Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Center

Praktijkervaring met kosten-effectiviteitsstudies

Raf Mertens

Structuur van de presentatie

1. **Korte voorstelling van het KCE**
2. **Stakeholder involvement: rode draad in jaarverslag 2011**
3. **Health Research System en Instituut (regeerakkoord)**
4. **KCE projecten in 2011**
5. **Overzicht toekomstige projecten**

Wat is het KCE?

- een federale instelling van openbaar nut (parastataal)
- opgericht dec 2002, eerste studies in 2004
- wetenschappelijk objectief en onafhankelijk
- **KCE** = Federaal **K**enniscentrum voor de Gezondheidszorg - **C**entre Fédéral d'**E**xpertise des Soins de Santé

Wat doet het KCE ?

Onafhankelijk advies aan beleidsmakers over alle aspecten van gezondheidszorg en ziekteverzekering

Hoe?

verzamelen en analyseren van **objectieve informatie** uit gegevens gezondheidszorg, wetenschappelijke literatuur en klinische praktijk

hiermee **wetenschappelijke studies** uitvoeren en **expertise** opbouwen


+ 175 rapporten
sinds start activiteiten
KCE in 2003

Het KCE-team

- ✓ artsen
- ✓ economisten
- ✓ data analysten
- ✓ juristen
- ✓ sociologen
- ✓ statistici
- ✓ ….

Totaal:56 (niet-VTE)

directie: 4 staf: 8

secretariaat:7 experten: 37

Een paar voorbeelden

- **Is Neonatale Screening op Mucoviscidose aangewezen in België?**
- **Een eerste stap naar het meten van de performantie van het Belgische gezondheidszorgsysteem**
- **Kosteneffectiviteit van antivirale behandeling voor chronische hepatitis B in België.**
- **Gebruik van point-of care systemen bij patiënten met orale anticoagulatie: een Health Technology Assesment**
- **Terugbetaling van Radioisotopen in België**
- **Organisatie en financiering van genetische diagnostiek in België**

HSR

(organisation, financing)

Health services

Reimbursement

Patient

HTA

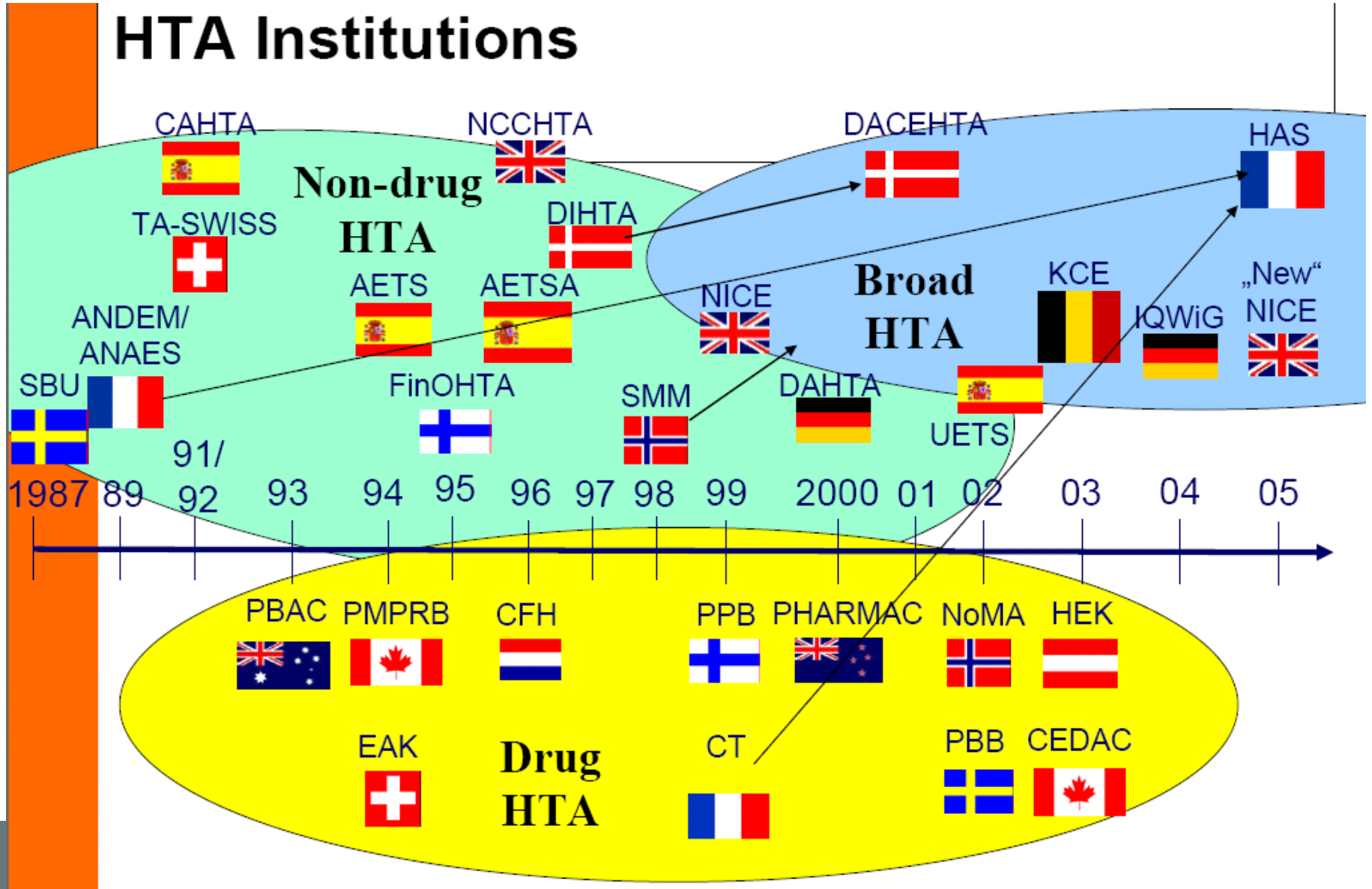
GCP

(guidelines)

