Atherothrombosis Management: What Can We Afford?
Thomas D. Szucs
University of Zurich

Overview

- What’s the challenge?
- What’s the data?
- Where’s the future?
What’s the challenge?

What is economics?

“The study of how men and society end up CHOOSING to employ SCARCE RESOURCES that could have ALTERNATIVE USES.”

Paul Samuelson, Nobelpreisträger (1980)
Health care technology and economic output

Economic Productivity (GDP)

Health care expenditure

Life expectancy

* Drugs and vaccines

“We cannot be a strong nation unless we are a healthy nation“

President Franklin D. Roosevelt

1 additional life year life expectancy → 4 % increase in GDP

Why economic evaluations?

- **Alternative**: market forces to decide who should get what
- But, is there a **perfect** market in health care?
What’s the data?

- Cardiovascular disease burden
- Cardiovascular care quality
- Cost-effectiveness of anti-atherothrombotic Rx
Disease burden

Costs of myocardial infarction in Europe

1 $ = 1.5 CHF = 1820 LIT = 1.82 DM = 17.2 ATS = 0.62 GBP = 1.06 EUR

Levy E. Pharmacoeconomics 2003; 21: 651-9
**Stroke: a major health burden**

- 1.3 mio ischemic strokes in US and Western Europe annually
- Responsible for 7-15% of deaths
- Primary cause of adult disability
- Second most important cause of dementia
- Third leading cause of death worldwide
- One in six survivors will suffer a second stroke within 5 years

---

**Costs of stroke in Europe**

![Costs of stroke in Europe](chart.png)

Levy E. Pharmacoeconomics 2003; 21: 651-9
**Epidemiology and Costs of Stroke in Switzerland**

- N=19123
- Prevalence: 4.4 %
- Male: 55 %
- Age 66.6 (SD 0.9) years
- Mean age at death 73.8 (SD 1.1) years
- ALOS acute care: 34.9 (SD 3.5) days
- Rehab stay: 116.5 (SD 98) days
- Labour force participation
  - 20% back to work (42% reduced productivity)
  - 51% permanently disabled
  - 24% died

Szucs TD, 2005

---

**Burden of peripheral arterial disease**

- Affects approximately 12%
- North America and Europe: 16% of people above 55 years (30-40 % symptomatic)
- 64% of men and 84% of women with an abnormal ABI are **asymptomatic**
- Rotterdam study: **asymptomatic** PAD: 8% (55-59 yrs) and 57% (>85 yrs)
Atherothrombosis is commonly found in more than one arterial bed*

*Cerebrovascular disease

24.7% 7.4% 29.9%

3.8% 3.3% 11.8%

19.2%

Coronary disease

Peripheral arterial disease

*Data from CAPRIE study (n=19,185)
Quality

Management of CHD in primary care

Errors of omission: CRUSADE
NSTE ACS care in 430 hospital 89,500 Pts

Aspirin Beta Blockers Heparin GP IIb-IIIa
Leading Centers
Lagging Centers

Paradoxical care: therapy for
ACS in the elderly

<table>
<thead>
<tr>
<th></th>
<th>&lt;75 yrs</th>
<th>≥75 yrs</th>
<th>Adj. OR (95%CI)**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>92</td>
<td>88*</td>
<td>0.91 (0.83, 1.00)</td>
</tr>
<tr>
<td>Beta-Blocker</td>
<td>79</td>
<td>75*</td>
<td>0.91 (0.84, 0.99)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>41</td>
<td>32*</td>
<td>0.82 (0.76, 0.88)</td>
</tr>
<tr>
<td>Gp 2b3a</td>
<td>41</td>
<td>22*</td>
<td>0.64 (0.59, 0.69)</td>
</tr>
<tr>
<td>Cath (≤48 hrs)</td>
<td>46</td>
<td>16*</td>
<td>0.51 (0.42-0.59)</td>
</tr>
<tr>
<td>PCI (≤48hrs)</td>
<td>32</td>
<td>14*</td>
<td>0.60 (0.55, 0.66)</td>
</tr>
</tbody>
</table>

* Unadjusted p<0.05 ** Comparison of age ≥75 with <75 yrs. Adjusted for gender, race, comorbidity, cardiac markers, insurance status, hospital features, and clustering effects (elderly treated, similar outcomes).

