APPLICABILITY OF MEASURING HEALTH RELATED QUALITY OF LIFE IN HEALTH CARE DECISION MAKING

Brno, 18 April 2024

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CV András Inotai

Affiliation
- Associate Professor (Center for Health Technology Assessment, Semmelweis University)
  - 10+ years of teaching experience
- Head of Pharmaceutical Policy Research (Syreon Research Institute)
  - 15 years of research experience in pharmaceutical policy, pharmacoeconomics, HTA and patient centric healthcare

Scientific appointment
- President, ISPOR Hungary Chapter/Hungarian Health Economics Association (2014-15)

Research track
- 60+ peer-reviewed scientific publications in health economics, pharmaceutical policy, HTA and patient centric healthcare
- Selected list of publications: https://pubmed.ncbi.nlm.nih.gov/?term=inotai+a&sort=pubdate&size=20

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Did you know that

- compared to women men tend to leave shorter …
- …but have better health related quality of life?

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Areas covered

- Paradigm shift in medicine: emerging role of patients and patient reported outcomes in healthcare
- Quality of life, health related quality of life (HRQoL)
- Measuring HRQoL, EQ-5D, value set
- Health status of the Hungarian population: 2000 vs 2022
- Population norms from the perspective of clinicians
- Perspective of payers - Quality adjusted life years (QALYs)

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Paradigm shift in medicine
The emerging role of PROs

- Lower incidence of acute high mortality diseases (infectious diseases) increase life expectancy on developed (and) developing) countries
- Higher prevalence of chronic conditions with disability along with increasing life longevity
- Improving quality of life is becoming increasingly important besides improving life longevity
- Patient reported outcomes (PROs) – information coming directly from patients on their own health status
  - Valuing health states based on PROs is relatively new and gaining increasing relevance in the field of Medicine
  - Psychometrics: Discipline in psychology to measure PROs – new application in clinical trials

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Health Outcome Measurement

- Biological/physiological parameters
  - (blood cholesterol level mmol/l)
- Observer Reported Outcomes (ObsROs, by non-clinician observer e.g. teacher or caregiver)
  - Focus on observable signs of behaviors
- Clinician Reported Outcomes (ClinROs)
  - Clinician Global Impression, ECOG Performance Score
- Patient Reported Outcomes (PROs)
  - Reported directly: Quality of life
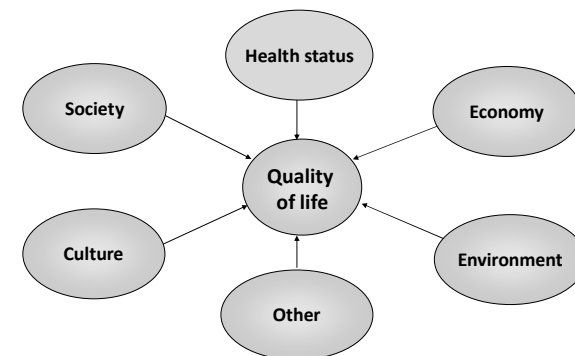 - Reported indirectly: Adherence

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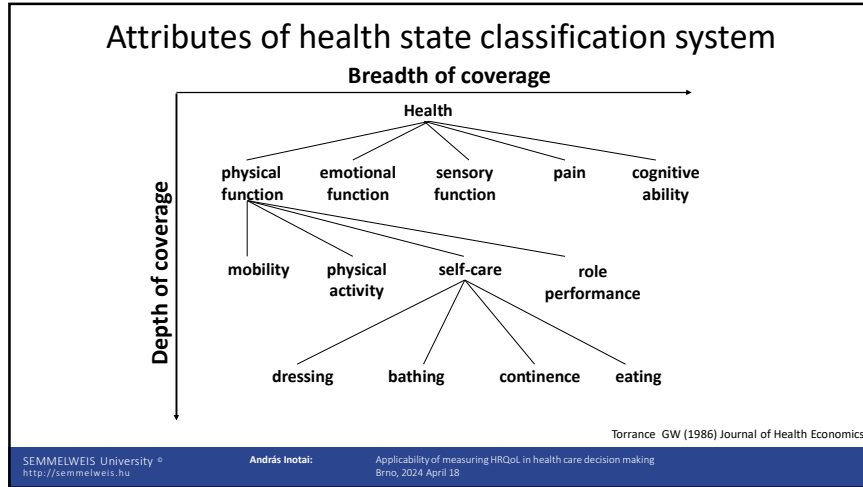"We should set the highest value not on living but on living well"