Technology

Disease

Europese context



Health Technology Assessment (HTA)

evaluatie van medische technologie of behandeling

- werkt het?
- is het veilig?
- meerwaarde in vgl met vroegere aanpak?
- verhouding kost-gezondheidswinst (kosten-effectiviteit)?
- impact budget gezondheidszorg?

HTA rapporten in 2011

- implantatie van een aortakunstklep (TAVI)
- zuurstoftherapie thuis
- hepatitis B en C: opsporen en behandelen
- pneumokokkenvaccins voor jonge kinderen

What is a true innovation?

Innovative = : Additional clinical efficacy or effectiveness

Relative efficacy

Relative effectiveness

More good than harm

As compared to current care

1 or more alternatives

Under ideal circumstances

Under usual circumstances of healthcare practice

What is a valuable innovation?

Previously unmet needs are filled

For Patients

For society

If it is additionally cost-effective (cost/QALY , Budget impact)

A small test

- **This is a new test for the until very recently unknown EBMS**

The test has a sensitivity of 96%

and a specificity of 85 %.

The prevalence of EBMS is 5%.

If your patient tests positive, what is the probability she effectively has EBMS?

90% 75 % 50 % 25% 10% ??

	Diseased	OK		PPV
Test +	48	142	190	48/190=25%
Test −	2	808	810	
Total	50	950	1000	

