ADAPTING LITERATURE-BASED REMISSION RATES FOR CHRONIC SPONTANEOUS/IDIOPATHIC URTICARIA TO THE NEEDS OF A HEALTH ECONOMIC MODEL: A KAPLAN-MEIER APPROACH


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BACKGROUND

- Remission, where symptoms spontaneously resolve, is seen in patients with chronic urticaria (CU)
- Chronic spontaneous urticaria (CSU), also known as chronic idiopathic urticaria (CIU), is a subtype of CU
- Limited literature currently exists regarding remission rates among patients with CU and CSU/CIU, and available estimates vary
- Due to the requirements of economic modeling (e.g., cycle length), these estimates cannot be incorporated directly

OBJECTIVE

- To adapt published remission rates in CSU patients to the needs of an economic model, using various statistical methods

METHODS

- A systematic review was conducted to identify literature on the natural course of CSU, with a focus on spontaneous remission rates
- From this systematic review, four studies were selected on the basis of a similar study population to the target population in the economic model
  - Beltrani et al. (2002)
  - Toubi et al. (2004)
  - van der Valk et al. (2002)
  - Nebiolo et al. (2005)
- All the four papers reported the proportion of patients that would have undergone/not undergone remission at different time points
- The study by Nebiolo et al. reported data for two populations, (i) CSU/CIU only and (ii) all forms of CU; therefore, a total of five populations were considered
- A four-step approach was undertaken to identify the best possible distribution fit for data extrapolation and to generate appropriate remission rates
  1. The data reported in each of the papers was extracted and converted to be in the same format
  2. The extracted data in the suitable format were then used to run a Kaplan-Meier analysis
  3. Several statistical distributions (exponential, log-normal, Weibull and log-logistic) were tested to identify the distribution best fitting the remission estimates
  4. Values obtained from the best fit distribution were further converted into rates for each 4-week cycle length

RESULTS

- The curve fit using different statistical distributions for all four papers are presented below (Figure 1)
- A summary of remission rates over 1, 3, 5, 10 and 20 years are depicted in (A)
- Table 1 presents the Kolmogorov-Smirnov (KS) distance, i.e., differential estimates between the expected values and the actual fit values. A lower value means that the distribution is a better fit.

CONCLUSION

- This approach provides a robust statistical method for adapting the literature estimates as per the requirements of an economic model
- Due to the wide range of remission estimates in the literature face validation via expert clinical opinion is recommended

REFERENCES

3. Toubi E et al. Allergy 2001;56(10):786-793

CONFLICT OF INTEREST

- GP, SG, SB, AH and MMB are employees of Novartis
- DMcB and JG are employees of RTI Health Solutions
- AM has received research support/consultancies/meeting expenses from Novartis, UGM Pharma and EQA

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FUNDING

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Figure 1. The four-step methodology

A HEALTH ECONOMIC MODEL: A KAPLAN-MEIER APPROACH

SPONTANEOUS/IDIOPATHIC URTICARIA TO THE NEEDS OF

• To adapt published remission rates in CSU patients to the needs of an economic model, using various statistical methods

RESULTS

BACKGROUND

The study by van der Valk et al. (2002) reported data for two populations, (i) CSU/CIU only and (ii) all forms of CU; therefore, a total of five populations were considered

A systematic review was conducted to identify literature on the natural course of CSU, with a focus on spontaneous remission rates

All CU patients

CSU patients

Figure 3. Curve fit using different distributions on data points from van der Valk

Figure 2. Curve fit using different distributions on data points from Beltrani and Toubi

Table 1. K-S distance values for the fitted distributions

<table>
<thead>
<tr>
<th>Distribution</th>
<th>Beltrani (CSU patients)</th>
<th>Toubi (CSU patients)</th>
<th>van der Valk (CSU patients)</th>
<th>Nebiolo (all CU patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exponential</td>
<td>0.081</td>
<td>0.079</td>
<td>0.160</td>
<td>0.054</td>
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<tr>
<td>Lognormal</td>
<td>0.200</td>
<td>0.001</td>
<td>1.66e-16</td>
<td>0.0428</td>
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<tr>
<td>Weibull</td>
<td>0.179</td>
<td>0.019</td>
<td>1.66e-16</td>
<td>0.0261</td>
</tr>
<tr>
<td>Log-logistic</td>
<td>0.461</td>
<td>0.081</td>
<td>0.1205</td>
<td>0.1105</td>
</tr>
<tr>
<td>Exponential</td>
<td>0.152</td>
<td>0.012</td>
<td>2.22e-16</td>
<td>0.0233</td>
</tr>
</tbody>
</table>

• A summary of remission rates over 1, 3, 5, 10 and 20 years are depicted in Figure 5A. Yearly remission rates across 20 years are presented in Figure 5B. As the remission rates were calculated per 4-week cycle length, details for the first year are presented in Figure 5C.

Figure 5. Summary of remission in patients over time by source

(A) Years from symptom onset or diagnosis

<table>
<thead>
<tr>
<th>Years</th>
<th>Beltrani (CSU patients)</th>
<th>Toubi (CSU patients)</th>
<th>van der Valk (CSU patients)</th>
<th>Nebiolo (all CU patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
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<td>6.19%</td>
<td>2.24%</td>
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<tr>
<td>3</td>
<td>8</td>
<td>13.17%</td>
<td>6.84%</td>
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<tr>
<td>5</td>
<td>12</td>
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<td>9.03%</td>
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<td>15.38%</td>
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<td>46</td>
<td>22.88%</td>
<td>21.94%</td>
<td>4.18%</td>
</tr>
</tbody>
</table>

(B) Probability of not remitting

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Probability of not remitting</th>
</tr>
</thead>
<tbody>
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<tr>
<td>40</td>
<td>0.00</td>
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<tr>
<td>45</td>
<td>0.00</td>
</tr>
<tr>
<td>50</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Figure 4. Curve fit using different distributions on data points from Nebiolo

(F) Remission rates (%) as a function of years from symptom onset or diagnosis

CONCLUSION

- This approach provides a robust statistical method for adapting the literature estimates as per the requirements of an economic model
- Due to the wide range of remission estimates in the literature face validation via expert clinical opinion is recommended to determine appropriate model inputs

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