

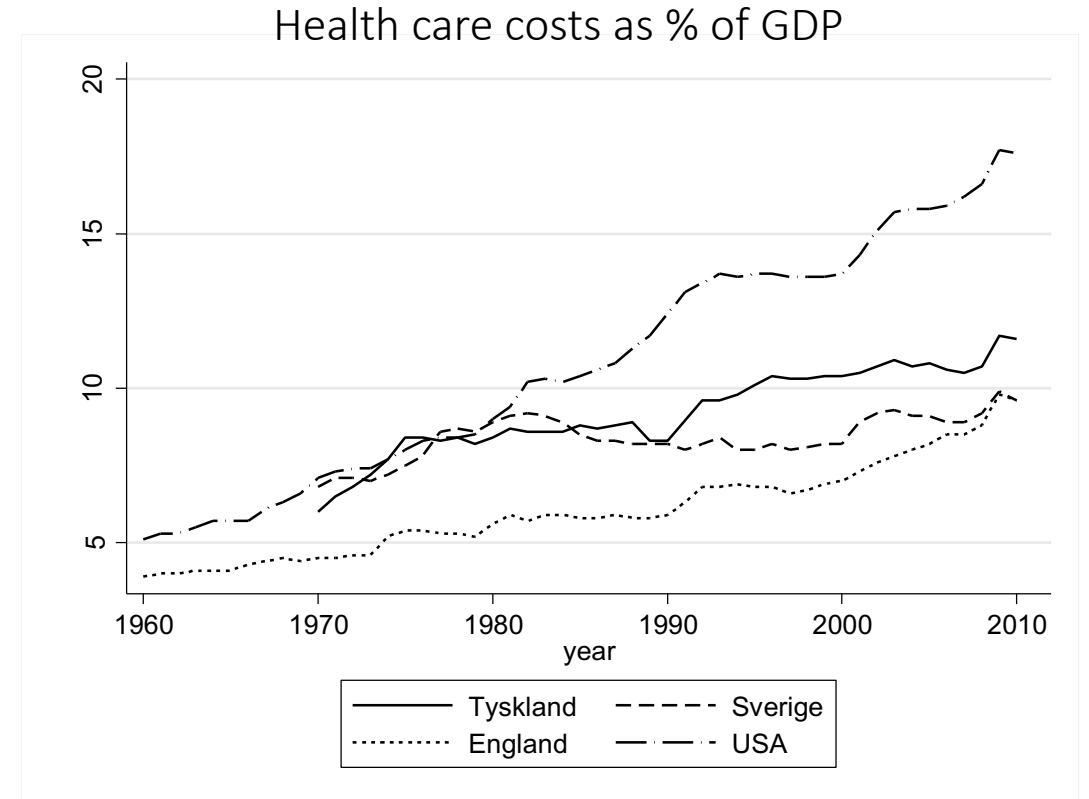
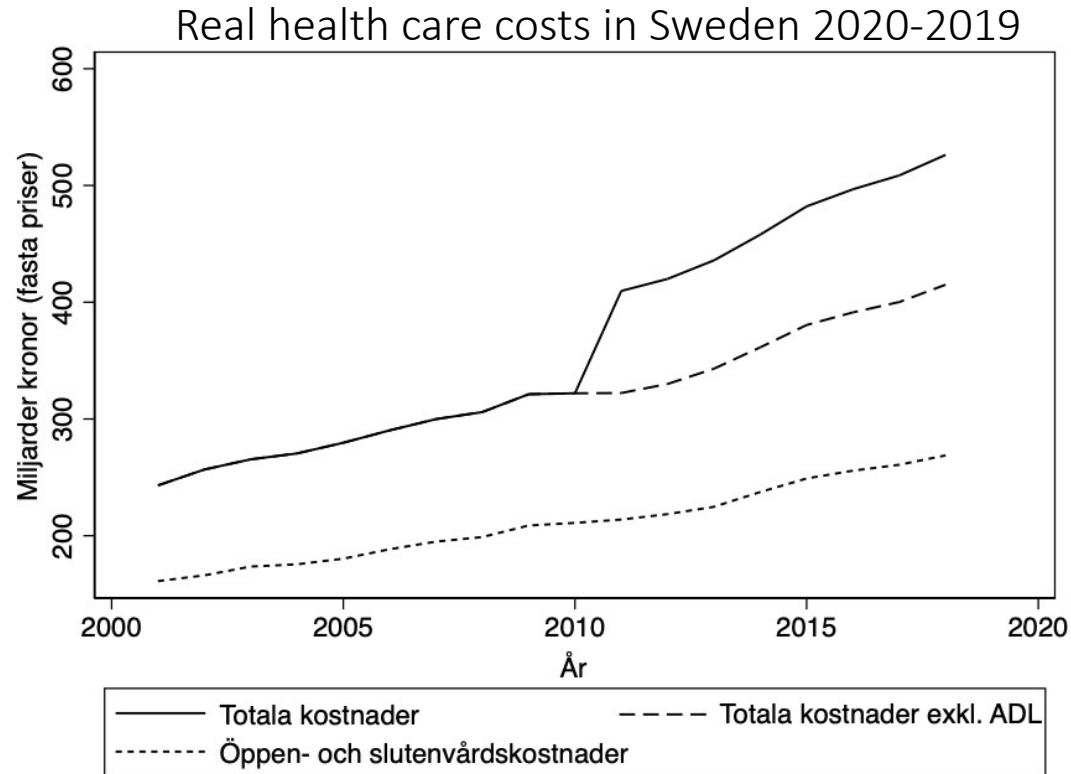
Applied Cost-Effectiveness Analysis

