



# ADVANCEMENTS IN THE ECONOMIC EVALUATION OF MEDICINES IN EUROPE. PRESENT SITUATION AND FUTURE PERSPECTIVES

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# CONTENT

- Methodology
- Economic evaluation and decision making
- Data
- Implementation and impact

# METHODOLOGY

- Outcome measurement
  - QALY or no QALY, that is the question
  - Arguments for and against QALY
  - A practical compromise
- Perspective on costs
  - Guidelines differ between countries
  - Arguments for a social perspective
  - A practical compromise

# PROS AND CONS OF QALY

- Pros
  - Health can be described as changes in life expectancy and quality of life
  - Comparisons possible over a wide range of clinical outcomes
- Cons
  - Unclear relation to individual and social preferences for health
  - May not totally capture the value of a new medicine

# A PRACTICAL COMPROMISE

- Start with number of life years gained
- Provide an estimate of changes in quality of life
  - Ideally several point estimates since QoL is an AUC
- Adjust the estimate of LYG for quality of life
  - Analyse effect of adjusting survival for QoL (-)
  - Analyse effect of including QoL benefit (+)
- Use alternative effect measures when possible
  - Cost per event avoided
  - Cost per successfully treated patient

# ARGUMENTS FOR A SOCIAL PERSPECTIVE

## EUR J HEALTH ECON (2009) 10:357-59

Eur J Health Econ

DOI 10.1007/s10198-009-0173-2

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EDITORIAL

**Ten arguments for a societal perspective in the economic evaluation of medical innovations**

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1-2. Consistent with the theoretical foundations for social cost benefit analysis

# TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE



## **A SOCIETAL PERSPECTIVE FOR ECONOMIC EVALUATION IS THE CLASSIC APPROACH TO ASSESSING THE PROFITABILITY OF SOCIETAL INVESTMENTS.**

- This is e.g. the standard approach in the assessment of different environmental, and transport safety programmes affecting health.
- There is no reason why economic evaluation of programmes affecting health in the health care sector should deviate from this standard.
- Adopting a payer instead of a social perspective will create a bias against investments in improved health through health care spending



3. If health gains are valued from a social perspective, so should costs

## TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE



# IT HAS BEEN WIDELY ACCEPTED THAT ECONOMIC EVALUATIONS SHOULD INCLUDE ALL POTENTIAL HEALTH EFFECTS, POSITIVE AS WELL AS NEGATIVE (SIDE EFFECTS)

- It is not logical to have a social perspective on health benefits and not costs
  - Analytical position
- Cost-effectiveness analysis can be performed within a specific budget perspective if outcome is services, not health
  - Productivity analysis
- Why should health effects measures as QALYs be included, but not the value of the costs avoided which was spent to compensate for them

4. A restricted payer perspective will lead to suboptimal decisions for allocation of resources; effecting both static and dynamic efficiency

## **TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE**



# ECONOMIC EVALUATIONS BASED ON A FIXED BUDGET MAY LEAD TO SUBOPTIMAL DECISIONS

- Switching costs to other parties may make an investment attractive
  - Prevention within and outside the health care sector
- What is within and outside the budget is a policy decision
- Costs outside the budget period is not counted
- How do we know if a consequence has an impact on the budget or not?

