Interest of Health Economic Analyses in the Management of Postmenopausal Osteoporosis

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- **Model structure**

- Health states and transitions
- Transition probabilities
- Cycle length and number of cycles
- Cost ~ effectiveness (Quality Adjusted Life Years QALY)
- Tracker variables

\[
\text{Total cost} = C_0 + C_1 + C_2 + \ldots + C_N
\]

\[
\text{Total effectiveness} = E_0 + E_1 + \ldots + E_N
\]
Transition probabilities

– Fracture incidence (by age)
– Target population
– Prior fractures ~ clinical risk factors
– Mortality rates ~ mortality excess (hip and vertebral)

Cost (healthcare payer perspective)

– Direct cost of fracture

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>From 16.579 to 20.306</td>
</tr>
<tr>
<td>Vertebral</td>
<td>2.429</td>
</tr>
<tr>
<td>Wrist</td>
<td>2.159</td>
</tr>
<tr>
<td>Other</td>
<td>3.573</td>
</tr>
</tbody>
</table>

– Annual long term cost of hip fracture

<table>
<thead>
<tr>
<th>Age range</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-69 years</td>
<td>1.102</td>
</tr>
<tr>
<td>70-79 years</td>
<td>1.272</td>
</tr>
<tr>
<td>80-89 years</td>
<td>2.544</td>
</tr>
<tr>
<td>90-99 years</td>
<td>3.392</td>
</tr>
<tr>
<td>&gt; 100 years</td>
<td>5.088</td>
</tr>
</tbody>
</table>
Markov microsimulation model

- **Utility values** (general population)

<table>
<thead>
<tr>
<th>Fracture</th>
<th>Years</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>1st year</td>
<td>0.797 (IC 0.770-0.825)</td>
</tr>
<tr>
<td></td>
<td>Subsequent years</td>
<td>0.8985 (IC 0.885-0.910)</td>
</tr>
<tr>
<td>Clinical vertebral</td>
<td>1st year</td>
<td>0.720 (IC 0.660-0.775)</td>
</tr>
<tr>
<td></td>
<td>Subsequent years</td>
<td>0.931 (IC 0.916-0.946)</td>
</tr>
<tr>
<td>Wrist</td>
<td>1st year</td>
<td>0.940 (IC 0.910-0.960)</td>
</tr>
<tr>
<td></td>
<td>Subsequent years</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>1st year</td>
<td>0.910 (IC 0.880-0.940)</td>
</tr>
<tr>
<td></td>
<td>Subsequent years</td>
<td>1</td>
</tr>
</tbody>
</table>

- **Proportional reduction of QALY according to fracture type**

Hiligsmann et al. Calcif Tissue Int. 2008;82:288-92
Model validation

- Internal validation
- External validation (predictive value of the model)
- Between model validation
- International experts ~ peer reviewed article
To model an intervention

- Fracture risk reduction: fracture type, offset of action, medication adherence
- Intervention cost
- Adverse events

\[ \text{ICER} = \frac{\Delta C}{\Delta E} \]

Cost-effectiveness thresholds

- Belgium: no (KCE)
- International: around €40000 - €45000 per QALY gained
Objectives

To evaluate the cost-effectiveness of bone densitometry screening for Belgian women combined with 5 years Alendronate therapy in osteoporotic women

To determine at which age bone densitometry screening is efficient

To compare universal screening with screening only women with clinical risk factors

To determine the impact of realistic persistence on the conclusions
Materials and methods (1)

A cost-utility analysis was performed

$P$ represents the prevalence of osteoporosis

$\Rightarrow$ Incremental cost per QALY gained
Economic evaluation of osteoporosis screening strategy conducted in the Province of Liège

– Women aged between 50 and 69 years
– Pre-screening with quantitative ultrasonometry (mobil units)

▪ Performance of ultrasound screening (428 patients)
  – 65.6% true positive, 78% false negative

▪ Screening follow-up (248 patients)
  – 16.5% no follow-up, 15.3% direct treatment, 68.2% DXA
  – 88.4% treatment after positive DXA
Simulated population:

Women aged from 55 to 85 years

Number of CRF: 0 → 4

Persistence: Optimal → realistic

Persistence level: X%-Y%-Z%

X = persistent at least 1 year; Y = persistent at least 2 years;
Z = persistent 5 years
COST-UTILITY OF MASS SCREENING FOR OSTEOPOROSIS IN WOMEN AGED 55-70 YEARS.

