

# A Systematic Review of Healthcare Resource Utilization and Direct Medical Costs in Hereditary Angioedema

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## Background

- Hereditary angioedema (HAE) is a rare, genetic disease characterized by debilitating swelling episodes in various parts of the body<sup>1</sup>
- HAE is associated with substantial and multifaceted burden for patients, caregivers, health systems<sup>2</sup>
- While previous literature has documented the economic impact of HAE on direct costs, productivity, and other indirect costs, no systematic literature reviews (SLRs) to date on this topic have been published
- As the HAE treatment landscape evolves, there is a need to better understand the economic value of HAE treatments, to inform decisions as well as to improve disease management, patient satisfaction, and quality of life

## Methods

- We conducted an SLR on economic outcomes, including healthcare resource utilization (HRU) and 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

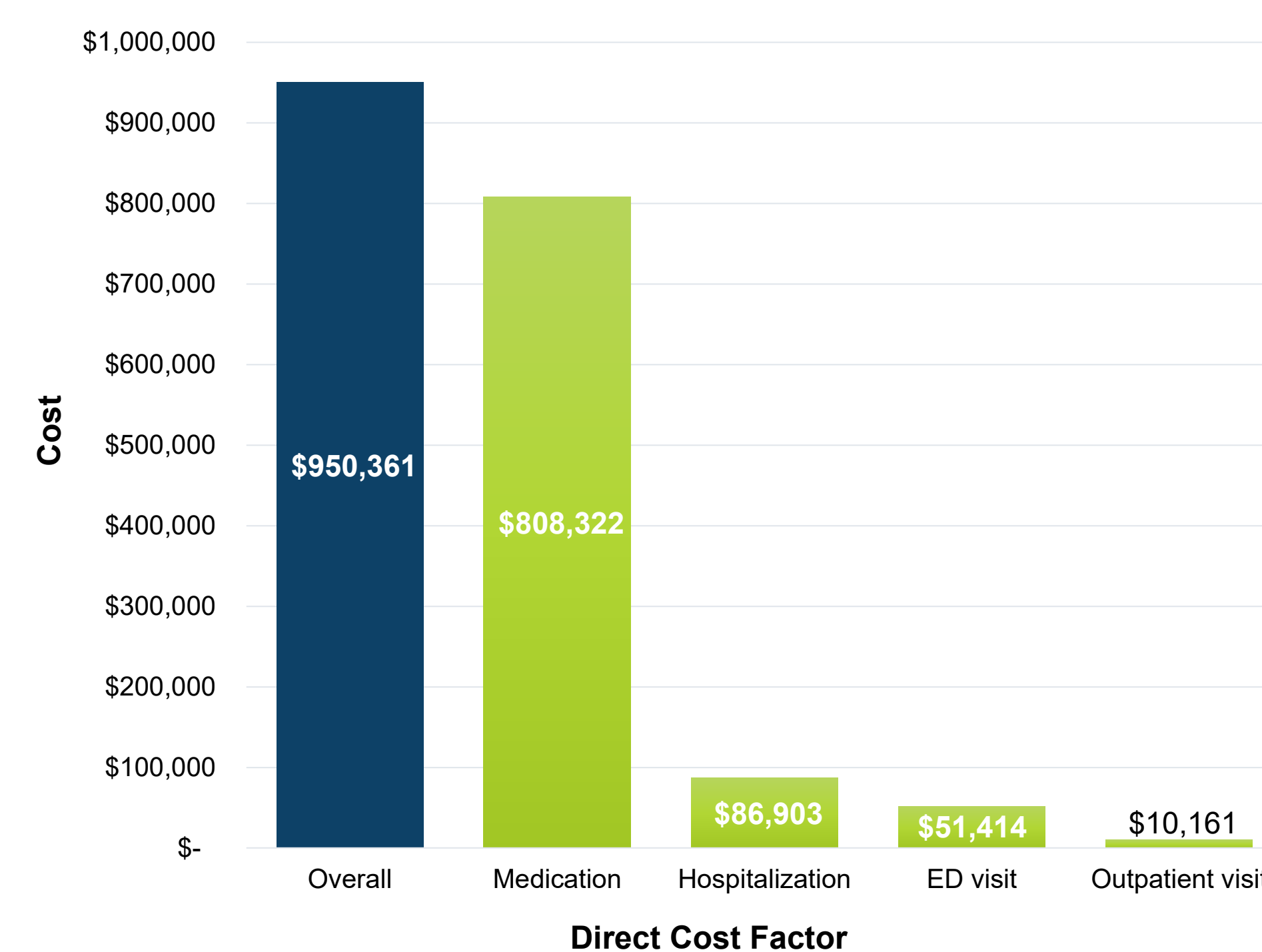
## References

- Radjicic C, Riedl MA, Craig TJ, et al. Patient perspectives on the treatment burden of injectable medication for hereditary angioedema. *Allergy Asthma Proc.* May 1 2021;42(3):S4-S10. doi:10.2500/aap.2021.42.210025
- Javaud, N., Bouillet, L., Rabetrano, H., Bitoun, A., Launay, D., Lapostolle, F., Reuter, P. G., Martin, L., Vicaut, E., Fain, O., Adnet, F., Durand-Zaleski, I., & SOS-HAE Collaborative Study Group (2019). Hereditary angioedema: Clinical presentation and socioeconomic cost of 200 French patients. *The journal of allergy and clinical immunology. In practice*, 7(1), 328–330. <https://doi.org/10.1016/j.jaip.2018.05.036>
- Castaldo, A. J., Jervelund, C., Corcoran, D., Boysen, H. B., Christiansen, S. C., & Zuraw, B. L. (2021). Assessing the cost and quality-of-life impact of on-demand-only medications for adults with hereditary angioedema. *Allergy and asthma proceedings*, 42(2), 108–117. <https://doi.org/10.2500/aap.2021.42.200127>
- K. Bowen, MD, MBA; B. Sahli, PharmD; and P.P. Gleason, PharmD, A.A. (2020 April). Hereditary Angioedema (HAE) Real-World Prophylactic and On-demand Treatment Cost in a 15 Million Commercially Insured Population: Comparison of C-1 Inhibitor (Haegarda®) versus Lanadelumab (Takhzyro®) Treated Members. [Poster Presentation].