5. Empirical studies support the risk of suboptimal decisions based on restricted view of benefits

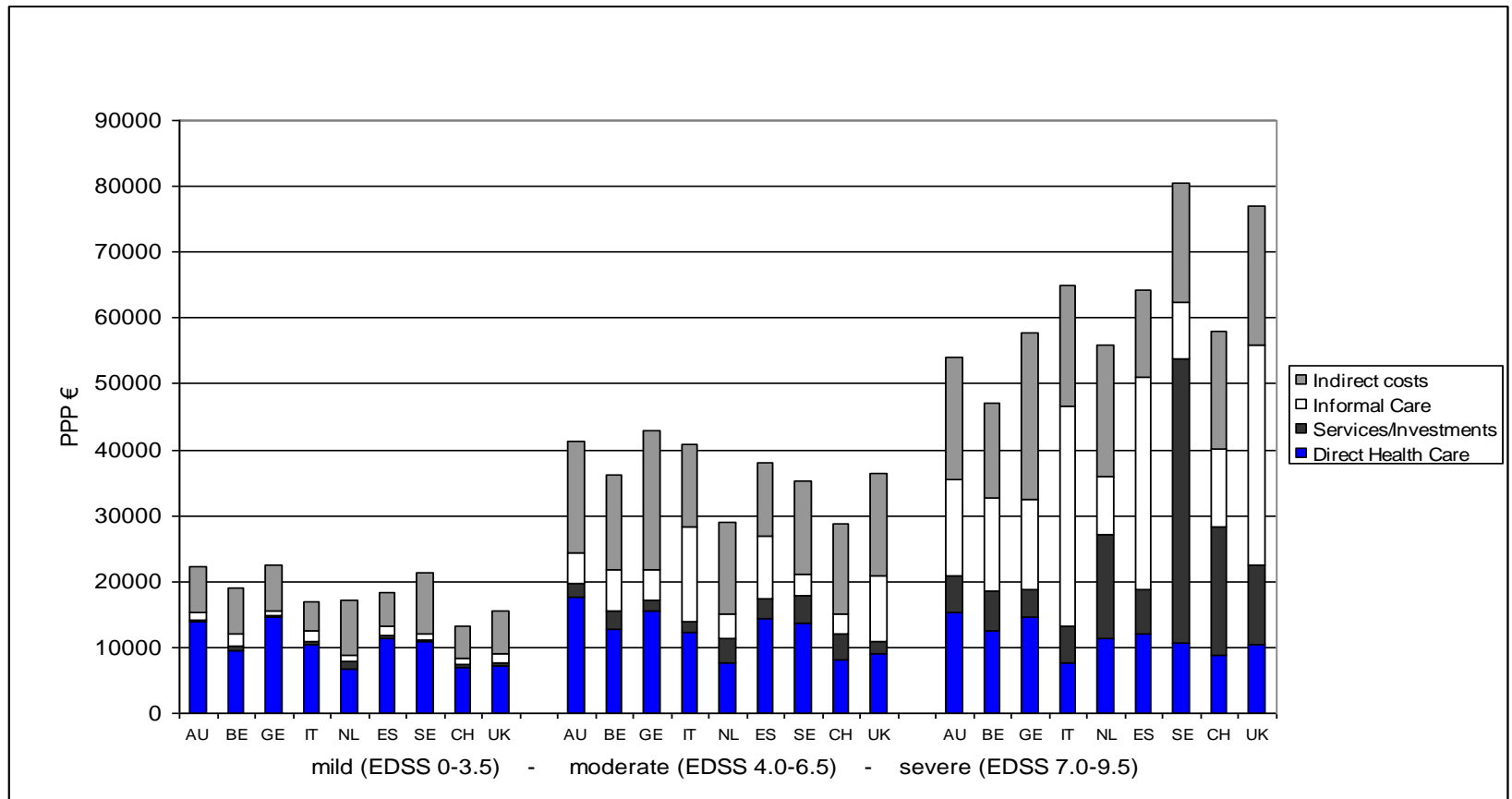
## **TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE**



Alzheimers disease. Hypothetical innovation offering a 50% reduction in disease progression for three years  
 Model simulation: lifetime costs of care, with and without treatment

	No treatment	Treatment	Difference	% of cost savings
Pharmaceuticals	49 159	49 393	235	0%
Direct medical	146 371	128 670	-17 701	17%
Community care	515 476	448 490	-66 986	66%
Informal care	245 371	228 604	-16 767	17%
<b>Total</b>	<b>956 377</b>	<b>855 158</b>	<b>-101 219</b>	<b>100%</b>

# Cost increase with progressing disease in MS (mean annual cost per patient, PPP€ 2005)



6-7. Payer perspectives cannot be defined in a consistent way, and thus QALYs will not have a consistent definition either

## **TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE**





# DEFINITION OF THE BUDGET IS OFTEN ARBITRARILY

- All health care costs both now and in the future
  - Including health care costs in added years of life
- Health care costs for a defined period only
  - Not including costs outside the studied disease
- In most countries there are several budgets
  - Difficult to define a consolidated budget, particularly in regionalized health care systems
  - Opportunities for transfers within and between budgets varies

# PROBLEM TO MEASURE AND INTERPRET QALYs IF THEY SHOULD INCLUDE EXTERNAL COSTS

- “Make sure that all benefits and costs are included, but only once”
  - Alan Williams (1976)
- “All changes in real resources should be measured and they can be classified in
  - Changes in service production
  - Changes in resources used by patients and their helpers
  - Changes in the gross domestic product
    - Alan Williams (1981)

