Assessing outcome of haemophilia treatment

The role of Health-Related Quality of Life (HRQoL)

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Van Creveldkliniek: 700 patients; 320 severe haemophilia
Outline

• HRQoL instruments
• HRQoL results in different studies
• Association of HRQoL with joint damage and treatment
Why perform outcome assessment?

Outcome in haemophilia is highly dependent on treatment

Outcome assessment

- Evaluate treatment results
  - Compare strategies
  - Improve treatment
  - Compare to other diseases
  - Improve outcome
Assessment of outcome: Perspective

- Patient
- Third Party Payer
- Society
Assessment of benefits: Perspective

- Patient: number of bleeds, joint function, arthropathy, disease-specific HRQoL
- Third Party Payer
- Society
Assessment of benefits: Perspective

- **Patient**
  - number of bleeds
  - joint function, arthropathy
  - disease-specific HRQoL

- **Third Party Payer**
  - doctor’s visits
  - hospital admissions
  - surgical procedures

- **Society**
Assessment of benefits: Perspective

- **Patient**
  - number of bleeds
  - joint function, arthropathy
  - disease-specific HRQoL

- **Third Party Payer**
  - doctor’s visits
  - hospital admissions
  - surgical procedures

- **Society**
  - labourforce participation
  - disability allowances, etc
  - HRQoL, Utility → QALY
Why is HRQoL essential?

Health Related Quality of Life

- ‘summary parameter’ for long-term patient relevant outcome
- translated into benefits from societal perspective ➔ QALY’s
### Assessment of Health Related Quality of Life

#### CHILDREN
**Generic**
- CHQ
- KINDL
- HUI*

**Specific**
- Hemo-Qol ('02)
- CHoKLAT ('04)

#### ADULTS
**Generic**
- SF 36
- EQ5D (Utility)*

**Specific**
- Hemofilia-Qol ('05)
- (MedTap)
  - Utility^Wasserman 2005*

* Preference based
Short Form 36 (SF36)

- physical function
- bodily pain
- physical role limitations
- general health

- social function
- mental role limitations
- mental health
- Vitality

Each domain: score 0 -100 (100 is optimum)

Physical summary scale (0-55)
Mental summary scale (0-55)
Euroqol (EQ-5D)

- mobility
- self-care
- usual activities
- pain/discomfort
- anxiety/depression

- Visual analogue scale (VAS)

\[ \text{EQ-5D}_{\text{utility}} (0-1) \rightarrow \text{QALY} \]
\[ \text{EQ-5D}_{\text{VAS}} (0-100) \]
Results of studies using the SF36 (1): cross-sectional Europe (n=903, Royal et al, ‘02)
SF 36: domain of ‘Physical Function’

10 questions, on limitations in:

• vigorous / moderate activities
• lifting/carrying groceries
• climbing stairs: > 1 flights/ 1 flight
• bending/kneeling/stooping
• walking: > 1 mile / 1 mile / 100 yards
• bathing & dressing
Results of SF36 and Euroqol (EQ5D)

In 6 studies, 56-903 patients

SF36 ‘physical function’ scores:

- ↓ than general population
- ↓/= with HIV infection
- ↓ with ↑ bleeds on OD
- ↓ with increasing age
- ↓ with severity of disease
- ↑ with prophylaxis

Euroqol (EQ5D)
Comparing SF36 and Euroqol (EQ5D)

<table>
<thead>
<tr>
<th></th>
<th>UK males</th>
<th>Miners ‘99</th>
<th>Trippoli ‘01</th>
<th>Pilot NL ‘06</th>
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</thead>
<tbody>
<tr>
<td>Number (% severe)</td>
<td>1466</td>
<td>164 (40%)</td>
<td>56 (57%)</td>
<td>22 (68%)</td>
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<tr>
<td>Age (yrs)</td>
<td>35-44</td>
<td>43.5</td>
<td>38.7</td>
<td>20.7</td>
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<tr>
<td>SF36- PF</td>
<td>91.9</td>
<td>62.3</td>
<td>73.6</td>
<td>93.4</td>
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<tr>
<td>SF36- PCS</td>
<td>52.0</td>
<td>38.7</td>
<td>44.7</td>
<td>51.2</td>
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<tr>
<td>Utility</td>
<td>1.00</td>
<td>0.77</td>
<td>0.68</td>
<td>0.91</td>
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<tr>
<td>Correlation SF36-utility</td>
<td>NA</td>
<td>0.59</td>
<td>0.64</td>
<td>0.63</td>
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</tbody>
</table>

Mean values
Conclusions on SF36 and EQ5D

- Physical domains/ components most sensitive in haemophilia
- Generic instruments:
  - able to pick up difference with general population
  - decrease HRQoL with age
  - only moderate correlation
  - able to pick up differences in haemophilia severity
Discrimination of haemophilia specific questionnaires: Hemofilia-Qol

10 centres in Spain
121 adults, (68% severe, 30% moderate, 2% mild)
Mean age 34.9 ± 11.9 yrs