What and why?

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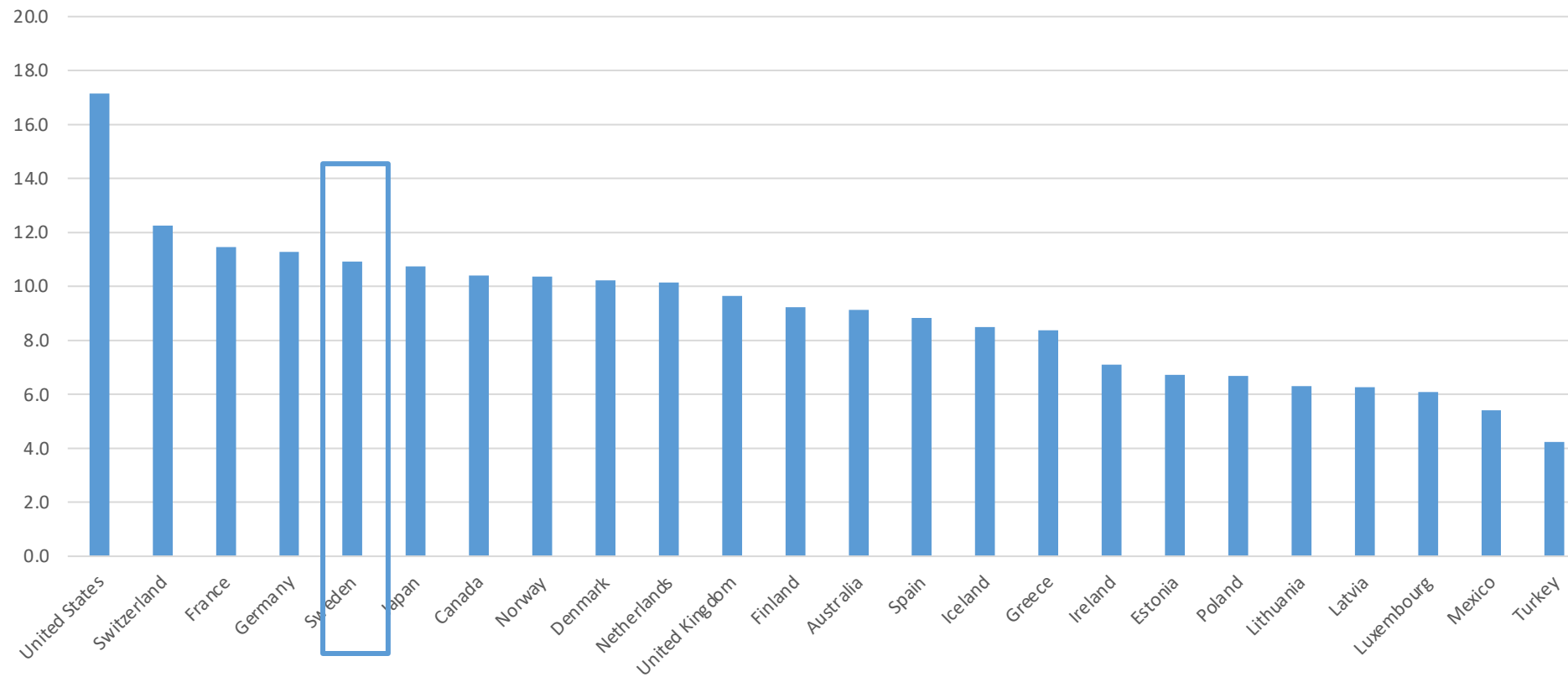
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Health care sector increasingly larger share of our economy