Socrates

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Determinants of QoL

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Slide 9: Attributes of health state classification system

Breadth of coverage

Depth of coverage

Health

- physical function
- emotional function
- sensory function
- pain
- cognitive ability

physical function →
- mobility
- physical activity
- self-care
- role performance

self-care →
- dressing
- bathing
- continence
- eating

Torrance GW (1986) Journal of Health Economics

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Slide 10: Classification of measures

	Profile	Index
Generic measures	NHP, SF-36, SF-12	EQ-5D, SF-6D, HUI2, HUI3, QWB
Specific measures	Kidney disease questionnaire	RAQoL, SGRQ

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EQ-5D-3L index

EQ-VAS

Under each heading, please tick the ONE box that best describes your health TODAY.

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

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

The best health you can imagine = 100; The worst health you can imagine = 0. YOUR HEALTH TODAY =

EuroQoL © EuroQol Group. EQ-5D™ is a trade mark of the EuroQol Group

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Slide 12: EQ-5D-3L index

- $3^5=243$ possible health states + death + unconsciousness
- PROs:
  - Simple,
  - Easy to understand,
  - Widely used – international references,
    - Comparability among diseases (even with a healthy population, and among different countries
  - Several validated translations in different languages to conduct multinational trials
- CONs:
  - Limited sensitivity to detect small changes

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Value sets

- Health states can be described by combination of statements of health-related quality of life measures.
- 'Value sets' are numerical expressions of how preferred a health state is.
- Reference points used in value sets:
  - 0.0 death (health states considered worse than death have negative weights)
  - 1.0 full health
- The provision of population-level health-related quality of life estimates (also known as 'population norms') is expected to improve the preciseness of patient-level clinical decision making, health economic and public health studies.
- However, preference towards these health states is influenced by culture, resulting in differences across populations.

EQ-5D value sets from UK (1997) and Hungary (2020)

Dimension	Level	Coefficient (UK)	Coefficient (HU)
	Constant	0.081	0.020
Mobility	1. level	0	0
	2. level	0.069	0.022
	3. level	0.314	0.648
Self-care	1. level	0	0
	2. level	0.104	0.051
	3. level	0.214	0.355
Usual activities	1. level	0	0
	2. level	0.036	0.025
	3. level	0.094	0.246
Pain / discomfort	1. level	0	0
	2. level	0.123	0.080
	3. level	0.386	0.338
Anxiety / depression	1. level	0	0
	2. level	0.071	0.078
	3. Level	0.236	0.258
	N3	0.269	-
Meas. interval		-0.594 to 1	-0.865 to 1

Health Status: 11223 UK

calculated index value (utility):
1.0 – 0.081 – 0.036
- 0.123 – 0.236 – 0.269 = **0.255**

Health Status: 11223 HU

calculated index value (utility):
1.0 – 0.020 – 0.025
- 0.080 – 0.258 = **0.617**

Drummond et. al. Methods for economic evaluation of health care programs. Oxford University Press, 1997
Fanni Rencz et al.. (2020) Parallel valuation of EQ-5D-3L and EQ-5D-5L by time trade-off in Hungary. VALUE IN HEALTH 23(9):1235-1245.