- Wilson, D. A., Bork, K., Shea, E. P., Rentz, A. M., Blaustein, M. B., & Pullman, W. E. (2010). Economic costs associated with acute attacks and long-term management of hereditary angioedema. *Annals of allergy, asthma & immunology* : official publication of the American College of Allergy, Asthma, & Immunology, 104(4), 314–320. <https://doi.org/10.1016/j.anaai.2010.01.024>
- Riedl, M. A., Banerji, A., Manning, M. E., Burrell, E., Joshi, N., Patel, D., Machnig, T., Tai, M. H., & Watson, D. J. (2019). Treatment patterns and healthcare resource utilization among patients with hereditary angioedema in the United States. *Orphanet journal of rare diseases*, 13(1), 180. <https://doi.org/10.1186/s13023-018-0922-3>
- S. E. Vande Walle, C. I. Stamer, P. P. Gleason, A.A. (2018, April). Hereditary Angioedema: A Comprehensive Integrated Medical and Pharmacy Claims Analysis of Utilization and Costs Among 15 Million Commercially Insured Members. [Poster presentation].
- Ohsawa I, Honda D, Nagamachi S, et al. Clinical manifestations, diagnosis, and treatment of hereditary angioedema: survey data from 94 physicians in Japan. *Annals of Allergy, Asthma & Immunology* : Official Publication of the American College of Allergy, Asthma, & Immunology. 2015 Jun;114(6):492-498. DOI: 10.1016/j.anaai.2015.03.010. PMID: 25872948.
- Banerji, A., Davis, K. H., Brown, T. M., Hollis, K., Hunter, S. M., Long, J., Jain, G., & Devercelli, G. (2020). Patient-reported burden of hereditary angioedema: findings from a patient survey in the United States. *Annals of allergy, asthma & immunology* : official publication of the American College of Allergy, Asthma, & Immunology, 124(6), 600–607. <https://doi.org/10.1016/j.anaai.2020.02.018>
- Mendivil, J., Murphy, R., de la Cruz, M., Janssen, E., Boysen, H. B., Jain, G., Ayyören-Pürsün, E., Hirji, I., & Devercelli, G. (2021). Clinical characteristics and burden of illness in patients with hereditary angioedema: findings from a multinational patient survey. *Orphanet journal of rare diseases*, 16(1), 94. <https://doi.org/10.1186/s13023-021-01717-4>
- Aggarwal S., Kumar S., Topaloglu O. (2018). Trends in Hospitalization Length of Stay and Costs in Patients with Hereditary Angioedema: Analysis of US National In-Patient Data for 2015. <https://doi.org/10.1016/j.jval.2018.04.1719>

