uteži uporabnosti?



**KOLIKO JE VREDEN
QALY?**



ENOTE: QALY in LYG (obe se pojavljajo)



Arbitrarno določene

Implicitne
Eksplisitne: večina držav, ki že ima zahtevo po FEKO študijah za reimbursiranje nima eksplicitno določene meje – izjema VB, Irska

Določene inštitucije (npr. WHO) oz. posamezniki predlagali mejne vrednosti

»Čvrste« in »mehke« meje

WTP in podobne raziskave

Pregledni članek: Hirth in sod. 2000

»Human capital«

Retrospektivne raziskave odločitev:

-George in sod. 2001 (v AUS)- nekonsistentna ICER meja, definirano območje meje
 -Devlin. 2003 (VB): med 35-48.000 funti na QALY


Izražene preference (revealed pref.)

Tveganje pri službi Varnost, nevezana na službo

Kontingenčno vrednotenje (WTP)

Študije na bolnikih :
 -Gyrd-Hansen, 2003;
 -Byrne et al., 2005;
 -King et al., 2005
 -ostali

EUROVAQ projekt
 -10 EU držav
 -CV merjenje ->risk reductions associated with safety improvements« na splošni populaciji
 ->elicitation of a willingness-to-pay-based value of a QALY based on discrete choice methods«



OVREDNOTENJE MEJNEGA PRIRASTKA STROŠKOV GLEDE NA PRIRASTEK UČINKOVITOSTI NA PODLAGI ALTERNATIVNIH STRATEGIJ ZDRAVLJENJA PACIENTOV S KONČNO LEDVIČNO ODPOVEDJO V SLOVENIJI

■ **METODE**

Izvedli smo analizo stroškovne učinkovitosti ter analizo stroškovne uporabnosti alternativnih strategij zdravljenja bolnikov s KLO v Sloveniji. Izdelali smo Markovski model ter kot orodje za postavitev modela in izračun rezultatov uporabili programsko opremo Tre Age Pro Suite 2005, različice 1.6.

■ **VIDIK RAZISKAVE**

Analizo smo izvedli z vidika plačnika zdravstvenih storitev, kjer smo upoštevali neposredne stroške povezane z zdravljenjem KLO.

■ **OBDOBJE ANALIZE**

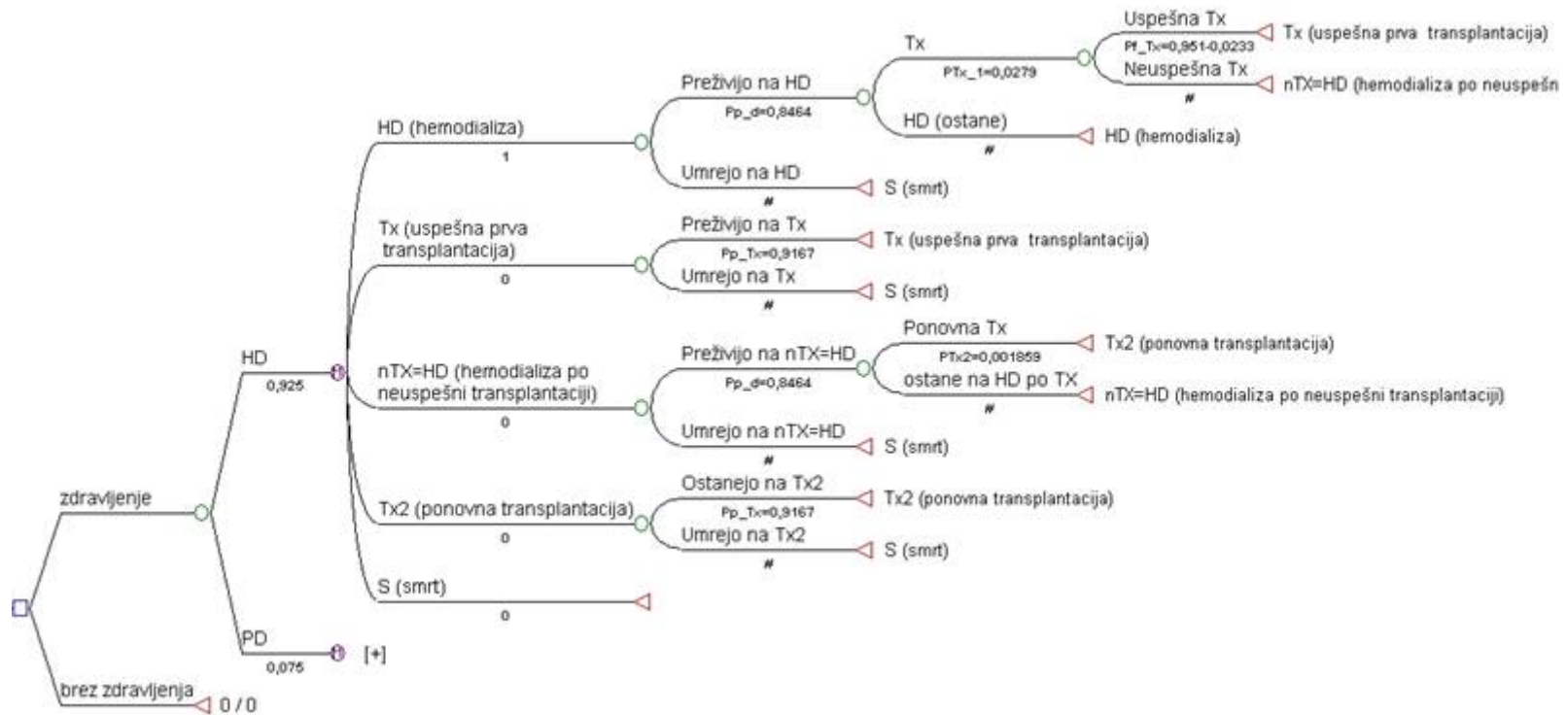
Analizo smo izvedli za obdobje 20 let.