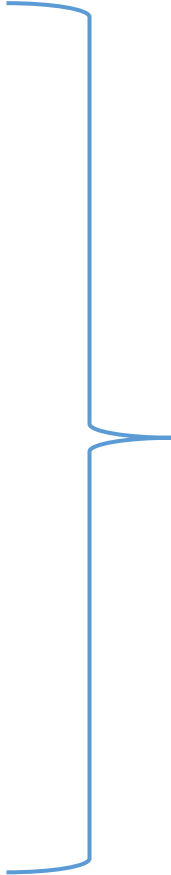
In Sweden, we allocate a relatively large share of our resources to health-care

Health care costs as % of GDP (OECD Health Data)



Basic economic facts

- We have limited resources
 - Health care staff
 - Physical & human capital
 - Time
 - Etc.
- We have unlimited demand
 - More & better prevention
 - Shorter waiting times
 - More novel drugs and medical technology
 - Etc.



We have to make choices and prioritize between relevant interventions

Stor besvikelse efter beslut från TLV att svenska män med avancerad prostatacancer nekas ny behandlingsmetod

Tandvårds- och läkemedelsförmånsverket (TLV) har nyligen beslutat att Zytiga, ett av väldigt få nya prostatacancerläkemedel som forskats fram under de senaste decennierna, inte ska ingå i högkostnadsskyddet. Vi på Janssen anser att TLV har tagit ett felaktigt beslut och står fast vid att Zytiga erbjuder en värdefull och kostnadseffektiv behandling för svenska män med avancerad prostatacancer. Janssen anser att TLV har gjort antaganden som ger en missvisande bild av värdet av Zytiga.

Tredje försöket att få subvention för läkemedel mot cystisk fibros



Economic perspectives on health-care

- Should we reimburse and subsidize a new medical technology?
- Always an alternative use of resources
 - If funding from the current health-care budget --> some other care will be displaced
 - If funding via re-allocation of the public budget --> displace educational, infrastructure, culture investments, etc.
 - If funding via higher taxes or out-of-pocket payments --> will displace private consumption

Economic perspectives on health-care

“Giving priority to one group of people means taking it away from another group, though for obvious reasons politicians tend not to dwell on this implication, leaving us to infer, from what is not said, who the ‘low priority’ groups are. In any honest and open discussion of these issues, however, that implication must be faced squarely, and **we must not shrink from identifying who (implicitly) the ‘low priority’ people are,** in any particular system of health care.”

- Alan Williams 1988



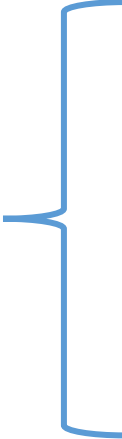
The (health) economic evaluation question

- Economic evaluations is an input to decision making for priority setting and the tool for public policy to identify efficient allocation of resources
- The task of an economic evaluation of a policy to identify, measure, and value the costs and benefits
- *“Is this intervention/policy/program worth to implement given all the other potential interventions that we could do with the same resources?”*