## Results

- We identified 66 studies. The majority of studies were observational (64%) and peer-reviewed (59%), and the most common study location was the United States (42%) (**Table 1**)
- Among 53 peer-reviewed and congress proceedings, 79% assessed HRU and direct costs in HAE
- Findings in the HAE publications revealed that total annual direct medical costs reached up to \$950,361 per patient, with medication accounting for the majority total direct costs (up to 85%, or \$808,322)<sup>3</sup> (**Figure 1**)
- Prophylaxis treatment was found to cost 2.42 times that of on-demand treatment only<sup>3,4</sup>

**Figure 1. Annual Medical Costs and Drivers Associated with HAE<sup>3,5</sup>**

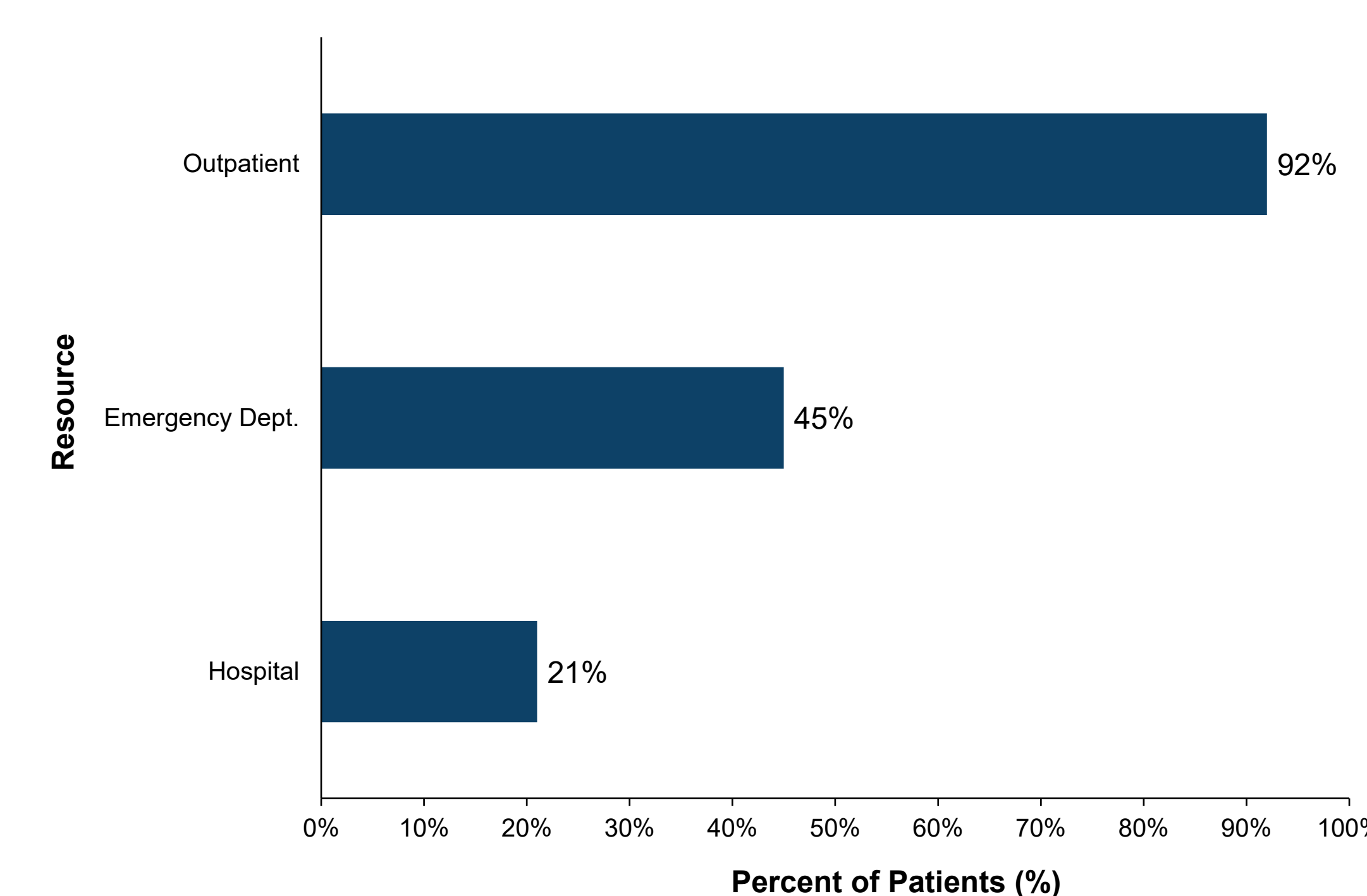


**Table 1. SLR Study and Sample Characteristics**

Characteristic	n (%)
<b>Total Number of Publications</b>	66 (100)
<b>Sample Size, number of patients</b>	
Minimum	1
Maximum	737
<b>Publication Type</b>	
Peer-Reviewed Research	39 (59.1)
Conference Proceeding	14 (21.2)
Economic Report	13 (19.7)
<b>Study Design</b>	
Observational	42 (63.6)
Economic Analysis/Modeling	23 (34.8)
RCT	1 (1.5)
<b>Study Location</b>	
United States	28 (42.4)
Europe	25 (37.9)
Other	13 (19.7)
<b>HAE Treatment Type, Studies*</b>	
On-Demand Treatment	20
Prophylactic Treatment	15