Prevalence : 50/1000=5%

Sensitivity: 48/50=96%

Specificity: 808/950=85%

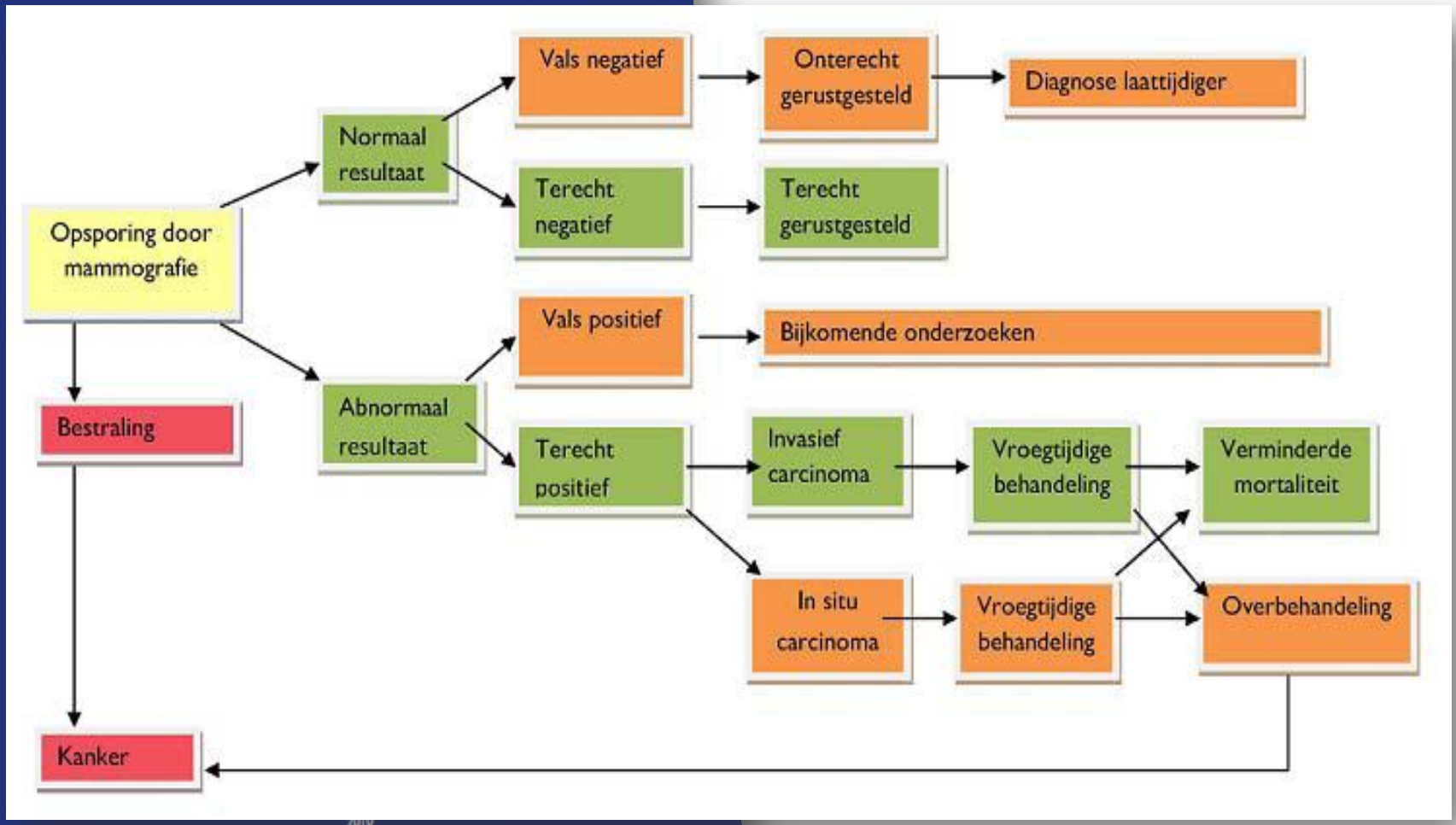
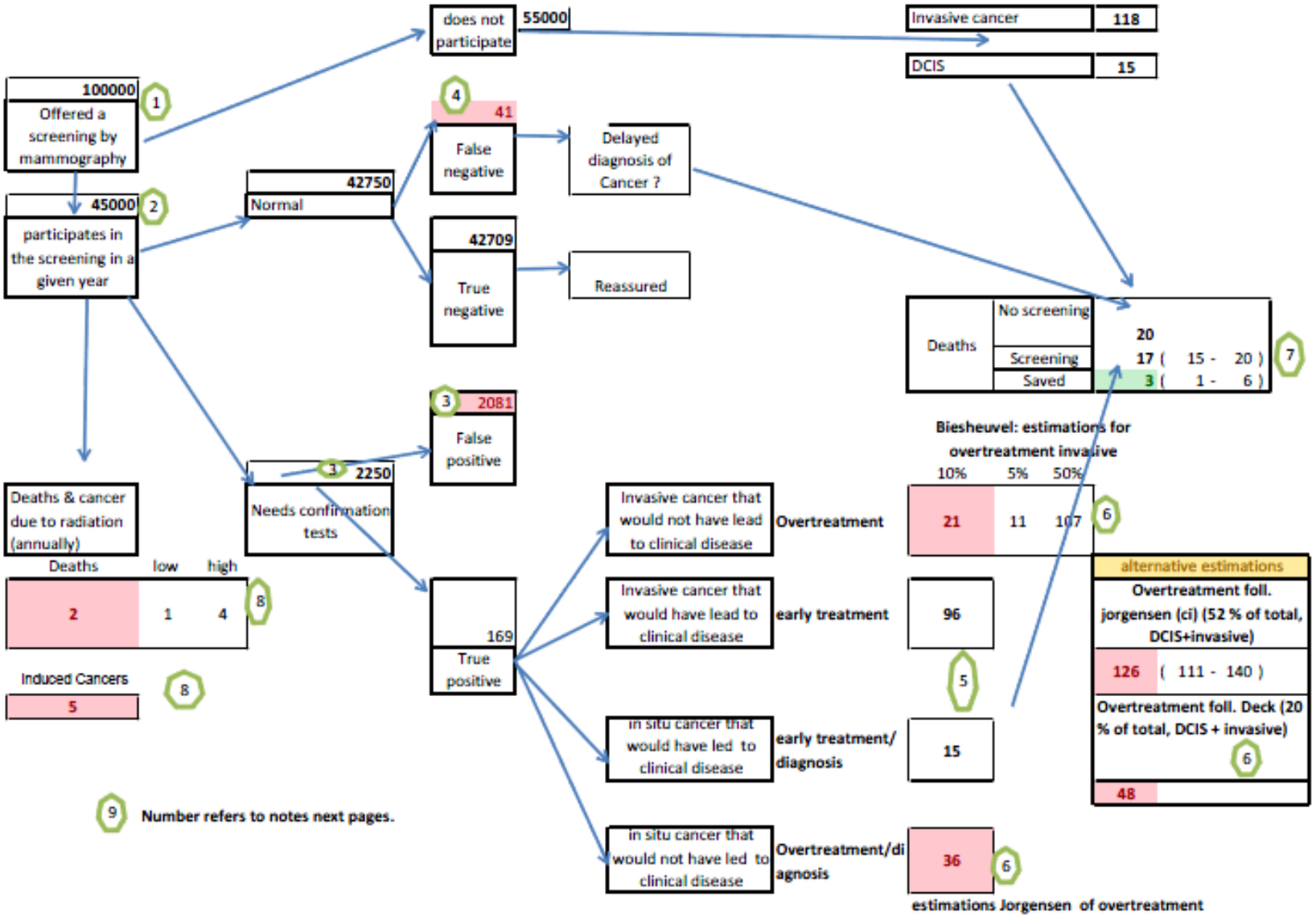

Opsporing door mammografie
Normaal resultaat
Vals negatief
Onterecht gerustgesteld
Diagnose laattijdiger
Terecht negatief
Terecht gerustgesteld
Abnormaal resultaat
Vals positief
Bijkomende onderzoeken
Terecht positief
Invasief carcinoma
Vroegtijdige behandeling
Verminderde mortaliteit
In situ carcinoma
Vroegtijdige behandeling
Overbehandeling
Bestraling
Kanker

Table 23: Simulation of the effects of offering screening for Belgium



JNCI Journal of the National Cancer Institute Advance Access published April 22, 2010

DOI: 10.1093/jnci/djq099

REVIEW

Overdiagnosis in Cancer

H. Gilbert Welch, William C. Black

Manuscript received September 3, 2009; revised March 1, 2010; accepted March 5, 2010.