The Ethical Platform in Swedish Health-Care Law

1. Human Dignity Principle → All humans have equal value and no priority setting are to be made based on personal characteristics or roles in society
2. Need & Solidary Principle → More resources should be allocated to groups with higher needs and severity of disease
3. Cost-effectiveness principle → When choosing between different interventions, should strive for a reasonable relationship between costs and effects (health outcomes)

Tools to assess the relationship between costs and effects

Type of evaluation	Measurement and valuation of costs	Identification of effects	Measurement and valuation of effects
Cost-minimization analysis (CMA)	Monetary units	Equal	None
Cost-effectiveness 	Cost-effectiveness analysis (CEA)	Monetary units	One or multiple consequences, but need to be combined in one measure <ul style="list-style-type: none"> - Saved life-years - Prevented cases - Etc
	Cost-utility analysis (CUA)	Monetary units	One or multiple consequences, but need to be combined in one measure <ul style="list-style-type: none"> - QALYs - DALYs - HYT (and other alternative metrics)
Cost-benefit analysis (CBA)	Monetary units	One or multiple consequences	Monetary units

Cost-effectiveness analysis

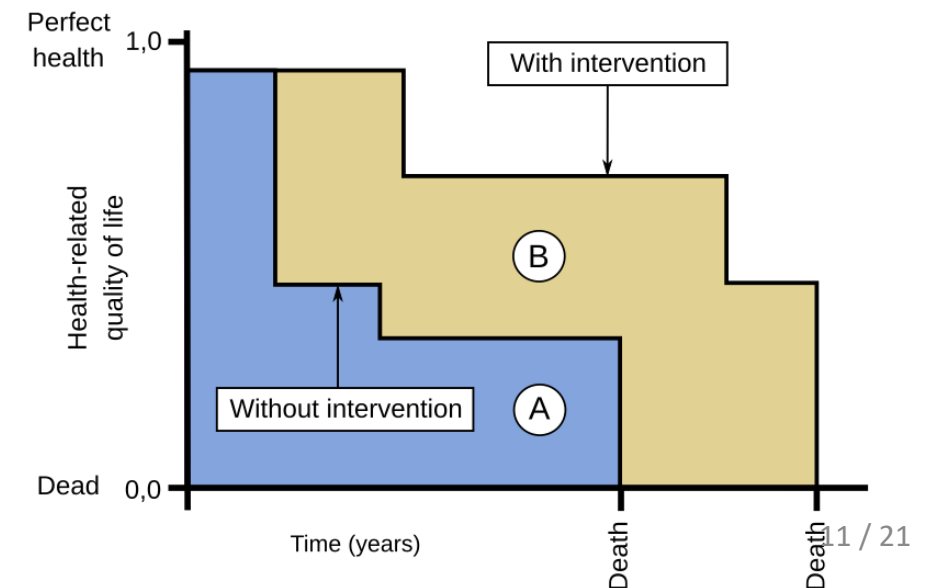
- Compares the costs and health outcomes (effects) of two (or more) interventions
- The result of a comparison between A and B is typically presented as the incremental cost-effectiveness ratio (ICER)