8. A budget perspective is inconsistent with decisions based on willingness to pay for a QALYs

## **TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE**



# A FIXED BUDGET IS INCONSISTENT WITH DECISIONS MADE ON A THRESHOLD FOR COST PER QALY

- The WTP for a QALY may vary over time and between diseases, groups of patients and the technology used
  - These valuation have and should have impact on budgets
- Research on the “value of a QALY” is meaningless unless the cost per QALY ratio is clearly and properly defined

9. Specific payer perspectives can be included in the social perspective

## **TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE**



10. A social perspective supports democratic decisions

# TEN ARGUMENTS FOR A SOCIAL PERSPECTIVE



# INVOLVEMENT OF ALL STAKEHOLDERS

- The HTA is not the decision – it is a help to make better decisions
- In all countries it is the population at large who both pays for and receive the benefits of new technologies
- A broad societal perspective on value, i.e. costs and benefits, facilitate informed discussion and decisions about access and use of new medical technologies

# A PRACTICAL COMPROMISE

- Start with a social perspective
- Report indirect costs separately
  - If relevant with both human capital and friction cost method
- Report cost in added years of life separately
  - If relevant present a separate estimate of health care cost in added years of life



# ECONOMIC EVALUATION AND DECISION MAKING

- Closer link between studies and decision
  - NICE 1999
  - LFN/TLV 2002 and National Guidelines 2005
  - AMNOG/IQWIG/
  - Greater role for economic evaluation
- But decisions must be made early
  - Lack of evidence for assessing relative effectiveness

# DATA

- Data from clinical trials
  - Limitations of RCT data for economic evaluations
    - Population, comparator and outcome
  - Opportunities for improvement
    - But not necessarily more economic data
    - Early engagement with HTA agencies (joint advice)
- Real life data
  - From efficacy to relative effectiveness
  - Different stakeholders – same data?

# EVIDENCE FOR REGULATORY DECISIONS

- Randomized clinical trials of efficacy and safety form the scientific basis for regulatory decisions on the balance between risks and benefits
- Clinical trials when used for assessment of relative effectiveness may suffer from
  - Having the wrong endpoints
  - Having the wrong comparator (placebo)
  - Studying the wrong patient population
- They may thus be interpreted in a different way by HTA and reimbursement bodies

# NEW CHALLENGES FOR REGULATORS

- Clinical trial data are seen as in-sufficient for assessment of safety
  - Risks are determined by the use of drugs in clinical practice
  - Need for more elaborate post-marketing studies for assessment of risk
- Clinical trial data are seen as in-sufficient for assessment of effectiveness
  - New guidelines needed for design of clinical trails
  - Need for post marketing follow up studies

# HOW CAN CLINICAL TRIALS BE IMPROVED?

- Designed to reflect real practice
  - Less influence on outcome from the experimental situation
- Choice of relevant end-points
  - Reflecting patient benefit
  - Useful for modelling long term effects
- Choice of relevant comparators
  - Active comparator rather than placebo
- Choice of relevant patient populations
  - The populations which the product will be used in

# BUT THERE ARE LIMITATIONS AND TRADE-OFFS FOR IMPROVEMENT

- Naturalistic design may compromise internal validity
- End-points may be relevant but increased measurement error
- More alternatives means more patients and longer study time
  - Increases costs
- Relevant patient populations may rise ethical issues
  - Higher risks

# PAYERS ARE INCREASINGLY ACCOUNTABLE FOR HEALTH OUTCOMES

- Focus in health care systems has shifted from input and throughput, towards output (health)
- Productivity and efficiency in health care delivery a growing concern
- Providers are incentivised to deliver better outcomes
  - Pay for performance (P4)

# INFORMATION ABOUT COST-EFFECTIVENESS IS INCREASINGLY IMPORTANT FOR PAYERS IN THEIR MANAGEMENT OF THE HEALTH CARE SYSTEM

- Decisions must be made about allocation of resources to improve efficiency, which involves priorities between effective technologies
- Relative effectiveness drives cost-effectiveness



# PROBLEMS WITH REAL LIFE STUDIES

- Problems with interpretation of data collected
  - Can be reduced by randomization but this may be difficult in many situations
- Quality of data obtained may be low
  - Can be managed but at a cost
- May take long time to get results
  - International collaboration may reduce the time
    - Most important for orphan drugs
- Will different stakeholders collaborate
  - One register – many stakeholders?