Correspondence to: H. Gilbert Welch, MD, MPH, Veterans Affairs Outcomes Group (111B), Department of Veterans Affairs Medical Center, White River Junction, VT 05009 (e-mail: h.gilbert.welch@dartmouth.edu).

about 25% of mammographically detected breast cancers,
50% of chest x-ray and/or sputum-detected lung cancers, and
60% of prostate-specific antigen–detected prostate cancers

wouldn't have caused symptoms or death

...tomography–detected lung cancer, neuroblas-
...kidney cancer. To address the problem, patients must be adequately informed of the nature and the magnitude of the trade-off involved with early cancer detection. Equally important, researchers need to work to develop better estimates of the magnitude of overdiagnosis and develop clinical strategies to help minimize it.

J Natl Cancer Inst 2010;102:1–9

A Theory of Medical Decision Making and Health: Fuzzy Trace Theory

Valerie F. Reyna, PhD

The tenets of fuzzy trace theory are summarized with respect to their relevance to health and medical decision making. Illustrations are given for HIV prevention, cardiovascular disease, surgical risk, genetic risk, and cancer prevention and control. A core idea of fuzzy trace theory is that people rely on the gist of information, its bottom-line meaning, as opposed to verbatim details in judgment and decision making. This idea explains why precise information (e.g., about risk) is not necessarily effective in encouraging prevention behaviors or in supporting medical decision making. People can get the facts right, and still not derive the proper meaning, which is key to informed decision making. Getting the gist is not sufficient, however. Retrieval (e.g., of health-related values) and processing interference brought on by thinking about nested or overlapping classes (e.g., in ratio concepts, such as probability) are also important. Theory-based interventions that work (and why they work) are presented, ranging from specific techniques aimed at enhancing representation, retrieval, and processing to a comprehensive intervention that integrates these components. ***Key words:*** *decision aids; risk communication; informed decision making; risk perception; behavior change.* ***(Med Decis Making 2008;28: 850–865)***

Examples of Some of the Effects in Judgment and Decision Research Explained by Fuzzy Trace Theory

Base rate neglect:
posttest probability estimates do not adequately reflect prior probabilities

Conjunction fallacy:
conjunction is ranked as more probable than constituent of conjunction

Disjunction fallacy:
disjunction is ranked as less probable than constituent of disjunction

Framing effect:
risk aversion for gains and risk seeking for losses

Frequency effect:
frequencies rated as more probable than equivalent percentages

Hindsight bias:
memories for earlier predictions are distorted in the direction of later outcomes

Overestimating small risks:
rare events are perceived as more likely than they actually are

