Evidence-based medicine versus patient-centered care
Chronicle of an announced clash?’

Raf Mertens
What is the KCE?

- **Federal** (para-stat.B)
- **Est’d 2002**

Scientific, objective and independent advisory body for policy makers and healthcare providers on all aspects of healthcare and health insurance
The KCE-team

- physicians
- economists
- data analysts
- lawyers
- sociologists
- statisticians
- ...

**Total**: 60 (non-FTE)

- management: 4
- staff: 8
- administration: 7
- experts: 40
Values of the KCE

- Scientific excellence and quality
- Independence and objectivity
- Deontology (e.g. conflicts of interest)
- Dialogue and consultation
- Transparency and good management
- Health system performance, accessibility and safety
- Patient- and client-oriented
• External experts with financial or professional ties to institutions or industry may have conflicts of interest -> request to declare potential conflicts of interest

• Internal expert: clause in the employment contract
250 reports since first publications in 2004
A paradigm shift:

From Eminence-Based Medicine to Evidence-Based Medicine

- Personal Clinical experience
- Pathophysiology and common sense
- Authority and expertise
- “Schools”

- Empirical evidence
- Quality of study design
- Absence of bias and reproducibility
- Internationally shared methods
Competences and Research Methods

- Medicine
- Nursing
- Epidemiology
- Public health
- Health economics
- Sociology
- Statistics
- Law
- Literature searches
- Data analysis
- Modelling
- Surveys
- Qualitative research
- International comparisons
**Systematic review**

**Formulate question**
- Select outcomes
- Rate importance

**Outcomes across studies**

Create evidence profile with GRADEpro

**Rate quality of evidence for each outcome**

Randomization increases initial quality

1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

Grade down
Grade up

1. Large effect
2. Dose response
3. Opposing bias & Confounders

**Summary of findings & estimate of effect for each outcome**

**Grade overall quality of evidence across outcomes based on lowest quality of critical outcomes**

**Recommendation or health care action**

**Grade recommendations**
- For or against (direction) ↓↑
- Strong or conditional/weak (strength)

By considering balance of:
- Quality of evidence
- Balance benefits/harms
- Values and preferences

Revise if necessary by considering:
- Resource use (cost)

**Formulate Recommendations** (↓↑ | ⊕...)
- “The panel recommends that ....should...” (↑↑ | ⊕...)
- “The panel suggests that ....should...” (↑? | ⊕...)
- “The panel suggests to not ....” (↓? | ⊕...)
- “The panel recommends to not...” (↓↓ | ⊕...)

**Guideline**

Source: Pr. Holger Schünemann
Natural history of an innovation

- Experimental, research
- Innovative, pioneers
- Routine use
- Case reports, Observational studies
- Cohort Studies, RCTs
- Real world trials
- Efficacy, safety
- Relative efficacy
- Relative effectiveness
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)

Real life users

RCT’s
Natural history of an innovation

Clinical guidelines

KCE

Relative effectiveness

Cost-effectiveness, ICER, budget impact

HTA, reimbursement advice

YES!

NO!
Cost-effectiveness
Incremental cost-effectiveness ratio (ICER)

Δ Costs

Less effective
More expensive

Less effective
Less expensive

More effective
Less expensive

More effective
More expensive

Δ Effectiveness (QALY)

20 000 € / QALY

8000 € / QALY

Cost - effectiveness

Incremental cost-effectiveness ratio (ICER)
Overall, 96% of the reviews recommended further research.
A small test

- This is the new **McMammaa** technique for breast cancer screening.
  *Multi-angle Computerized Mammography with Meta-Modular Array Adaptation*

The technique has a **sensitivity** of 95% and a **specificity** of 95%.
The **prevalence** of truly cancerous lesions is 0.4%.

If your patient has a positive image, what is the probability she effectively has breast cancer

95%  90%  75%  50%  25%  10%  5%  ??
**McMammaa breast cancer screening + Echography**

<table>
<thead>
<tr>
<th></th>
<th>Cancer</th>
<th>OK</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result +</td>
<td>38</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Result -</td>
<td>2</td>
<td>9462</td>
<td>9464</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>9960</td>
<td>10,000</td>
</tr>
</tbody>
</table>

- **Prevalence**: $\frac{40}{10,000} = 0.4\%$
- **Sensitivity**: $\frac{38}{40} = 95\%$
- **Specificity**: $\frac{9462}{9960} = 95\%$
- **PPV**: $\frac{38}{536} = 7.1\%$
- **PPV**: $\frac{40}{790} = 5.1\%$

