Decision-making in the evaluation of medicines in Europe: challenges and reality

Anke Hövels, PhD

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Farmaco-epidemiologie en Klinische Farmacologie

Universiteit Utrecht

Content

- The Netherlands
- Role of economics in reimbursement in NL
- Case study from NL
- Economic evaluations and challenges
- Orphan drugs and HTA

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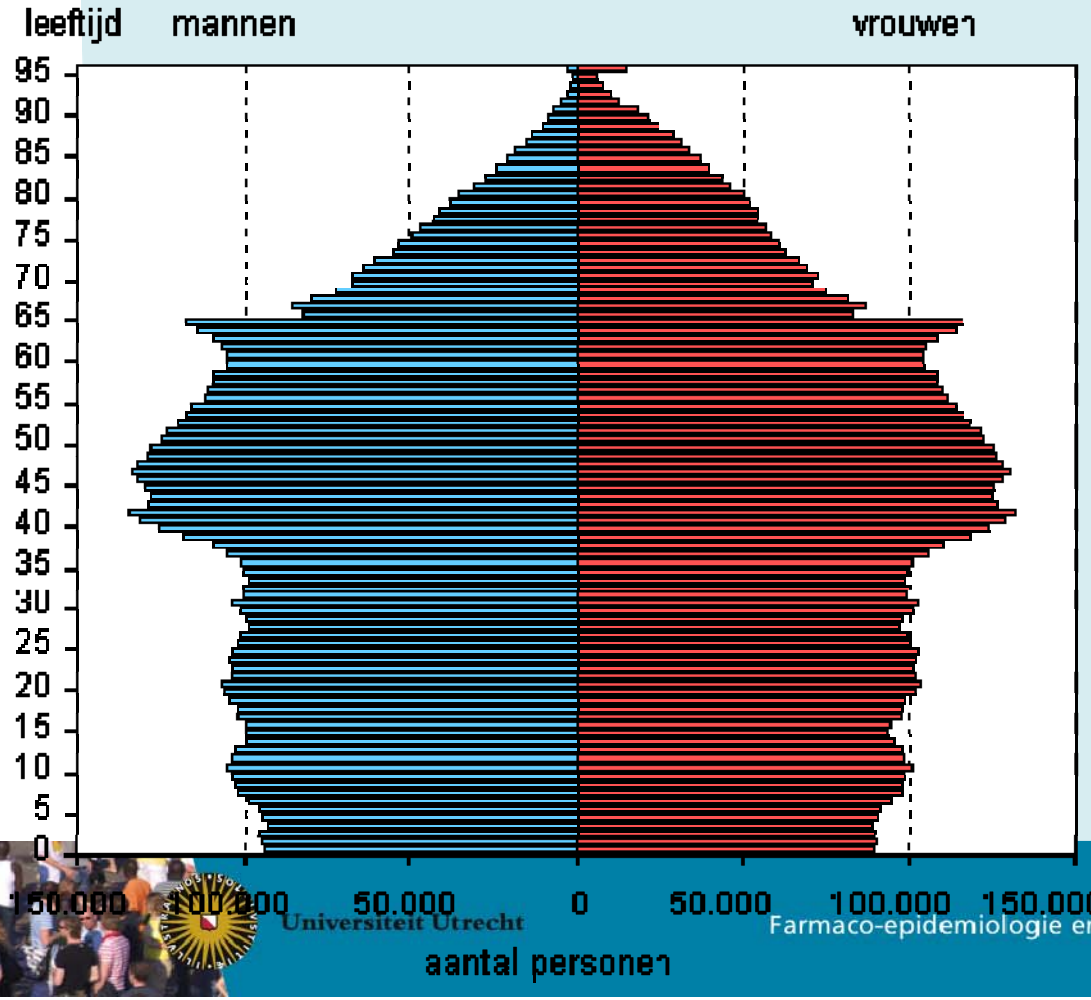
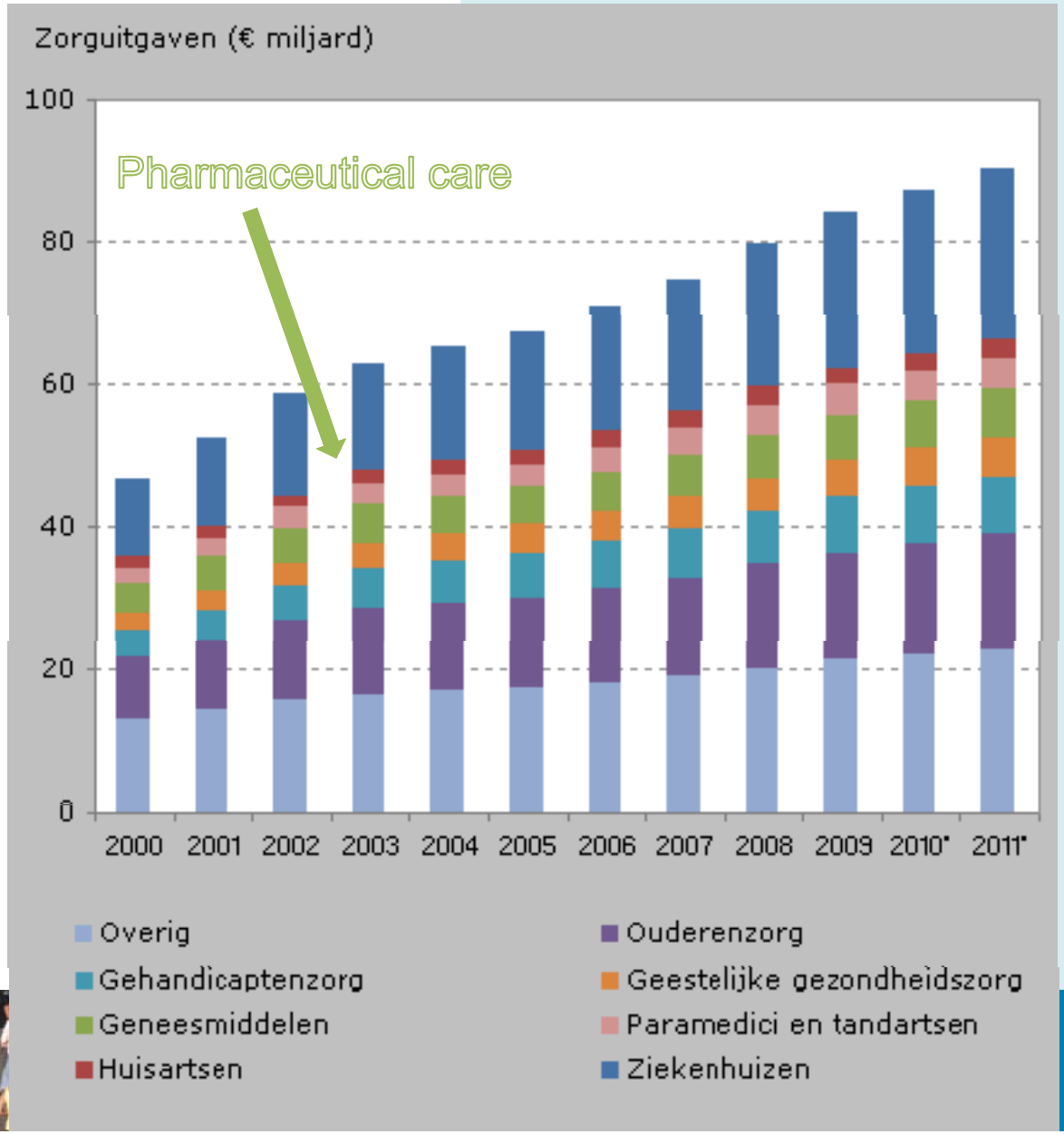
The Netherlands