- Monte Carlo microsimulation
- Screening by US followed by diagnosis (DXA) and treatment (Alendronate)
- Lifelong perspective
- Cost per QALY gained (1000Euros)
- Base Case
- Sensitivity analysis based on age of mass screening

Hiligsmann et al, 2007
COST-UTILITY OF MASS SCREENING FOR OSTEOPOROSIS IN WOMEN AGED 50-69 YEARS.

- Monte Carlo microsimulation
- Screening by US followed by diagnosis (DXA) and treatment (Alendronate)
- Lifelong perspective
- Cost per QALY gained (1000 Euros)
- ICER with 100% US+ getting DXA and 100% DXA+ getting treatment.
  QUS marginal cost: 5 Euros
  DXA marginal cost: 15 Euros

Hiligsmann et al, 2007
Cost-utility of strontium ranelate in the treatment of postmenopausal women

Hiligsmann et al. Osteoporosis Int. 2009
Strontium ranelate

5 year treatment

Efficacy (Relative Risk):

- Hip fracture: 0.57 (CI 95%: 0.33 – 0.97)
- Clinical vertebral fracture: 0.76 (CI 95%: 0.65 – 0.87)
- Wrist and other fractures: 0.82 (CI 95%: 0.69 – 0.98)

=> TROPOS study – low BMD aged 74 years and older

Annual treatment cost: € 526.46

5 year offset time (linearly increase)

no adverse events
Results: base case

<table>
<thead>
<tr>
<th>Cost (€) per QALY gained</th>
<th>Women with osteoporosis</th>
<th>Women with vertebral fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 70 years</td>
<td>15,997</td>
<td>19,486</td>
</tr>
<tr>
<td>Age 75 years</td>
<td>7,730</td>
<td>8,238</td>
</tr>
<tr>
<td>Age 80 years</td>
<td>CS</td>
<td>CS</td>
</tr>
</tbody>
</table>

CS = cost-saving
Results: univariate sensitivity analyses

<table>
<thead>
<tr>
<th>Cost (€) per QALY gained</th>
<th>Women with osteoporosis</th>
<th>Women with vertebral fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70 years</td>
<td>80 years</td>
</tr>
<tr>
<td><strong>Base case</strong></td>
<td>15,997</td>
<td><strong>CS</strong></td>
</tr>
<tr>
<td>Discount rates 5% (costs and effects)</td>
<td>26,948</td>
<td>5,564</td>
</tr>
<tr>
<td>0.7 time base case fracture disutility</td>
<td>19,845</td>
<td><strong>CS</strong></td>
</tr>
<tr>
<td>0.7 time base case fracture costs</td>
<td>20,524</td>
<td>11,707</td>
</tr>
<tr>
<td>0.7 time base case fracture risk</td>
<td>36,784</td>
<td>28,148</td>
</tr>
</tbody>
</table>

**CS** = cost-saving
Results: cost-effectiveness acceptability curve

Women with osteoporosis

Proportion Cost-Effective

Willingness to Pay per QALY gained

- Age 70 years
- Age 75 years
- Age 80 years
Conclusion

Strontium ranelate is a cost-effective strategy when compared to Calcium and Vitamin D in postmenopausal Belgian women over 70 years of age either with osteoporosis or with a prevalent vertebral fracture.
« Cost-effectiveness of Strontium Ranelate vs. Risedronate »
Results: base-case analysis

Incremental cost-effectiveness ratio (cost in € per QALY gained) of strontium ranelate versus no treatment and risedronate according to age and population

<table>
<thead>
<tr>
<th>Age</th>
<th>Strontium vs. no treatment</th>
<th>Strontium vs. Risedronate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T-score ≤ -2.5</td>
<td>PVF</td>
</tr>
<tr>
<td>Age 70 years</td>
<td>21,365</td>
<td>23,330</td>
</tr>
<tr>
<td>Age 75 years</td>
<td>15,307</td>
<td>16,518</td>
</tr>
<tr>
<td>Age 80 years</td>
<td>10,164</td>
<td>6,015</td>
</tr>
</tbody>
</table>

, CS = Cost Saving
Cost-effectiveness of Denosumab vs branded and generic Bisphosphonates
The cost-effectiveness (expressed in cost in € per QALY gained) of denosumab compared with no treatment for women aged 60 to 80 years with BMD T-score \( \leq -2.5 \) or prevalent vertebral fracture.