HEALTH STATUS OF THE HUNGARIAN POPULATION
2000 vs 2022

Population health survey 2000

- N=5503 (age 18+)
- Instrument: EQ-5D-3L
- Value set used to quantify EQ-5D-3L dimensional responses: UK
- Small sample size for age 65+
- Update was necessary

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Baseline survey data (2022)

Characteristics	Total	
N, %	11910	100
Sex		
Women	6466	54.3
Men	5444	45.7
Age (year)		
12-17	578	4.9
18-24	818	6.9
25-34	1456	12.2
35-44	1664	14.0
45-54	1945	16.3
55-64	1892	15.9
65-74	2176	18.3
75-84	1105	9.3
85+	276	2.3
Geographical region (residence)		
Budapest (Central Hungary)	1364	11.5
Pest (Central Hungary)	1005	8.4
Central Transdanubia	1433	12.0
Western Transdanubia	1280	10.8
Southern Transdanubia	1310	11.0
Northern Hungary	1557	13.1
Northern Great Plain	2153	18.1
Southern Great Plain	1808	15.2

Ctd.		
Education (highest level completed)*		
Less than 8 years in primary school	438	3.7
Primary school	2481	21.0
Secondary school	6447	54.5
University	2469	20.9
Occupation**		
Employed/self-employed	5907	49.6
Unemployed	247	2.1
Pensioner	999	8.4
Student	4023	33.8
Other inactive***	723	6.1
Household size		
1	2180	18.3
2	4083	34.3
3	2349	19.7
4	1916	16.1
5	950	8.0
6	267	2.2
7-9	165	1.4

Inotai et al. Population-level norm values by EQ-5D-3L in Hungary - a comparison of survey results from 2022 with 2000. Manuscript under review

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Statistical methods

- Primary sampling units (PSUs) were settlements, and the secondary sampling units were dwellings in Hungary. The settlements were stratified by county and size.
- All household members aged 12 years or older were included in the survey.
- Design **weights** were calculated based on the sampling design. After the data collection, these **were calibrated to correct for nonresponse by geographical region to population size, biological sex and age distribution, development category of the settlement, and household size, so that we could provide unbiased estimates on the level of the population.**
- To include 11910 respondents aged 12 or more, 15058 individuals were contacted in 7578 households, resulting in a response rate of 79%. Of all the EQ-5D-3L questionnaires, 2.81% were self-administered online, 46.64% by telephone interview, and 50.55% by personal interview, between 1st April and 2nd May 2022.
- Mean EQ-5D-3L index values with their 95% confidence intervals were estimated for the target population by age and sex using "svy: mean" procedure with analytically derived variance estimator associated with the sample mean.

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Dimensional responses

dimension	mobility	self-care	usual activities	pain/ discomf	anxiety/ depr		mobility	self-care	usual activities	pain/ discomf	anxiety/ depr
male 12-15	98.3	98.6	97.8	98.6	99.2	female 12-15	99.6	99.8	99.1	97.3	97.4
male 16-17	99.2	97.9	97.9	99.2	92.6	female 16-17	100	100	100	99.2	94.9
male 18-24	97.7	98.3	96.9	96.8	93.5	female 18-24	97.7	97.9	98	95.1	94.7
male 25-34	98.4	99	98.3	94.1	94.2	female 25-34	98.3	99	97.9	94.8	94.2
male 35-44	96.8	99.8	98.6	92.7	94.2	female 35-44	98.2	99.1	98.2	91.8	93.2
male 45-54	92.9	98.2	94.6	86	90.2	female 45-54	92.8	98.2	94.9	84.8	87.5
male 55-64	83.1	96.6	88.6	71.7	85.1	female 55-64	81	95.2	87.1	69.3	81.2
male 65-74	63.1	90.3	79.9	55	80.2	female 65-74	60.7	90.5	76	46.6	70.1
male 75-84	41.5	75.4	56.8	34.3	68.3	female 75-84	35.8	76.3	54.8	26.8	58
male 85+	24.3	55.6	36.5	25.9	51.3	female 85+	18.7	48.9	31.8	16.9	50.9