- 16.7 inhabitants

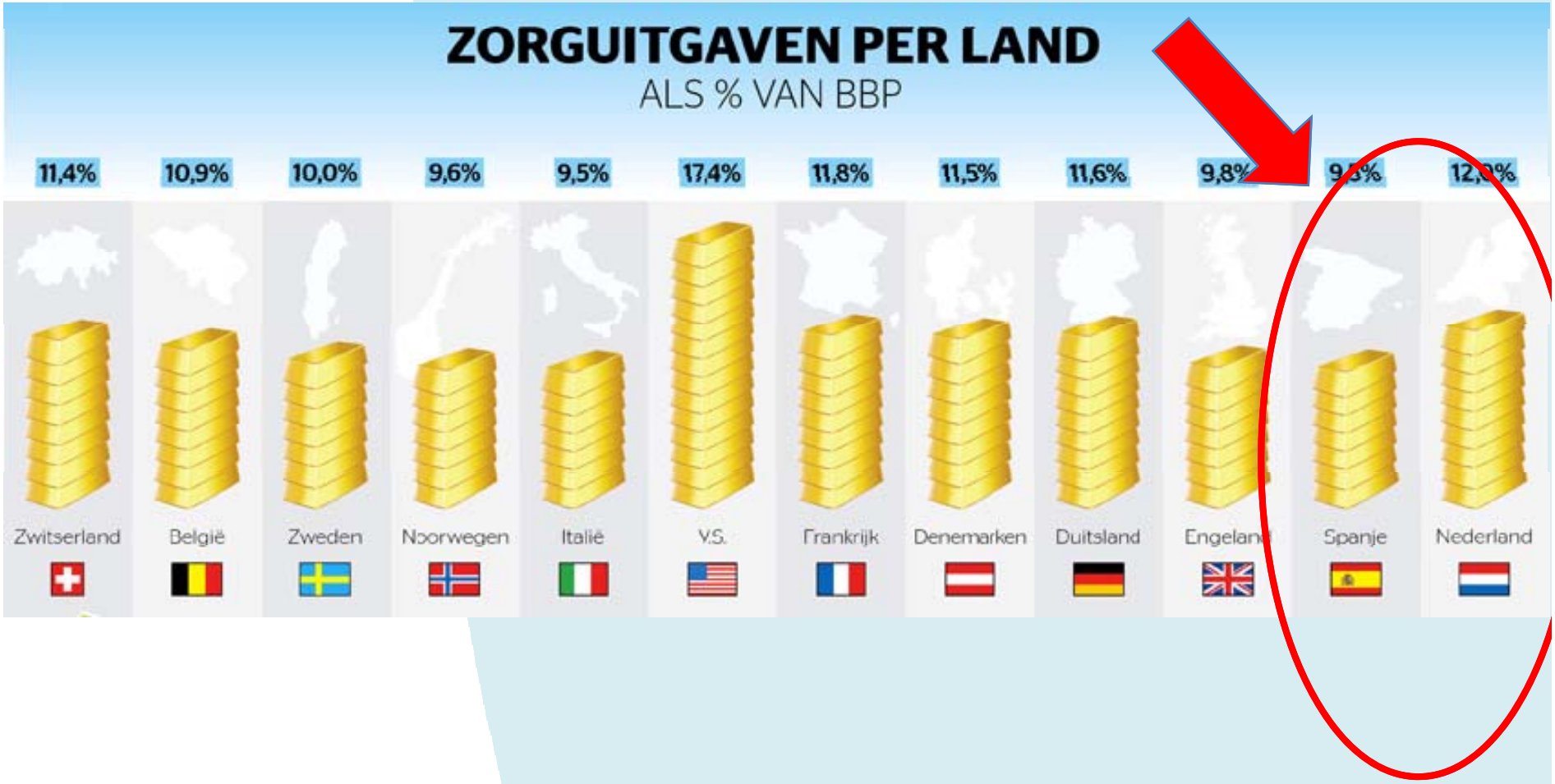


Health care costs



Health care spenditure: €5392 per inhabitant

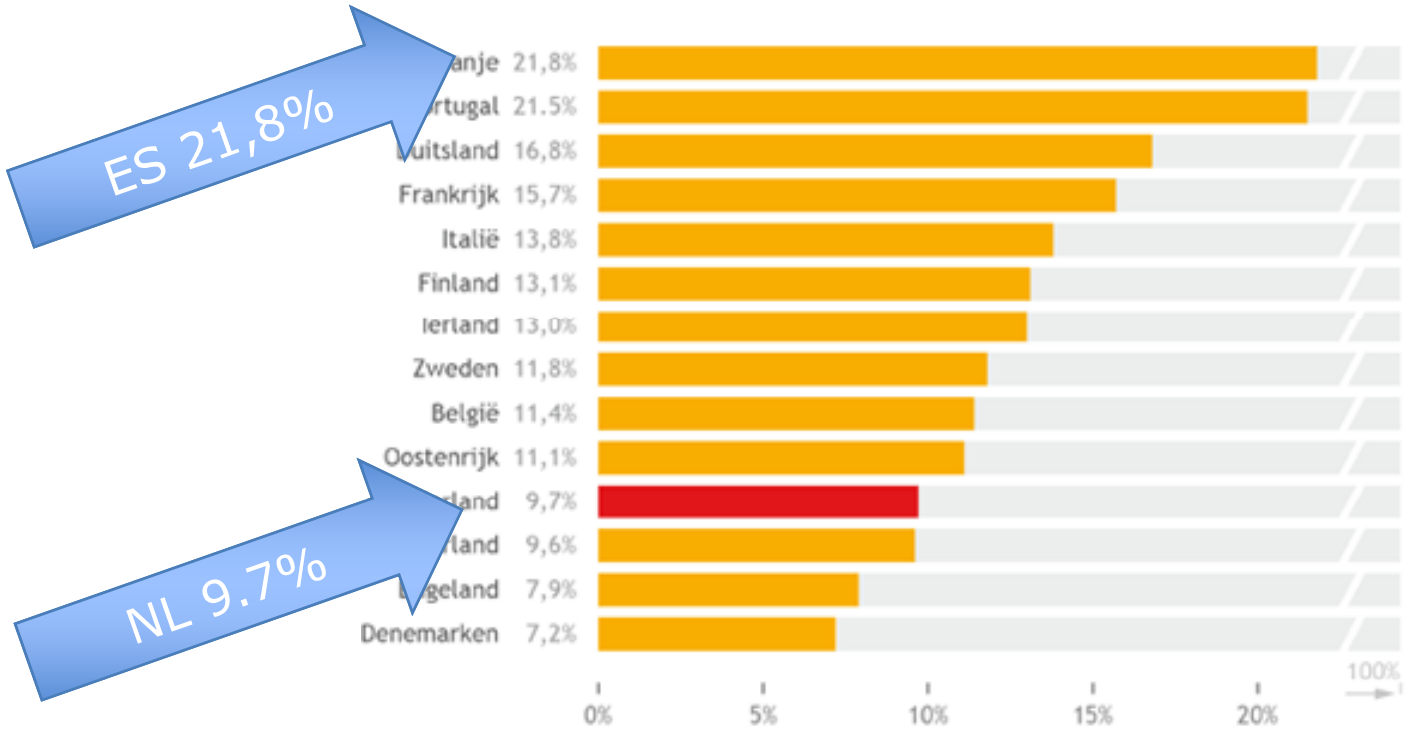
European perspective



Source: RIVM.nl

Costs of pharmaceuticals

Aandeel uitgaven aan farmaceutische hulp binnen totale zorg-uitgaven in 2009 (in procenten)



