A Systematic Review of Socioeconomic Burden in Hereditary Angioedema

Timothy Craig, DO1; Kristen A. Cribs, PhD MPH2; Shawn Czado3

1The Pennsylvania State University, College of Medicine, Allergy, Asthma and Immunology, Hershey, PA, USA; 2Alkene LLC, Manchester Center, VT, USA; 3KalVista Pharmaceuticals, Inc., Cambridge, MA, USA

References

- Background
  - Hereditary angioedema (HAE) is a rare, genetic disease characterized by debilitating swelling episodes in various parts of the body.
  - Over the past decade, several treatment options for HAE have emerged; however, concerns regarding the financial impact of these therapies on patients, caregivers, and healthcare systems persist.
  - Previous literature indicates that HAE is associated with substantial direct medical costs, however, indirect costs are not as well-characterized.
  - This study aimed to comprehensively evaluate and synthesize the current body of evidence around the socioeconomic burden of HAE on patients and caregivers.

- Methods
  - We conducted an SLR on economic outcomes, including indirect costs, among patients with HAE, including those using prophylactic and/or on-demand HAE therapies, in accordance with PRISMA guidelines.
  - Searches were conducted in PubMed, Embase, and Google Scholar.
  - Article inclusion was limited to English peer-reviewed and grey literature published between January 1, 2007 and July 1, 2022.
  - Two independent reviewers assessed literature eligibility and abstracted data.
  - We adjusted all costs for inflation to 2022 USD.

- Results
  - We identified 66 studies. The majority of studies were observational (64%), and the most common study location was the United States (42%) (Table 1).
  - Among these 66 studies, 41 assessed socioeconomic burden in HAE, revealing annual costs up to $57,238, which reflects both patient and caregiver indirect costs.
  - Factors contributing to indirect costs included reduced work productivity, travel, childcare, and caregiver burden.
  - The most significant driver of indirect patient costs was reduced hours and lower labor market participation (up to $20,156 or 35% of total indirect costs) (Figure 1).
  - Caregiver indirect costs accounted for up to 14% of total indirect costs, with lower productivity and/or presenteeism being the most significant driver ($5,395) (Figure 2).

- Discussion
  - This SLR revealed substantial socioeconomic burden for patients with HAE and their caregivers, with indirect costs being driven largely by decreased productivity and labor market participation.
  - We also found HAE to impede patient work productivity and attendance, with more severe impacts observed as attack severity increased.
  - Understanding indirect costs related to HAE, which are often underappreciated, is crucial to facilitating holistic HAE disease management approaches that benefit patients, caregivers, and society.

Table 1. SLR Study and Sample Characteristics

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Total Number of Publications</th>
<th>Study Location</th>
<th>Sample Size, number of patients available</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Economic Report</td>
<td>13 (19.7)</td>
<td>United States</td>
<td>20</td>
<td>20</td>
<td>137</td>
</tr>
<tr>
<td>Conference Proceeding</td>
<td>25 (37.9)</td>
<td>United States</td>
<td>28</td>
<td>28</td>
<td>517</td>
</tr>
<tr>
<td>Observational</td>
<td>48 (74.6)</td>
<td>United States</td>
<td>28</td>
<td>28</td>
<td>517</td>
</tr>
<tr>
<td>Original Research</td>
<td>48 (74.6)</td>
<td>United States</td>
<td>28</td>
<td>28</td>
<td>517</td>
</tr>
</tbody>
</table>

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

<table>
<thead>
<tr>
<th>Attack Severity*</th>
<th>Range of number of days missed per attack</th>
<th>Mean number of days missed per attack</th>
<th>Range of mean WPAI work productivity loss</th>
<th>Range of mean WPAI activity impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (range)</td>
<td>1.0 – 3.3</td>
<td>9.0 – 19.9</td>
<td>22.11 – 25.40</td>
<td>20.6 – 33.88</td>
</tr>
<tr>
<td>Mild</td>
<td>0.5 – 2.2</td>
<td>19.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>1.0 – 1.8</td>
<td>16.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Severe</td>
<td>1.8 – 5.5</td>
<td>28.2</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Severity was assessed using study-specific categories for mild, moderate, and severe attacks.

Conclusions

- Findings indicated “moderate” levels of impairment related to work productivity loss and activity impairment, as measured by the Work Productivity and Activity Impairment Questionnaire (WPAI): 22 – 25% and 21 – 34%, respectively.
- Days missed per year ranged from 9.0 – 19.9, with up to 28.2 days missed for severe attacks.

Acknowledgements

- The authors thank Emily B. Johnson and Sabrina D. Johnson for their assistance with data collection and analysis.

Disclosure

- This study was sponsored by KalVista Pharmaceuticals, Inc. SC is an employee of KalVista Pharmaceuticals, Inc. No authors received compensation for their involvement in this research.

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs

Table 2. Work/School Absenteeism Due to HAE

Figure 1. Maximum Annual Patient Indirect Costs

Figure 2. Annual Caregiver Indirect Costs