EQ-5D-5L Utility Index for different countries

Basler Biometrische Sektion

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This is joint work with

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Agenda

// Background and Problem Statement
// Methods
// Results
// Discussion and Conclusion
Background EQ-5D

One of the most frequently used generic questionnaires to assess health states and utilities

‘EuroQol EQ-5D-3L’ with 5 dimensions and 3 levels of severity introduced in 1990

5805 hits for „EQ-5D“ in PubMed; ~48,600 in Google Scholar (2018-04-03)

EQ-5D-5L introduced in 2005

EQ-5D-5L

// 5 Dimensions
  // Mobility
  // Self-care
  // Usual activities
  // Pain / discomfort
  // Anxiety / depression

// 5 Levels
  // No
  // Slight
  // Moderate
  // Severe
  // Extreme / unable

// 3125 (= 5^5) possible health states

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY
- I have no problems in walking about
- I have slight problems in walking about
- I have moderate problems in walking about
- I have severe problems in walking about
- I am unable to walk about

SELF-CARE
- I have no problems washing or dressing myself
- I have slight problems washing or dressing myself
- I have moderate problems washing or dressing myself
- I have severe problems washing or dressing myself
- I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)
- I have no problems doing my usual activities
- I have slight problems doing my usual activities
- I have moderate problems doing my usual activities
- I have severe problems doing my usual activities
- I am unable to do my usual activities

PAIN / DISCOMFORT
- I have no pain or discomfort
- I have slight pain or discomfort
- I have moderate pain or discomfort
- I have severe pain or discomfort
- I have extreme pain or discomfort

ANXIETY / DEPRESSION
- I am not anxious or depressed
- I am slightly anxious or depressed
- I am moderately anxious or depressed
- I am severely anxious or depressed
- I am extremely anxious or depressed

Devlin et al 2017. Figure 1
Valuation

Each health state is rated with anchors

// 1 ≈ perfect health
// 0 ≈ death
// Negative values are possible

Health states are rated by the general public, i.e., not by the sick people in a given state

Valuations are by country

Several methods used to elicit the valuations, e.g.,

// time trade-off: “I’d rather live 5 years in perfect health than 10 years with condition A.”
// discrete choice experiment: “I prefer extreme pain over severe depression + severe difficulties walking.”
// A (non-random) sample of the health states is directly evaluated, all valuations are then derived from a model.
Quality adjusted life-years

QALYs = area under the curve
A = QALYs without intervention
B = QALYs gained by intervention

By Jmarchn - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=67001576
Why are QALYs important?

NICE aims to spend less than £20,000 to £30,000 per QALY

That is not a hard limit; it will go almost twice as high for end-of-life drugs

https://www.nice.org.uk/advice/lgb10
Recall

Health valuations are elicited by country

Some differences are to be expected, e.g., if you need a wheel chair
Problem Statement

How important are the differences between countries?

How to analyze EQ-5D-5L in a multi-national trial?
Agenda

// Background and Problem Statement

// Methods

// Results

// Discussion and Conclusion
### Data – elicidated sets

86 of the 3125 states were elicidated to model all 3125 states

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients (n) participated</th>
<th>Age range</th>
<th>Range of EQ-5D-5L</th>
<th>No of health states</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>1209</td>
<td>18-89</td>
<td>-0.148 to 0.949</td>
<td>86</td>
</tr>
<tr>
<td>England</td>
<td>996</td>
<td>18-75+</td>
<td>-0.281 to 0.951</td>
<td>86</td>
</tr>
<tr>
<td>Japan</td>
<td>1026</td>
<td></td>
<td>-0.025 to 0.895</td>
<td></td>
</tr>
<tr>
<td>Korea</td>
<td>1085</td>
<td>19-60+</td>
<td>-0.066 to 0.833</td>
<td>86</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1003</td>
<td>18-80+</td>
<td>-0.446 to 1</td>
<td>86</td>
</tr>
<tr>
<td>Uruguay</td>
<td>794</td>
<td>20-83</td>
<td>-0.264 to 1</td>
<td>86</td>
</tr>
</tbody>
</table>
Data – „crosswalk“ sets