Ratio/numerosity bias:
focus on relative magnitude of numerators

Questions to KCE

- **Does A work better than placebo ?**

  → Efficacy

- **Does A work better than B ?**

  → Relative efficacy

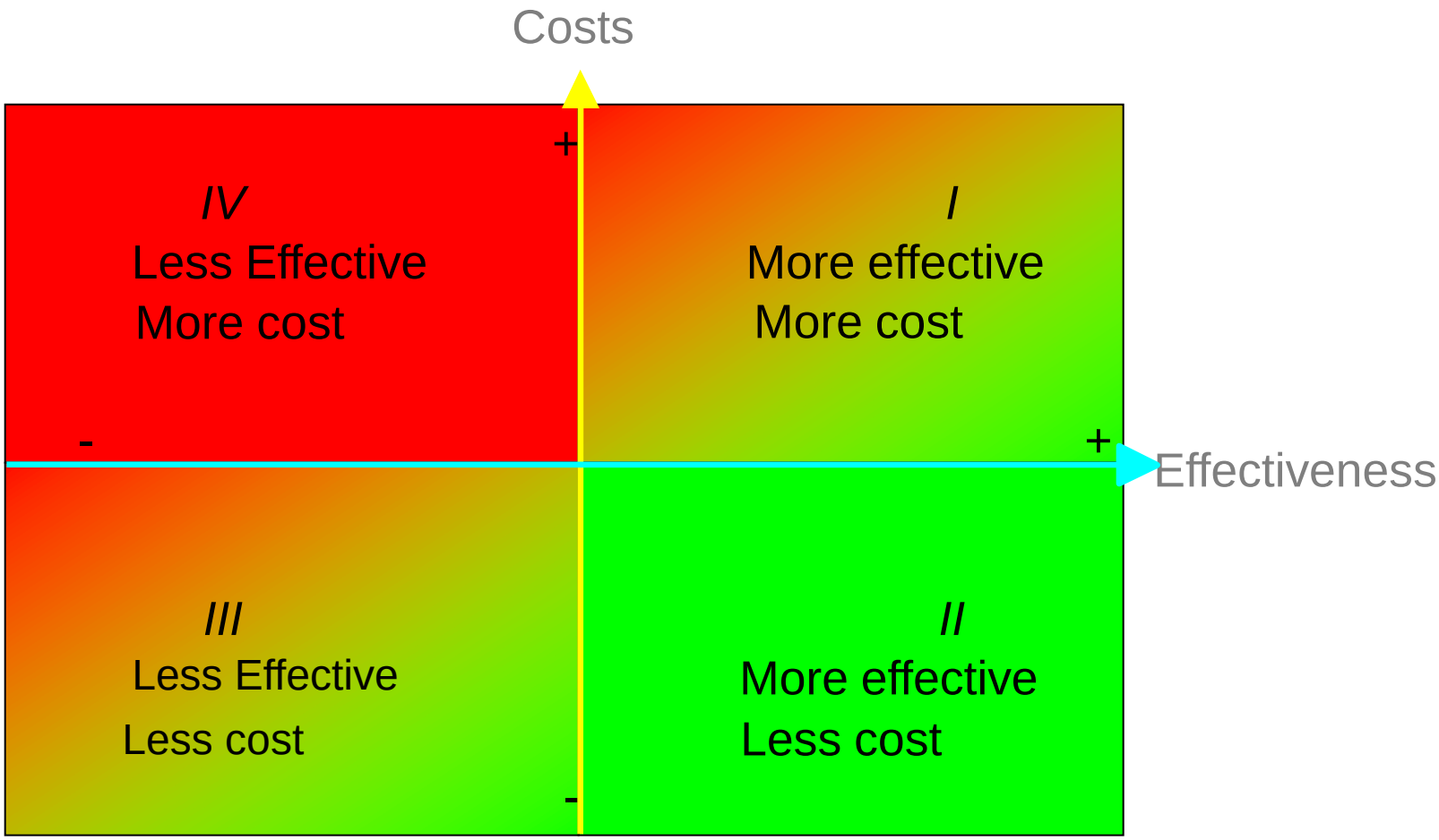
- **… also in real life ?**

  → Relative effictiveness

- **at an acceptable cost ?**

  → Cost-effectiveness

Cost-effectiveness
Incremental cost-effectiveness ratio (ICER)




Richtlijnen voor farmaco-economische evaluaties in België
KCE reports 78A
Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
2008
Drempelwaarden voor kosteneffectiviteit in de gezondheidszorg
KCE reports 100A
2008

12 Pharmacoeconomic Guidelines

1. **Literature review**
2. **Perspective of the evaluation**

3. **Target population**
4. **Comparator**

5. **Analytic technique**
6. **Study design**
7. **Calculation of costs**

8. **Valuation of outcomes**
9. **Time horizon**

10. **Modelling**
11. **Handling uncertainty**
12. **Discount rate**

Population
Intervention
Comparator
Outcome

Methods
Techniques

Literature review

McGauran *et al. Trials* 2010, **11**:37
http://www.trialsjournal.com/content/11/1/37

TRIALS

Open Access

REVIEW

Reporting bias in medical research - a narrative review

Natalie McGauran*, Beate Wieseler, Julia Kreis, Yvonne-Beatrice Schüler, Heike Kölsch and Thomas Kaiser

in the assessment of health care interventions. Several prominent cases
ample, in the reporting of trials of antidepressants, Class I anti-arrhythmic
im of this narrative review is to gain an overview of reporting bias in the
bias and selective outcome reporting. We explore whether these types of
well-known cases noted above, in order to gain an impression of how
e, we screened relevant articles on reporting bias that had previously been
ty and Efficiency in Health Care in the context of its health technology
rk, together with the reference lists of these articles.
ons comprising around 50 different pharmacological, surgical (e.g. vacuum-
ltrasound), and preventive (e.g. cancer vaccines) interventions. Regarding
eporting bias were, for example, identified in the treatment of the following
chizophrenia, anxiety disorder, attention-deficit hyperactivity disorder,
ovascular disease, gastric ulcers, irritable bowel syndrome, urinary
mellitus type 2, hypercholesterolaemia, thyroid disorders, menopausal
varian cancer and melanoma), various types of infections (e.g. HIV, influenza
cases involved the withholding of study data by manufacturers and
t by manufacturers to suppress publication. The ascertained effects of
on of efficacy and the underestimation of safety risks of interventions.
read phenomenon in the medical literature. Mandatory prospective
study data via results databases need to be introduced on a worldwide scale.
v of research data, help fulfil ethical obligations towards patients, and ensure a
in the health care system.