# IMPLEMENTATION AND IMPACT

- Management of uncertainty
  - Coverage by evidence development
  - Pay for performance
- Measurement and management
  - Can we see any impact so far?
  - Obvious problems with implementation
    - As with other political and administrative decisions

## Mobilisation of resources

Until the 1970s focus was on expansion of resources and access

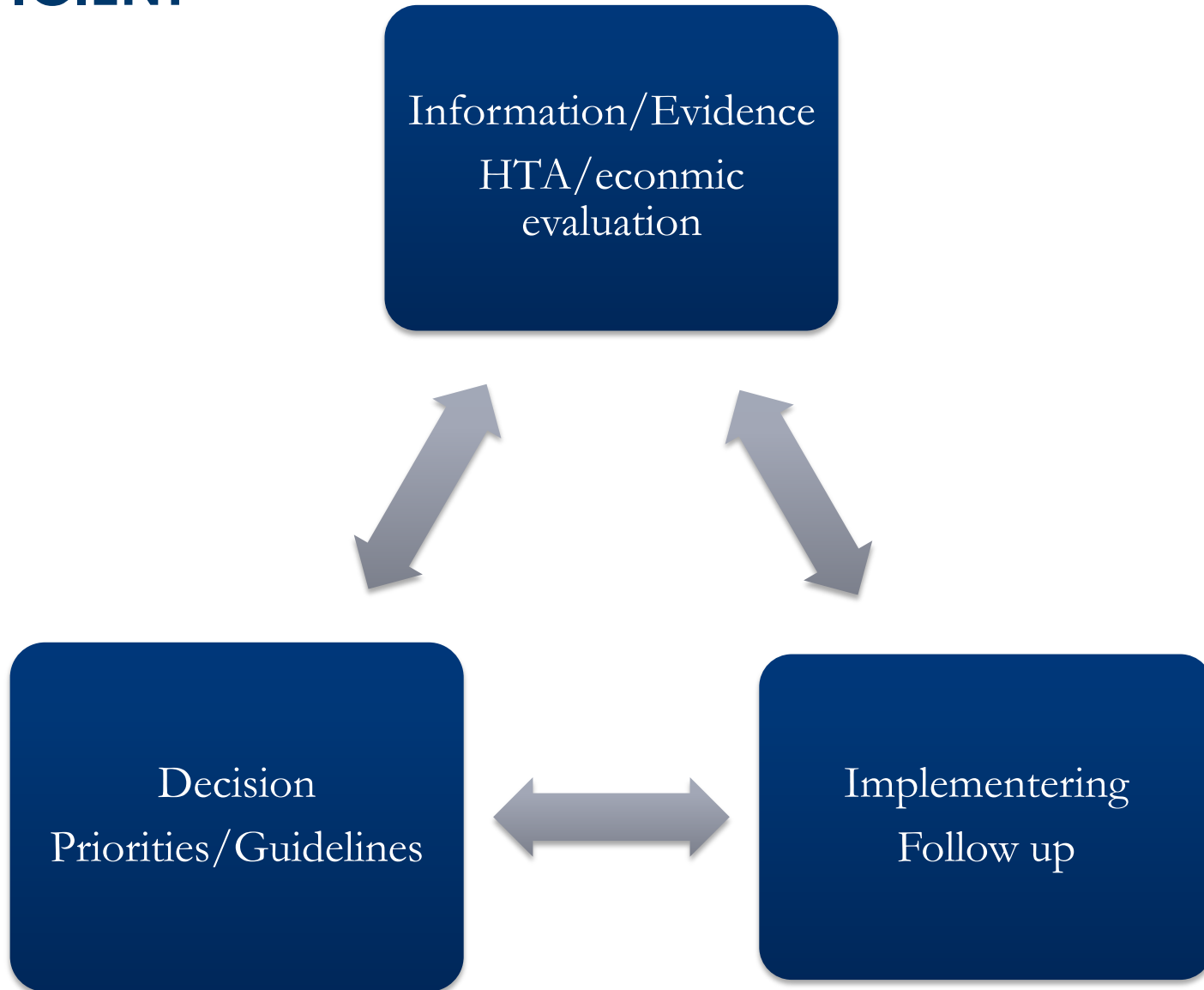
## Structure and processes

After the oil price chock, re-organisation (re-invention) was the solution to improvement in access

## Outcome

Today health care management focus on outcome and cost-effectiveness;  
Health and quality of care

# RIGHT DECISION IS NECESSARY BUT NOT SUFFICIENT



# PERFORMANCE BASED REIMBURSEMENT A COMMON PLAYING FIELD FOR PAYERS AND INDUSTRY?

# REIMBURSEMENT DECISIONS ARE RESTRICTED (OPTIMIZED) IN DIFFERENT WAYS

- Co-payments, pre-use authorization, quantity and dose limitations, coverage by evidence development, restricted reimbursement, outcomes guarantees, conditional treatment continuation , only in research, only with research, price volume agreements, .....
- Reimbursement is not only yes or no!!!!
  - Marketing under an open ended insurance is a thing of the past