% reporting **no problems** in each dimension

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Dimensional differences between male and female

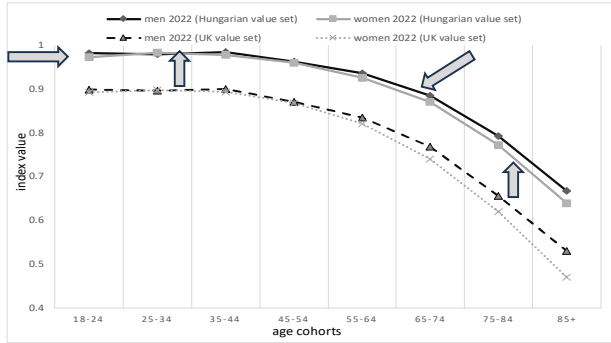|	mobility	self-care	usual activities	pain/ discomf	anxiety/ depr
12-15	-1.3	-1.2	-1.3	1.3	1.8
16-17	-0.8	-2.1	-2.1	0	-2.3
18-24	0	0.4	-1.1	1.7	-1.2
25-34	0.1	0	0.4	-0.7	0
35-44	-1.4	0.7	0.4	0.9	1
45-54	0.1	0	-0.3	1.2	2.7
55-64	2.1	1.4	1.5	2.4	3.9
65-74	2.4	-0.2	3.9	8.4	10.1
75-	5.7	-0.9	2	7.5	10.3
85+	5.6	6.7	4.7	9	0.4

% reporting **no problems** in each dimension
Red: female report more problems. Blue: male report more problems

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The impact of value set: whose preference matters?

Legend: men 2022 (Hungarian value set) — women 2022 (Hungarian value set) — men 2022 (UK value set) — women 2022 (UK value set)

Y-axis: index value; X-axis: age cohorts (18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+)

Inotai et al. Population-level norm values by EQ-5D-3L in Hungary - a comparison of survey results from 2022 with 2000. Manuscript under review
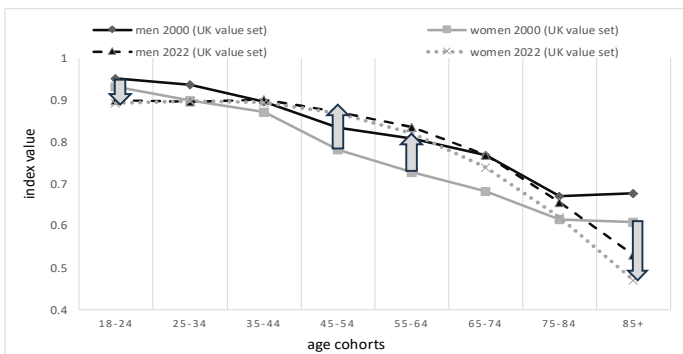
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Dimensional changes 2000 vs 2022

	dimension	mobility	self-care	usual ac	pain/disc	anx/depr		mobility	self-care	usual act	pain/disc	anx/dep
	level	L2+L3	L2+L3	L2+L3	L2+L3	L2+L3		L2+L3	L2+L3	L2+L3	L2+L3	L2+L3
2000	men 18-34	2.5	0.9	1.8	14.8	15	men 18-34	0.6	-0.4	-0.4	9.9	9
	men 35-64	17	4.8	13.2	35.8	30	men 35-64	8.6	3.1	20.3	20.3	20.2
	men 65+	38.9	17.1	30.9	55.9	40.5	men 65+	-6.6	1	1.5	3.2	15.5
	women 18-34	3.2	0.3	2.8	18.2	26.1	women 18-34	1.3	-1.1	0.7	13.1	20.5
	women 35-64	20.7	5.3	15.6	48	44.5	women 35-64	11.8	2.9	30.5	30.5	32.1
	women 65+	49.4	19	35.5	68.4	54.3	women 65+	-2.1	1.1	0.4	5.6	18.6
2022	men 18-34	1.9	1.3	2.2	4.9	6						
	men 35-64	8.4	1.7	5.6	15.5	9.8						
	men 65+	45.5	16.1	29.4	52.7	25						
	women 18-34	1.9	1.4	2.1	5.1	5.6						
	women 35-64	8.9	2.4	6.3	17.5	12.4						
	women 65+	51.5	17.9	35.1	62.8	35.7						

