PSYNC

			15 P
		2 E	5 B
		Experimental	
	32 Gh	57 La	
	Ghent	Lab	

Cost-effectiveness of
mental health care interventions

Keynote:
**Prof. Dr.
Lieven Annemans**

17/01/2020

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Onderbergen 1, 9000 Gent.

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An introduction to health economic evaluations, with a focus on mental healthcare

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Outline

I. **Why health economic evaluations**

II. Basics of cost-effectiveness analysis

III. Models

IV. Prospective health economic evaluations

V. Health economic evaluations and decision making

Q&A

Q&A

Q&A

The conflicting goals of healthcare policy
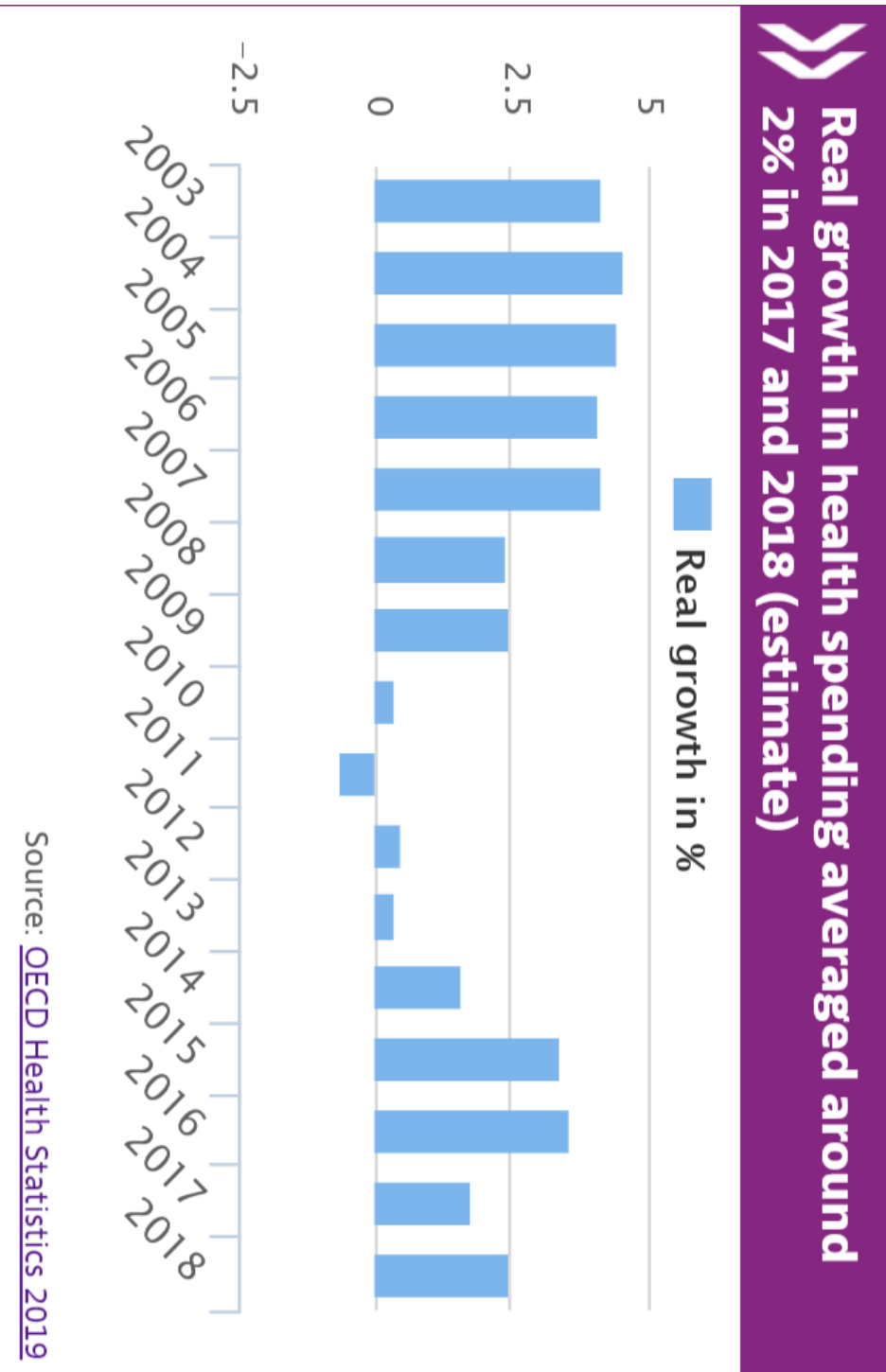
Typical characteristics of the health care system

- <u>Uncertainty</u>   ↑ **Mental health**
  - → Health insurance
    - Moral hazard,
    - "adverse selection"
- <u>Asymmetric information</u>   ↑ **Mental health**
  - → Possibility of supplier-induced demand!
- <u>Externalities</u>   ↑ **Mental health**
  - – Societal consequences of illnesss

→ **Crucial role for governments**

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OECD 2008

Annual growth of public health expenditure in the OECD

Real growth in health spending averaged around 2% in 2017 and 2018 (estimate)

Real growth in %

Source: OECD Health Statistics 2019

→ **Recommended approach**

to **optimize the health of the population within the limits of the available resources,** and within an **ethical framework** built on equity and solidarity principles.

EU Council of Ministers of Health Dec 2010

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What does it mean for innovative technologies/medicines/programmes?

→ *"We need to <u>make available</u> innovative technologies/medicines/programmes that offer an <u>added therapeutic/societal benefit</u> at an <u>acceptable cost</u> and <u>fill unmet medical needs</u>"*

→ Decisions on pricing, reimbursement, recommending usage, …. more and more based on health economic evaluations

- OECD 2003
- EU Council of Ministers of Health Dec 2010

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New health programmes → costs and effects

Costs and savings

Possible Study Perspectives

- <u>Society</u>: both costs/savings within and outside the healthcare sector
    - Includes cost of absenteeism and presenteeism
    - Includes transportation costs
- <u>Health care payers</u>: only costs/savings within the health care sector

    (NOTE: third party payer & patients)
- <u>Hospital</u>: only costs/savings incurred by the hospital

SOCIETY

HEALTH CARE SECTOR

HOSPITAL
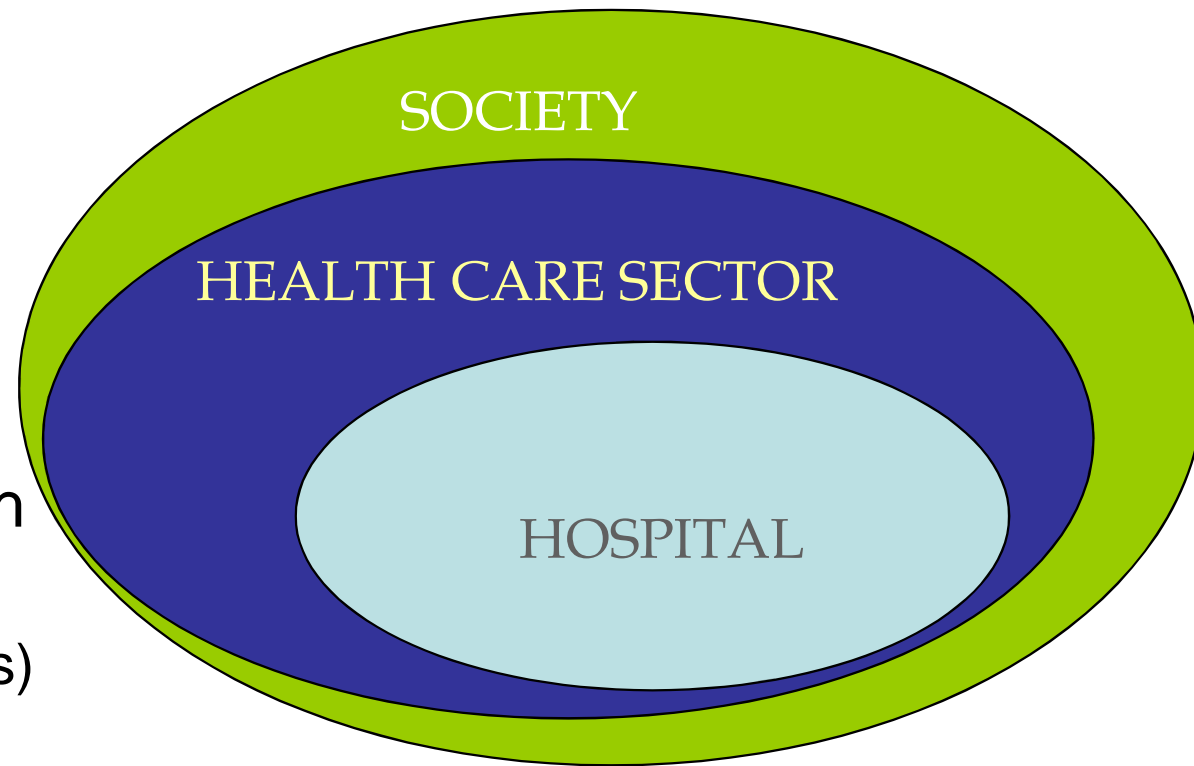
Andlin-Sobocki P et al. The mission is remission - health economic consequences of achieving remission in antidepressant treatment of depression (costs in SKR)
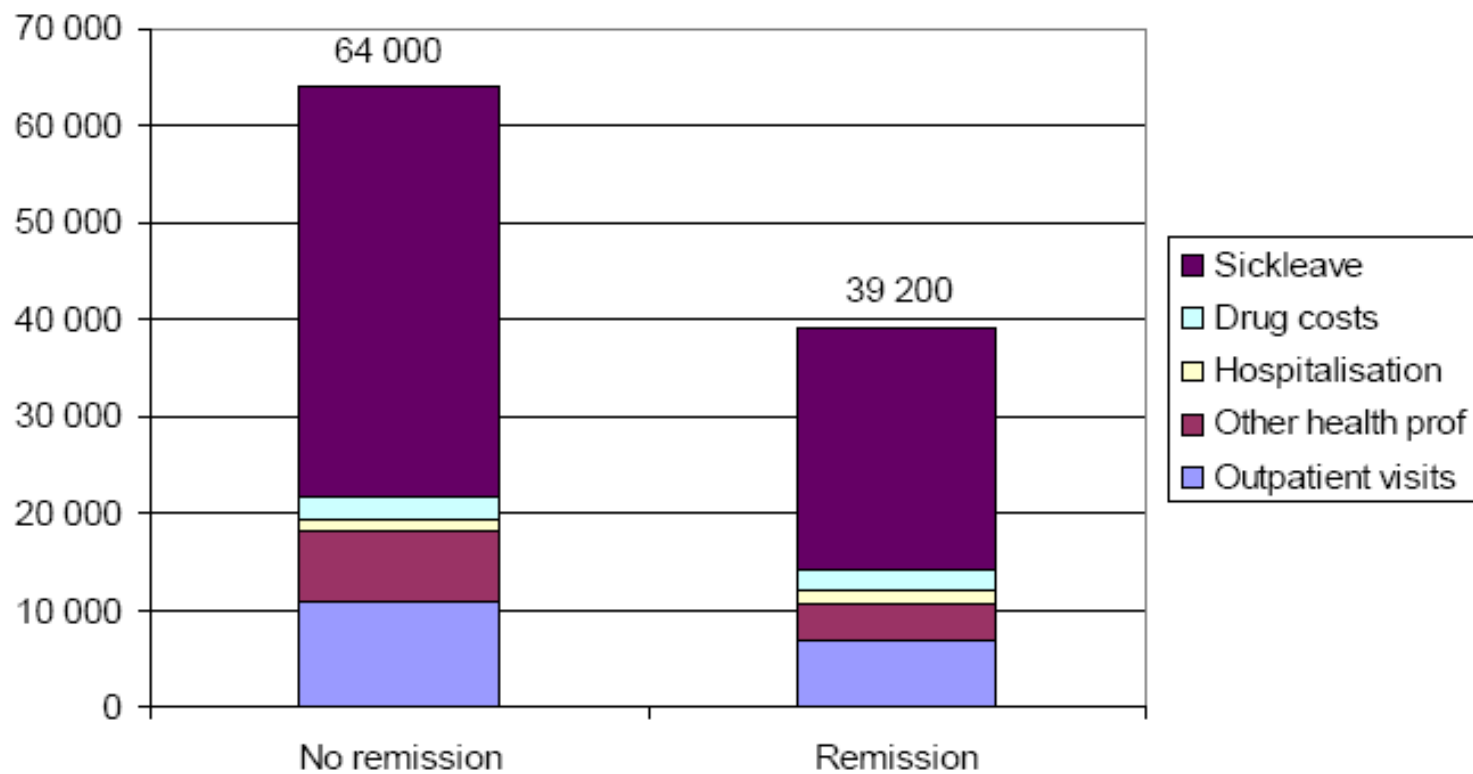
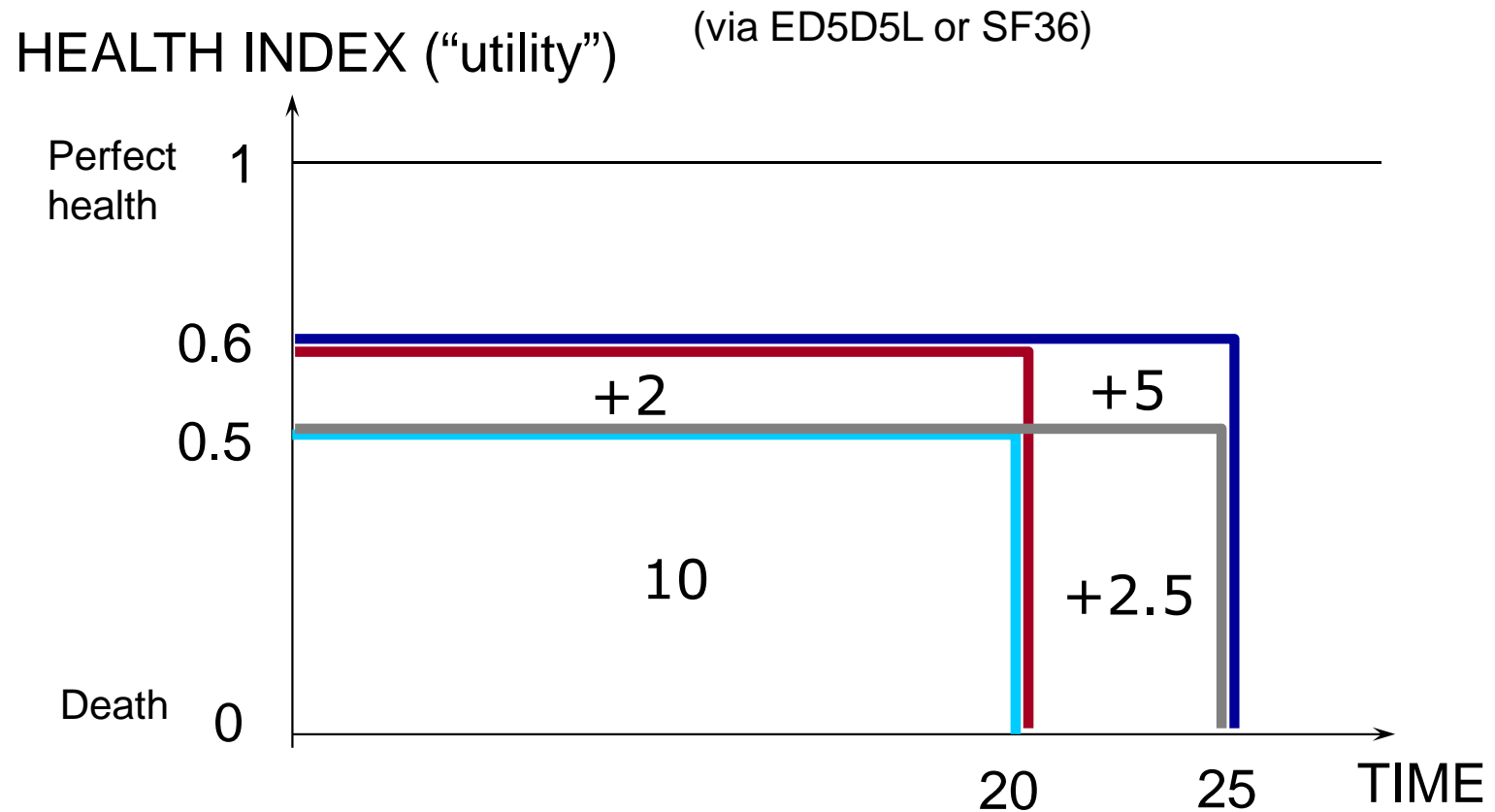**Depression-related 6-month cost per patient by remission attainment status**