Bron: Stichting Farmaceutische Kengetallen, 2011

Increase is caused by

- Aging population: 15%
- Increase in prices: 35%
- Other (increase in # of patients, technology development, broadening of indications): 50%
- This has a profound effect on public health, in light of finite health budgets

Source: RIVM.n

Health care costs are paid for by:

- Basic Insurance: 68.6%
- Government (taxes): 14.3%
- Out of pocket patient: 9.6%
- Additional insurance: 4%
- Other: 3.5%

Source: RIVM.n

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Inequalities in oncology care: Economic consequences of high cost drugs

Maartje G.H. Niezen[a,*], *Elly A. Stolk*[b], *Adri Steenhoek*[a], *Carin A. Uyl-De Groot*[b]

[a]*Institute for Health Policy and Management, Erasmus MC Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands*
[b]*Institute for Medical Technology Assessment (iMTA), Erasmus MC Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherl*

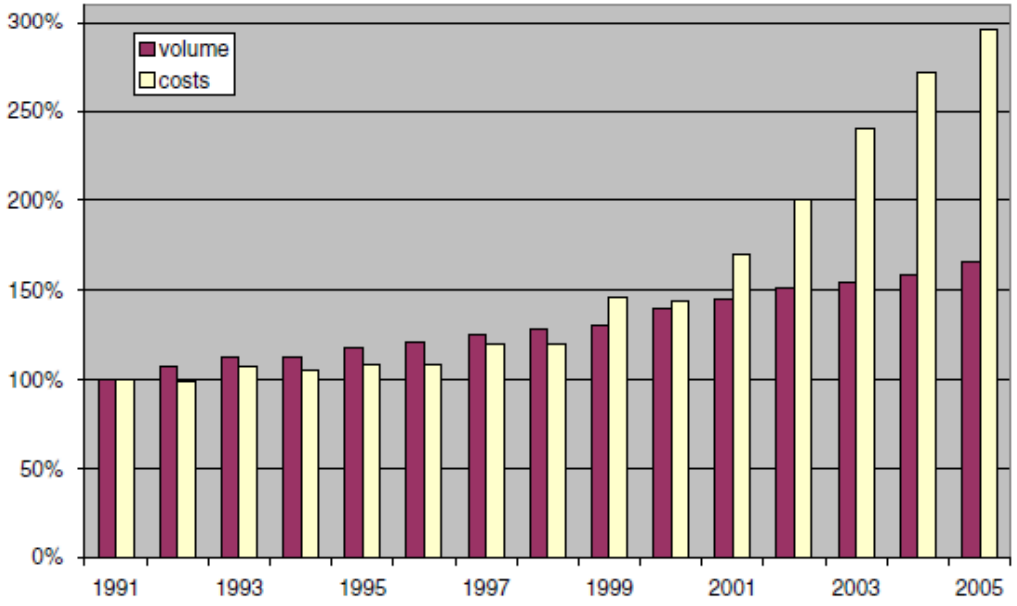


Fig. 1 – Hospital drugs: development in volume and expenditures since 1991 (1991 = 100%).

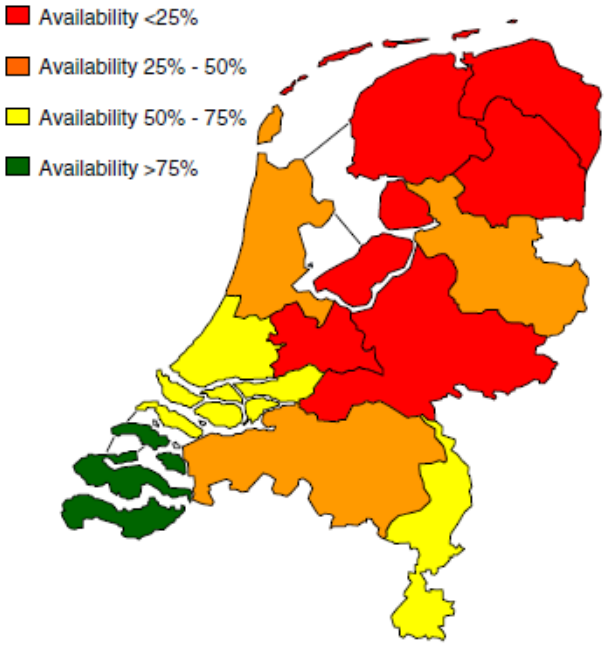
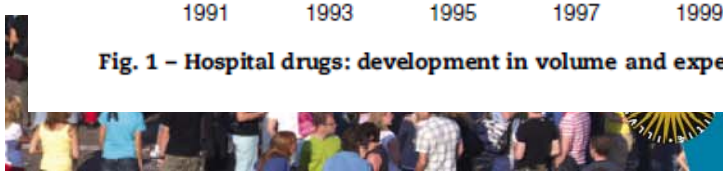
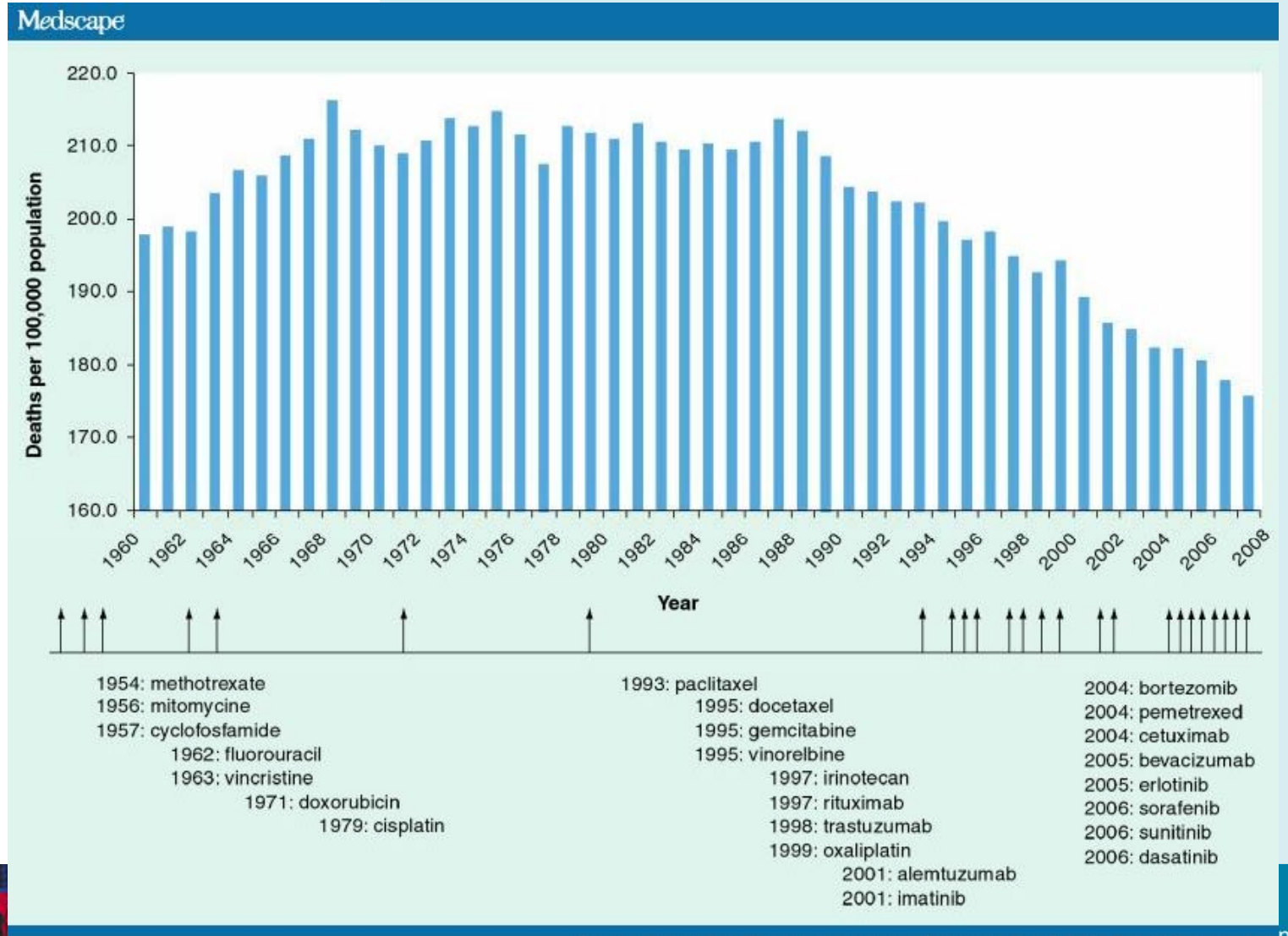