$$ICER = \frac{Cost_A - Cost_B}{Effectiveness_A - Effectiveness_B}$$

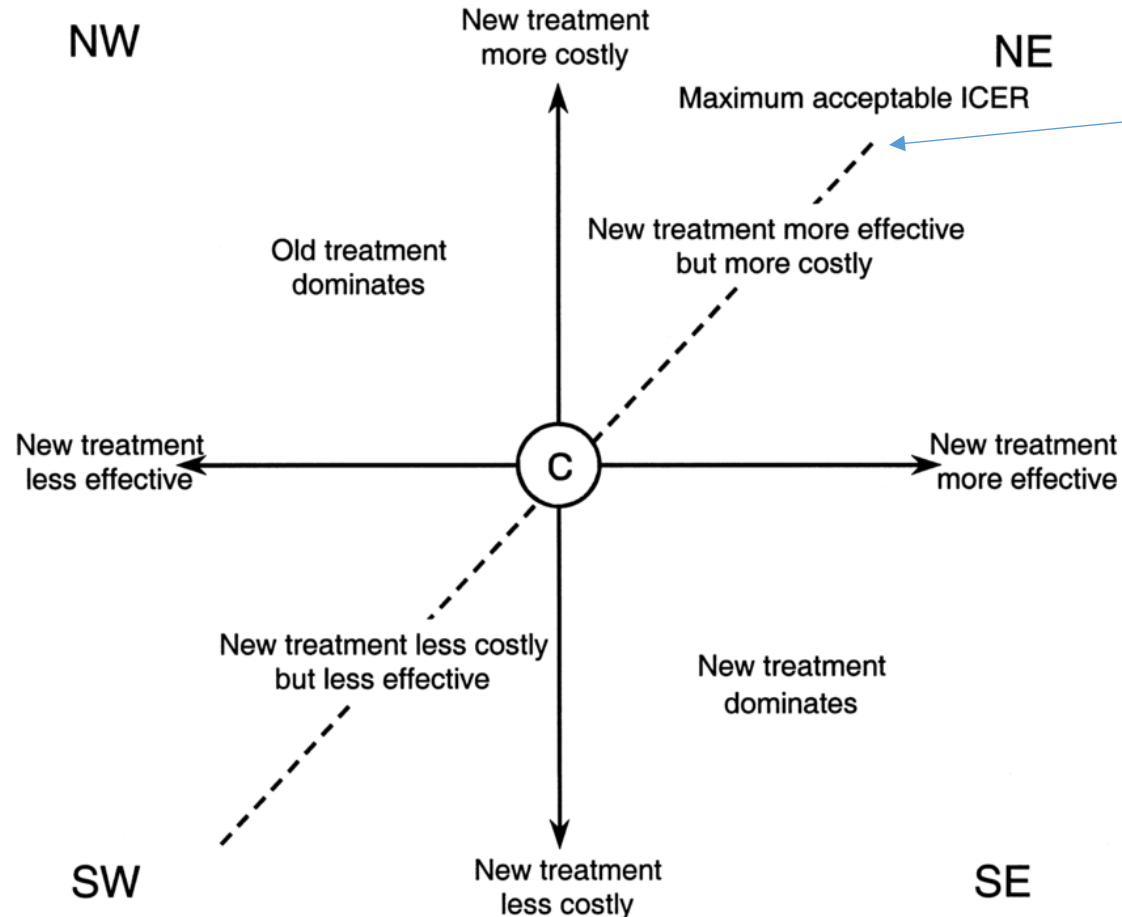
$$ICER = \frac{Cost_A - Cost_B}{QALY_A - QALY_B}$$

Cost-effectiveness analysis: measuring health outcomes

- Costs are measured in SEK, USD, Euro, etc.
- Health outcomes (effects) should preferably be measured in a generic final endpoint
 - Quality Adjusted Life Years (QALYs) has been the most common metric in applied CEA (CUA) for some time now
 - Combines length of life with quality of life



Cost-effectiveness analysis: input to decision-makers



Maximum acceptable ICER?

- Sweden: 500 000 – 1 million SEK/QALY
- UK: 20,000 – 30,000 GBP/QALY
- US: 100,000 – 150,000 USD/QALY

Applied CEA – two main approaches

- Trial-based CEA
 - Individual-level data on costs and health outcomes from trials or registries
- Model-based CEA
 - Mathematical decision-model (decision-trees, Markov cohort models, microsimulation models, ...) that are populated with secondary data from trials, registries, administrative list prices, etc.
- Often a combination of the two
 - A trial rarely has the required follow-up to model all relevant costs and health outcomes --> frequently see studies using trial-based CEA (within-trial period) with long-term modeling using a Markov cohort model

Trial-based CEA: case study

- Cost-effectiveness of revascularization vs best medical therapy for patients with intermittent claudication
- RCT data including 158 patients from Sahlgrenska University Hospital
- Cost data collected from the hospital cost per patient system (each resource use multiplied by a unit cost)
- Health outcomes in QALYs based on self-assessed HRQoL using EQ5D instrument

Circulation: Cardiovascular Interventions
Volume 13, Issue 1, January 2020
<https://doi.org/10.1161/CIRCINTERVENTIONS.119.008450>