Peterson, ACC 2004
CRUSADE 4th Quarter
Cost-effectiveness

Cost-effectiveness plane

<table>
<thead>
<tr>
<th>Δ costs</th>
<th>More expensive</th>
<th>Less effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>More expensive</td>
<td>More effective</td>
<td>More effective</td>
</tr>
<tr>
<td>Less expensive</td>
<td>Less effective</td>
<td>Less effective</td>
</tr>
</tbody>
</table>

EVALUATION
All is relative...

Current thresholds for the cost per quality adjusted life year gained

<table>
<thead>
<tr>
<th>Country</th>
<th>Threshold cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>AUS$ 42-76000</td>
</tr>
<tr>
<td>Canada</td>
<td>CAN$ 20-100000</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Euro 20000</td>
</tr>
<tr>
<td>Sweden</td>
<td>SEK 500000</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>£ 30000</td>
</tr>
<tr>
<td>United States</td>
<td>US$ 50-100000</td>
</tr>
</tbody>
</table>
Two types of economic analyses

- **Within trial analysis**
  - Resource utilisation and costs of clinical trial
  - Non trial related resources also included
  - High internal validity, low external validity

- **Beyond trial analysis**
  - Resource utilisation and costs extrapolated
  - Modelling required
  - Low internal validity, high external validity

---

CURE: Incremental costs per patient (over 9 months, within trial analysis)

<table>
<thead>
<tr>
<th>Difference (Clopidogrel – Placebo)</th>
<th>Canada (Can$)</th>
<th>Sweden (SEK)</th>
<th>UK (£)</th>
<th>US (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial costs during hospitalisation including study drug</td>
<td>-334</td>
<td>-1320</td>
<td>-56</td>
<td>-203</td>
</tr>
<tr>
<td>Follow up costs a</td>
<td>494</td>
<td>3465</td>
<td>264</td>
<td>654</td>
</tr>
<tr>
<td>Mean difference in costs per 9 months</td>
<td>161</td>
<td>2145</td>
<td>208</td>
<td>451</td>
</tr>
</tbody>
</table>

* a includes costs of recurrent hospitalisation and study drug over 9 months

Lamy A. Circulation 2002; 106: Suppl.II: 3721
**CURE: Incremental cost per event avoided with clopidogrel plus aspirin versus aspirin (within trial analysis)**

Weintraub W. PharmacoEconomics 2004; 22 (Suppl.4): 29-41

---

**CURE: long term cost-effectiveness analysis**

- **Method**: Markov model with 6 health states
  - At risk
  - First year with stroke
  - Following years with stroke
  - First year with MI
  - Following years with MI
  - Death
- **Cohort**: 64 years, 61% male
- **Results**:
  - Survival clopidogrel: 9.65 years
  - Survival placebo: 9.77 years
  - 0.117 life-years gained

CURE: long term cost-effectiveness analysis: Direct costs only

€160 0.117
Life years gained

€ 1365 per life year gained


CURE: long term cost-effectiveness analysis

<table>
<thead>
<tr>
<th>Country</th>
<th>Net direct costs €</th>
<th>Net indirect costs €</th>
<th>Cost per LYG (direct costs only) €</th>
<th>Cost per LYG (total costs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DK</td>
<td>64</td>
<td>-209</td>
<td>549</td>
<td>Dominant</td>
</tr>
<tr>
<td>SF</td>
<td>510</td>
<td>-214</td>
<td>5048</td>
<td>€ 2935</td>
</tr>
<tr>
<td>S</td>
<td>160</td>
<td>-214</td>
<td>1365</td>
<td>Dominant</td>
</tr>
<tr>
<td>N</td>
<td>137</td>
<td>-219</td>
<td>1171</td>
<td>Dominant</td>
</tr>
<tr>
<td>USA</td>
<td>343 $</td>
<td>-219</td>
<td>$ 4910</td>
<td>Dominant</td>
</tr>
<tr>
<td>A</td>
<td></td>
<td></td>
<td>€ 4146</td>
<td></td>
</tr>
<tr>
<td>NL</td>
<td>-17</td>
<td></td>
<td>Dominant</td>
<td></td>
</tr>
</tbody>
</table>

Weintraub W. Circulation 2003; 108: 1925
Schwarz B. Pharmacoeconomics German Research Articles 2004; 2: 31-41
Van Hout B. Value in Health 2003; 6: 667
PCI-CURE: Incremental cost € per event avoided (within trial analysis)

Reported cost-effectiveness ratios for cardiovascular interventions

Weintraub W. PharmacoEconomics 2004; 22 (Suppl.4): 29-41
Cost-effectiveness of cardiovascular interventions in Switzerland

Where’s the future?
Greatest problem: one size doesn’t fit all!