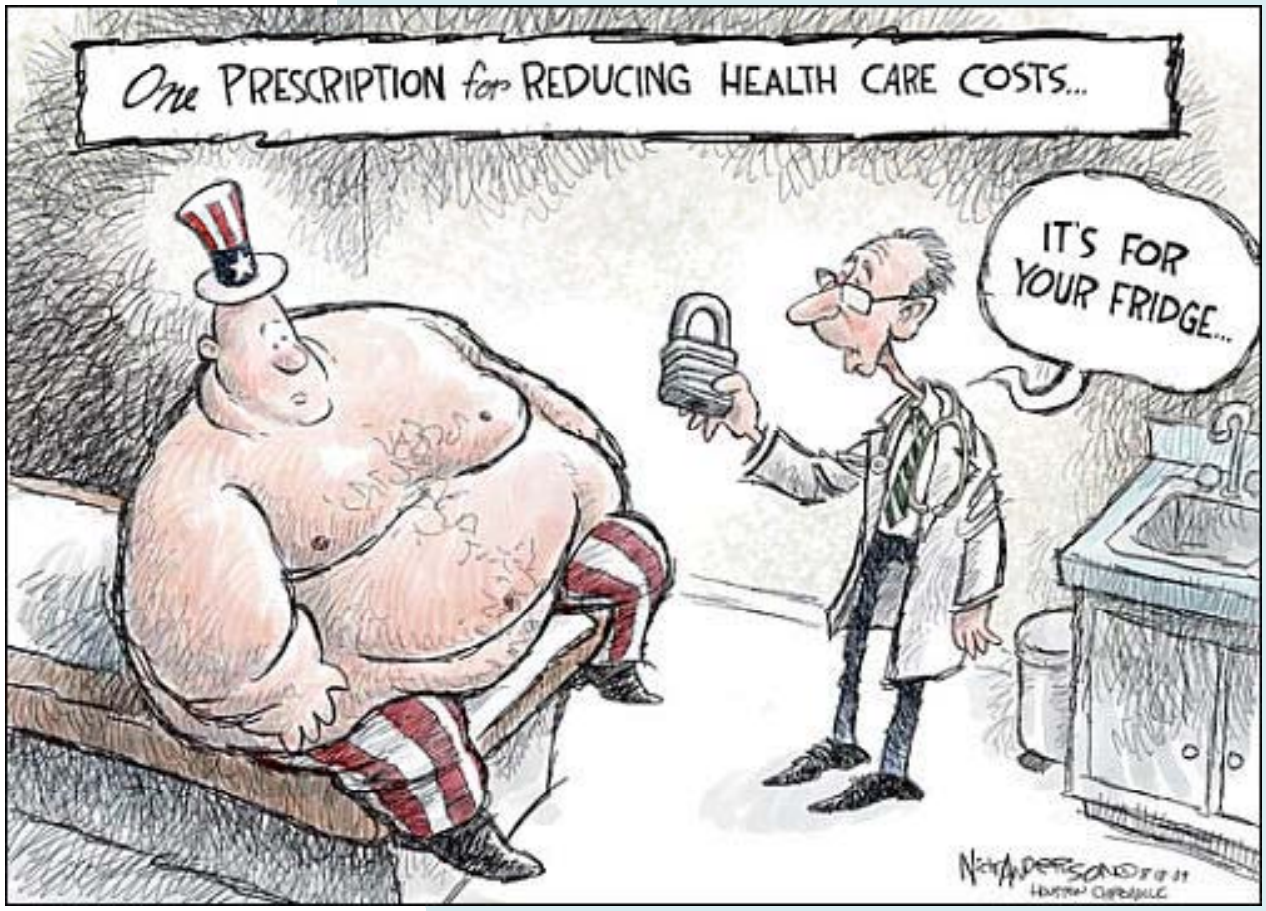
Fig. 5 – Estimated availability of trastuzamab (herceptin®) in Dutch regions (Figure reproduced from[2]).