PERIPHERAL VASCULAR DISEASE

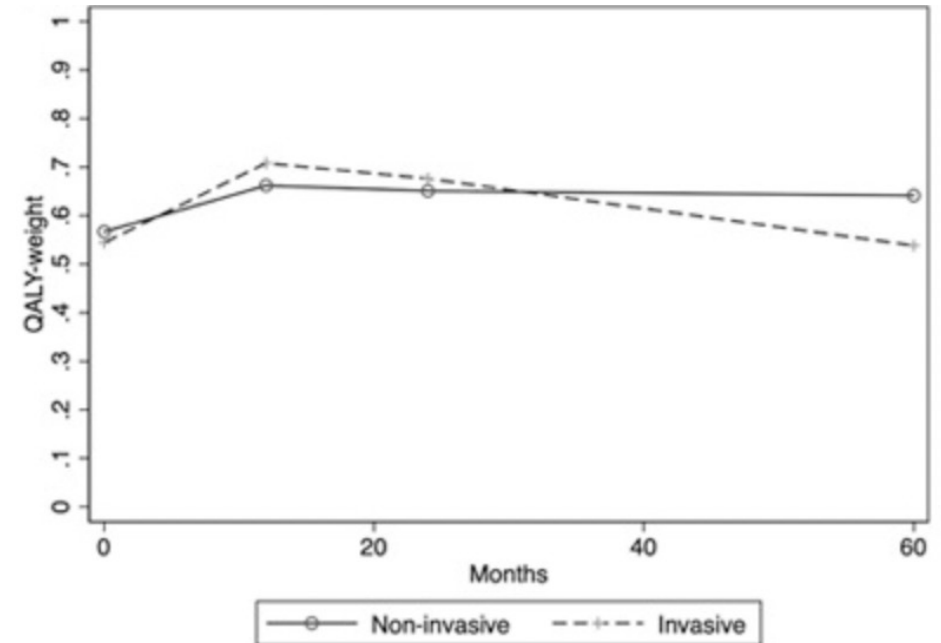
Absence of Long-Term Benefit of Revascularization in Patients With Intermittent Claudication

Five-Year Results From the IRONIC Randomized Controlled Trial

Henrik Djerf, MD, Johan Millinger, MD, Mårten Falkenberg, MD, PhD, Lennart Jivegård, MD, PhD, Mikael Svensson, PhD, and Joakim Nordanstig, MD, PhD