Health Effects

Quality
Adjusted
Life
Years

EQ-5D-5L

EQ-5D Domain		Response Category
Mobility	1	I have no problems walking
	2	I have slight problems walking
	3	I have moderate problems walking
	4	I have severe problems walking
	5	I am unable to walk
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
		I have severe problems washing or dressing
		I am unable to wash or dress myself
Usual Activities		I have no problems doing my usual activities
		I have slight problems doing my usual activities
		I have moderate problems doing my usual
		I have severe problems doing my usual activities
		I am unable to do my usual activities
Pain or 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 or 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

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Algorithm: to a utility score

EQ-5D-5L value set for England		Example: the value for health state 23245	
constant	1.000	Constant	=1.000
Mobility = 2	0.057	Minus MO level 2	-0.057
Mobility = 3	0.074		
Mobility = 4	0.207		
Mobility = 5	0.255		
Self care = 2	0.059		
Self care = 3	0.083	Minus SC level 3	-0.083
Self care = 4	0.176		
Self care = 5	0.208		
Usual activities = 2	0.048	Minus UA level 2	-0.048
Usual activities = 3	0.067		
Usual activities = 4	0.165		
Usual activities = 5	0.165		
Pain/discomfort = 2	0.059		
Pain/discomfort = 3	0.079		
Pain/discomfort = 4	0.244	Minus PD level 4	-0.244
Pain/discomfort = 5	0.298		
Anxiety/depression = 2	0.072		
Anxiety/depression = 3	0.099		
Anxiety/depression = 4	0.282		
Anxiety/depression = 5	0.282	Minus AD level 5	-0.282
		State 23245	=0.286

Example: "utilities" in depressed patients in primary care
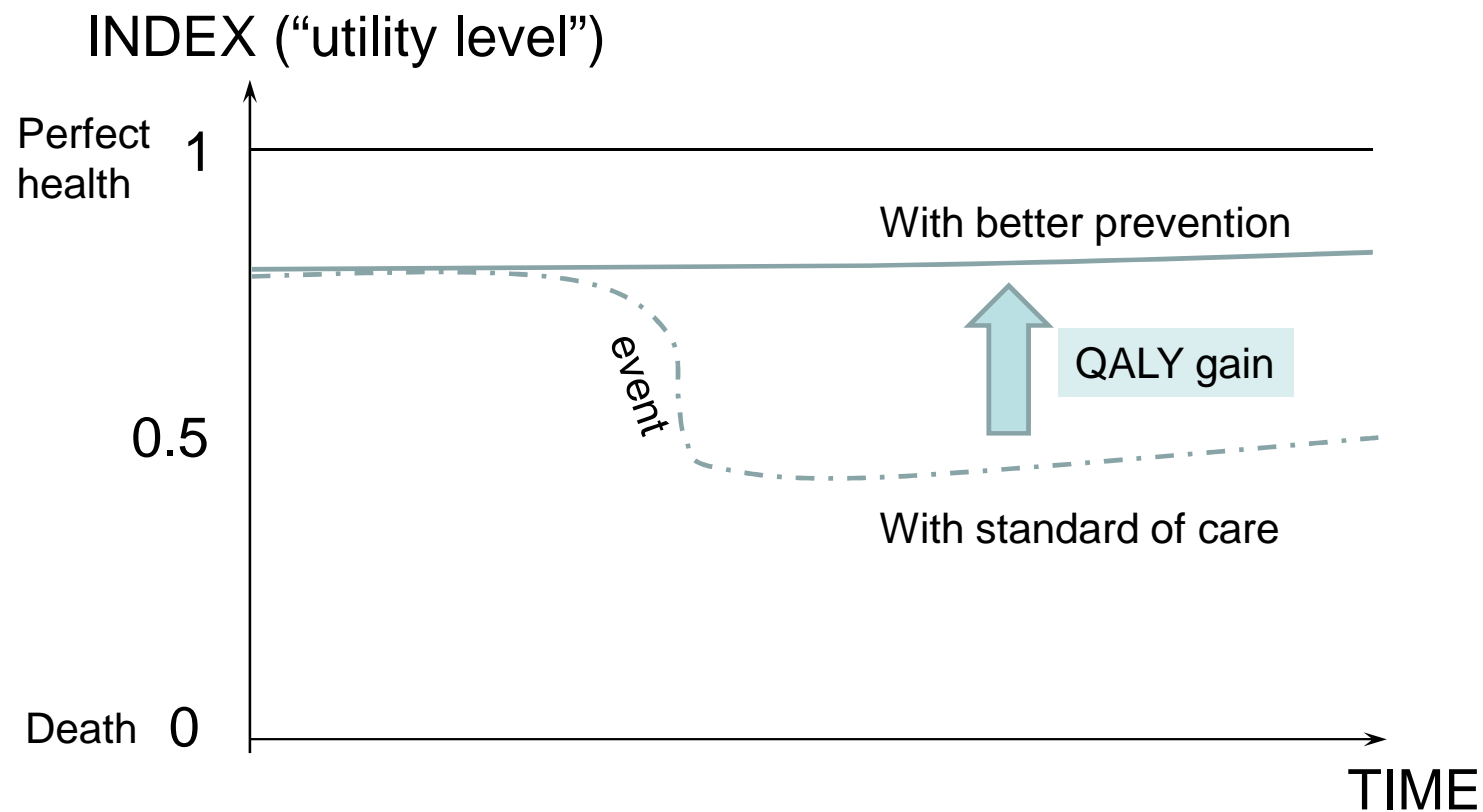
Utility scores by disease severity over time

Sobocki P, et al. Value Health. 2007 Mar-Apr;10(2):153-60.
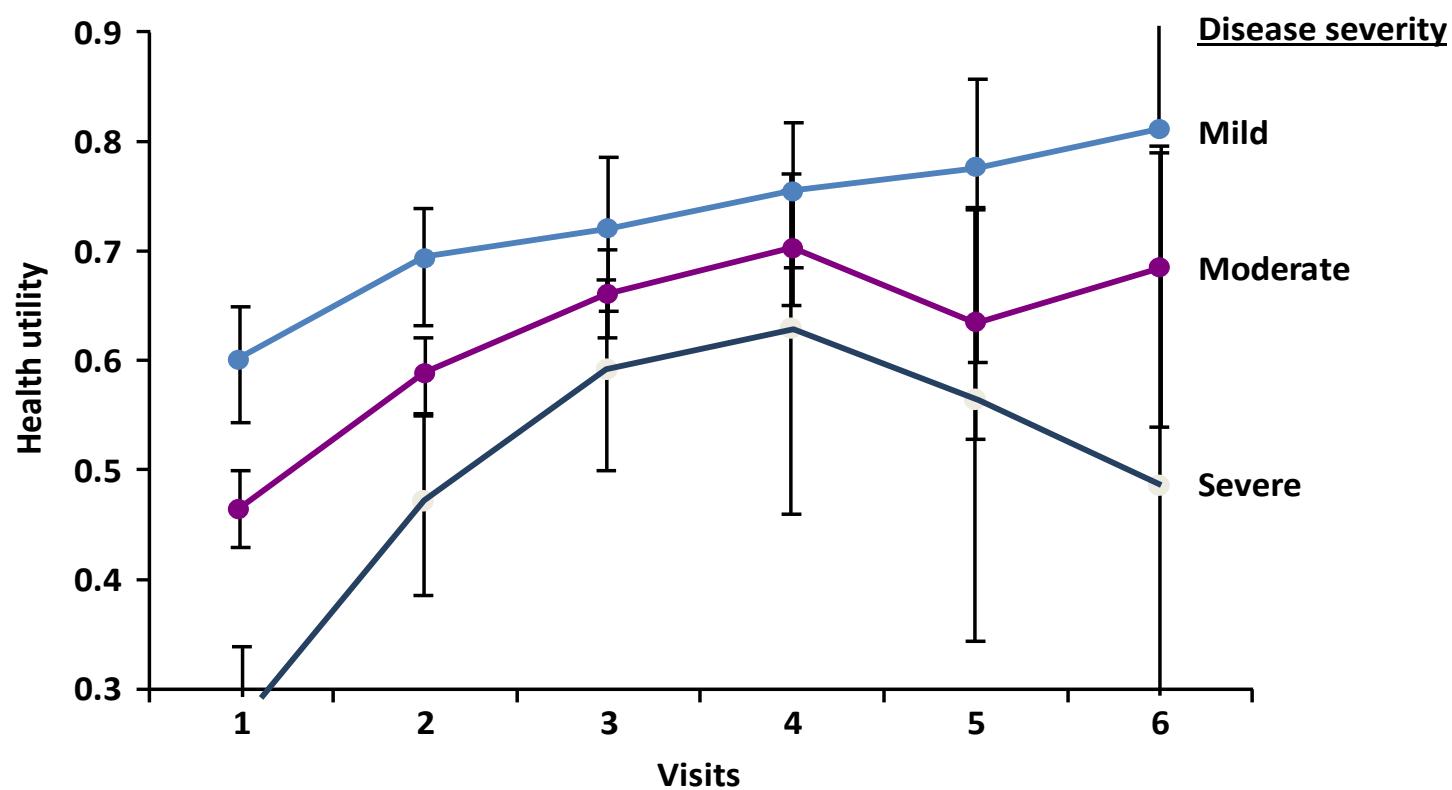
Gain in QALY by avoiding progression

INDEX ("utility level")

Perfect health — 1

0.5

Death — 0

QALY gain

With new therapy

With standard of care

Now

TIME
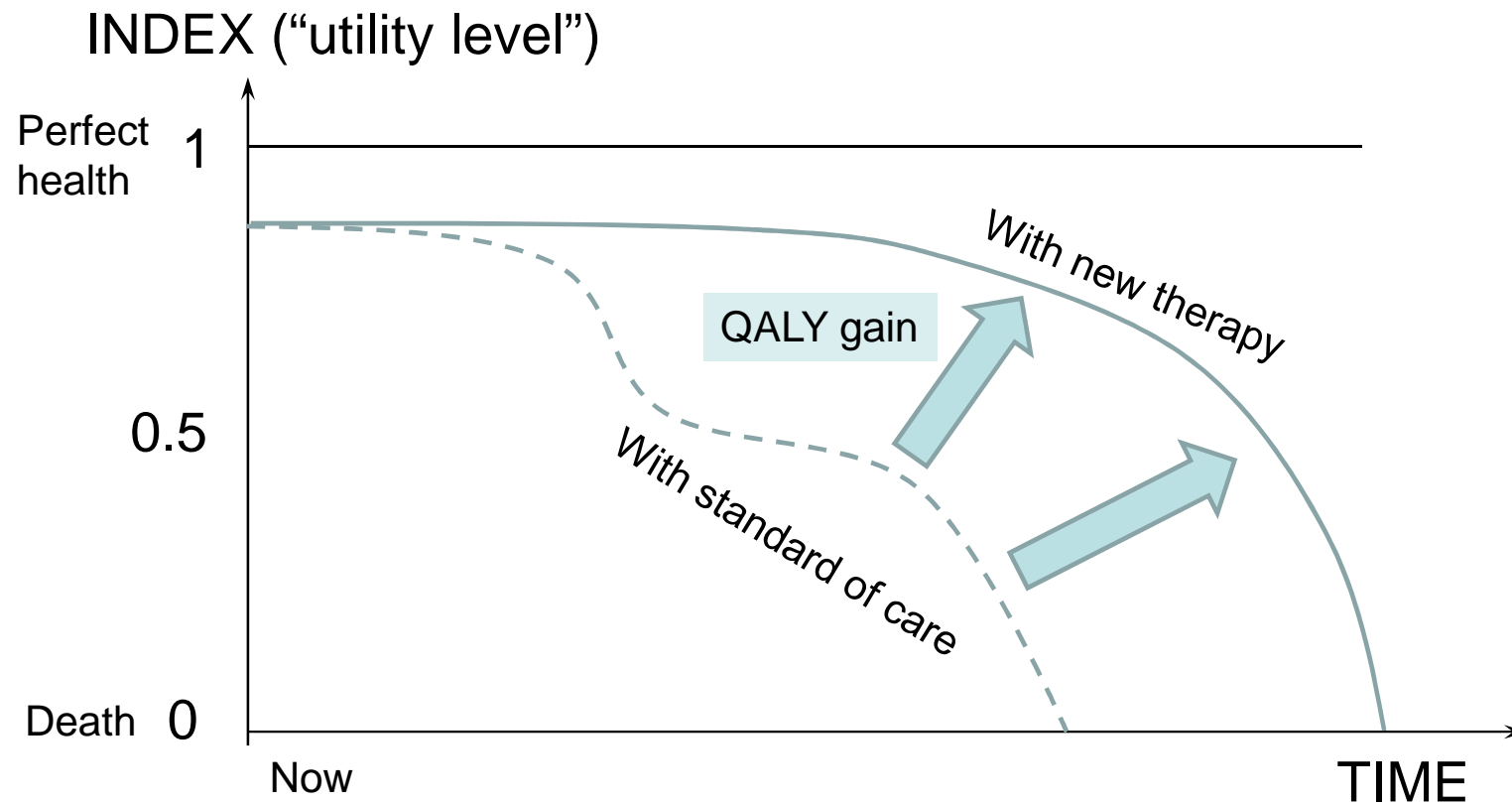
Example schizophrenia

Stable schizophrenia	0.919 (0.023)
Weight gain	0.825 (0.028)
Diabetes	0.769 (0.036)
Hyperprolactinemia	0.815 (0.030)
Relapse	0.604 (0.042)
EPS	0.722 (0.037)