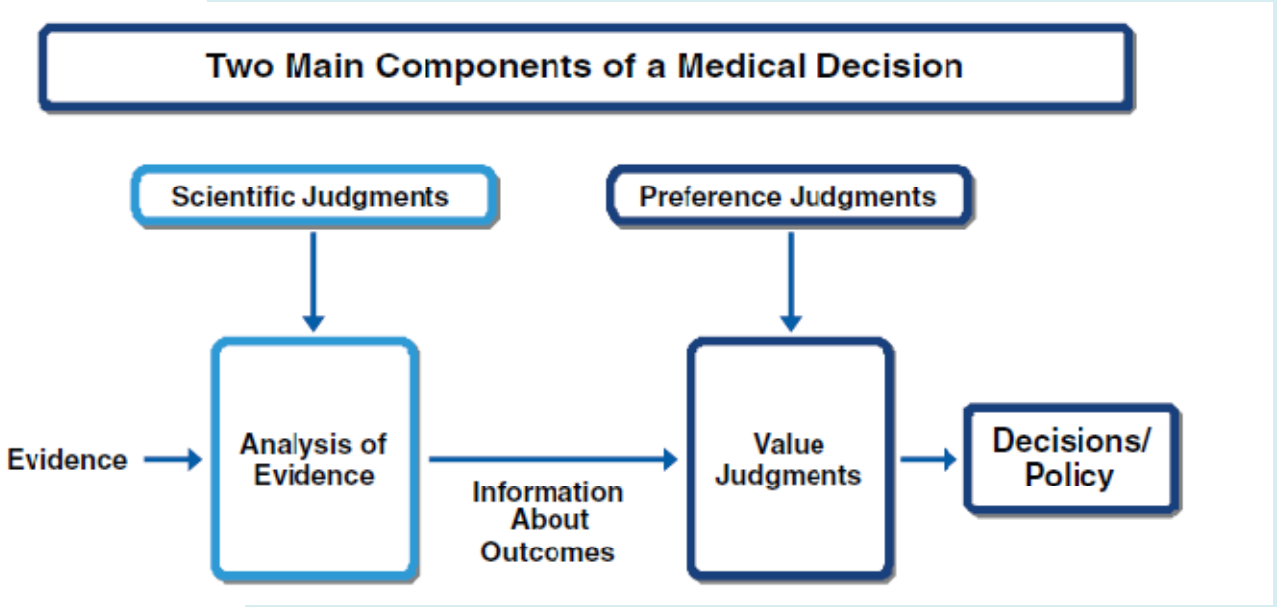
Deaths per 100,000 of malignancies



Value for all this money.. Decision making?



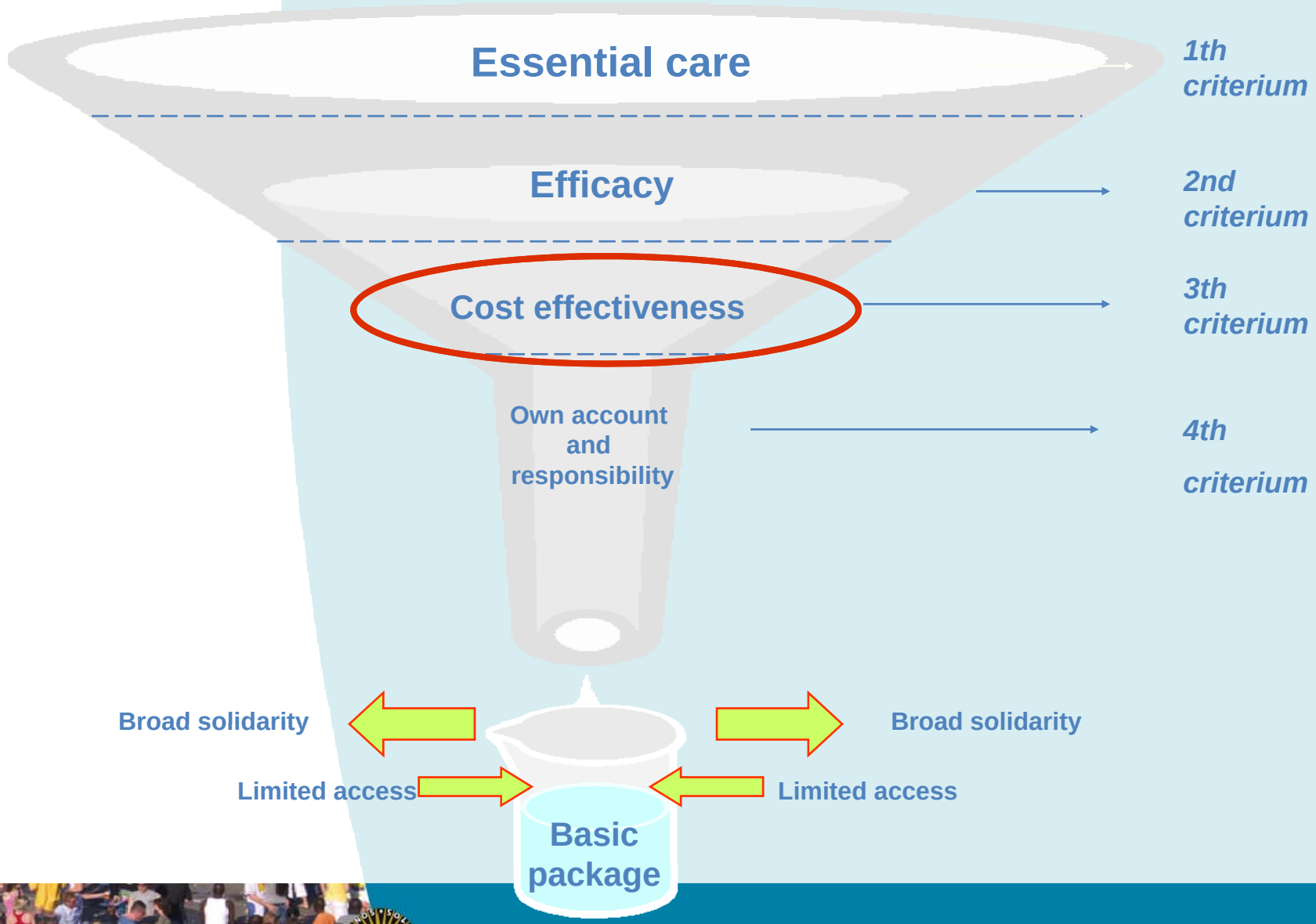
Components of a Medical Decision



Assessment component

Appraisal component

The funnel of Dunning



Decisons on pharmaceutical innovations

- **Efficacy**
- **Safety**
- **Quality**

Regulatory agencies

➡ **market authorisation**

- **Therapeutic value**
- **Efficiency**
- **P.E.**

Reimbursement agencies

➡ **advice to government / payers** ➡ **access, reimbursement (insurance) package**

Therapeutic value

"The sum of the values of all relevant properties of a given drug, together determining the relative position of this drug within therapy as compared to other available treatment options."