# Trust is good but control is better?

- “However, lack of sufficient, timely and relevant evidence makes HTA-driven coverage and reimbursement decisions difficult, if not impossible.”
- There is a lack of evidence but also a need to follow up that decisions are followed
  - Payers do not trust that information to prescribers is enough to implement the decisions

# What's in it for payers?

- Waste of money is new major risk
  - High cost per patients
  - Small patient populations
- Funding in health care shifting from input to output
  - From budgets and fee for service
  - Capitation and disease management
- Pay per pill not consistent with criteria for cost-effectiveness
  - Focus on indication and alternatives



# Performance-based agreements

Current use in oncology and future trends



# THE ISSUES

- Relative effectiveness and cost-effectiveness are not criteria for decisions about adoption and use of new cancer drugs
- This gives HTA and reimbursement bodies acting on behalf of payers increasing influence
- However, lack of sufficient, timely and relevant evidence makes HTA-driven coverage and reimbursement decisions difficult, if not impossible.

# POTENTIAL SOLUTIONS

- Asking for more data before decision is made
  - Will increase costs
  - Will delay introduction
- Coverage by evidence development
  - Data collection to verify effectiveness and cost-effectiveness in approved indications
- Performance based agreements (P4P)
  - Payment depend on observed outcome
  - Change the distribution of risk between payers and manufacturers

## WHY ARE PAYERS INTERESTED IN P4P?

- Waste of money is new major risk
  - High cost per patient for new targeted treatments
  - Wrong use has high opportunity cost
- Funding in health care shifting from input to output
  - Away from budgets and fee for service
  - Towards capitation and disease management
- Pay per pill not consistent with criteria for cost-effectiveness
  - Focus on indication and alternatives

# Is cancer “special”?

- In terms of uncertainty at market authorization?
- In terms of cost per patient?
- In terms of opportunities to define indications and follow up use and effectiveness in clinical practice?

# EXPERIENCES SO FAR

- Oncology drugs dominate among the performance based agreements we know today
  - In Italy, 16 out of 18 agreements are cancer drugs
- Many performance based agreements are simple price discounts
  - Payment related to number of cycles given
- Most agreements use response as criteria for performance

# PERFORMANCE GUARANTEES

## CANCER

Green <sup>24</sup> , 2006	UK	Multiple myeloma	Johnson and Johnson	National health service	J & J agreed to reimburse the NHS in either cash or product for patients who do not respond (Response measure: 50% decrease in serum M protein) after 4 cycles of treatment with <b>Velcade</b> . Responding patients receive additional 4 cycles.
Pollack, 2007	US	Breast Cancer	Genomic Health	United Healthc are	United Healthcare agreed to reimburse the <b>OncotypeDx</b> test for 18 months while it and Genomic Health monitor the results. If the number of women receiving chemotherapy exceeds an agreed upon threshold, even if the test suggests they do not need it, the insurer will negotiate a lower price.
Thomson, 2008	UK	Colorectal cancer	Merck	Primary care trust	Rebate direct to primary care trust on the cost of any vials of <b>Cetuximab</b> used for patients who do not achieve a pre-agreed clinical outcome ('nonresponders') at up to 6 weeks (up to an agreed maximum of 3200 milligrams).

# WILL P4P LEAD TO MORE EFFICIENT HEALTH CARE DELIVERY?

- The studies evaluating P4P are very few and of low quality
- P4P efficiency could not be demonstrated in a systematic review of published studies
- But we must recognise the problems to give a clear answer to this question
  - Controlled experiments are not difficult to undertake and interpret



# POINTS FOR DISCUSSION

- Genuine uncertainty versus asymmetric information
  - Can industry and payers a common information base?
- Pay for drug or outcome
  - Performance payment make the industry responsible for efficiency in the health services
  - Responsibility without influence?
  - New business model?
- Pay for performance as a vehicle for differential pricing in high and low income countries



## FUTURE OF ECONOMIC EVALUATION OF MEDICINES

- Focus on the most important issues in health policy
  - Outcome and cost-effectiveness
- Can be developed to include dynamic aspects
  - Management of pharmaceutical innovation
- Not perfect, but better than the alternatives
  - Roll back of public finance and increased co-payments
    - Limits access to those who can pay
  - Political "muddling through" (Charles Lindblom)
    - Not rational and democratic