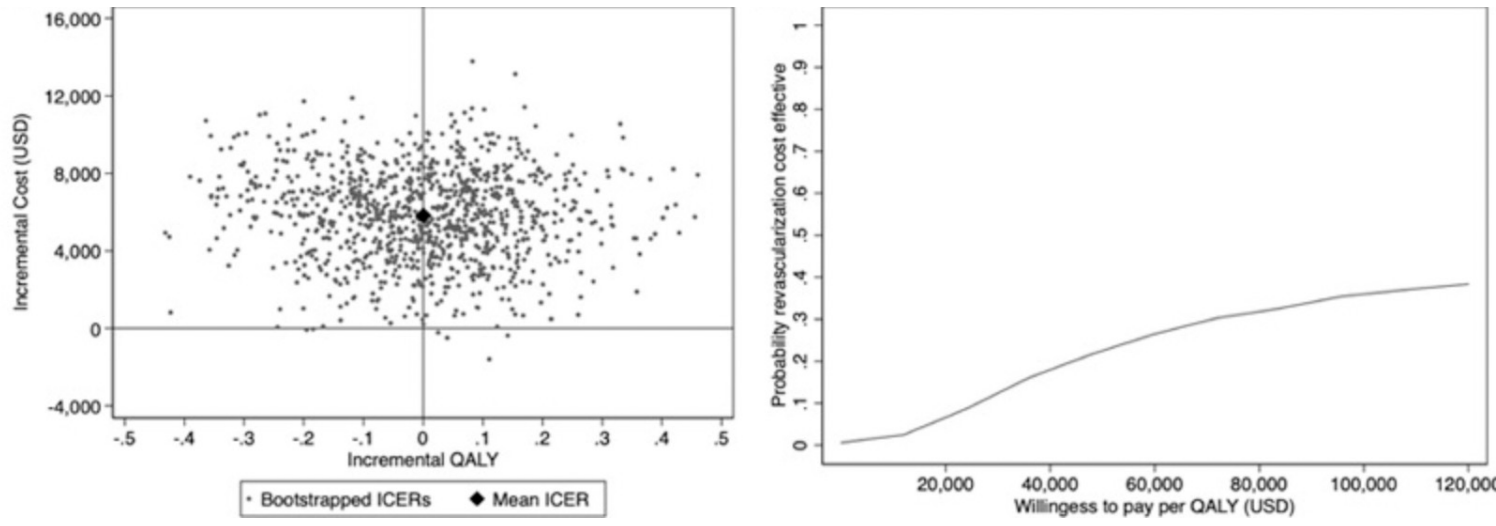
Trial-based CEA: case study

- QALYs measured as the area under the curve
- QALY-weight (“utility score”) is indexed
 - 1 = best possible health state
 - 0 = equal to being dead
- Exists many “tariffs” (value sets) that map responses to generic HRQoL surveys to the QALY-weight (EQ5D, SF36, HUI, etc.)
- Follow-up 5 years – a patient with best possible health state during entire follow-up have 5 QALYs



Trial-based CEA: case study



	Complete Case Analysis Including Deaths (n=130)		Full Sample Results Based on Multiple Imputation (n=158)	
	Cost per Patient	QALYs	Cost per Patient	QALYs
Difference, invasive vs noninvasive	6133 (972 to 11 292)	-0.10* (-0.45 to 0.25)	5849 (1202 to 10 496)	0.001 (-0.32 to 0.32)
ICER	Invasive treatment dominated (more expensive and worse health outcome)		\$5 503 448 per QALY	



Revascularization for patients with intermittent claudication is most likely **not** a cost-effective intervention

Assessing uncertainty using non-parametric bootstrapping

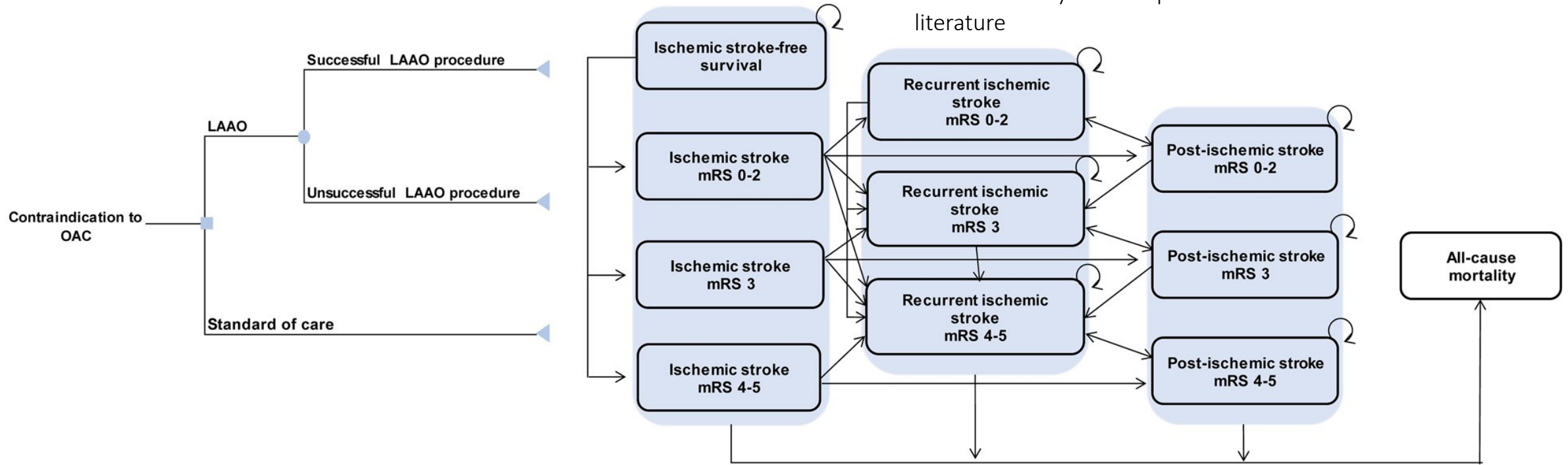
Model-based CEA: case study

Cost-effectiveness analysis of left atrial appendage occlusion in patients with atrial fibrillation and contraindication to oral anticoagulation 
Frida Labori , Josefine Persson, Carl Bonander, Katarina Jood, Mikael Svensson
European Heart Journal, Volume 43, Issue 13, 1 April 2022, Pages 1348–1356,
<https://doi.org/10.1093/eurheartj/ehab847>