% reporting **any L2 or L3 problems** in each dimension
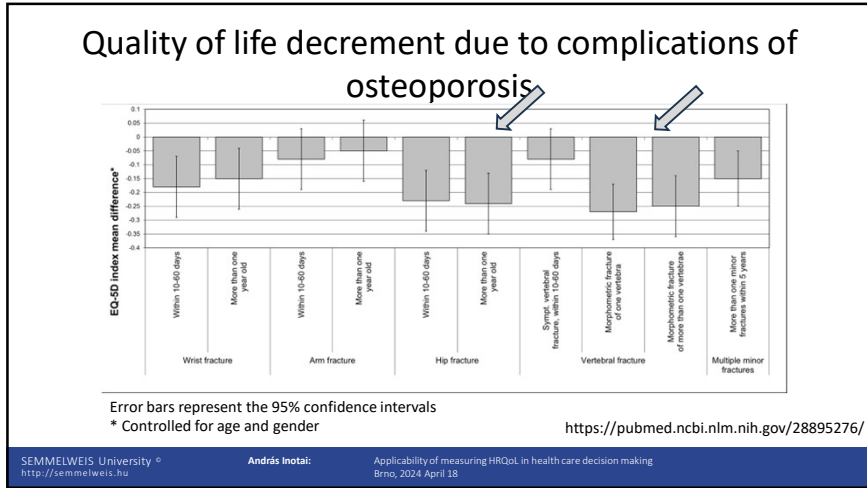Red: improvement over 22 year,
Blue: deterioration over 22 years

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2000 vs 2022

Legend: men 2000 (UK value set) — women 2000 (UK value set) — men 2022 (UK value set) — women 2022 (UK value set)

Y-axis: index value; X-axis: age cohorts (18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+)
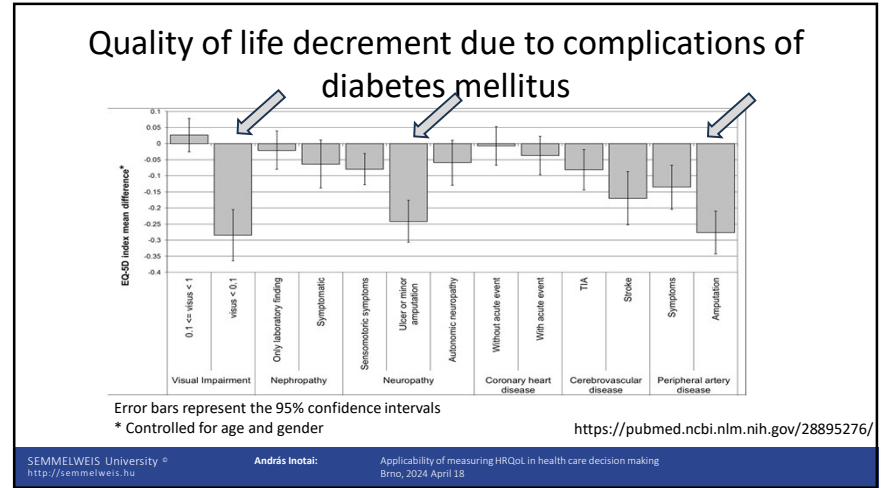
Inotai et al. Population-level norm values by EQ-5D-3L in Hungary - a comparison of survey results from 2022 with 2000. Manuscript under review