Briggs et al. 2008

Gain in QALY by avoiding an event

INDEX ("utility level")

Perfect health — 1

With better prevention

event

QALY gain

0.5

With standard of care

Death — 0

TIME

Cost-effectiveness: 3 possibilities

L. Annemans. Health economics for non-economists. Pelckmans Pro, June 2018
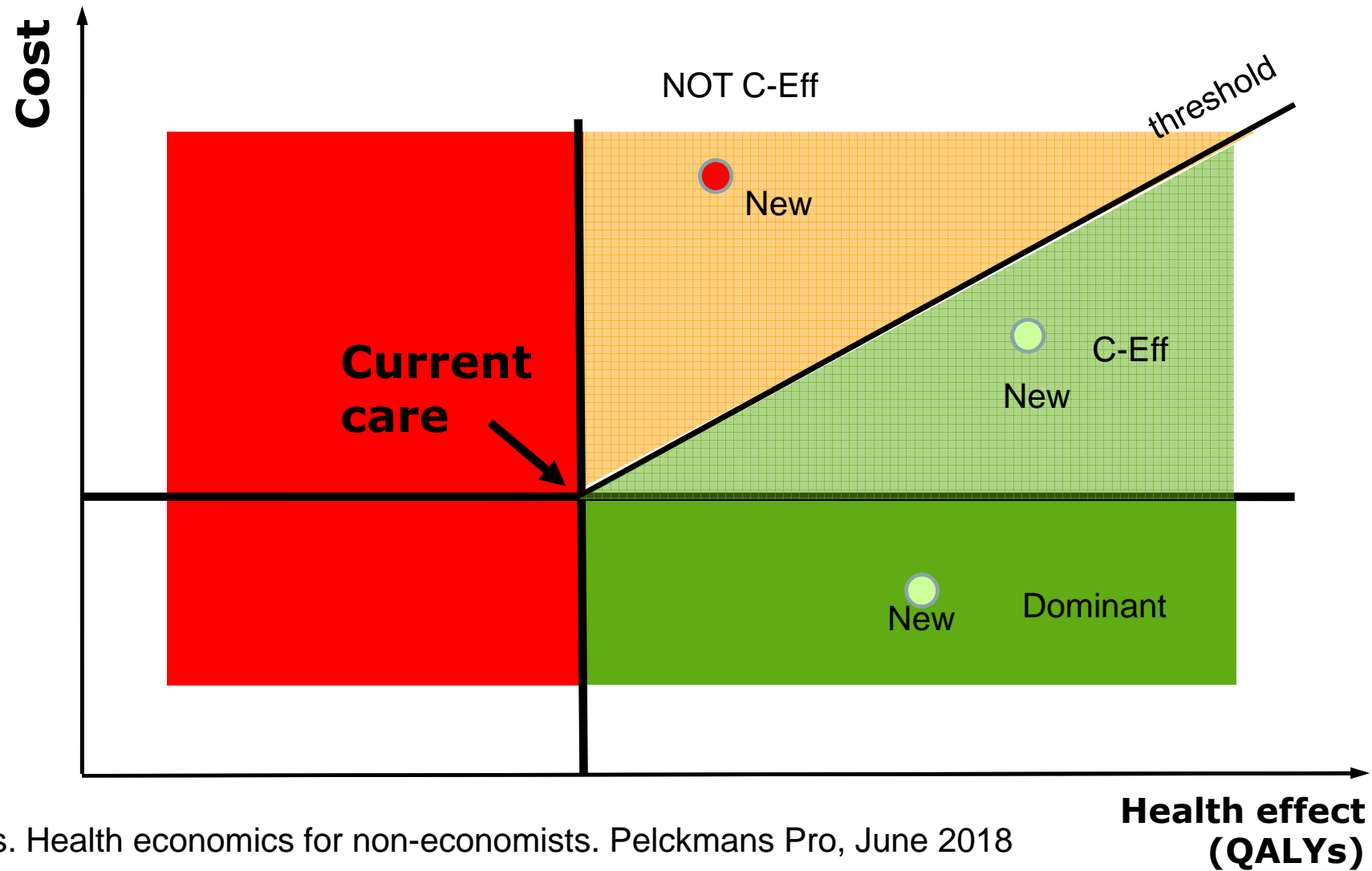
Example: assertive community treatment in patients with schizophrenia: dominant

Figure 1. 12-Month Outpatient Costs and Hospitalization Costs, Assertive Community Treatment (ACT) Versus Standard Care (SC)[a]

Effect: 10 QALYs per 100 patients

Legend:
- □ Outpatient treatment costs
- ■ Inpatient treatment costs

Hospitalization costs, ACT < SC ($P < .001$)
Outpatient costs, ACT > SC ($P < .001$)
Total costs, ACT < SC ($P = .27$)

Costs, €

Intervention (ACT)   Control (SC)
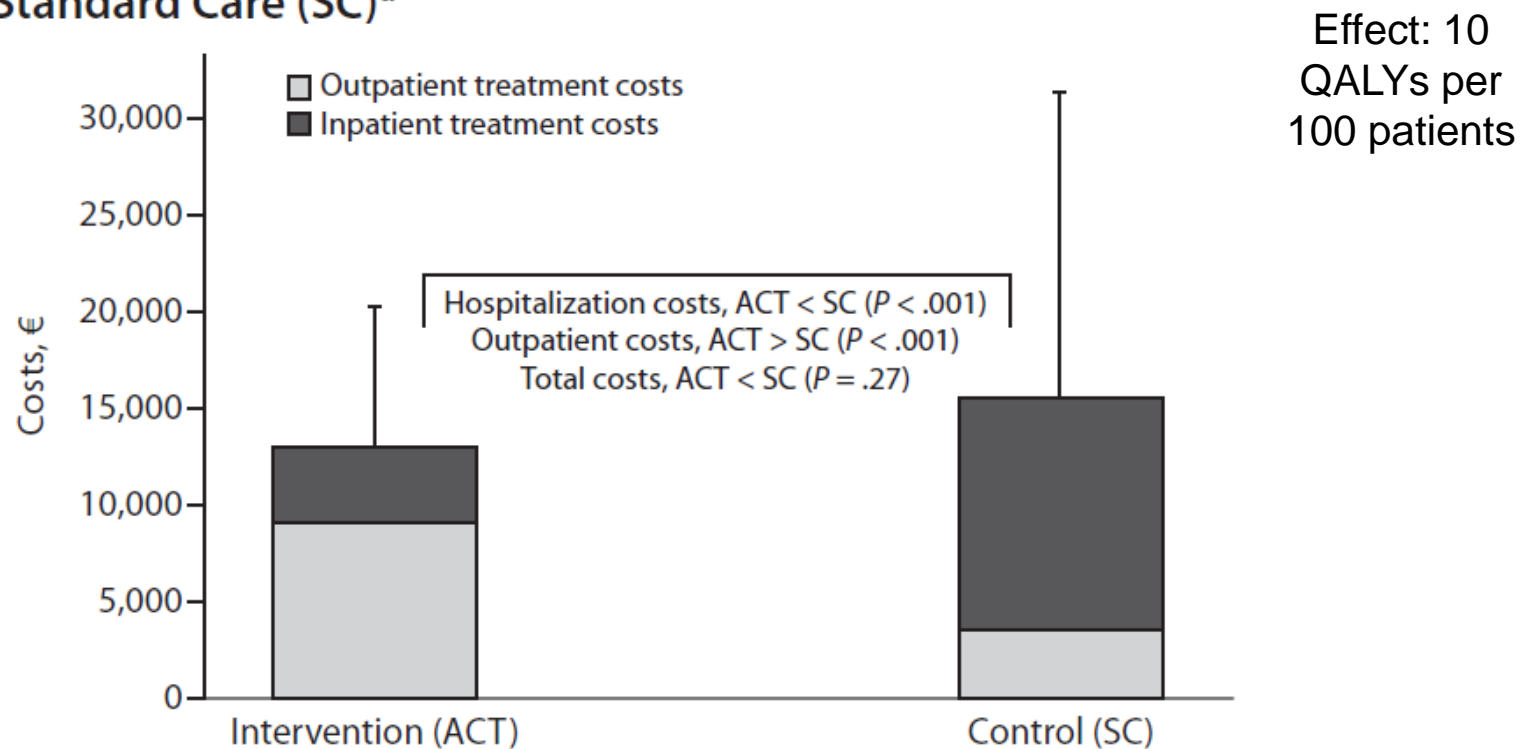
Karow et al, J Clin Psychiatry 2012

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So the KEY outcome is the

Incremental Cost-Effectiveness Ratio (ICER)

$$ICER = \frac{C_{new} - C_{current}}{Eff_{new} - Eff_{current}}$$

Which then needs to be under the threshold!

Note: Cost difference = net cost (= including possible savings/extras)
Note 2: some authors prefer ICUR (incremental **cost-utility** analysis)
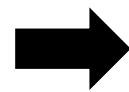
Where is the threshold?

- BENCHMARKING
  e.g. cost-effectiveness of caring for a dialysis patient
  historically **50,000 $ per QALY (+/- 200,000$ for 4 QALYs)**
  (note: now +/- 100,000$ per QALY)

- WHO - CHOICE **Highly cost-effective** (< GDP per capita);
  Cost-effective (between one and three times GDP per capita);
  (e.g. Belgium = +/- €37000)
  (recently challenged by the WHO)

- At the discretion of the decision maker (official: England: 30,000£
  per QALY; not official: Belgium 40,000€/QALY)
  (recently challenged)

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BUT suppose: another new therapy for major depression

cost

20,000€

health benefit

0.2 QALYs

➡ 100,000€/QALY
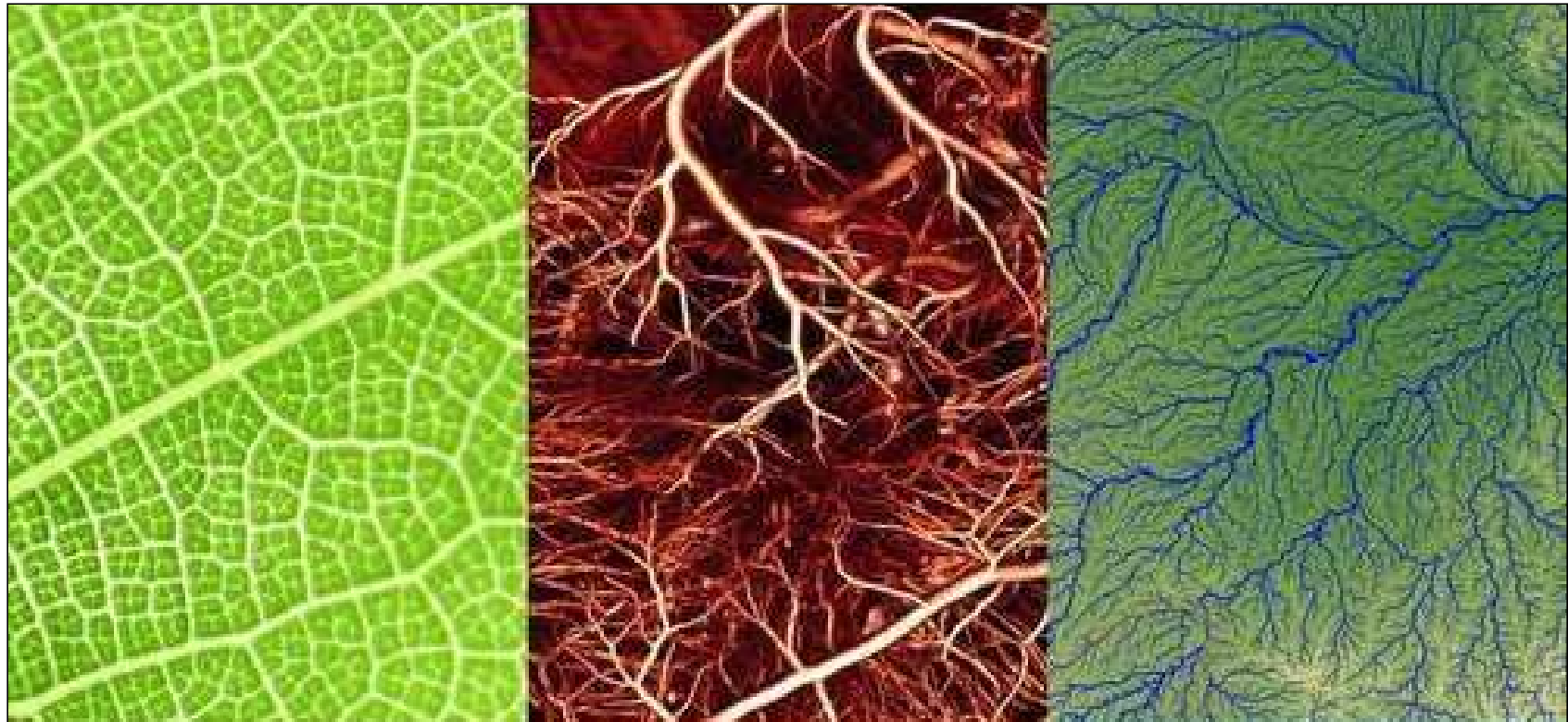
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Note