Based on patients’ completion of both the EQ-5D-3L and the EQ-5D-5L descriptive systems, the Crosswalk Project established a link between the EQ-5D-5L and the EQ-5D-3L descriptive system, for which value sets in more countries are available. By using the crosswalk link function and the individual responses to the EQ-5D-5L descriptive system, the single index value for the EQ-5D-5L can be estimated.

Belgium, Denmark, Europe, Finland, France, Germany, Japan, Netherlands, New Zealand, Slovenia, Spain, Thailand, UK, US, Zimbabwe.

The crosswalk value were downloaded from the EuroQol.org website.
Data – real study

Not all possible health states occur often in real life, e.g. the combination “unable to walk“, „extreme pain“, „unable to wash or dress myself“ but „no problems doing my usual activities“ seems rather unlikely.

To gauge the effects of the different valuations in practice the baseline EQ-5D-5L states of a real study were evaluated for each of the countries.
For each of the 3125 possible health states the difference between the two countries with the highest and the lowest valuation was calculated.

These differences were analyzed by descriptive statistics including boxplots and histograms.

The differences in valuations between two different health states were also calculated and analyzed for each pair of distinct health states.

For the clinical trial we used the observed health states of 313 patients
Agenda

// Background and Problem Statement

// Methods

// Results

// Discussion and Conclusion
Maximal Difference between Countries – Elicitated sets

Lowest difference 0.0173 for health state “45512”

Highest difference 0.642 for health state “44444”. (-0.289 in The Netherlands and at +0.353 in Uruguay)

The median discrepancy across all 3125 possible health states was 0.260 with IQR 0.182 to 0.371
Scatter plot by Country – Elicitated sets
Maximal Difference between Countries – Crosswalk sets

Smallest difference was 0.100 for health state “11111”

Largest difference was 0.626 for health state “15155” with Japan scoring +0.440 and the UK -0.186.

For 99% of the health states the difference was larger than 0.190

The median difference was 0.417 across the 3125 possible health states with an IQR of 0.337 to 0.490.
Scatter plot by Country – Crosswalk sets

Denmark="1"
France="2"
Germany="3"
Japan="4"
Netherlands="5"
Spain="6"
Thailand="7"
UK="8"
US="9"
Zimbabwe="10"
Systematic differences and differences in the valuation of change

In almost all health states, Germany reported higher valuations than France.

Large discrepancies between the countries were also observed when analyzing changes from one health state to another health state.

In many cases not only the magnitude of the change was different between the countries but also the direction of the change.

A change from health state “44444” to “55511” is valued as an improvement of 0.679 units in The Netherlands and as a worsening of 0.169 units in Uruguay.
Valuations of sample study (n=313)