■ **IZIDI ANALIZE**

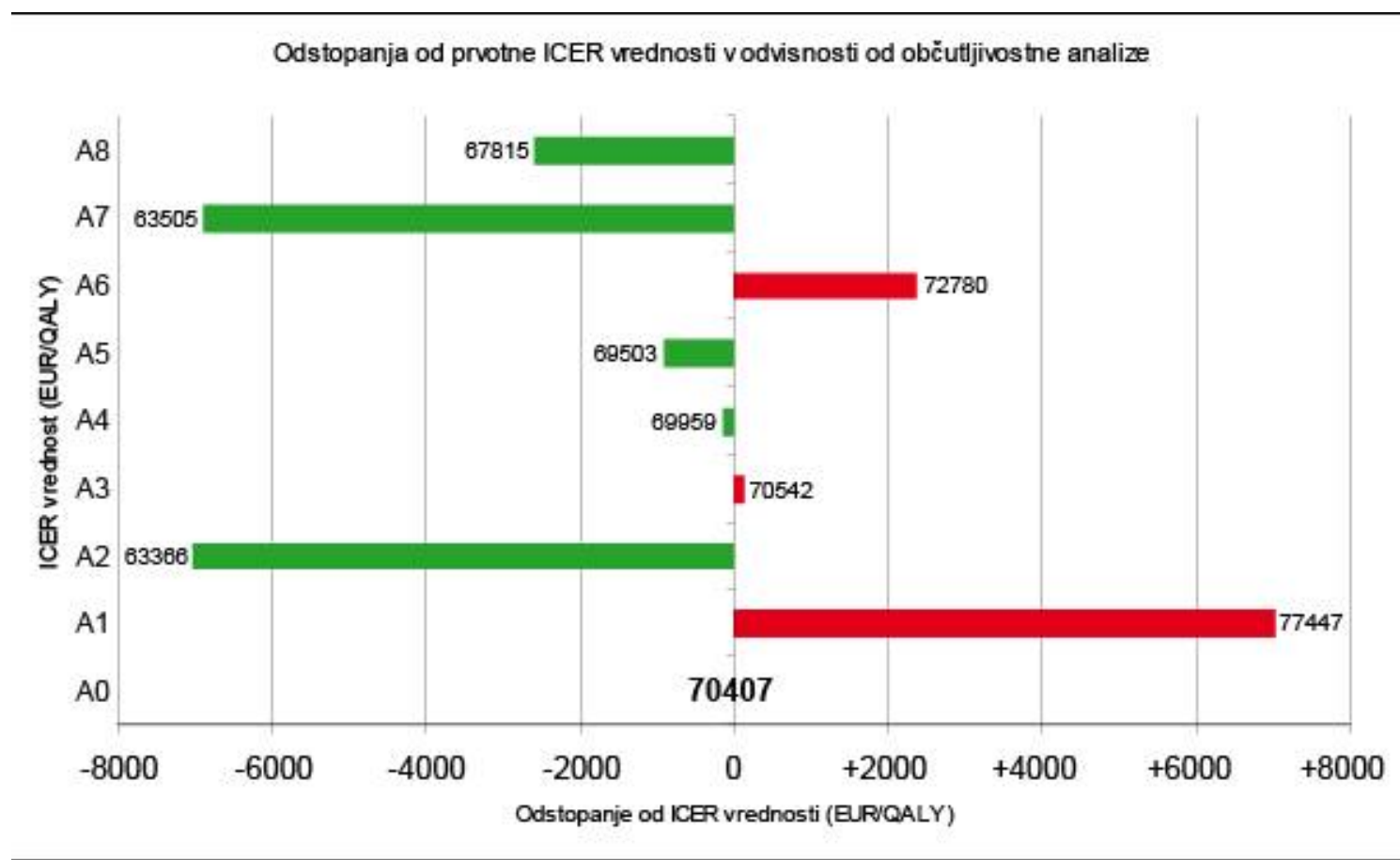
Kot izide analize smo spremljali preživetje, stroške ter učinkovitost zdravljenja KLO glede na strategijo brez zdravljenja. Kot učinkovitost smo enkrat upoštevali pridobljena leta življenja (LYG), drugič pa leta zdravstveno kakovostnega življenja (QALYs). Na podlagi kumulativnih stroškov ter učinkovitosti smo določili tudi prirastek stroškov glede na prirastek učinkovitosti.