Assessing therapeutic value

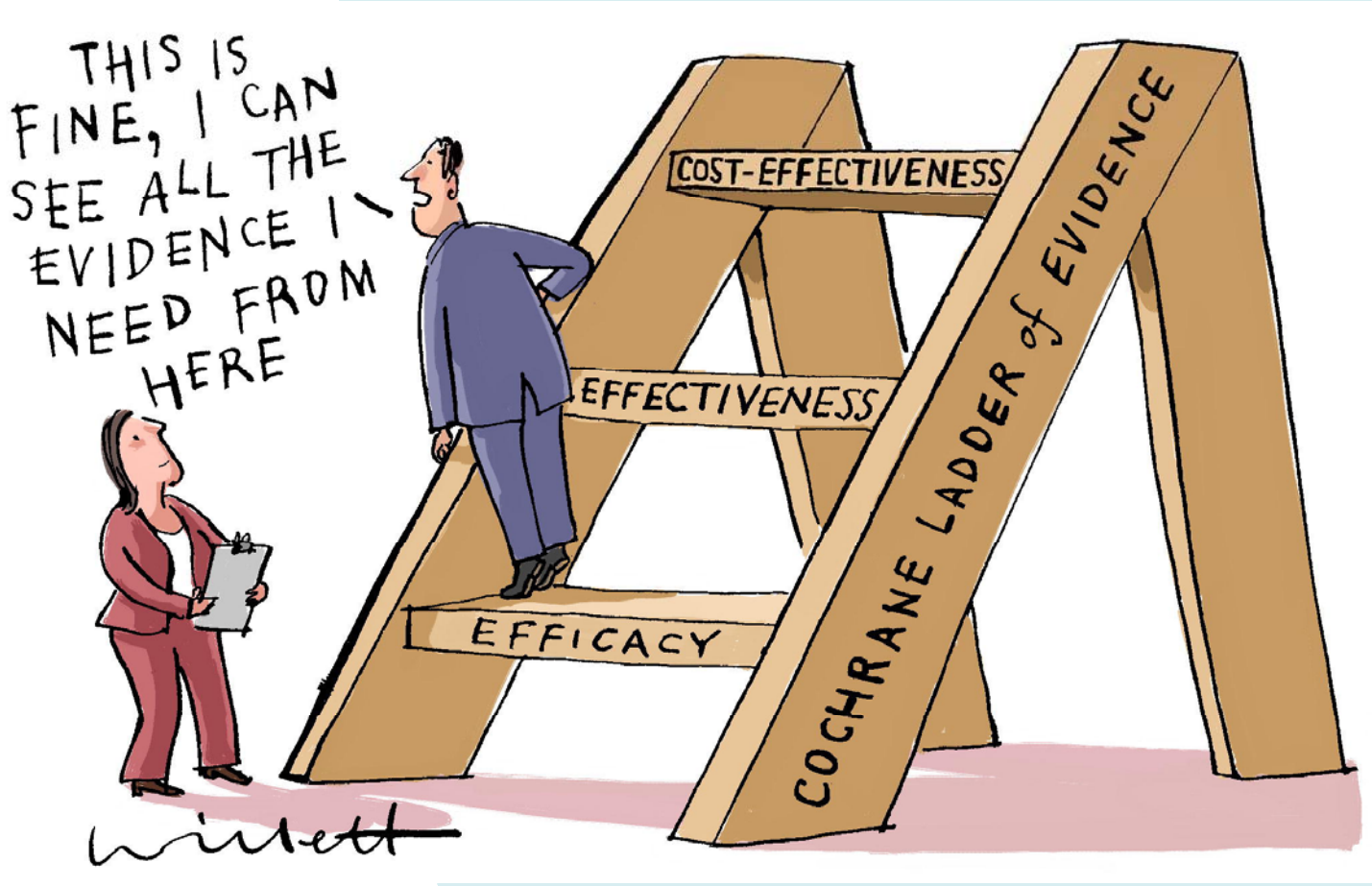
Compare to:

- Standard treatment

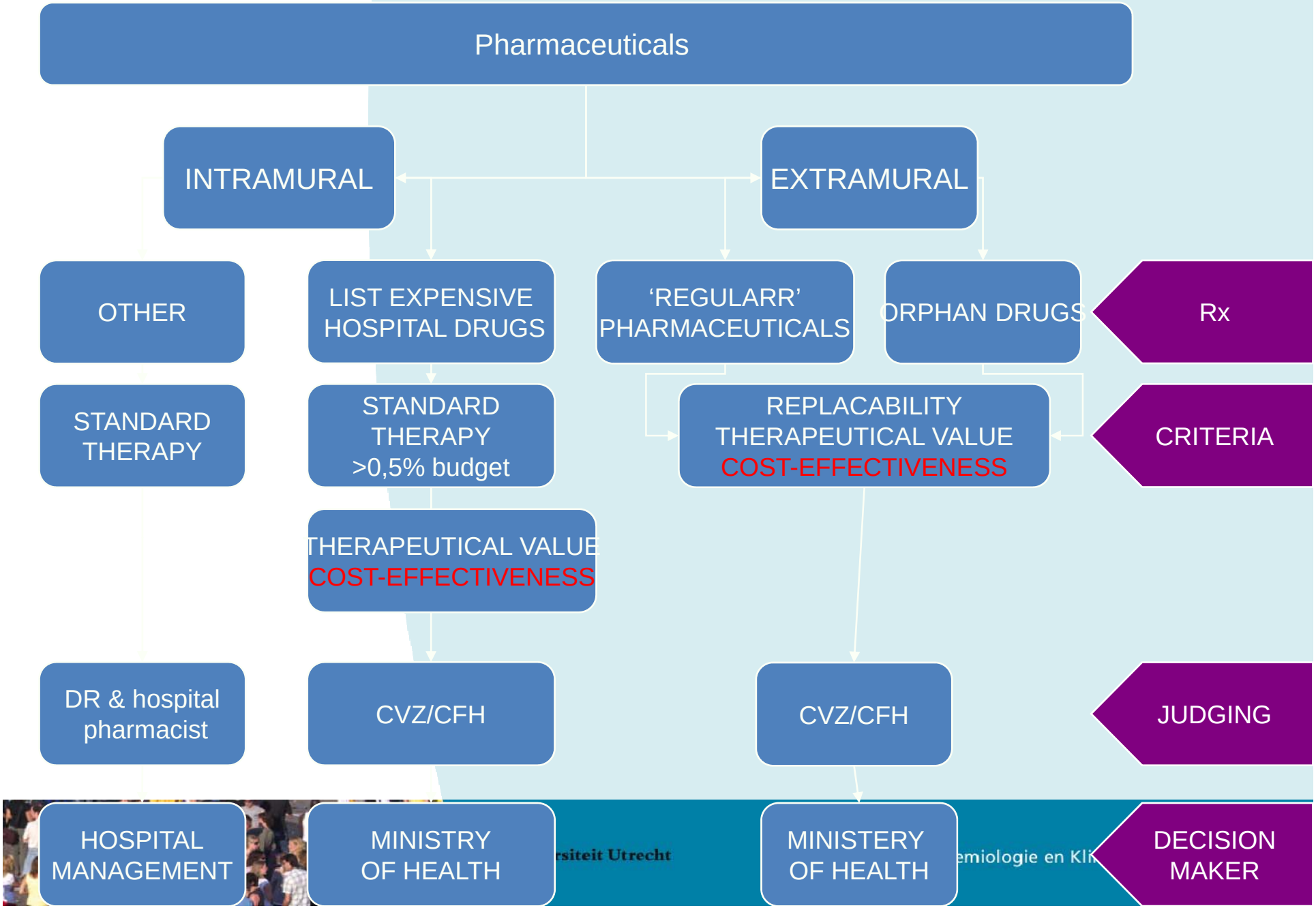
Relevant specifications:

- Efficacy/effectiveness
- Side effects
- Applicability
- Quality of life
- Ease of use

Strong evidence package needed



Reimbursement in The Netherlands



Expensive drugs → conditional reimbursement

- More than 0,5% total annual national hospital pharmacy budget (>2,5 mln.) prognosis
- Therapeutical value shown/standard therapy
- Preliminary reimbursement for 3-4 years
- In this time: collect data on therapeutical value, patient subgroups & cost-effectiveness
- At T=0 the required data are determined in meeting of all involved parties (CVZ, applicants)
- NB: pharmaceutical industry cannot apply: applicants are usually university hospitals or physican associations.