Cost analysis = an economic evaluation whereby effects are not considered

Cost-minimisation = an economic evaluation whereby effects are considered (proven) to be equal

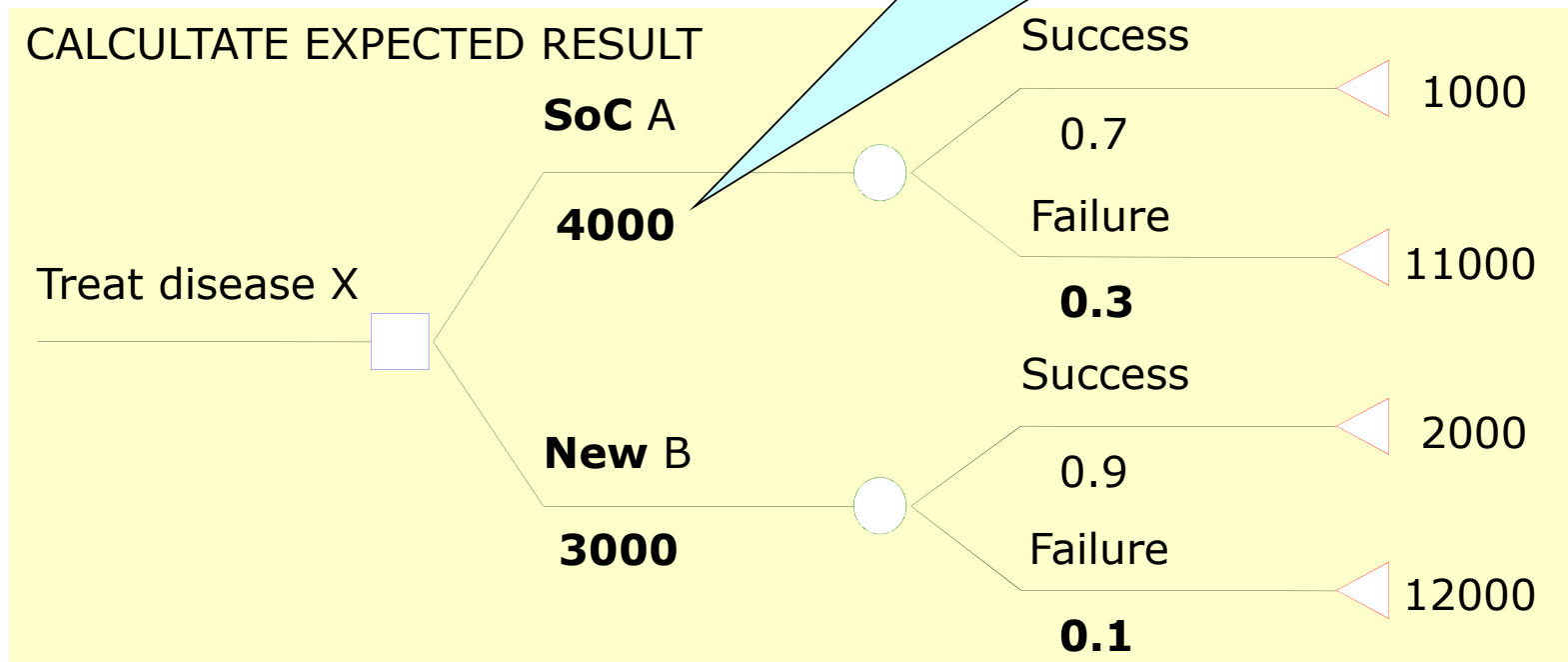# III. Models

Method = decision tree ; example

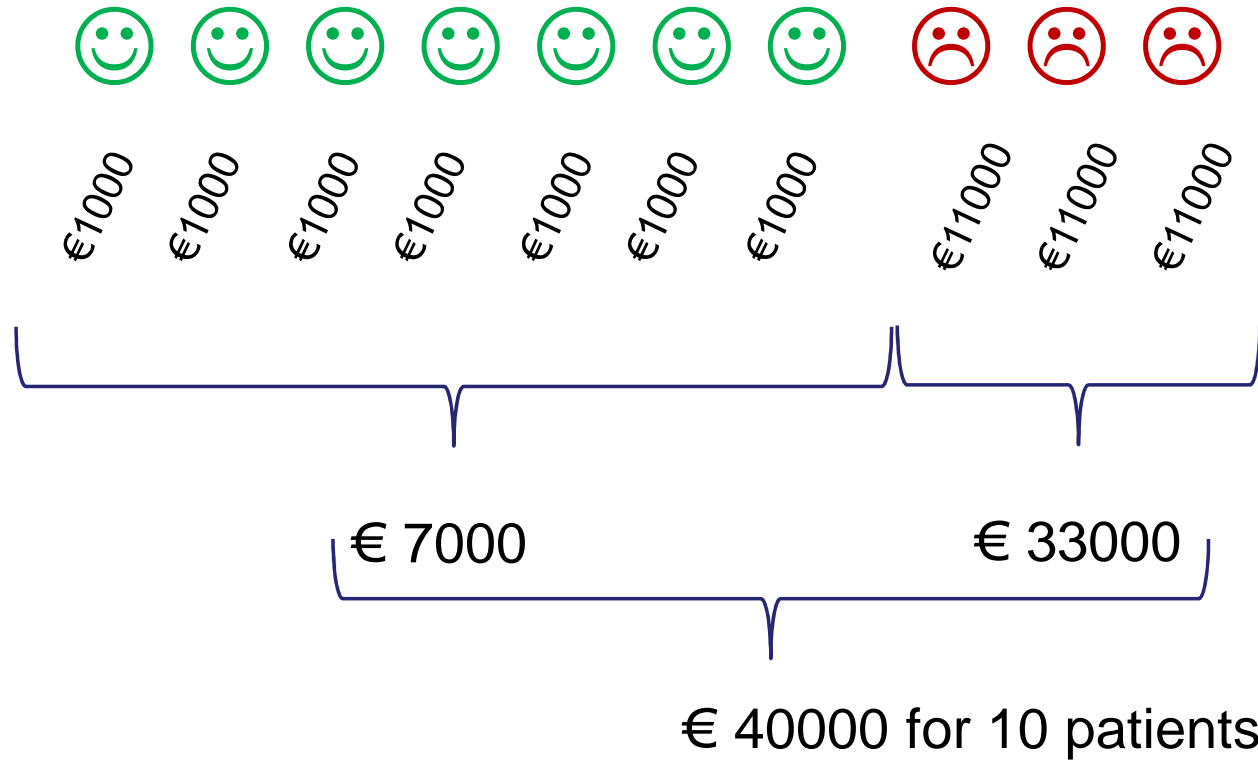Cost treatment A (Standard of Care) = 1000
Cost new treatment B = 2000
Cost of "failure" = **10000***

* Needs separate study to obtain data

7/10 x 1000 + 3/10 x 11000

CALCULTATE EXPECTED RESULT

SoC A

4000

Treat disease X

Success

1000

0.7

Failure

11000

0.3

Success

2000

New B

0.9

3000

Failure

12000

0.1

30

Calculation for treatment A, <u>per 10 patients</u>

€1000 €1000 €1000 €1000 €1000 €1000 €1000   €11000 €11000 €11000

€ 7000   € 33000
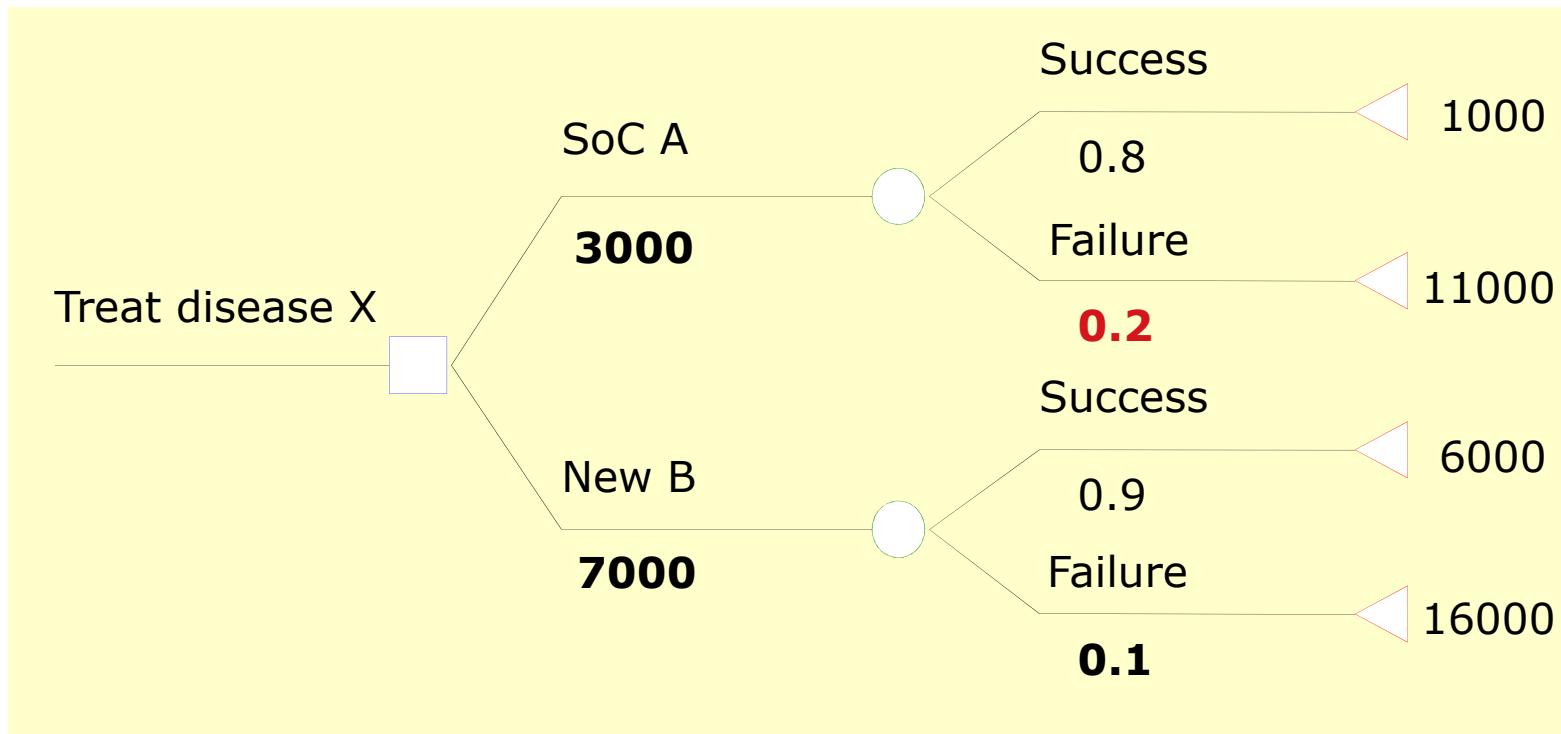
€ 40000 for 10 patients

→ €4000 per patient

FASTER: 0.7 x 1000 + 0.3 x 11000 = 4000

Change inputs → new result

Cost treatment A = 1000
Cost new treatment B = 6000
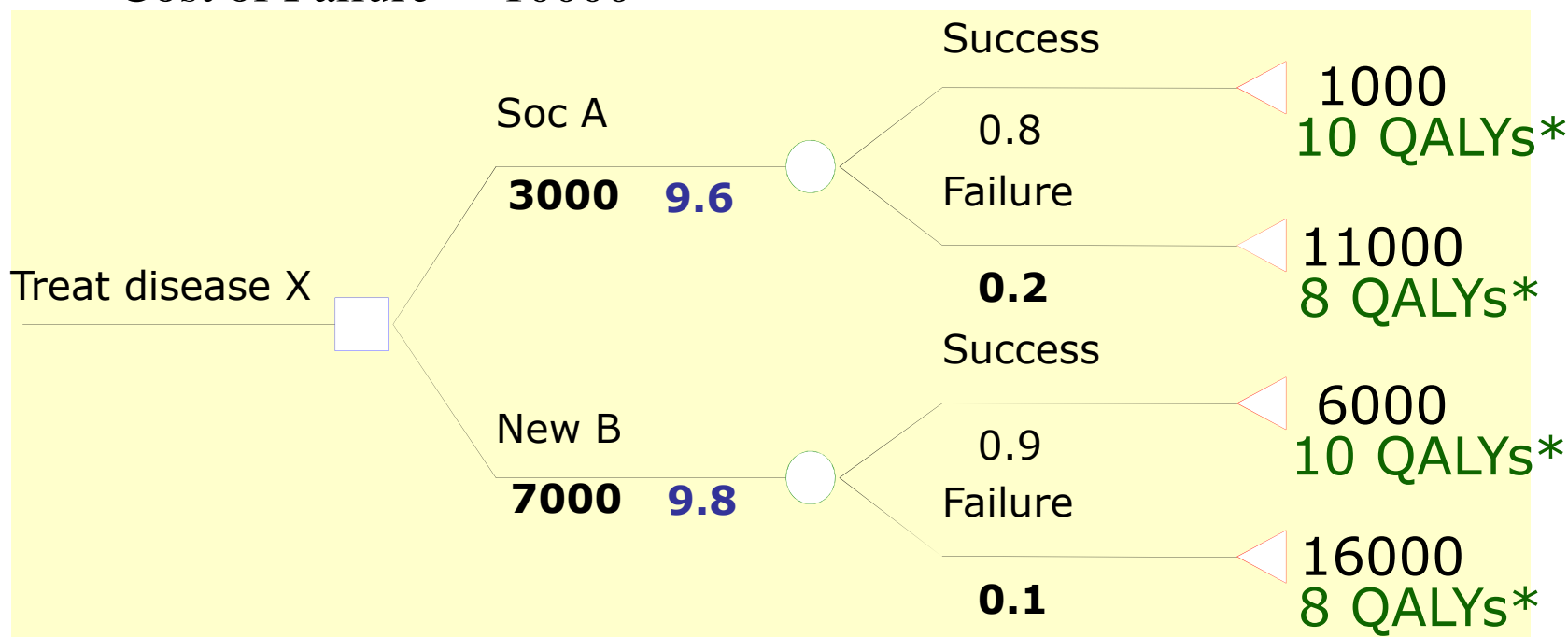Cost of Failure = 10000

What about the QALYs?