Over a period of 10 years, half of the women will have had a positive result.
Diagnostic mammography in women with a breast lump

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<tr>
<td>Result +</td>
<td>3800</td>
<td>600 4400</td>
</tr>
<tr>
<td>Result −</td>
<td>200</td>
<td>5400 5600</td>
</tr>
<tr>
<td>Total</td>
<td>4000</td>
<td>6000 10.000</td>
</tr>
</tbody>
</table>

Prevalence: 4000/10.000 = 40%

Sensitivity: 3800/4000 = 95%

Specificity: 5400/6000 = 90%

PPV: 3800/4400 = 86%
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.
A double debate

- The figures – divergent interpretations of the literature, and a lot of uncertainty
- The values – what weight to attribute to a false positive result, overdiagnosis, overtreatment vs. avoided cancer deaths
Transcatheter aortakunstklep implantatie (TAVI): een Health Technology Assessment actualisatie

KCE report 163A
Trancatheter aortic valve replacement (TAVI)

- Follow-up study after publication of new Partner-Study results

- 18.000 € (i.e. 6x classical valve)
- Intervention 2x more expensive
- No superiority in vast majority of patients, and still safety concerns
- Only recommended in anatomiclly inoperable patients
Publication bias and selective reporting in the PARTNER TAVI trial

Hans Van Brabandt, Mattias Neyt

Objective
- To illustrate selective reporting of data from a trial on transcatheter aortic valve implantation (TAVI).

Methods
- Baseline characteristics and mortality data are available from the PARTNER Pivotal trial (NEJM 2010;363).
- Mortality Data from the PARTNER Continued Access Study were identified from FDA files. Patients’ baseline characteristics were requested from the investigators, the study sponsor (Edwards) and the FDA.

Data from the PARTNER trial

<table>
<thead>
<tr>
<th></th>
<th>Pivotal Trial</th>
<th>Continued Access</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVI Standard</td>
<td>TAVI Standard</td>
</tr>
<tr>
<td>N</td>
<td>N=179</td>
<td>N=41</td>
</tr>
<tr>
<td>1-year mortality n (%)</td>
<td>55 (30.7)</td>
<td>13 (34.3)</td>
</tr>
<tr>
<td></td>
<td>-19%</td>
<td>+13%</td>
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<tr>
<td></td>
<td>89 (49.7)</td>
<td>10 (21.6)</td>
</tr>
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A Continued Access Study enables sponsors to extend patient enrolment in a pivotal trial, while a market application in the US is being investigated. Its design is exactly the same as the pivotal trial.

Results
The investigators, the sponsor, and the FDA all refused to provide additional data to explain the unexpected findings. They considered them resulting from random variation.
Discussion

- Apart from bad luck, the opposing findings (Pivotal vs. Cont’d Access) may result from protocol violations, different approaches to “standard therapy”, ...
- We encouraged both the investigators and the NEJM to publish these troublesome data, to no avail.
- A 2-year follow-up paper of the PARTNER trial in NEJM (2012;366) still ignores those data.
- In our view, this behaviour is both ethically and scientifically unacceptable.
Figure 2. Cost Effectiveness of TAVI

Problem 1: Which do you choose?  
Get 900€ for sure  OR  90% chance to get 1000€

Problem 2 : Which do you choose?  
Lose 900€ for sure  OR  90% chance to lose 1000€
Source: Kahneman. Thinking, fast and slow
80-plusser moet hartklep zelf betalen in België

24/12/2012 | Guy Tegenbos

De ziekteverzekering wil geen reguliere terugbetaling voor de Tavi-hartklep, hoewel die vaak de hoogbejaarden nog jaren kwiek leven geeft.

Van een reguliere terugbetaling van de Tavi-hartkleppen die via de lies kunnen worden ingebracht, wil de Belgische ziekteverzekering nog altijd niet weten. Die dure hartkleppen (15 à 20.000 euro per stuk, de prijs van een VW Golf) zijn aangewezen bij patiënten bij wie een openhartoperatie te mijden is, bijvoorbeeld als de borstholte verzakt is door vorige ingrepen of door bestralingen.