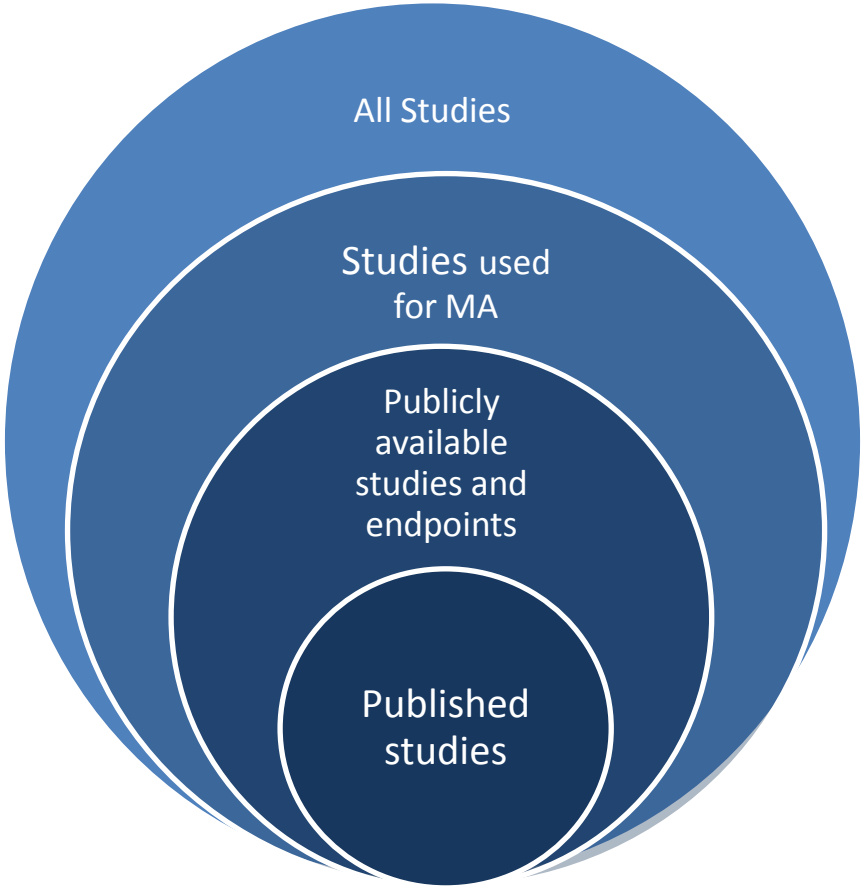
"We identified reporting bias in 40 indications comprising around 50 different pharmacological, surgical, diagnostic, and preventive interventions. Regarding pharmacological interventions, cases of reporting bias were, for example, identified in the treatment of the following conditions: (…)

depression,
bipolar disorder,
schizophrenia,
anxiety disorder,
attention-deficit hyperactivity disorder,
Alzheimer's disease,
pain,
migraine,
cardiovascular disease,
gastric ulcers,
irritable bowel syndrome,
urinary incontinence,
atopic dermatitis,
diabetes mellitus type 2,
hypercholesterolaemia,
thyroid disorders,
menopausal symptoms,
cancer (e.g. ovarian cancer and melanoma),
infections (e.g. HIV, influenza and Hepatitis B),
acute trauma

Many … manuf… manuf… reporti… undere… …bt by …fects of …he

IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

Availability of effectiveness data



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PLoS MEDICINE

Conflicts of Interest at M
Industry-Supported Rand
Factors and Revenue – C

Andreas Lundh[1,2¤*], **Marija Barbateskovic**[1],

1 The Nordic Cochrane Centre, Rigshospitalet, Copenhagen, Denmar
Copenhagen, Denmark

Abstract

Background: Transparency in reporting of confli
journals. Publication of large industry-supporte
sales and thereby be a source of conflicts of in
journal impact factors and revenue.

Methods and Findings: We sampled six major
BMJ, *JAMA*, The *Lancet*, and *New England Jou*
published in 1996–1997 and 2005–2006 using
we investigated citations of industry-supported
contacted journal editors and retrieved tax information on income from
industry support varied between journals, from 7% in *BMJ* to 32% in *NEJM* in 2005–2006.
more frequently cited than trials with other types of support, and omitting them from the impact factor
decreased journal impact factors. The decrease varied considerably between journals, with 1% for *BMJ* to 15% for *NEJM* in
2007. For the two journals disclosing data, income from the sales of reprints contributed to 3% and 41% of the total income
for *BMJ* and The *Lancet* in 2005–2006.

Conclusions: Publication of industry-supported trials was associated with an increase in journal impact factors. Sales of
reprints may provide a substantial income. We suggest that journals disclose financial information in the same way that they
require them from their authors, so that readers can assess the potential effect of different types of papers on journals'
revenue and impact.

Richard Smith

(editor of the BMJ and chief executive of the BMJ Publishing Group from 1991 to 2004):

(…) A third of the trials in the *New England Journal of Medicine* are funded by industry with almost another half having mixed funding that includes a drug company.
Editors know well that they may be able to sell a million dollars worth of reprints of such an article, with a profit margin of perhaps 70%. In other words publishing that one paper will lead to $700 000 on the bottom line.

Defining relative efficacy vs. relative effectiveness

Efficacy (RCT)

Age, sex, ethnicity

Disease stage, severity

Comorbidities

Dosage/administration route

Short-term vs. Long-term

Effectiveness ('Real life' study)

Modelling (extension of time horizon; extrapolation intermediate outcomes; pooling from multiple trials – meta analyses)

pragmatic trials, effectiveness trias)