- Cost-effectiveness of percutaneous left atrial appendage occlusion (LAAO) compared to standard stroke prevention care for patients with atrial fibrillation (AF) and contraindicated to oral anticoagulation
- No RCT for this intervention and patient group currently published (one ongoing)
- Increasingly popular intervention in cardiology

Model-based CEA: case study

- Markov cohort model for a hypothetical cohort with age 74 at start of model
- Modeled using 1-year cycle lengths for each treatment arm until entire cohort is dead
- Transition probabilities, quality of life, and costs used to populate the model identified from systematic reviews and meta-analyses from published literature



Each state in the model is associated with a given cost and HRQoL per cycle length

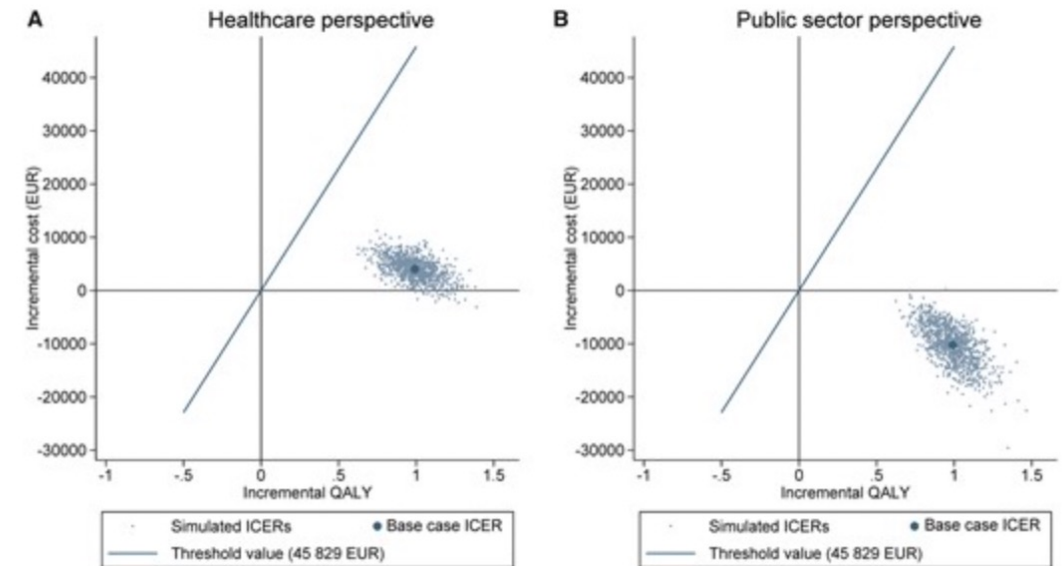
Model-based CEA: case study

Table 4 Mean costs and health outcomes per patient from the Markov model

	LAAO	Standard of care	Difference
Costs			
Healthcare perspective	19 032 EUR	15 022 EUR	4010 EUR
Public sector perspective	21 029 EUR	31 281 EUR	-10 252 EUR
Health outcomes			
QALYs	7.11	6.12	0.99

EUR, Euro; LAAO, left atrial appendage occlusion; QALY, quality-adjusted life-year.

Model results indicate that likely that LAAO is cost-effective



Sensitivity analysis using Monte-Carl simulation where each parameter in the model has a specified uncertainty range

Conclusion

- Cost-effectiveness analysis an input to health-care decision making and priority setting
- More influential in some health care jurisdictions (e.g., UK, Canada, Australia, Netherlands, Sweden) and particularly for certain types of care (most systematically for prescription drugs)
- Uncertainty with long-term effectiveness and costs of treatments a big issue

Swedish language intro to the subject



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