PRELIMINARY MEETING CVZ+APPLICANTS

SUBMISSION OF DOSSIER

AGREEMENT ON DATA COLLECTION PLAN (T=0)

EMEA MA

DATA COLLECTION T=0 –T=4

REEVALUATION OF: BUDGET IMPACT COST-EFFECTIVENESS THERAPEUTICAL VALUE (T=4)

DECISION ON DEFINITIVE REIMBURSEMENT ?

Dossier T=0

- Budget impact prognosis (more than 2.5 million)
- Preliminary cost-effectiveness analysis
- Description of therapeutical value
  - Efficacy
  - Effectiveness
  - Safety
  - Ease of use
- Plan on data collection

Dossier T=4

- Actual budget impact (> 2.5 million??)
- Actual cost-effectiveness? More cost-effective in certain subgroups?
- Therapeutical value maintained in daily practice?

Cost-effectiveness??

Economic evaluations

- Cost minimization → Which one is the cheapest? (€)
- Cost-effectiveness → What do I invest to gain outcomes? (€/effect)
- Cost-utility → What do I invest to gain 1 QALY? (€/QALY)

Challenge 1: Calculating the QALY

- Survival
- Quality of life

} QALY's

QALY

- A Quality Adjusted Life Year (QALY) is a combination of the value (between 0 and 1) of a certain health state and the amount of time (LY) spent in that health state.

  0 = Death

  1 = Perfect health

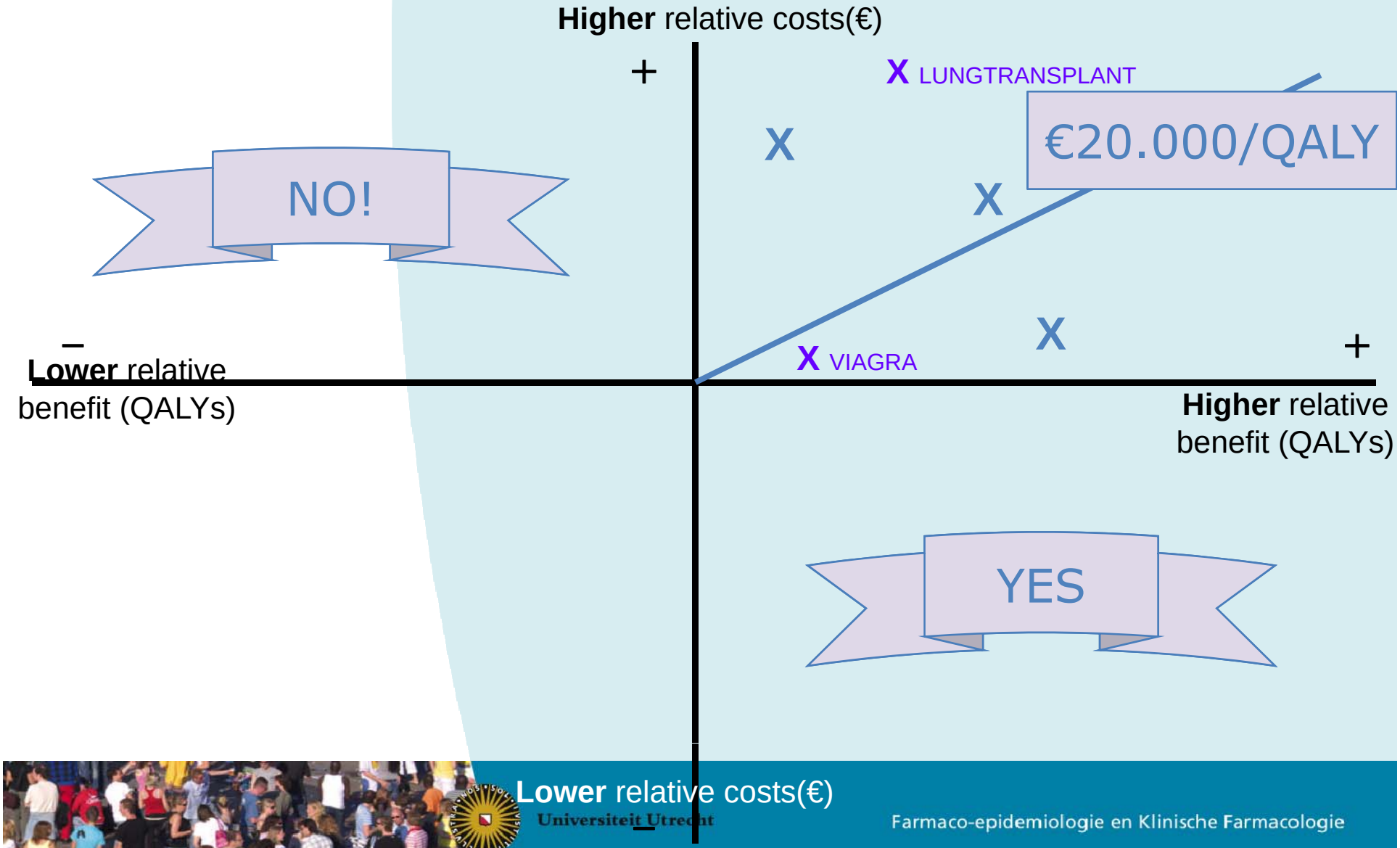
Utility: International perspective

Imagine a patient who :

- Is confined to bed
- Has some problems washing or dressing himself
- Has some problems with any usual activities
- Has no pain or discomfort
- Is not anxious or depressed

- **Utility value of this patient according to the general population in:**
- Sweden: 0,36
- Spain: -0,05
- Uk: 0,15
- Malaysia: 0,47

Challenge 2: A QALY is a QALY is a QALY

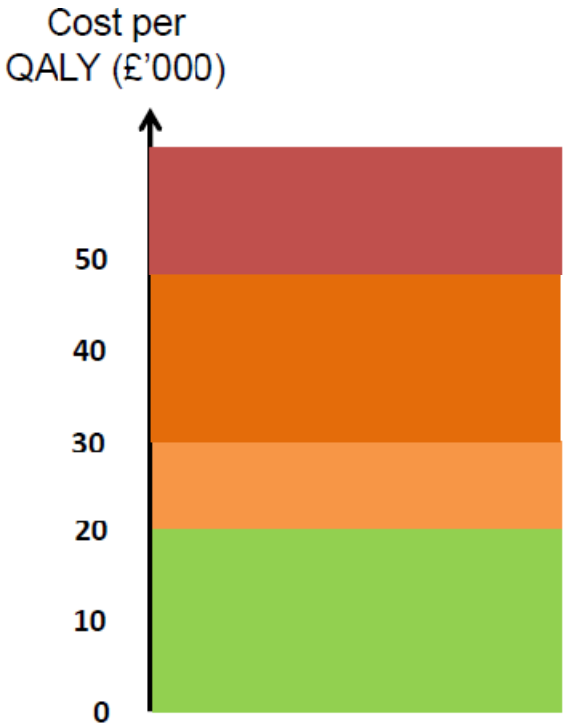


QALY league table

Intervention	$ / QALY
GM-CSF in elderly with leukemia	235.958
EPO in dialysis patients	139.623
Lung transplantation	100.957
End stage renal disease management	53.513
Heart transplantation	46.775
Didronel in osteoporosis	32.047
PTA with Stent	17.889
Breast cancer screening	5.147
Viagra	5.097
Treatment of congenital anorectal malformations	2.778