Cost treatment A =1000

Cost medicine B = 6000

Cost of Failure = 10000

If disease: -2 QALYs*

* Needs again separate study to obtain data

Treat disease X

Soc A
3000 **9.6**

Success
0.8
1000
10 QALYs*

Failure
0.2
11000
8 QALYs*

New B
7000 **9.8**

Success
0.9
6000
10 QALYs*

Failure
0.1
16000
8 QALYs*

ICER = 4000/0.2 = 20000 € /QALY gained

Incremental Cost-Effectiveness Ratio

What is 'Failure' in such decision trees? Some examples

Failure?

Depression   ·······

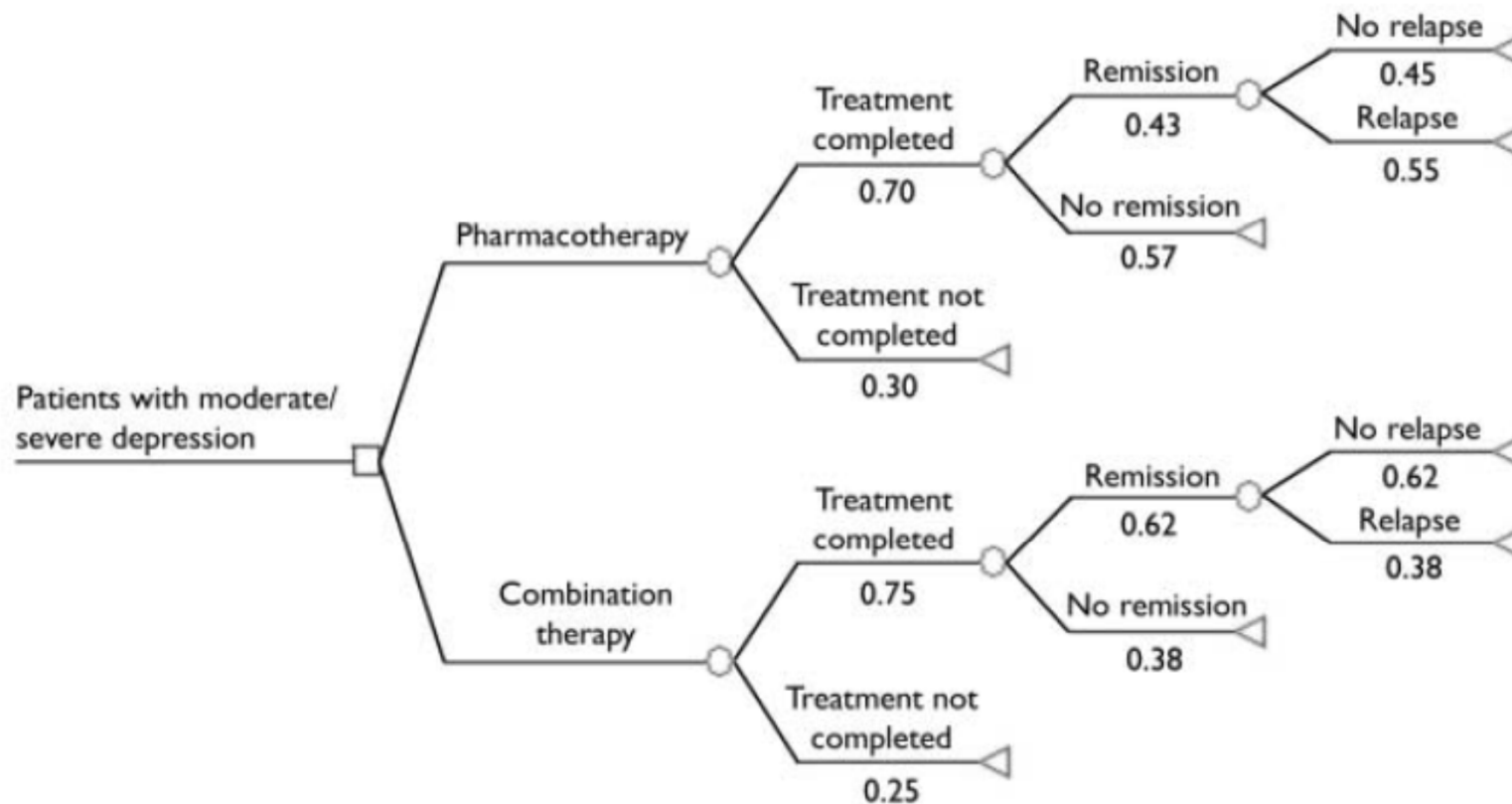Schizophrenia   ·······

Alcohol dependence   ·······

Alzheimer's   ·······

…

Example : Depression: combination (psycho + pharma) vs pharma alone

Note: Psuccess = 0.70*0.43*0.45 = 0.135

Simon et al, Br J Psych, 2006

Results (15 months)

	Pharmaco-therapy	Combination therapy	Difference
Costs, £[1]			
Total healthcare cost per person	660	1297	637
Effects			
Probability of successful treatment per person	0.14	0.29	0.16
QALY per person with severe depression	0.52	0.63	0.11
QALY per person with moderate depression	0.84	0.89	0.04
Cost-effectiveness, £[1] (95% CI)			
Cost per additional successfully treated patient	4056 (1400–18 300)		
Cost per QALY gained with severe depression	5777 (1900–33 800)		
Cost per QALY gained with moderate depression	14 540 (4800–79 400)		

Simon et al, Br J Psych, 2006

Example 2 depression

Annemans et al. PharmacoEconomics 2014
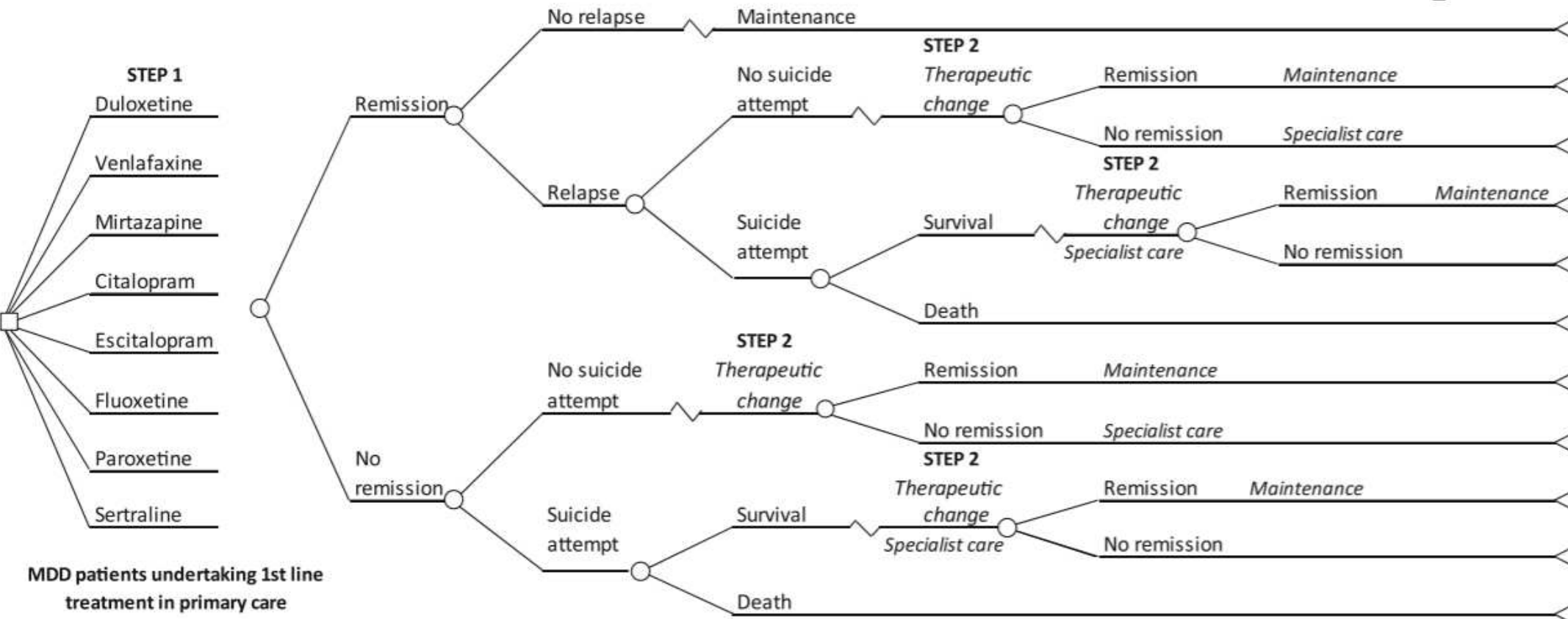
Markov models

Principle:

- Patients are in disease specific <u>health states</u>
- Time is divided into periods (<u>cycles</u>)
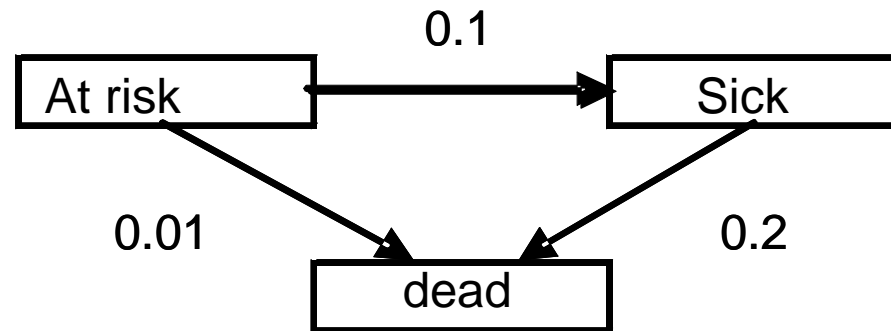- During each cycle the patient can move from one health state to another (transition).

  The risk of this transition = "<u>transition probability</u>"

Note:
Medline citations ["QALY" AND "Markov"] up to now: > 3000 citations

Markov Model – simple example

- 3 health states (at risk, sick, death); 1 cycle = 1 year

|	Upon start	after 1 year	after 2 years	after 3 years
At risk	1000	890	792	705
Sick	0	100	169	214
Dead	0	10	39	81
Total	**1000**	**1000**	**1000**	**1000**

100 – 20 + 89 = 169

Changing the model

NEW PREVENTIVE TREATMENT: At risk → sick: **0.05 per year! (50% reduction)**

	Upon start	after 1 year	after 2 years	after 3 years
At risk	1000	940	884	831
Sick	0	50	87	114
Dead	0	10	29	<u>56</u>
Total	**1000**	**1000**	**1000**	**1000**