<table>
<thead>
<tr>
<th>Value Set</th>
<th>Mean</th>
<th>Std Dev</th>
<th>Minimum</th>
<th>Lower Quartile</th>
<th>Median</th>
<th>Upper Quartile</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>0.698</td>
<td>0.208</td>
<td>0.019</td>
<td>0.572</td>
<td>0.765</td>
<td>0.860</td>
<td>0.949</td>
</tr>
<tr>
<td>England</td>
<td>0.713</td>
<td>0.229</td>
<td>-0.117</td>
<td>0.558</td>
<td>0.786</td>
<td>0.893</td>
<td>1.000</td>
</tr>
<tr>
<td>Japan</td>
<td>0.699</td>
<td>0.176</td>
<td>0.161</td>
<td>0.581</td>
<td><strong>0.717</strong></td>
<td>0.831</td>
<td>1.000</td>
</tr>
<tr>
<td>Korea</td>
<td>0.704</td>
<td>0.173</td>
<td>0.172</td>
<td>0.560</td>
<td>0.765</td>
<td>0.830</td>
<td>1.000</td>
</tr>
<tr>
<td>Netherlands</td>
<td>0.622</td>
<td>0.273</td>
<td>-0.289</td>
<td>0.449</td>
<td>0.717</td>
<td>0.848</td>
<td>0.953</td>
</tr>
<tr>
<td>Uruguay</td>
<td>0.818</td>
<td>0.147</td>
<td>0.240</td>
<td>0.730</td>
<td><strong>0.861</strong></td>
<td>0.927</td>
<td>1.000</td>
</tr>
<tr>
<td>Denmark (cw)</td>
<td>0.677</td>
<td>0.175</td>
<td>0.083</td>
<td>0.555</td>
<td>0.722</td>
<td>0.797</td>
<td>1.000</td>
</tr>
<tr>
<td>France (cw)</td>
<td>0.604</td>
<td>0.268</td>
<td>-0.169</td>
<td>0.402</td>
<td>0.635</td>
<td>0.839</td>
<td>1.000</td>
</tr>
<tr>
<td>Germany (cw)</td>
<td>0.742</td>
<td>0.202</td>
<td>0.069</td>
<td>0.595</td>
<td><strong>0.806</strong></td>
<td>0.887</td>
<td>1.000</td>
</tr>
<tr>
<td>Japan (cw)</td>
<td>0.665</td>
<td>0.132</td>
<td>0.127</td>
<td>0.571</td>
<td>0.671</td>
<td>0.740</td>
<td>1.000</td>
</tr>
<tr>
<td>Netherlands (cw)</td>
<td>0.658</td>
<td>0.212</td>
<td>0.088</td>
<td>0.503</td>
<td>0.713</td>
<td>0.833</td>
<td>1.000</td>
</tr>
<tr>
<td>Spain (cw)</td>
<td>0.666</td>
<td>0.241</td>
<td>-0.198</td>
<td>0.509</td>
<td>0.729</td>
<td>0.857</td>
<td>1.000</td>
</tr>
<tr>
<td>Thailand (cw)</td>
<td>0.570</td>
<td>0.199</td>
<td>-0.124</td>
<td>0.432</td>
<td><strong>0.582</strong></td>
<td>0.723</td>
<td>1.000</td>
</tr>
<tr>
<td>UK (cw)</td>
<td>0.610</td>
<td>0.235</td>
<td>-0.107</td>
<td>0.442</td>
<td>0.696</td>
<td>0.768</td>
<td>1.000</td>
</tr>
<tr>
<td>US (cw)</td>
<td>0.714</td>
<td>0.158</td>
<td>0.188</td>
<td>0.605</td>
<td>0.777</td>
<td>0.826</td>
<td>1.000</td>
</tr>
<tr>
<td>Zimbabwe (cw)</td>
<td>0.710</td>
<td>0.131</td>
<td>0.303</td>
<td>0.621</td>
<td>0.743</td>
<td>0.810</td>
<td>0.900</td>
</tr>
</tbody>
</table>

(cw): crosswalk set
Agenda

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Discussion

The EQ-5D-5L utilities of health states vary substantially between the different countries.

// The median difference was 0.417 for the crosswalk sets and 0.315 for the countries with elicited value sets across all 3125 possible health states.

// For the sample study the valuations by 0.114 for the countries with elicited value sets and by 0.224 for the crosswalk sets.

NICE is critical of -5L: “Currently the 5L valuation set is not recommended for use.“

For health economic modelling the value set of that specific country should be used.

For a clinical trial using different value sets (e.g., the German one for patients from Germany and the French one for patients from France) is, in our view, not interpretable.
Conclusion

Beware of the huge country differences.

When analyzing multinational clinical studies, several country-specific value sets should be used to evaluate treatment effects.

Using just one country set, e.g. the one from England, provides results that are only valid for that country.
References


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Bye-Bye