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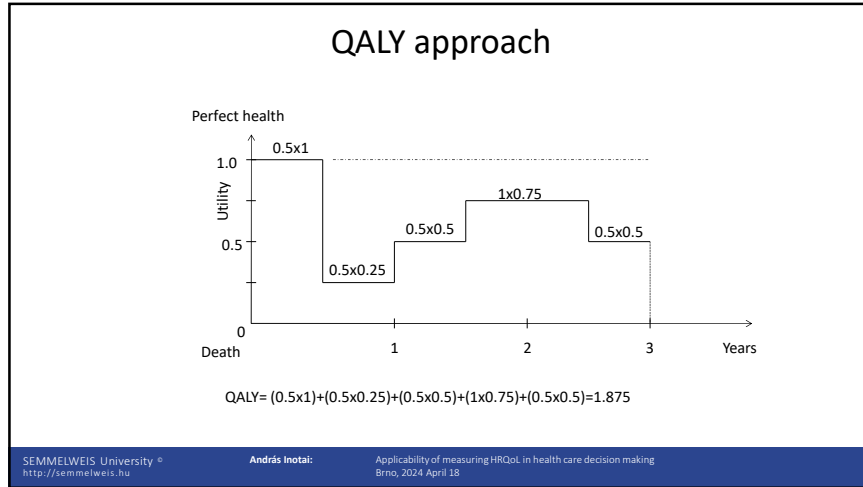## Slide 24

POPULATION NORMS FROM THE PERSPECTIVE OF CLINICIANS

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Slide 25

Quality of life decrement due to complications of osteoporosis

Error bars represent the 95% confidence intervals
* Controlled for age and gender

https://pubmed.ncbi.nlm.nih.gov/28895276/

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Slide 26

Quality of life decrement due to complications of diabetes mellitus

Error bars represent the 95% confidence intervals
* Controlled for age and gender

https://pubmed.ncbi.nlm.nih.gov/28895276/

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THE PERSPECTIVE OF DECISION MAKER:
QUALITY ADJUSTED LIFE YEARS (QALY)

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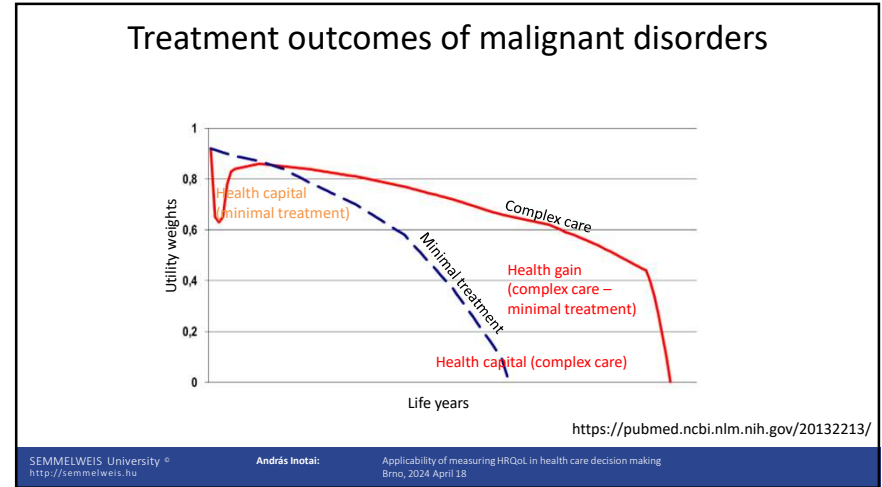
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How to interpret and compare the clinical benefits of health technologies?

- 50% reduction of epilepsy attacks
- 50% reduction of tumor size
- 15% improvement in lung functions
- 4 points improvement in ADAS-Cog score
- 20% less patients need symptomatic therapy
- 2 points improvement in the 10-point pain VAS scale

Which outcome is more important?