Model <u>predicts</u> less deaths

Example: depression

Camacho EM, et al. BMJ Open 2016

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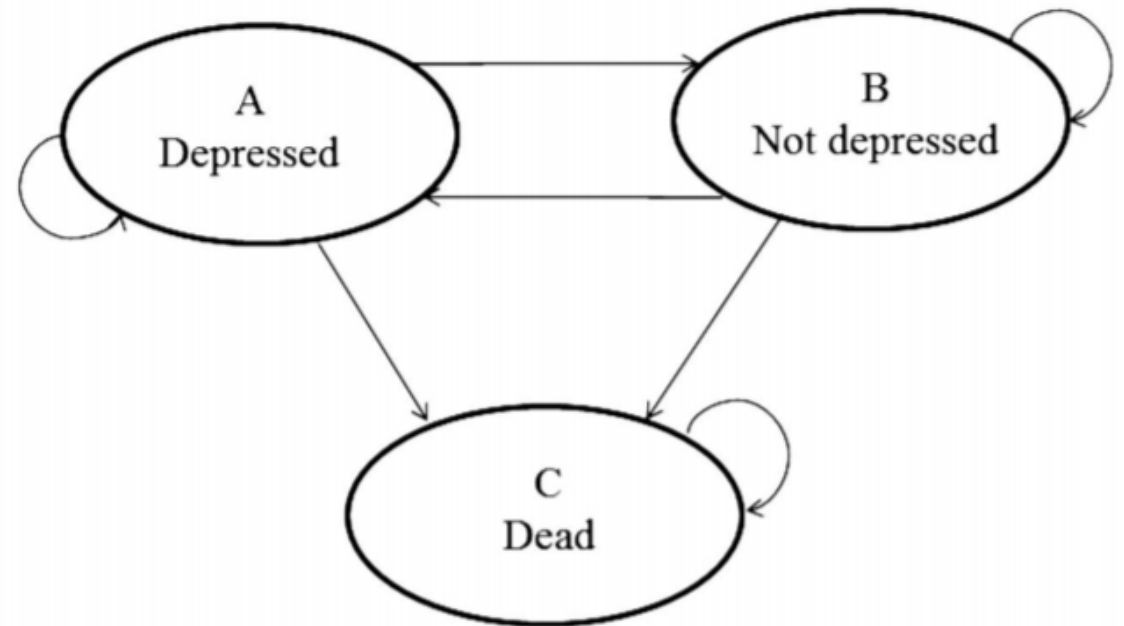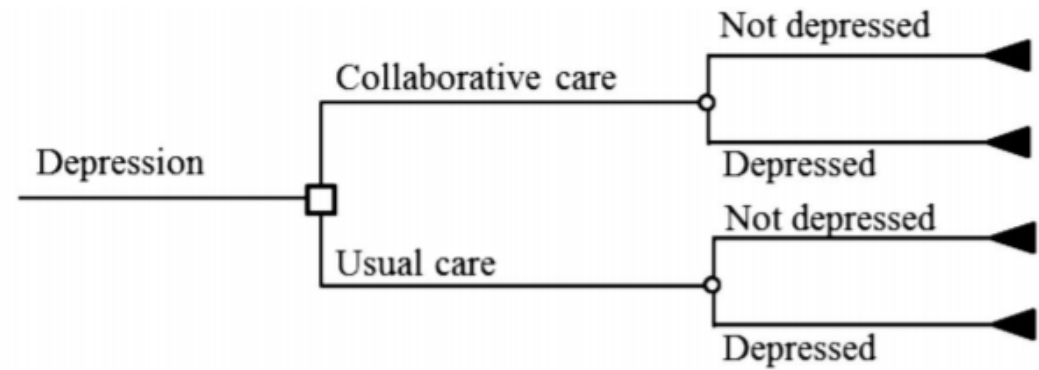
The terminal nodes (◄) of the decision tree correspond to Markov states A and B, representing the pathway from the tree into the Markov model
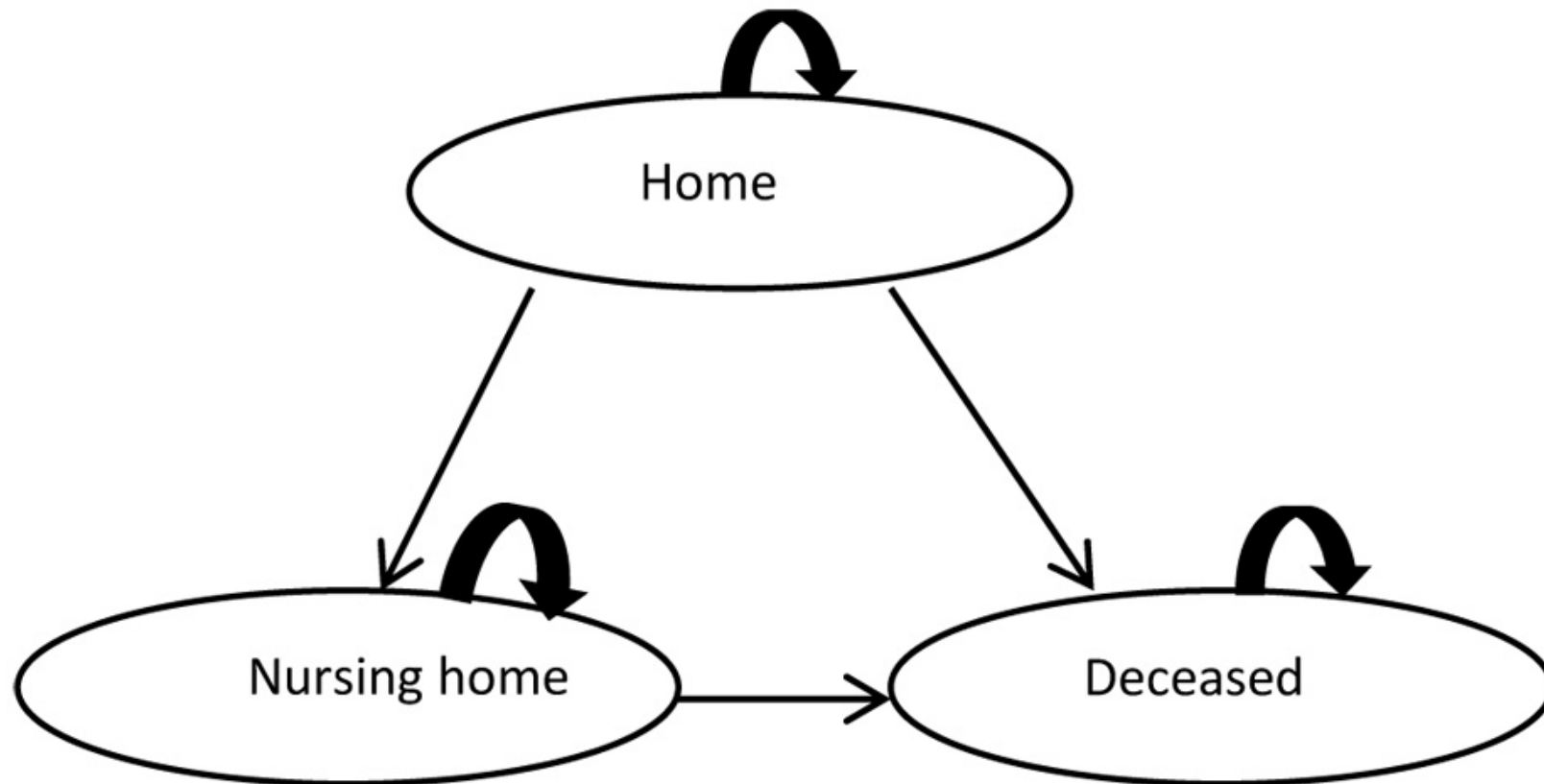
Alzheimer's

Alzheimer's dementia: budget impact and cost-utility analysis of a combination treatment with a cholinesterase inhibitor and memantine in Switzerland

Alena M. Pfeil[a], Reto W. Kressig[b], Thomas D. Szucs[a]

Model Pfeil et al (2012)

Pfeil et al. Swiss Med Wkly. 2012;142:w13676

Results Pfeil et al (2012)

Tx	Survival (yrs)	Time Home	Time Nursing Home	QALYs	COSTS
ChE-I	3.33	2.65	0.48	1.87	67394
ChE-I + M	3.33	3.3	0.03	1.99	39738
Diff	0	+0.45	-0.45	+0.12	-27656

Pfeil et al. Swiss Med Wkly. 2012;142:w13676

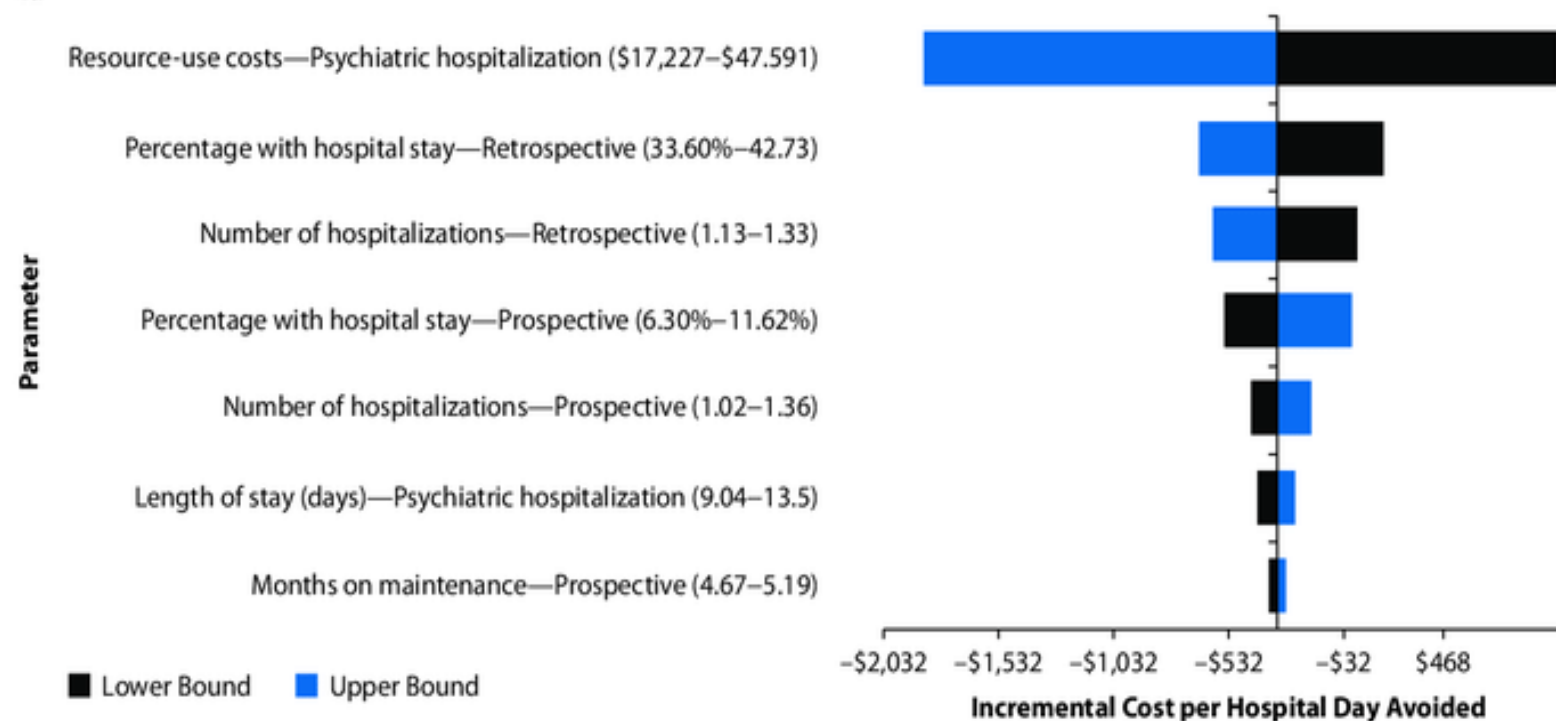# HOW TO MAKE MODELS CREDIBLE AND RELIABLE?

1. Validation of structure: does the structure reflect real life? → clinical experts
2. Validation of calculations: → peer review
3. Validation of outcomes: compare outcomes predicted by the "current" arm with real observations
4. Show various sensitivity analyses

Example: Tornado diagram

4a

Parameter	
Resource-use costs—Psychiatric hospitalization ($17,227–$47.591)	
Percentage with hospital stay—Retrospective (33.60%–42.73)	
Number of hospitalizations—Retrospective (1.13–1.33)	
Percentage with hospital stay—Prospective (6.30%–11.62%)	
Number of hospitalizations—Prospective (1.02–1.36)	
Length of stay (days)—Psychiatric hospitalization (9.04–13.5)	
Months on maintenance—Prospective (4.67–5.19)	

■ Lower Bound ■ Upper Bound

–$2,032   –$1,532   –$1,032   –$532   –$32 $468

Incremental Cost per Hospital Day Avoided

Wilson et al, 2016 – retrospective prospective analysis on switching to aripriprazole once monthly

Probabilistic sens. Analysis (= Monte Carlo analysis): example

Available data:
Purchase cost of no prevention = 0
Purchase cost of prevention = €4000
Cost of a r e l a p s e = €10000
Chance of a r e l a p s e without prevention = 30%
Chance of a r e l a p s e with prevention = 20%
QALYs without a r e l a p s e = 10
QALYs with a r e l a p s e = 6

DETERMINISTIC RESULT?

ICER = **?**

No prevention

No relapse

0.700 10 QALY

3000   8.8 QALY

relapse

At risk for CHD

0.300 6 QALY

No relapse

Prevention

0.800 10 QALY

6000   9.2 QALY

relapse

0.200 6 QALY
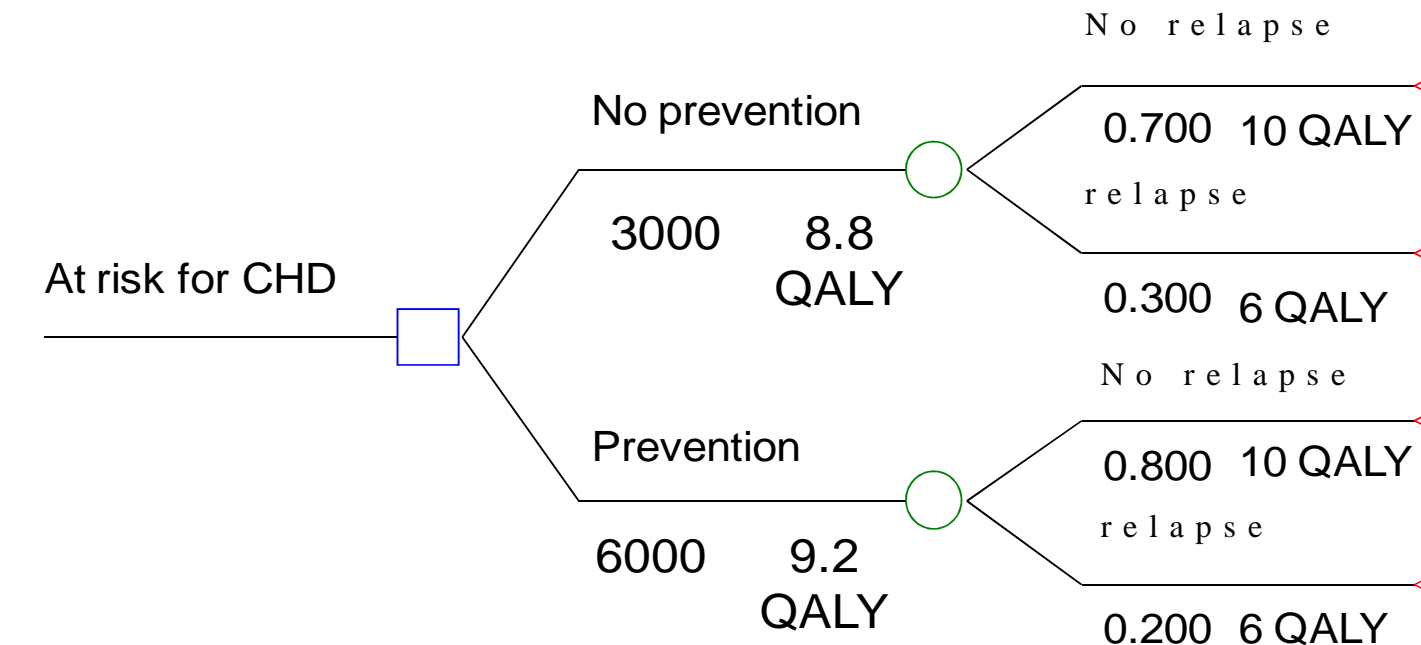
R e l a p s e = s c h i z o p h r e n i a « a t t a c k »

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Probability *distribution* of inputs

- Suppose the cost of prevention is not €4,000 as was originally the case, but a normal distribution with average = €4,000 and standard error = €500.

- The cost of a relapse is not €10,000, but a normal distribution with average = €10,000 and standard error = €1,000.