<table>
<thead>
<tr>
<th>Population</th>
<th>Age (years)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>60</td>
<td>70</td>
<td>80</td>
</tr>
<tr>
<td>BMD T-score ( \leq -2.5 )</td>
<td>25,061</td>
<td>8,948</td>
<td>-642</td>
</tr>
<tr>
<td></td>
<td>(22,018-28,830)</td>
<td>(7,885-9,871)</td>
<td>(-2254,1643)</td>
</tr>
<tr>
<td>Prevalent vertebral fracture</td>
<td>28,420</td>
<td>11,314</td>
<td>829</td>
</tr>
<tr>
<td></td>
<td>(27,140-30,448)</td>
<td>(10,003-12,936)</td>
<td>(-1214,1912)</td>
</tr>
</tbody>
</table>

Hiligsmann et al. Bone 2010;47:34-40
• Lifetime costs, QALYs, number of fractures and ICER (expressed in cost in € per QALY gained) of denosumab compared with oral bisphosphonates in osteoporotic women aged 70 years

<table>
<thead>
<tr>
<th>Lifetime outcomes (per patient)</th>
<th>Denosumab</th>
<th>Branded alendronate</th>
<th>Generic alendronate</th>
<th>Risedronate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with BMD T-score ≤-2.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costs, €</td>
<td>12 561</td>
<td>12 312</td>
<td>12 169</td>
<td>12 565</td>
</tr>
<tr>
<td>QALYs</td>
<td>10.4424</td>
<td>10.4248</td>
<td>10.4248</td>
<td>10.4202</td>
</tr>
<tr>
<td>Number of fractures</td>
<td>1.2122</td>
<td>1.2393</td>
<td>1.2393</td>
<td>1.2386</td>
</tr>
<tr>
<td>ICER, €/QALY (95% CI)</td>
<td></td>
<td>14 120 (10 109, 16 765)</td>
<td>22 220 (18 628, 24 780)</td>
<td>-209 (-4 003, 1 681)</td>
</tr>
</tbody>
</table>

BMD = bone mineral density; CI = confidence interval; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-years

Hiligsmann et al. Pharmacoeconomics. In press
- Incremental cost-effectiveness ratio (expressed in cost in € per QALY gained) of denosumab compared with oral bisphosphonates according to age in women with BMD T-score \( \leq -2.5 \)
Tornado diagram for one-way sensitivity analyses (conducted on treatment parameters) on the cost-effectiveness of denosumab compared with generic alendronate in women aged 70 years with BMD T-score ≤-2.5

Base case: €22 220/QALY

- 2-year offset time for Dmab and GA
- 2-year offset time for Dmab
- Dmab cost 15% lower
- No monitoring costs
- Lower GA cost for discontinuing patients (a)
- Full compliance for GA
- GA cost 50% lower
- Dmab cost 15% higher
- Dmab cost 30% higher
- GA adherence 25% higher (b)
- Dmab cost 50% higher

Lower GA cost for discontinuing patients (a)
Full compliance for GA
GA cost 50% lower
Dmab cost 15% higher
Dmab cost 30% higher
GA adherence 25% higher (b)
Dmab cost 50% higher
Clinical and economic implications of non-adherence with osteoporosis medications
Background

Poor adherence is a major issue in osteoporosis management

BUT the clinical and economic consequences of non-adherence have not been well described

Objective

To estimate the clinical and economic implications of therapeutic adherence to bisphosphonates therapies
Adherence to therapy definitions (ISPOR, 2008)

- Compliance: “The extend to which a patient acts in accordance with the prescribed interval, and dose of regimen”

- Persistence: “The duration of time from initiation to discontinuation of therapy”

Scenarios for persistence:

- **Real-world persistence** (Rabenda et al., OI, 2008): 30%, 12%, 18% and 15% of patients go off therapy after 3 months, 6 months, 1 year and 2 years respectively

- **Full persistence** over 3 years

- Real-world persistence **25% and 50% lower**
Impact of medication compliance on the cost-effectiveness of bisphosphonates compared to no treatment.
Conclusion

Non-adherence with osteoporosis medications results

- in worsening health outcomes
- in a significant change in the cost-effectiveness of treatments

⇒ Adherence-enhancing interventions would be worthwhile, both in clinical and economic terms
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