Challenge 3: Thresholds..
NICE & Cost-effectiveness:

Cost effectiveness



End of Life medicines - Supplementary Advice

Need to identify an increasingly strong case with regard to same factor

Make explicit reference to:

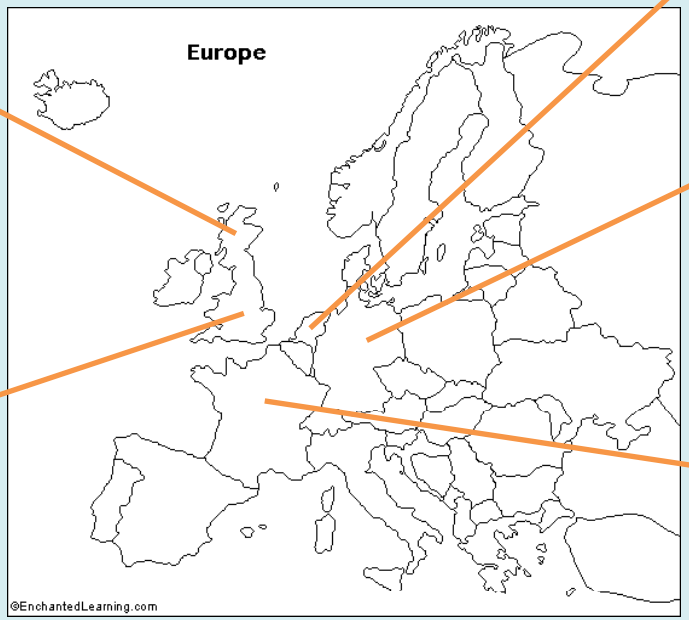
- Certainty
- HRQoL adequately captured?
- Innovative nature
- Non-health objectives of the NHS

Pharmacoeconomics and orphan drugs

Specific regulations for market access

SMC applies modifiers to ICER thresholds for orphan drugs that:
•Substantially improve life-expectancy or QoL
•Can be targeted to a subgroup
•If other therapeutic options are absent
•That bridge to another definitive therapy
•Are licensed alternatives of unlicensed, established, treatments

NICE "end of life" guidance allows higher ICER threshold for orphan drugs that extend life expectancy of rare conditions



NL: No mandatory PE for orphan drugs

DE: Medical additional benefit is considered to be shown by EMA authorization (for ODs with sales<50 M Euro), however, the extent of the additional benefit and therapeutic significance must be quantified.

FR: ATU system allows for early reimbursement before EMA authorization if njo alternative treatments exist.

Not always driven by rarity, but more often by severity or absence of alternatives

Reality: Case study from NL

- Myozyme for Pompe disease
- Intramural (IV) orphan drug registered for:
- ‘long-term enzyme replacement therapy (ERT) in patients with a confirmed diagnosis of Pompe disease (acid α-glucosidase deficiency).Myozyme is indicated in adults and paediatric patients of all ages.’

Pompe's disease

- **Glycogen storage disease type II** (also called **Pompe disease** or **acid maltase deficiency**) is an autosomal recessive metabolic disorder which damages muscle and nerve cells throughout the body.

- The **infantile form** usually comes to medical attention within the first few months of life. Median age at death in untreated cases is 8.7 months and is usually due to cardiorespiratory failure.

- The **late onset form** has a slower progression. Prognosis depends on the age of onset on symptoms with a better prognosis being associated with later onset disease.

In NL

- 100 patients in total suffer from Pompe disease
- All are treated in the same university hospital (EMC, Rotterdam)
- No other pharmaceutical treatments available
- In 2006 reimbursement through the list expensive hospital drugs was applied for by EMC

T=0 (2007)

- Therapeutical value: positive, since no other therapy is available
- Prognosis of total annual costs: € 30.567.000,-: (Assuming 90% of patients will be treated yearly with myozyme)
- Cost-effectiveness: no indication available due to small number of patients

Study:

- Research question:
  - What is the cost-effectiveness of Myozyme compared to supportive care?
  - How and in who is Myozyme used in daily practice?

- Data collection
  - Retrospectively and prospectively data on all patients with Pompe disease in NL are collected.

T=4 (2011)

- Therapeutical value only for patients with classical form (n=13)
- Real annual costs: € 41 million
- Cost-effectiveness:
  - Infant form: €300 000 / QALY (improved survival and QoL)
  - Late onset form: €15 million- €33 million/QALY (slightly improved survival and no improvement QoL)

Conclusion from case study:

- CVZ Advice:

- Stop reimbursement for late onset form of Pompe disease (n=±80) effective immediately
- Continue reimbursement for infant form of Pompe disease (n=±13)

And then… media:

'Hoeveel mag 28 meter lopen van een Pompe-patiënt kosten?'

OPINIE - Hanneke Kouwenberg en John Bijl – 01/08/12, 09:00

'Succes Pompe-middel ondersc

Myozyme, het medicijn tegen de ziekte van Pompe
ANP

Toegevoegd: ma

De belangenv
patiënten zegt
pati ten baat
genee
dan het
zorgverz

Het Col
o

belangenvereniging.

Advies: stop met dure medicijnen

VZ vindt de behandelingen voor Pompe en Fabry te

Toegevoegd: zondag 29 jul 2012, 1
Update: zondag 29 jul 2012, 17:31

Door Rinke van den Brink en
van der Parre

Het CVZ, het College voor Zorgverzekeringen, wil stoppe
het vergoeden van dure medi
voor enkele zeldzame ziekten
staat in twee conceptadviezen
de minister van Volksgezondh
in handen zijn van de NOS

Media responds shocked:
Should costs be the reason
to stop reimbursement of
drugs that only affect a very
small population?

Univers

ne Farmacologie

What now?

- CVZ/CFH still want to stop reimbursement for Pompe disease, non-classical form (n=80)
- However, a slow transition period is advised in which patients currently treated with Myozyme will continue treatment
- In addition new negotiations start with the manufacturer to lower the price

Future

- Conditional reimbursement in future for all drugs
- More focus on which patient group benefits most instead of €/QALY
- New discussions around the role of cost-effectiveness


College voor Zorgverzekeringen

Kosteneffectiviteit in de zorg

Op weg naar een genuanceerd en geaccepteerd gebruik van kosteneffectiviteitsgegevens in de zorg

Datum 30 september 2013

Summary

- Economics has to play a role in decision making in health care due to the rising costs
- Pharmacoeconomics is a new science and still has some important challenges
- Many countries apply health economics in some form in decision making

Thank you for your attention!