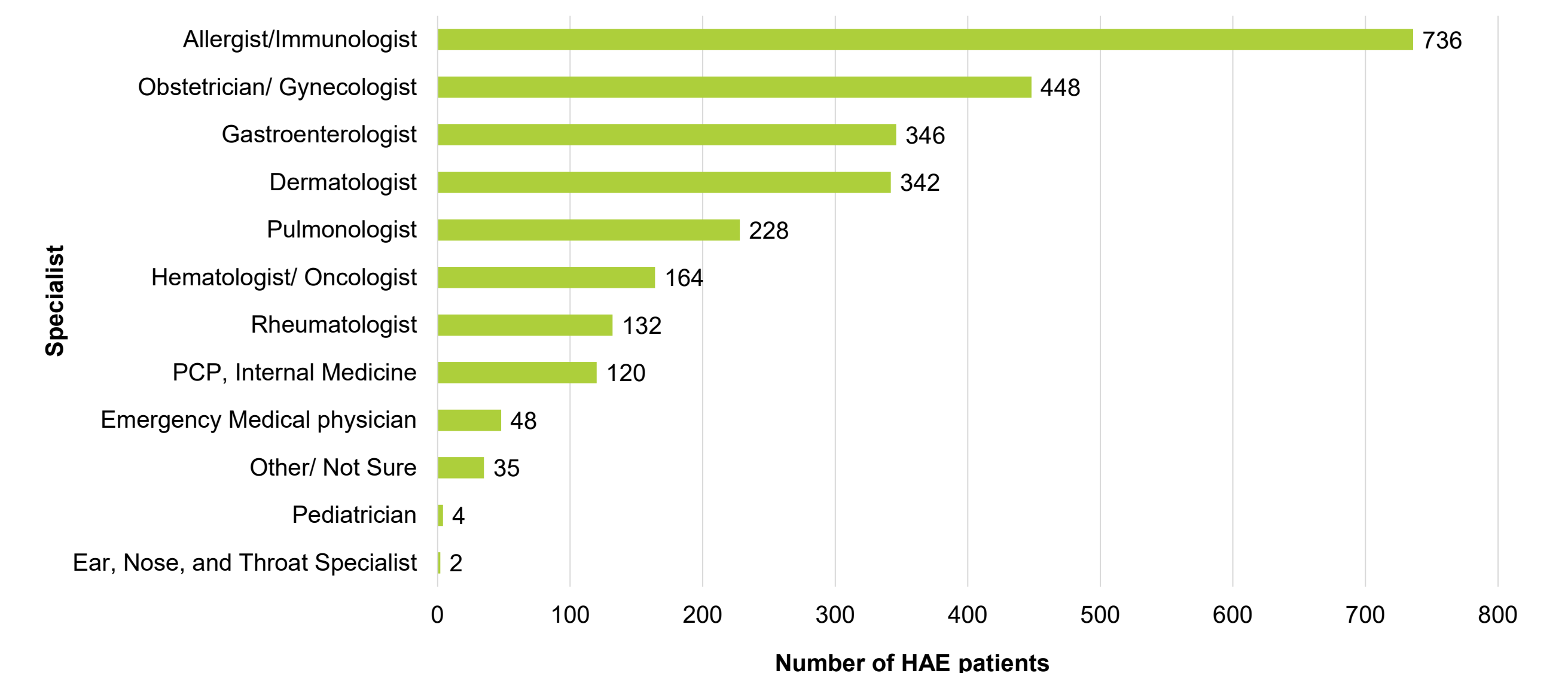
\*32 studies assessed an HAE therapy; some assessed both on-demand and prophylactic treatments

**Figure 2. Percent of Patients Requiring at Least 1 Resource Visit Per Year<sup>6,7,8</sup>**



- For HRU outcomes, 92% of HAE patients using prophylactic and/or on-demand therapy required at least one outpatient visit,<sup>6</sup> 45% required at least one emergency department (ED) visit,<sup>7</sup> and 21% required at least one inpatient stay annually<sup>8</sup> (**Figure 2**)
- Patients required between 2.7 – 3.7 outpatient visits,<sup>9</sup> 1.94 ED visits, and 1.04 inpatient visits annually<sup>10</sup> with a length of stay (LOS) per admission of up to 8 days<sup>11</sup>
- Most HAE patients required specialist office visits, where the most common type of medical profession seen was an allergist/immunologist (28.3%)<sup>5,10</sup> (**Figure 3**)

**Figure 3. Medical Professionals Typically Seen by Patients with HAE<sup>4,9</sup>**



## Conclusion

- This SLR found that, despite the emergence of new HAE therapies in the past decade, individuals with HAE still experience high HRU, regardless of using prophylaxis
- We found direct costs to be largely driven by medication costs, with prophylactic therapies costing more than twice that of on-demand therapies
- As the HAE treatment landscape evolves, there is opportunity to introduce patient-centered treatment options that improve disease control, thereby minimizing HRU and costs, as well as enhance patient satisfaction and quality of life

## Acknowledgements

The authors thank Alkemi LLC contributors Betsy J. Lahue and Laloo A. Perriello, who assisted with abstract writing and editing.

## 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.



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