RA DISEASE: Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes pain, stiffness and also limited motion and function of joints.

HAQ: The Health Assessment Questionnaire (HAQ) is a self-report questionnaire measuring disability level of patients with RA by the HAQ-index on a scale from 0 (no difficulty) to 3 (unable to do).

OBJECTIVE: The main objective of this study is to estimate the impact of the level of functional status and disability on health service cost related to RA disease in Hungary.

DEPENDENCE: Although it is straightforward to think that higher disability implies higher costs, the nature of the relationship is unclear.

COUPULA: Nowadays there are more and more recent copula models aimed at describing the behavior of multivariate data sets.

JOINT DISTRIBUTION: Instead of fitting only trend lines for the expected value of the cost the entire bivariate distribution has been modeled.

Figure 1. Density curves of Gaussian (θ=0.5 on the left) and Student-t (θ=0.05; df=4 on the right) copulas.

PROS: Non-linear structures are applicable / No restrictions on marginal distributions.

CONS: Testing the goodness-of-fit (GOF) and handling covariates are complicated.

GOF: The performance of the different model assumptions can be compared by GOF procedures based on the function.

MIXTURE: In practical applications it is possible that the marginal distributions are not continuous, in such cases mixture models can be used. Similarly to zero-inflated models there is often positive probability observed at zero, these can be estimated easily by relative frequencies (y,y,y,y,y) as in Table 1.

H(x,y) = Pr[X,Y] ≤ (x,y) = C(F(X),G(Y))

where F and G are the marginal distribution functions and C is the copula distribution function.

MODELS: There are several parametric families available, for elliptical families the parameters of the copula are written as (θ,θ,θ,θ) as in Table 1.

H(X,Y) = p_0 + p_1 Pr[X ≤ x] + p_2 Pr[Y ≤ y]

(1−p_3 − p_4 − p_5) Pr[X,Y ≤ (x,y)]


OUTPUT: After the model estimation any conditional expectations (see Table 2.) or conditional probabilities (see Figure 3.) become obtainable.

COVARIATES: Covariates can be included as additional model parameters e.g. gender/age/treatment type etc.

MORE FAMILIES: Different parametric assumptions can be applied, e.g. asymptotic dependence/independence or between.

REFERENCES


The empirical marginal distributions (black lines) and their parametric versions (red lines) assuming normal distribution for HAQ (μ=1.4 and σ=0.7) and log-normal distribution for the inpatient cost (μ=9.4 and σ=0.6) are presented in the upper panels of Figure 2. The dependence parameter of the Gaussian copula is 0.375 (0.07) which is significantly greater than zero (p-value<0.01).

Figure 2. Marginal distribution of HAQ and Cost. Density of the bivariate joint model. Difference between K functions, respectively.

SUMMARY

RESULTS: Average costs in out/inpatient care and total cost have been estimated based on the fitted mixture models. The actual values are summarized in Table 2. There is positive dependence found in all cases which means that the average cost increases with higher values of HAQ indices.

Table 2. Expected costs of out/inpatient care and total cost

<table>
<thead>
<tr>
<th>HAQ Index</th>
<th>Expected Cost of Outpatient Care</th>
<th>Expected Cost of Inpatient Care</th>
<th>Expected Total Cost (including Outpatient)</th>
<th>Expected Total Cost (excluding Outpatient)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0.5)</td>
<td>574</td>
<td>568</td>
<td>1130.78</td>
<td>1030.79</td>
</tr>
<tr>
<td>Medium (1.5)</td>
<td>577</td>
<td>584</td>
<td>1163.97</td>
<td>1062.97</td>
</tr>
<tr>
<td>High (2.5)</td>
<td>580</td>
<td>573</td>
<td>1173.90</td>
<td>1073.90</td>
</tr>
</tbody>
</table>

Table 3. Conditional distribution functions at low/in between HAQ values.

Figure 3. Conditional distribution functions at low/in between HAQ values.

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AC: HAQ-indices of RA patients were collected in the Arthritis Center (AC) of Buda Hospital of Hospitaliters Brothers of St. John from 1st January 2001 to 31st March 2014.

NHIFA: RA patients were also identified in the database of National Health Insurance Fund Administration (NHIFA) and further parameters as e.g. relevant treatments and health service costs (in- and outpatient) were collected from 1st January 2005 to 31st July 2013.


MERGE: After merging AC (497 patients) and NHIFA (43 836 patients) database the 2-dimensional patterns of the HAQ-index measurements versus costs (sum of relevant costs in the following year) and several covariates became available for bivariate modeling.

STUDY PERIOD: There have been 324 patients with 2115 HAQ-index observations available in the AC-NHIFA merged database from 1st January 2005 to 31st July 2013.

EXCHANGE RATE: HUF/USD currency conversion has been made according to the quarterly average rate of the Central Bank of Hungary (2014 Q2)