Effectiveness

Real world trial

Real world no trial

vs. best alternative
nical outcome

Relative effectiveness

Post marketing study with comparator

come

Absolute efficacy

Medical claims data

No comparator

Absolute

Adapted from :Pharmaceutical forum

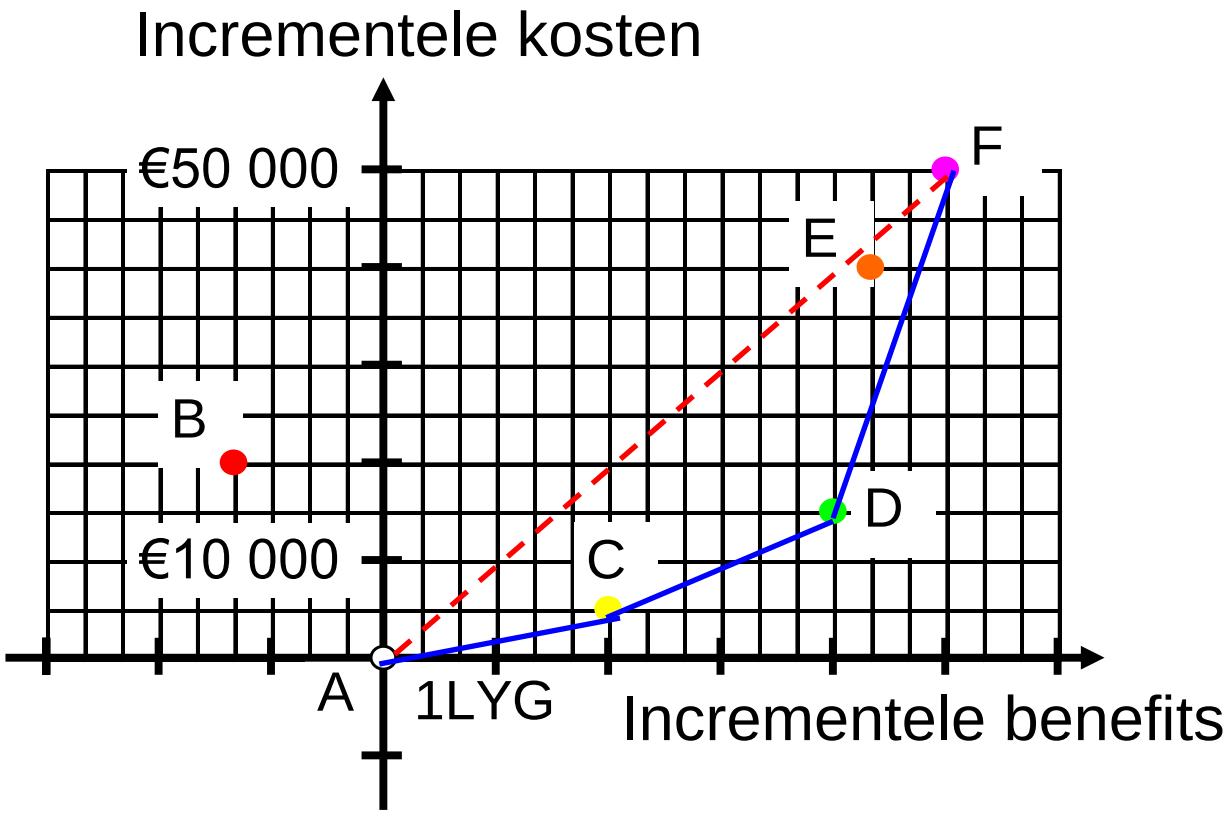
Choice of a comparator

Placebo

Best available alternative

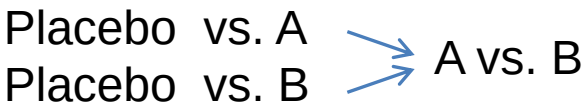
Comparator

- **Cost-efficiency frontier**



2. Choice of a comparator (cont'd)

Modelling, indirect comparison?



- many methodological issues
- not accepted / preferred by many MS
- guidelines needed