- The number of QALYs if there is no relapse is not 10, but a normal distribution with an average of 10 and a standard error of 1.

- The number of QALYs in case of a relapse is not 6, but a normal distribution with an average of 6 and a standard error of 1.

Computer runs the model **500** times. *For every new calculation, the computer takes a value chosen **at random** from the respective probability distributions.*

When the model is calculated for the first time, for example, the computer might use:

- Cost of prevention   = €3,790 (and not €4,000)
- Cost of relapse   **= €8,530** (and not €10,000)
- Number of QALYs without relapse = 10.5 (and not 10)
- Number of QALYs with relapse   = 6.2 (and not 6).
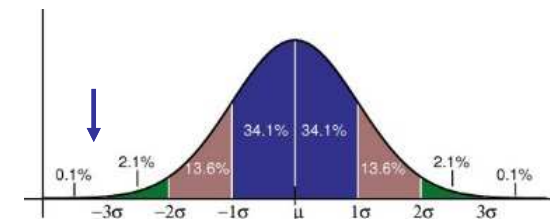
→ With these inputs, the model leads to an ICER of € 6,712 per QALY (check ☺)

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→ Probabilistic sensitivity analysis
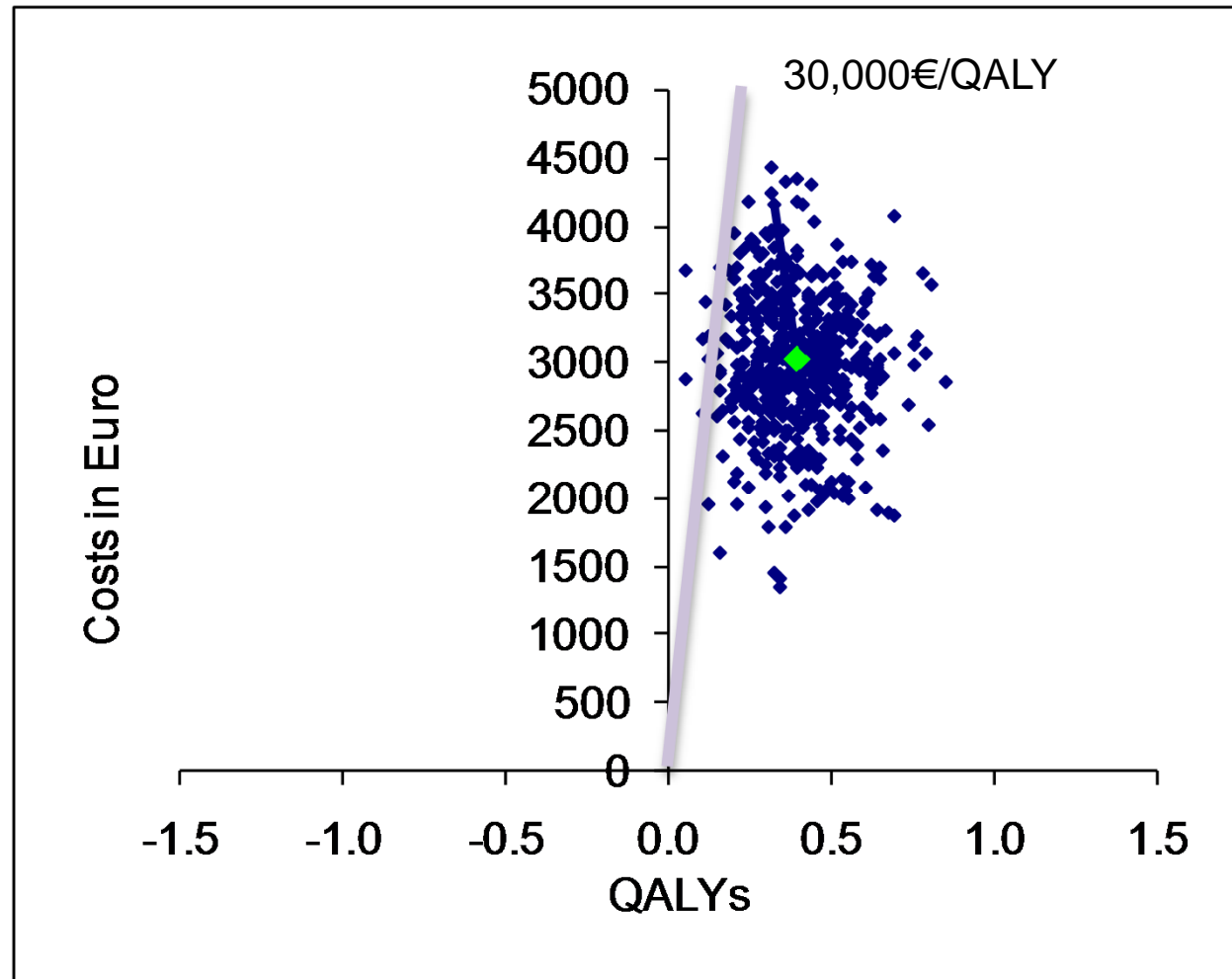
Role of indication/use

The ICER for memantine is £'32,100 per/QALY.

The probability that memantine is cost-effective in a moderate to severe cohort compared with BSC at a WTP of £'30,000 per QALY is 38% (and 28% at a WTP of £'20,000 per QALY).

Bond et al, Health Technol Assess. 2012;16(21):1-470.

In conclusion: which model when?

- "All models are wrong, but some are useful"
  (B. Jönsson)
- "Different models have different strengths and weaknesses. The task of the modeler is to find the best type of model to match the problem to be solved" (D. Eddy)
- Mostly
  - acute disease without sequelae → decision tree
  - Sequelae, recurrence, chronic, … → Markov
  - Very complex: discrete event simulation

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Prospective Research for Health Economic Evaluations.
Some Conflicts Between the Clinical Purpose and the Health Economic Purpose.

We have an IDEA!

- We are preparing a comparative clinical trial
Let us also collect economic (<u>= medical resource use</u>) data <u>within</u> the trial ("piggy-backing")!

GOOD IDEA or BAD IDEA?

- There may be some <u>conflicts</u>…

Does it have an implication for trials

Purpose, environment and instructions of a clinical trial

The clinical trialist view

The health economist's view

- Purpose = Authorisation
- Controlled environment
- Strict protocol instructions

- Purpose = Reimbursement
- Real life environment
- "Do what you normally do"

Patients, Time Horizon, Drop-outs

- Exclude confounders

  - Avoid co-morbidities
  - Avoid elderly

- Limited time

- Drop-outs not analysed

- Only exclude if contra-indicated

  - Include co-morbidities
  - Include elderly

- Time to include all relevant costs and outcomes

- Follow Drop-outs

In conclusion

- **High internal validity**
- **Low external validity**

- **Low internal validity**
- **High external validity**

Compromise: pragmatic/naturalistic trial?

1. Start with an original clinical trial protocol

2. Discuss inclusion and <u>exclusion</u> criteria

3. Discuss with clinical experts the differences between protocol and <u>real life practice</u>
   → obtain consensus on *mandatory* visits reflecting as much as possible real life

4. Plan measures to <u>follow up drop outs</u> (e.g. diary, nurse calls,…) (informed consent!)

NOTE: Relative effectiveness = the extent to which an intervention does <u>more good than harm</u> <u>compared to one or more intervention alternatives</u> for achieving the ***desired results*** when provided <u>under the usual circumstances of health care practice</u>.

Efficacy   Effectiveness

Highly selected	**Patients**	Closer to real life
Placebo/"golden standard"	**Comparator**	Most likely to be replaced
Surrogate endpoints	**Outcomes**	Clinical Relevant Endpoints
Strict protocol instructions	**Design**	Closer to routine follow up

Cost-effectiveness of Cognitive Behavioral Therapy for Depressed Youth Declining Antidepressants

John F. Dickerson, PhD,[a] Frances L. Lynch, PhD,[a] Michael C. Leo, PhD,[a] Lynn L. DeBar, PhD,[b] John Pearson, MD,[a] Gregory N. Clarke, PhD[a]
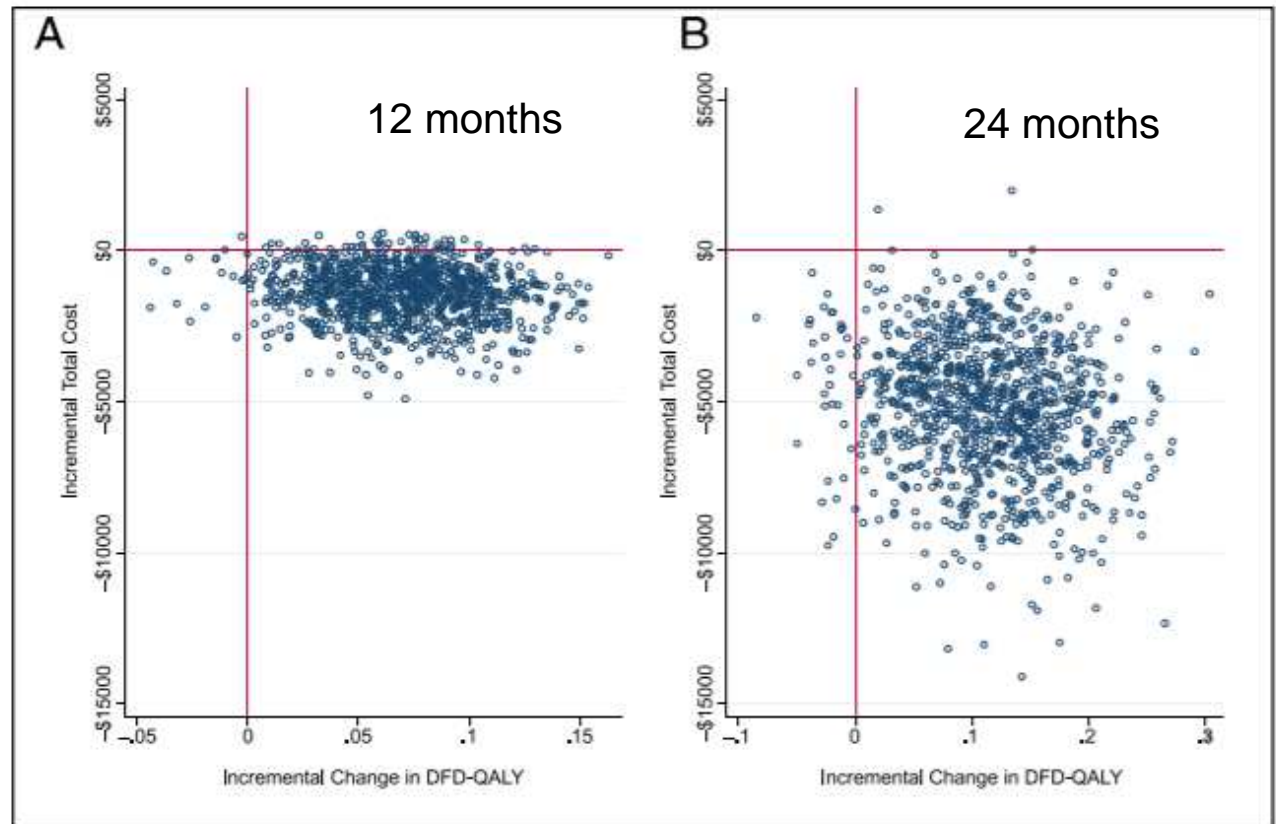
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I. Why health economic evaluations

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V. **Health economic evaluations and decision making**

Three challenges!

1. Medical need

2. Budget impact and financial incentives

3. Uncertainty

Medical Need

(Scitovsky)

Low need
→ no funding

Acceptable health

High need
→ more solidarity
→ invest more

NL: first attempt for adapted thresholds

Zorginstituut Nl (ZIN):
variable threshold

- €80,000 per QALY for severe condition, even up to €100,000 at end-of life
- €50,000 per QALY for moderate burden
- €20,000 per QALY for mild burden

Willingness to pay for a QALY

Health burden to the patient

ZIN. Kosteneffectiviteit in de praktijk | 26 juni 2015
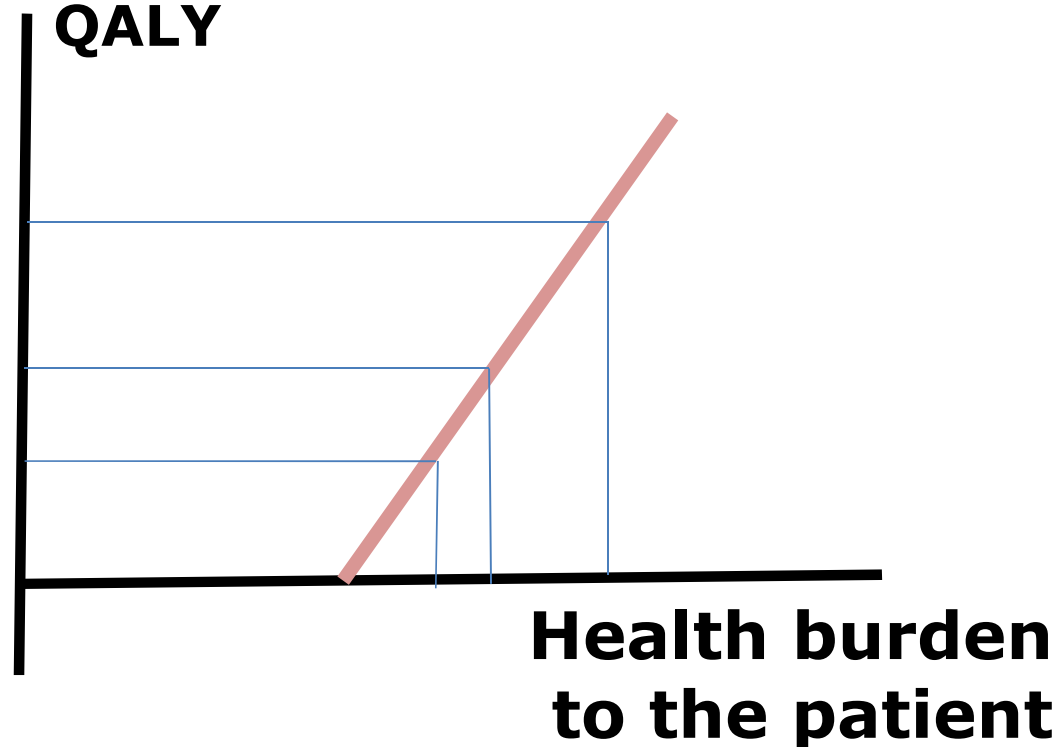
→ 2nd element : Budget impact

"The economic and equity rationale for carrying out budget impact analyses is <u>opportunity cost</u> = benefits forgone by using resources in one way rather than another"
→ There is a need for economic evaluations to address the issue on how to allocate resources *efficiently*, and for budget impact studies to address the issue of *affordability*

→   Need for well documented estimates at population level!
→   Need for very clear description of the target population
→   Need for a stratified approach wherever possible

How to deal with the paradox: cost-effective but unaffordable?