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Slide 29: QALY approach

Perfect health

QALY= (0.5x1)+(0.5x0.25)+(0.5x0.5)+(1x0.75)+(0.5x0.5)=1.875

Slide 30: Treatment outcomes of malignant disorders

https://pubmed.ncbi.nlm.nih.gov/20132213/

Slide 31: Relevance of QALY

- QALY is suitable to **aggregate** different dimensions of health outcomes (e.g. in the case of complex oncology treatment):
  - Long-term life years gain
  - Short-term QoL deterioration (due to AEs)
  - Long-term QoL improvement
- QALY is suitable to estimate the magnitude and sign of aggregate health gain
- Set up objective ranking between health technologies through ensuring **comparability**
  - QALY league table
- Calculation of QALYs and estimating utilities is **standardised**
- Critique of QALY has a wide literature

Slide 32: Full economic evaluation - when is it cost-effective?

$$ICER^* = \frac{Cost_{NEW} - Cost_{ALT}}{QALY_{NEW} - QALY_{ALT}}$$

$$= \frac{\Delta Cost}{\Delta QALY}$$

*Incremental cost-effectiveness ratio

Slide 33

Cost effectiveness plane

- QALY loss
- QALY gain
- More costs
- Savings
- Dominated
- CE Ratio
- CE Ratio
- Dominant
- Costs
- QALYs

| NW dominated |
| SW CE ratio |
| NE CE ratio |
| SE Dominant |

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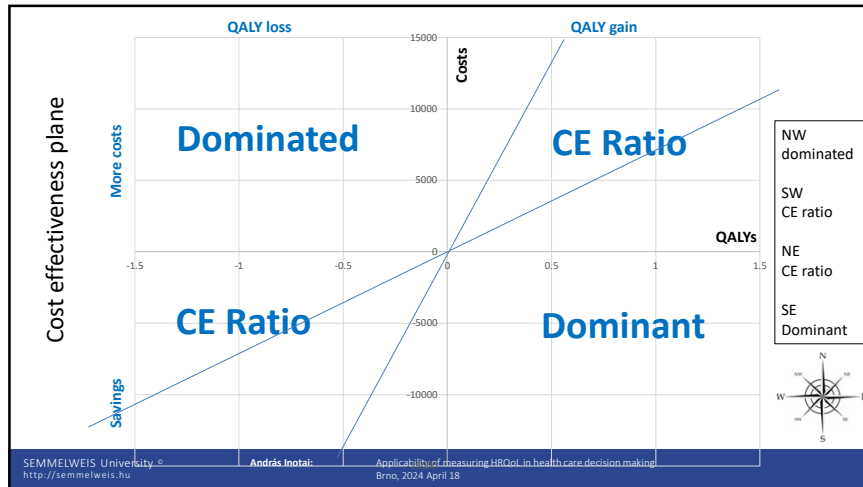
Take-home messages

- Patient Reported Outcomes earn increased importance in medicine
- HRQoL can be measured by many tools, including EQ-5D-3L instrument
- 'Value sets' are numerical expressions of how preferred a health state (e.g. an EQ-5D-3L state) is.
- Population norm values are used as a reference to estimate the HRQoL decrement of a patient population with different diseases
- QALY is a universal health outcome measure which considers both quality of life (utility) and quantity of life (life longevity)
- QALY is used in cost utility analyses to estimate value for money of health technologies (e.g. pharmaceuticals)

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Implications

- SUKL applies cost-effectiveness analyses for pharmacoeconomic evaluations. Attemps were made to estimate willingness to pay threshold (CZK/QALY)*.
- Interestingly, according to EuroQoL website,
  – there are no population norms available for EQ-5D-3L/5L for Czechia
  – there is no value set available for EQ-5D-3L/5L for Czechia
- If EQ-5D-3L is used to estimate QALYs, international value sets are available

*Haluska M et al. Cost-Effectiveness Threshold in the Czech Republic: Are ICERS Still Growing? an Updated Analysis. Value Health 2020;23:2S660

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Questions

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