Comparison of outcomes

surrogate outcomes

short vs. long term

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KCE

Trastuzumab bij vroegtijdige stadia van borstkanker

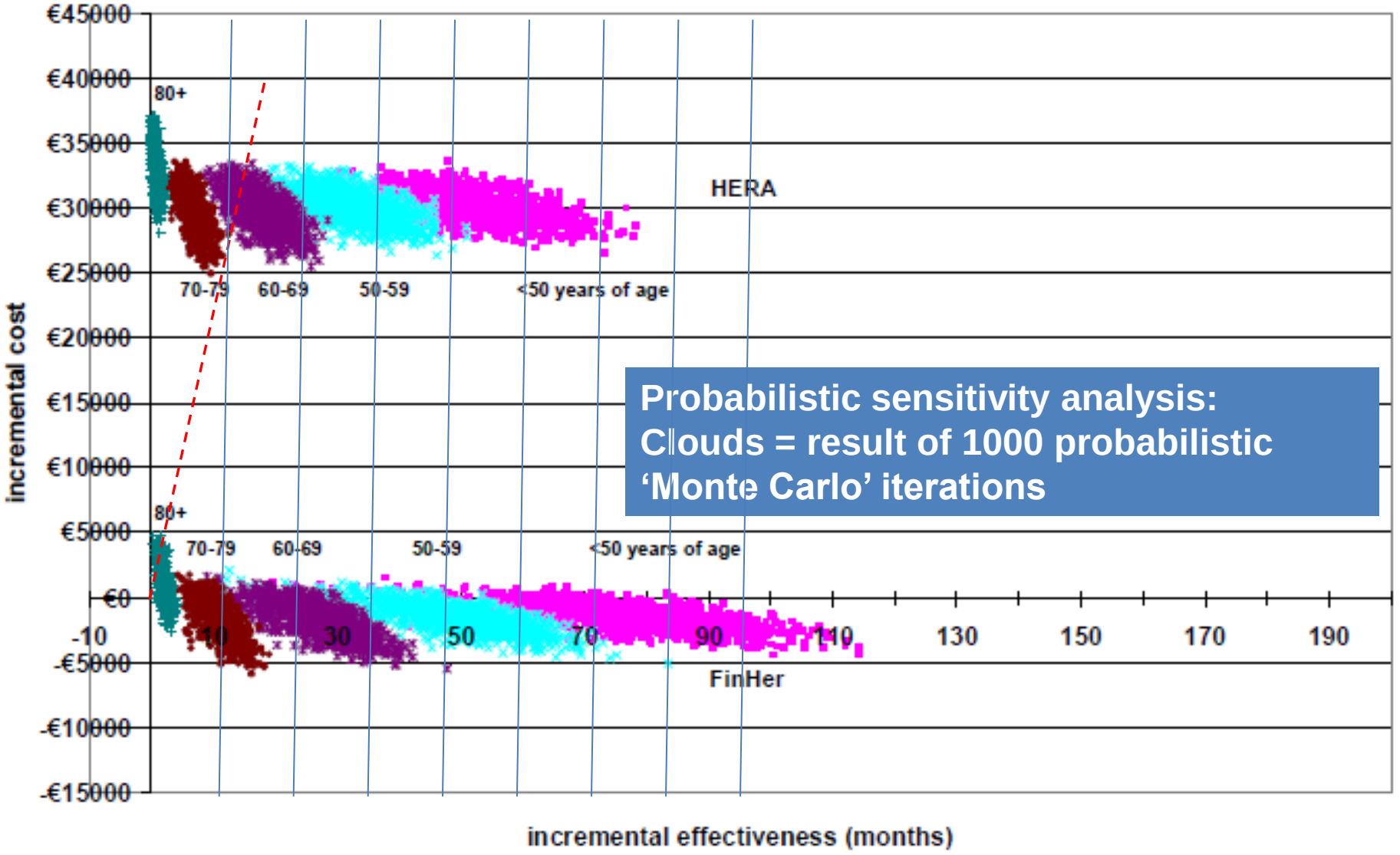
KCE reports vol. 34A

Tabel 1. Ontwerp van de studies met trastuzumab in vroegtijdige vormen van borstcarcinoom

Studiecode, regio, patiënten (pat.) en inclusiecriteria	Anthracycline vooraf (of nadien in FinHer/E2198)	Trastuzumab start in combinatie	Trastuzumab sequentieel na	Trastuzumab regime
B31, US, 2 armen: 1960? pat, N+ of N0 high-risk	doxorubicine +cyclophosphamide (AC)	Paclitaxel		2 mg/kg/wk 1 jaar
N9831, US, 3 armen: 3046 pat, N+ of N0 high-risk	doxorubicine +cyclophosphamide		paclitaxel (arm B)	2 mg/kg/wk 1 jaar
		paclitaxel (arm C)		
HERA, ex-US, 3 armen: 5090 pat, N+ of N0 with T1c	geen anthracycline (6%), doxorubicine zonder taxane (23%), epirubicine zonder taxane (45%), anthracycline + taxanes (26%)		alle chemotherapie	6 mg/kg/3wk 1 jaar 6 mg/kg/3wk 2 jaar
BCIRG006, globaal, 3 armen: 3222 pat, N+ of N0 high-risk	doxorubicine +cyclophosphamide	docetaxel arm		2 mg/kg/wk 1 jaar
	geen anthracycline voor of na	docetaxel + carboplatin		
FinHer, Finland, 2 armen: 232 pat, N+ of N0 >2cm	na: 5FU+epirubicin +cyclophosphamide (FEC)	docetaxel or vinorelbine		2 mg/kg/wk 9 weken
E2198, US, 2 armen: 200 pat, N+, stadium II of IIIa	na: doxorubicin +cyclophospham			2 mg/kg/wk 10 weken
			deels ook na chemotherapie	2 mg/kg/wk 10 w voor + 1y na AC

This regimen was not tested in a phase III trial, nor submitted for market approval!

Incrementele kosten-effectiviteit voor de HERA en FinHer studie, per leeftijdscategorie; Stadium II tumoren



Probabilistic sensitivity analysis: Clouds = result of 1000 probabilistic 'Monte Carlo' iterations

Cost-effectiveness versus Cost-utility

- **Cost-effectiveness analysis**
  - **Major outcome = life years gained**
  - **No other patient-relevant outcomes expressed in different units**
- **Cost-utility analysis**
  - **Major outcome = improving Health-related quality of life**
  - **Multiple patient-relevant outcomes expressed in different units**
  - **Results also expressed i.t.o. Cost/LYG or /QALY**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Dispensing and Administration of Medication in Hospitals:
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Health Technology Assessment & Health Services Research, Denmark, has joined INAHTA network
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Monday September 20, 2010
EUnetHTA Joint Action – new phase in EUnetHTA development
Focusing on scientific cooperation in HTA in Europe, thirty four government appointed organisations from the EU Member States, Accession Countries and EEA work together to help developing reliable, timely, transparent and transferable information to contribute to HTAs in European countries.
The EUnetHTA Joint Action builds on the achievements of
previous European initiatives including
and the Pharmaceu
The EUnetHTA JA (2010-2012) has received funding from the European Union, in the framework of the Health Programme.
Go directly to
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Samenwerking op Europees niveau

Richtlijn *'transborder health care'*
voorziet in de oprichting van een
Europees netwerk van HTA agentschappen

Op de hoogte blijven van KCE-rapporten, vacatures, contracten,…www.kce.fgov.be

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Bedankt voor uw interesse!

Vragen ?