ELSEVIER

Resolving the "Cost-Effective but Unaffordable" Paradox: Estimating the Health Opportunity Costs of Nonmarginal Budget Impacts

CrossMark

James Lomas, MSc, PhD[1,*], Karl Claxton, MSc, PhD[1,2], Stephen Martin, MSc, PhD[2], Marta Soares, MSc, PhD[1]

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How to link all of this?
Value Informed & Affordable Prices

L. Annemans. Health economics for non-economists. Pelckmans Pro, June 2018

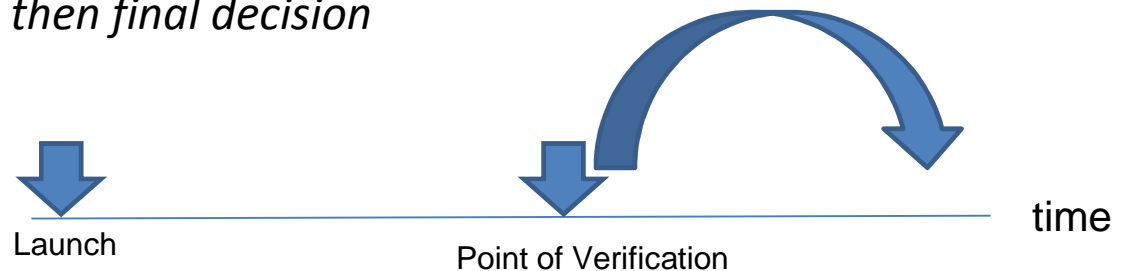# Problem 3: *uncertainty*

outcomes based agreements!
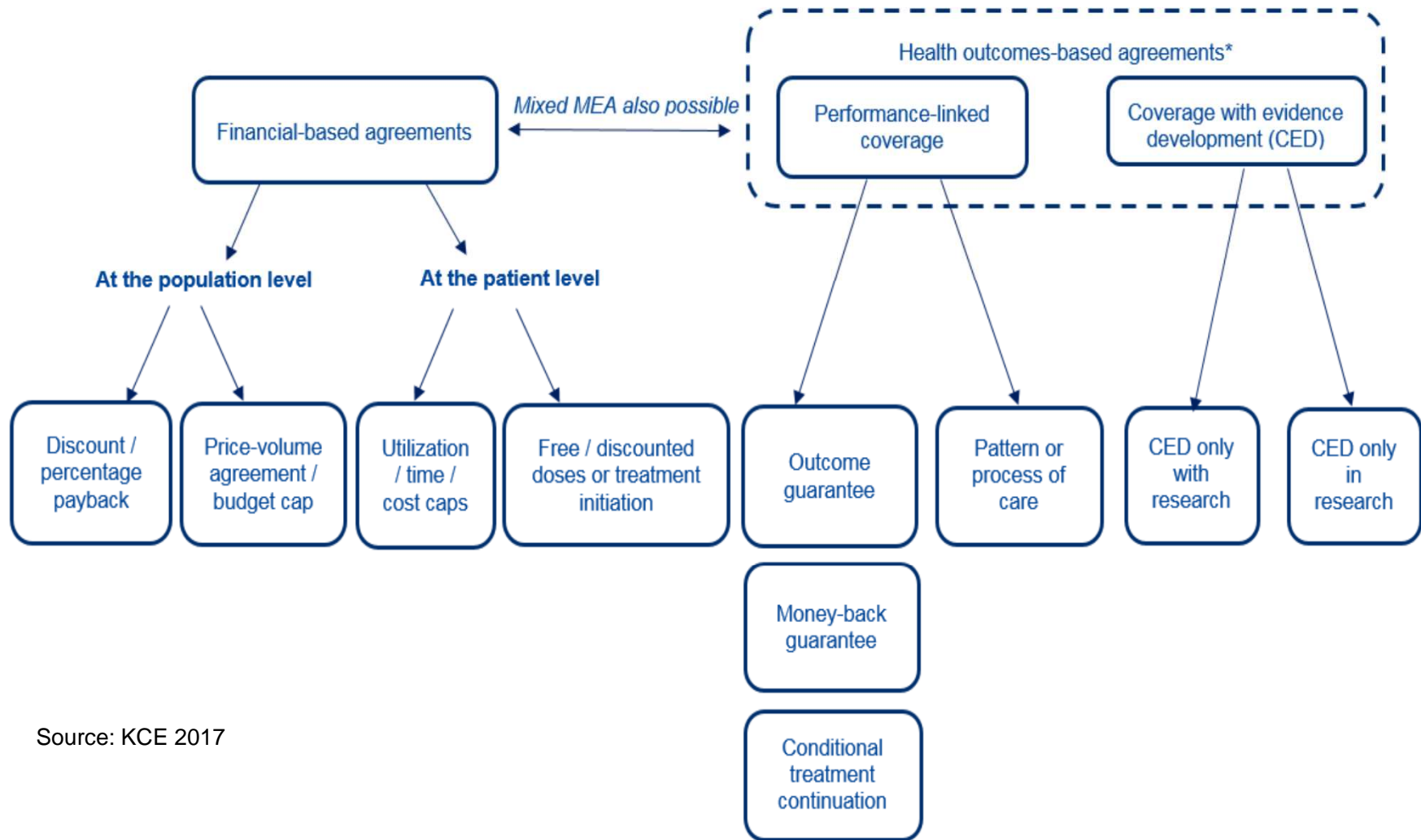
Source: KCE 2017

Key approaches on population level

1. Coverage upon evidence development

   - *Temporary approval, then final decision*

   Launch   Point of Verification   time

2. Performance Linked Reimbursement (outcomes guarantee)

   - *Not as good as promised → industry pays back*

   Launch   Point of Verification   time
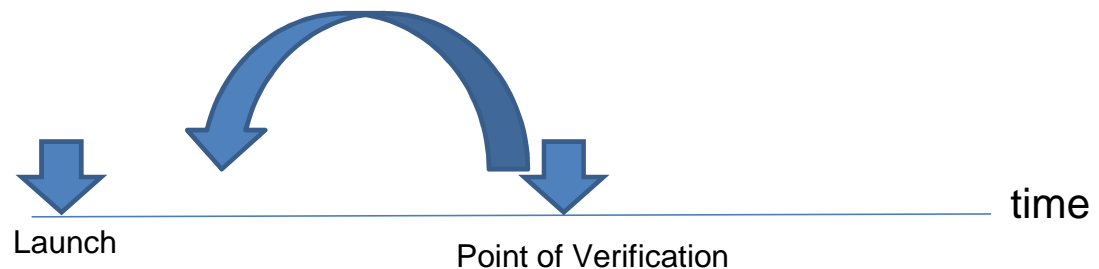
Yes, but..

- Administrative burden
- Confounders
- Treatment is part of broader treatment sequence
- Role of health professionals
- Role of patients?
- Data quality
- Is a registry really real life?
- …

Discussion

- The basics are straightforward
- 2 main methods: modelling or prospective
- Need for sensitivity analysis
- Other elements play a role in decision making
- Increasing need for real life data

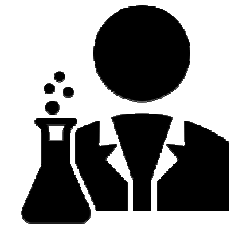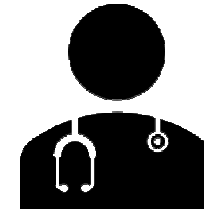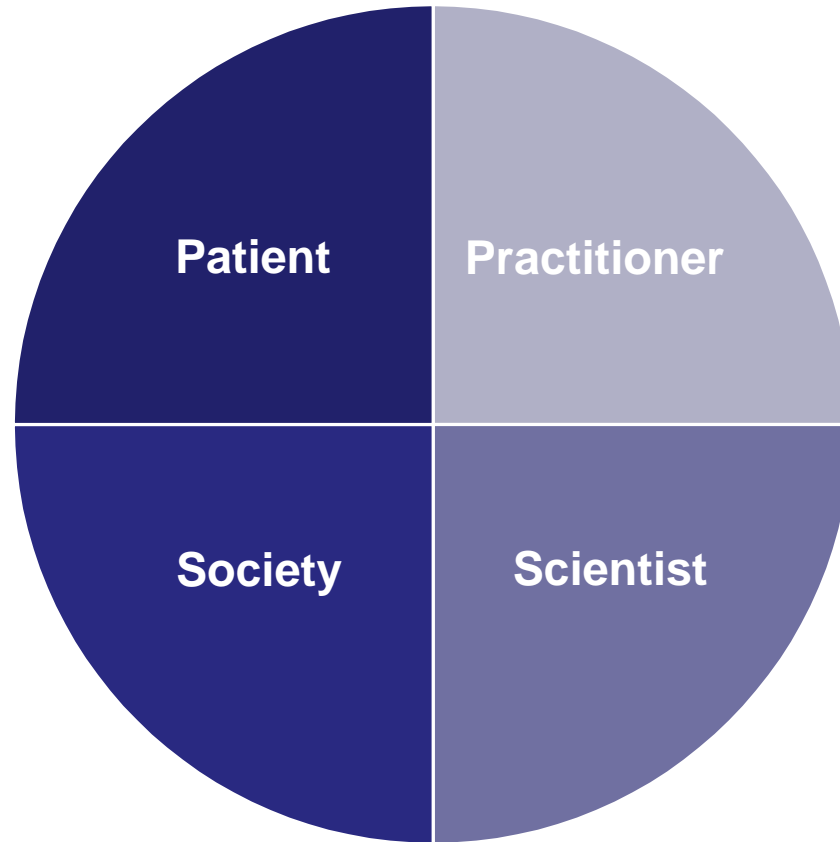Annemans L. Health Economics for non-economists.
Pelckmans Pro, June 2018.
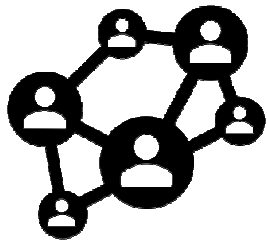*https://nolledz.com/product/health-economics-for-non-economists/*
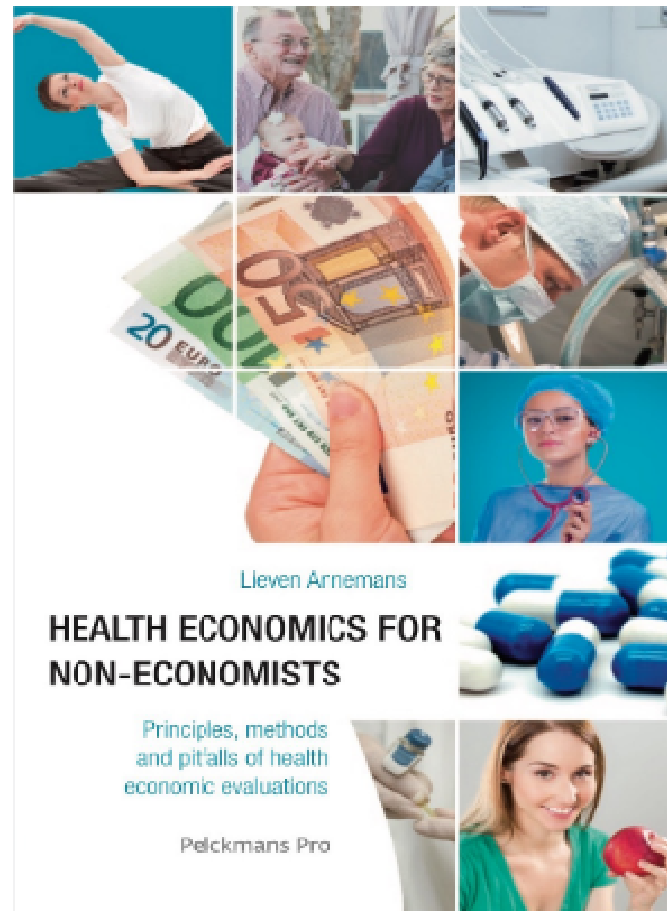
Discussion

The impact of an economical discourse on mental health care and its stakeholders

Moderators:

dr. Femke Truijens & dr. Melissa De Smet

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The impact of an economical discourse on patients

Patient (service user) perspective

- *What does it ==cost me== when cost-effectiveness drives my treatment?*
  - *Freedom of choice, available time, number of sessions, autonomy, shared decision making,…*

- *If cost-effective therapy does not work (fast enough) for me, ==it says there's something wrong with me.==*

The impact of an economical discourse on practitioners and clinical practice

Practitioner perspective

- *Who gains what? Therapeutic value for patients is ==not translatable== to economical value.*

- *Putting health care into economical terms makes therapy (intervention) a ==commodity.==*

- *Commodifying treatments introduces ==exclusion== of the toughest psychiatric (more complex) cases.*

The impact of an economical discourse on science and scientists

Scientist perspective

- *It's not my job. Economic evaluation interferes with scientific rigor*!

- *When funding agencies focus on cost-effectiveness, they shape research agenda's*

- *Quantification of experiences cannot be translated directly in economic calculations*

- *Cost-effectiveness emphasizes cure rather than care*

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The impact of an economical discourse on society

Societal perspective

- *To keep mental health care <mark>affordable</mark>, patients should be stimulated to <mark>end therapy as quickly as possible</mark> (stepped-care-model)*

- *Cost-effectiveness will enlarge the focus on <mark>prevention,</mark> screening, testing and evaluation: this <mark>interferes</mark> with people's privacy and right to decide for themselves.*

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Evaluate this course!

https://nl.surveymonkey.com/r/D79X72J