COST-EFFECTIVENESS VARIATIONS

- C-E ratios vary across sub-groups (or cohorts) based on:
  - clinical presentation
  - sociodemographics
  - nature of treatment

“How cost-effective, in which patients, under what conditions?”
Targeting high risk patients is a cost-effective means for introducing new treatments (tirofiban)

Increase in ACS budget (%)

Events avoided

Cost per event avoided (£)

Cohen DJ. Circulation 2004; 110: 508-14

From drug/device specific towards guideline-based economics...
**Scenario 1: Cost consequences of DES with moderate increase of first PCI and w/o further substitution of CABG**

<table>
<thead>
<tr>
<th>Year</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary revascularisations</td>
<td>16172</td>
<td>16415</td>
<td>16661</td>
<td>16911</td>
<td>17164</td>
</tr>
<tr>
<td>% PCIs of primary revascularisations</td>
<td>0.77</td>
<td>0.77</td>
<td>0.77</td>
<td>0.77</td>
<td>0.77</td>
</tr>
</tbody>
</table>

**Base case analysis - Δ DES-BMS = CHF 745 / per patient**

- Costs revascularisation with BMS: 352.2, 357.4, 362.8, 368.2, 373.8
- Costs revascularisation with DES: 342.8, 348.9, 353.9, 358.5, 363.8

**Worst case scenario - Δ DES-BMS = CHF 673 / per patient**

- Costs revascularisation with BMS*: 305.3, 309.9, 314.5, 319.2, 324.0
- Costs revascularisation with DES: 313.7, 318.4, 323.2, 328.1, 333.0
- Δ DES-BMS (Mio. CHF): 8.4, 8.6, 8.7, 8.8, 8.9

Source: TD et al. Kardiovask Med 2005 (Feb)

---

**Base-case assessment of combination statin/ezetimibe therapy versus statin monotherapy under the ESC and IAS guidelines.**

<table>
<thead>
<tr>
<th>Statin monotherapy under IAS guidelines</th>
<th>Statin/ezetimibe combination therapy under IAS guidelines</th>
<th>Statin monotherapy under ESC guidelines</th>
<th>Statin/ezetimibe combination therapy under ESC guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of treatment with per patient (CHF)</td>
<td>807</td>
<td>882</td>
<td>742</td>
</tr>
<tr>
<td>Incremental cost per patient (CHF) vs no treatment</td>
<td>381</td>
<td>456</td>
<td>320</td>
</tr>
<tr>
<td>Events avoided/10,000 patients treated (9)</td>
<td>35</td>
<td>45</td>
<td>64</td>
</tr>
<tr>
<td>QALY per patient (yrs)</td>
<td>9.694</td>
<td>9.696</td>
<td>9.699</td>
</tr>
<tr>
<td>Incremental cost per patient (CHF) - combo- vs monotherapy</td>
<td>75</td>
<td>222</td>
<td></td>
</tr>
<tr>
<td>QALY’s gained/10,000 patients treated (yrs) - combo vs monotherapy</td>
<td>16</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>ICUR (CHF/QALY gain)</td>
<td>47'304</td>
<td>72'485</td>
<td></td>
</tr>
</tbody>
</table>

Dräger N et al. 2005 (forthcoming)
What did NICE reject?

- No routine extraction of wisdom teeth
- Digital hearing aids: more data necessary
- Laparoscopic surgery of colon cancer
- Autologous cartilage transplantation
- Docetaxol first-line Rx breast cancer
- Interferon beta und Glatirimer acetate for multiple sclerosis

Reasons for rejection:
Missing/insufficient clinical evidence,
not cost-effectiveness
Conclusions

- Atherothrombosis represents a major clinical and economic burden to society
- Health economic studies are an important tool in assisting informed decisions on prioritisation
- Focus will shift from drug/technology-only based evaluations towards guideline-oriented (economic) evaluations
- We can afford innovations, given that effectiveness and cost-effectiveness are proven

Don’t get lost in cost myopia!
TEN BUCKS A PILL FOR VIAGRA?! THAT'S ONLY FORTY DOLLARS A YEAR.