■ **DISKONTIRANJE STROŠKOV IN UČINKOVITOSTI**

Tako stroške kot tudi učinkovitost zdravljenja smo diskontirali z v praksi najbolj uporabljeno diskontno stopnjo – 5% na leto. V občutljivostni analizi smo analizirali tudi vpliv 3% diskontne stopnje.



- Rezultat:
 - ICER: 70.407 EUR/QALY
- Občutljivostna analiza





**Willingness to pay for a life-year gained
from the societal perspective**





Brief introduction

- Arbitrarily defined cost-effectiveness thresholds
 - \$20,000-\$100,000 per QALY or LYG
- Reviews of pas decisions:
 - Australia: unlikely to recommend a drug for which the additional cost per LYG exceeded AU\$76,000 and unlikely to reject it if this additional cost per LYG was below AU\$42,000.
- Studies exploring value of statistical life
- Studies measuring WTP for a change in quality of life score
- No published research is available that would directly assess how much a society values benefits of health technologies affecting survival



Methods

- Contingent valuation (“Willingness-to-pay”):
 - Methodology primarily developed by environmental economists (NOAA guidelines)
 - Seeks to elicit the **value** that people attach to the specific health care intervention by asking them **how much they would be prepared to pay** to obtain the benefits of the intervention.
 - Hypothetical market
 - Applied in the evaluation of various health care interventions
 - Methodological issues: Importance of careful study design when attempting to apply CV methodology to public policy

- Contingent valuation (CV) method was used to measure how much a general population in Slovenia was willing to pay for a new, hypothetical, oncology drug that prolongs survival.