15.000 tot 20.000 euro voor 3 tot 5 kwaliteitsvolle jaren voor 80'ers, is dat te veel?
Biologische hartklip wordt via de slagader met een Katheter tot in het hart geschoven en dan opengeplooid. Het Universitair Ziekenhuis Antwerpen (UA) was in 2008 het eerste in België om dat toe te passen. **23 ziekenhuizen in België willen Tavi's inplanten, een wereldrecord**, maar voor het aantal ingrepen in verhouding tot de bevolking, hoort België bij de absolute achterblijvers. Er is sprake van een 200-tal tot nu, allemaal betaald door de patiënten en de ziekenhuizen. België is het enige land waar de ziekteverzekering niet structureel terugbetaalt.

Prof. Chris Vrints (UZA): ‘Wij laten de patiënt zelf 5.000 euro betalen; de rest regelen wij via het innovatiefonds van ons ziekenhuis. Voor het tiental Nederlanders dat we hier jaarlijks opereren – dit ziekenhuis is het dichtstbij voor veel Zeelanders – betaalt de zorgverzekering alles.'

Voor hun aarzeling verwijzen alle Beslissende Belgen naar het Kenniscentrum Gezondheidszorg KCE, dat blijft zeggen dat de Tavi-techiek maar nuttig is voor 25 à 30 patiënten per jaar. Het raadt voor ouderenopenhartoperaties aan, zelfs als ze riskant zijn.
SYNTHÈSE
FAUT-IL UN DÉPISTAGE CARDIAQUE POUR LES JEUNES SPORTIFS ?
Personnes dépistées

1 000 000

... Parmi lesquelles 3000 personnes ont un problème cardiaque mais n’en sont pas conscientes

Questionnaire
Examen clinique
ECG au repos

€60 millions
Personnes dont les résultats sont anormaux et pour lesquelles des examens complémentaires sont nécessaires

...parmi lesquelles 3000 personnes ont un problème cardiaque mais n’en sont pas conscientes

1 000 000

2250 détectés

50 000 - 300 000

750 non détectés

Stress - désagrément

Cardiologue
ECG au repos et Echographie

€60 millions

+ €6-35 millions

+ coûts d’examens complémentaires
Jeunes qui deviennent “malades cardiaques”

1 000 000

... parmi lesquelles 3000 personnes ont un problème cardiaque mais n’en sont pas conscientes

50 000 – 300 000

Perception de maladie cardiaque

5000

Disqualification

Problèmes liés aux interventions

€60 millions

+ €6-35 millions

+ coûts d’examen complémentaires

+ coûts du suivi et du traitement
Effet net

Personnes dépistées
1 000 000

> 66 – 95 millions d’euros

Nombre de décès
-1? - +1?
Effet net

Personnes dépistées
1 000 000

> 66 – 95 millions d’euros

Nombre de décès
-1? - +1?
A clash of paradigms

Should the practice of medicine be a deontological or utilitarian enterprise?

Gerard Garbutt,1 Peter Davies2

ABSTRACT

There is currently an unrecognised conflict between the utilitarian nature of the overall NHS and the basic deontology of the doctor-patient interaction. This conflict leads to mistrust and misunderstanding between managers and clinicians. This misunderstanding is bad for both doctors and managers, and also leads to waste of time and resources, and poorer services to patients. The utilitarian thinkers (mainly managers and politicians) tend to value finite, short term, evidence based technical interventions, delivered according to specifications and contracts. They appear happy to break care up into smaller pieces, which can then be commissioned from multiple providers. The deontological thinkers (mainly doctors and other clinicians) tend to think about care delivered through a long term continuous relationship, and regard that relationship as therapeutic and salutogenic in itself. To them breaking care up into smaller fragments is a denial of what caring is really about. Very rarely are either or both sides of this debate fully aware of where their powerfully held and often well argued positions start from. In this paper we offer an appraisal of the strengths and weaknesses of both moral viewpoints as applied in1 suggest a way in which neither is pushed too far. We believe this reconciles doctors, managers and

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Problem structuring in health technology assessment: an argumentative approach to increase its usefulness.

Source: Margriet Moret-Hartman (2008)
# A clash of paradigms

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SYNTHÈSE
IMPACT VAN DE RAPPORTEN GEPUBLICEERD DOOR HET KCE TIJDENS DE PERIODE 2009-2011
Globaal resultaat

- Directe impact: 41%
- Indirecte impact: 30%
- Niet gemeten: 14%
- Geen impact: 10%
- In behandeling: 5%
KCE Reports 206Bs
Cancer du poumon à petites cellules et non à petites...
Thank you for your attention!