<table>
<thead>
<tr>
<th>Subscale (dimension)</th>
<th>No. of items</th>
<th>Change with Nr of bleeds</th>
<th>Change with Chronic pain</th>
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</thead>
<tbody>
<tr>
<td>Physical health</td>
<td>8</td>
<td>; $P = 0.000^*$</td>
<td>; $P = 0.000^{**}$</td>
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<tr>
<td>Daily activities</td>
<td>4</td>
<td>; $P = 0.003^*$</td>
<td>; $P = 0.000^{**}$</td>
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<tr>
<td>Joint damage</td>
<td>3</td>
<td>; $P = 0.000^*$</td>
<td>; $P = 0.002^*$</td>
</tr>
<tr>
<td>Pain</td>
<td>2</td>
<td>; $P = 0.000^{**}$</td>
<td>$P = 0.007^*$</td>
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<tr>
<td>Treatment satisfaction</td>
<td>2</td>
<td>$P = \text{NS}$</td>
<td>$P = 0.044^*$</td>
</tr>
<tr>
<td>Treatment difficulties</td>
<td>4</td>
<td>$P = \text{NS}$</td>
<td>$P = 0.073^{***}$</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>5</td>
<td>$P = \text{NS}$</td>
<td>; $P = 0.000^{**}$</td>
</tr>
<tr>
<td>Mental health</td>
<td>3</td>
<td>$P = \text{NS}$</td>
<td>; $P = 0.000^{**}$</td>
</tr>
<tr>
<td>Relationships and social activity</td>
<td>5</td>
<td>$P = \text{NS}$</td>
<td>; $P = 0.000^{**}$</td>
</tr>
<tr>
<td>Hemofilia-QoL (total score)</td>
<td>36</td>
<td>$P = 0.004^*$</td>
<td>; $P = 0.000^{**}$</td>
</tr>
</tbody>
</table>
Pediatric haemophilia specific questionnaires

**Haemo-Qol**
- Started from treaters' perspective
- 3 tools: age 4-7, 8-12, 13-16
- 2 tools: age 4-7, 8-16 (35 Q)
- Hemoqol Index: 4-16 yrs (8 Q)

**Domains**
- physical
- feeling
- view
- family
- friends
- others
- school
- treatment

**Summary score** 100-0

**CHOKLAT**
- Started from patients’ perspective
- One tool age 4-18
- Patient & parent form (35 Q)

**Domains: not specified**

**Correlation**
- Patients -0.74
- Parents -0.82

**Summary score** 0-100
Conclusions HRQoL questionnaires in haemophilia

**GENERIC**
- Physical domains/ components most sensitive in haemophilia
- Generic instruments:
  - able to pick up difference with general population
  - decrease HRQoL with age
  - only moderate correlation SF36 and EQ5D
  - able to pick up differences in haemophilia severity

**DISEASE SPECIFIC**
- able to pick up differences in haemophilia severity
- added domains on joint damage and treatment
- additional value??

  treatment > research?
Remaining questions:

Negative effect of age: caused by age or arthropathy?

Long-term effects of different treatment strategies on HRQoL?

→ study association of arthropathy with HRQoL
Association of arthropathy with HRQoL: Methods

Methods:
• 96 patients (88% severe, 12% moderate)
• Pettersson scores & SF 36 completed within 2.5 yrs

Outcome parameters:
• Pettersson score, 6 joints, 0-78 points
• score for ‘physical function’ of SF36, 0-100 points ‘PF’
• Physical component score of SF36, 0-55 points ‘PCS’

Multivariate regression analysis:
Association of Pettersson score with SF36 independent of age
mean age 28.6 years (range 13-54)
- Pettersson score to SF 36: mean 0.4 yrs (sd 1.1)
- median Pettersson score 13 (24% zero score)

patients divided according to Pettersson scores
- 0-4 points
- 5-27 points
- 28-78 points
Association of arthropathy with HRQoL: outcome according to Pettersson scores

Mean values
Effects of age in general population: physical function

- 19 yrs: 97
- 25 yrs: 94
- 41 yrs: 87
Association of arthropathy with HRQoL: outcome according to Pettersson scores

![Bar chart showing the association of arthropathy with HRQoL outcomes according to Pettersson scores. The chart displays data for age, PF expect, PF, and PCS categories with age ranging from 0 to 4, 5 to 27, 28 to 78, and PF expect and PCS scores for each age group.](image)
Association of arthropathy with HRQoL: age adjusted analysis

- Effect on Physical Function (PF):
  - 4.4 points/ 10 points increase in Pettersson score
    (CI: -7.8 to -1.1, p=0.01)

- Effect on Physical Summary Score (PCS):
  - 1.4 points/ 10 points increase in Pettersson score
    (CI: -3.0 to +0.2, p=0.07)

- NOT on other domains of SF36
Conclusions

• Effect of age on HRQoL is caused by both age and haemophilic arthropathy

• age-adjusted association of Pettersson scores
  – with domain of physical function (PF)
  – with physical summary score (PCS)
  – NOT with other domains of SF36
Future research:

• Use of HRQoL (and Utilities) as outcome for comparison of long-term results between treatment strategies

• Look for ‘point of no return’: threshold effect of joint damage on HRQoL?
## Two studies

<table>
<thead>
<tr>
<th>Severe haemophilia</th>
<th>Moderate haemophilia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NL-SW</strong></td>
<td><strong>NL-SW-DK</strong></td>
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<tr>
<td>Age 12-35</td>
<td>All ages</td>
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<tr>
<td>No inhibitors</td>
<td>No inhibitors</td>
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<tr>
<td><strong>Assessment</strong></td>
<td><strong>Assessment</strong></td>
</tr>
<tr>
<td>joint structure</td>
<td>joint structure by PT</td>
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<tr>
<td>joint function</td>
<td>joint function questionn</td>
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<tr>
<td>HRQoL</td>
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<td>physical activity questionn</td>
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<td>by PT</td>
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<td></td>
<td>questionn</td>
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