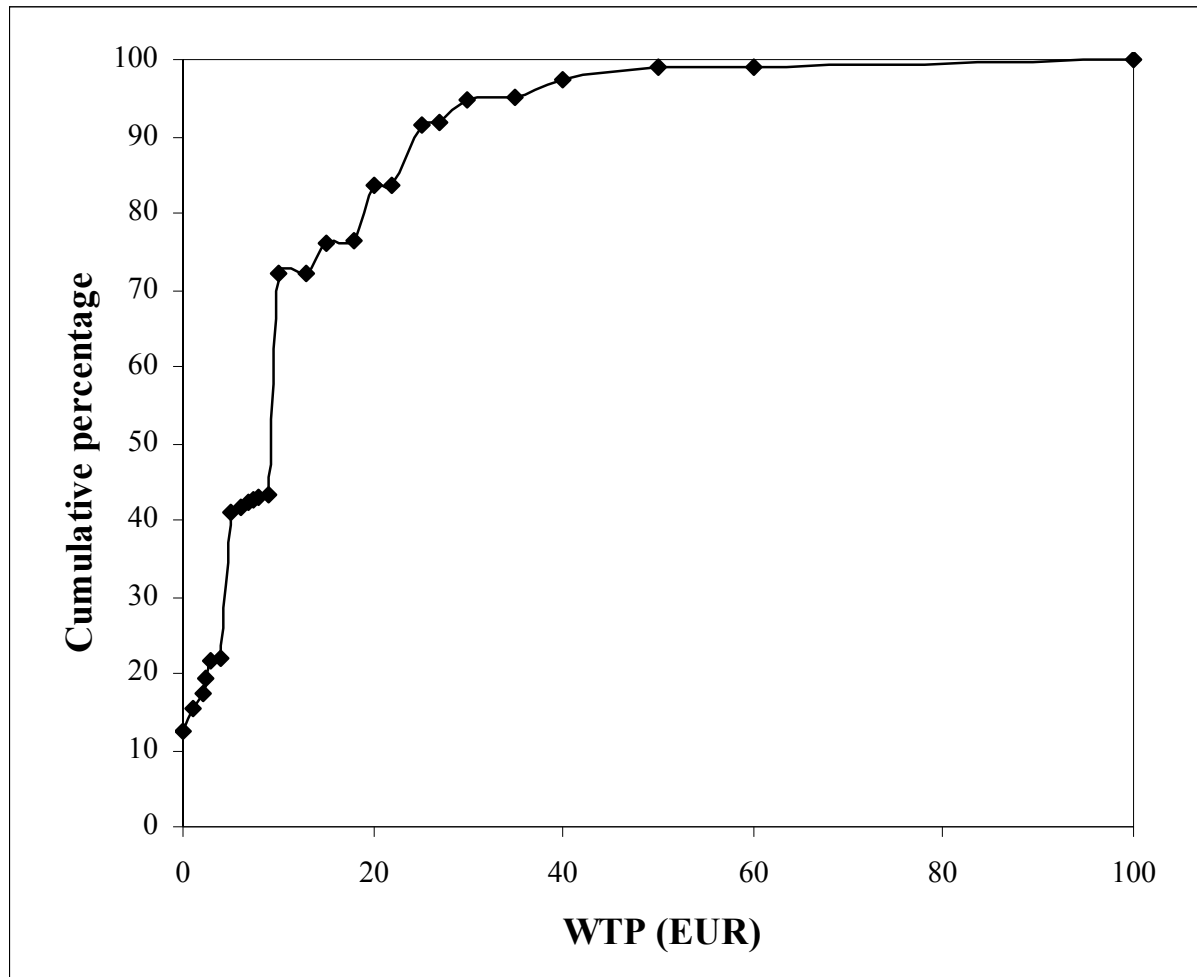
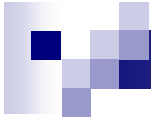
Methods (cont.)

- 1,500 questionnaires were mailed to a random sample of Slovenian general population above 18 years old
- A reminder postcard was sent to non-responders a week after the initial mailing.
- Questionnaire design
 - Validation: experts and convenience sample of the general population
 - Design: initial questions, presentation of scenario, WTP elicitation, scope tests and disclosure of socio-demographic data.
- WTP per life-year gained
 - average amount of money that an individual would pay for the rest of his life was divided by the benefit of the drug and the probability of needing the drug
 - discounting future costs and benefits

Results

- A 45% response rate (N=682)
- 600 valid, 82 protesting
- **Monthly WTP:**
 - 12.04 EUR for base-case scenario ([Figure](#))
 - Scope tests:

Lifetime risk of getting cancer (%)	Benefit of a new oncology drug	Average monthly WTP (EUR)
30	1 year	12.04
30	3 months	9.80
30	3 years	16.55
10	1 year	10.82
100	1 year	24.32



- **Construct validity:** predictors of the WTP

Variable	Unstandardized regression coefficients	p-value
Surviving cancer	0.257	0.009*
Anxiety about getting cancer	0.153	0.025*
Income	0.429	0.000*
* p<0.05		

- **WTP per life-year gained:** A diminishing marginal utility of survival prolongation

Lifetime risk of getting cancer (%)	Benefit of a new oncology drug	WTP per LYG (EUR)
30	3 months	61,909
30	1 year	19,921
30	3 years	8,917



- Criterion validity:
 - NEEDS study: app. 40,000 EUR/LYG (3 months survival benefit)
- Transferability to other countries: PPP
- Transferability to non-oncology setting