

Burden of Untreated Hereditary Angioedema Attacks Impact on Social, Mental, and Physical Health

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Background

- Hereditary angioedema (HAE) is a rare genetic disease associated with unpredictable, painful, and debilitating attacks of tissue swelling in various locations of the body that can be life-threatening depending on the location(s) affected
- Global HAE treatment guidelines recommend that people living with HAE should consider treating all attacks early upon recognizing them in order to reduce morbidity and mortality¹⁻³
- Despite availability of on-demand therapies, patients do not universally treat attacks⁴
- We examined the impact of the patients' last untreated attack on social, mental, and physical health

1. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline. *Allergy, Asthma & Clinical Immunology*. 2019;11/25 2019;15(1):72. doi:10.1186/s13223-019-0376-8

2. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3. doi:10.1016/j.jaip.2020.08.046

3. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAAACI guideline for the management of hereditary angioedema-The 2021 revision and update. *Allergy*. Jul 2022;77(7):1961-1990. doi:10.1111/all.15214

4. Radojicic, Cristine et al. Patient Perspectives On Early Use Of On-demand Treatment For Hereditary Angioedema (HAE) Attacks to Reduce Severity and Duration. *Journal of Allergy and Clinical Immunology*, Volume 151, Issue 2, AB143

Methods

- The US Hereditary Angioedema Association recruited participants with Type 1 or 2 HAE between April and June 2023
 - Recruitment was stratified to include approximately 50% of participants taking on-demand only and 50% receiving nonandrogen long-term prophylaxis (LTP) plus on-demand, at the time of their last treated attack
- Participants completed a 20-minute, self-reported, online survey that inquired about their last untreated HAE attack
- Participants had to be at least 18 years old and had at least 1 untreated attack in the past 3 months

Methods: Quality of Life Assessments



- Physical and social QoL was assessed using a modified version of the **Hereditary Angioedema Quality of Life Questionnaire (HAEA-QoLv2)**
 - **Physical impact of HAE** (energy level, sleep, and activity level)
 - Range from 1 (not at all) to 4 (severe/very severe)
 - **Social impact of HAE** (ex. felt embarrassed, felt socially isolated)
 - Range from 1 (strongly disagree) to 5 (strongly agree)
- **EuroQol Five-Dimensions Five-Levels (EQ-5D-5L)**, a self-report survey, was used to assess physical and mental QoL "today" (i.e., current QoL) and at the time of the last untreated attack
 - **EQ-5D-5L Index Score** = QoL composite of items across 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
 - Range from -0.59 (lowest possible health state) to 1 (best possible health state)
 - **Visual Analogue Score (VAS)** = Single-item, self-assessment of overall health status
 - Range from 0 ("worst imaginable health state") to 100 ("best imaginable health state")

Respondent Characteristics

	Total (n=20)	On-Demand Treatment Only (n=9)	On-Demand Treatment + LTP (n=11)
Current Age (years) Mean (SD)	39 (14.6)	45 (14.2)	33 (13.1)
HAE Type			
Type 1	80%	89%	73%
Type 2	20%	11%	27%
Gender			
Female	75%	67%	82%
Race / Ethnicity			
White	87%	89%	79%
Hispanic or Latino	9%	8%	14%
Black/African American	3%	3%	7%
American Indian/Alaskan Native	2%	0%	14%
Asian	3%	4%	0%
Other	1%	1%	0%

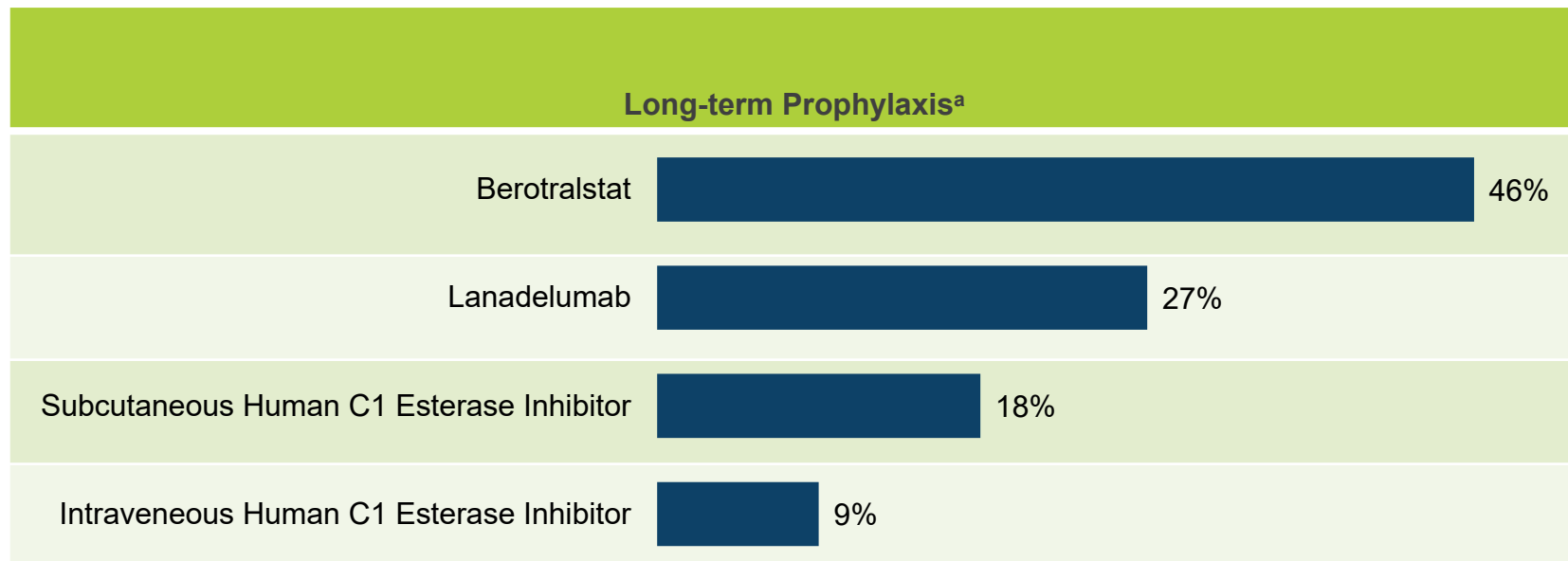
- On-demand treatment only participants and on-demand + LTP participants both reported having an average of 10 attacks over the past year
 - On-demand treatment only participants treated 22% of attacks
 - On-demand + LTP participants treated 64% of attacks

Prescribed On-demand Treatment at the Time of Last Untreated Attack

On-Demand Therapy		On-demand Treatment Only (n=9)	On-demand Treatment + LTP (n=11)
Icatibant	 75%	78%	73%
Plasma Derived C1 Esterase Inhibitor	 30%	22%	36%

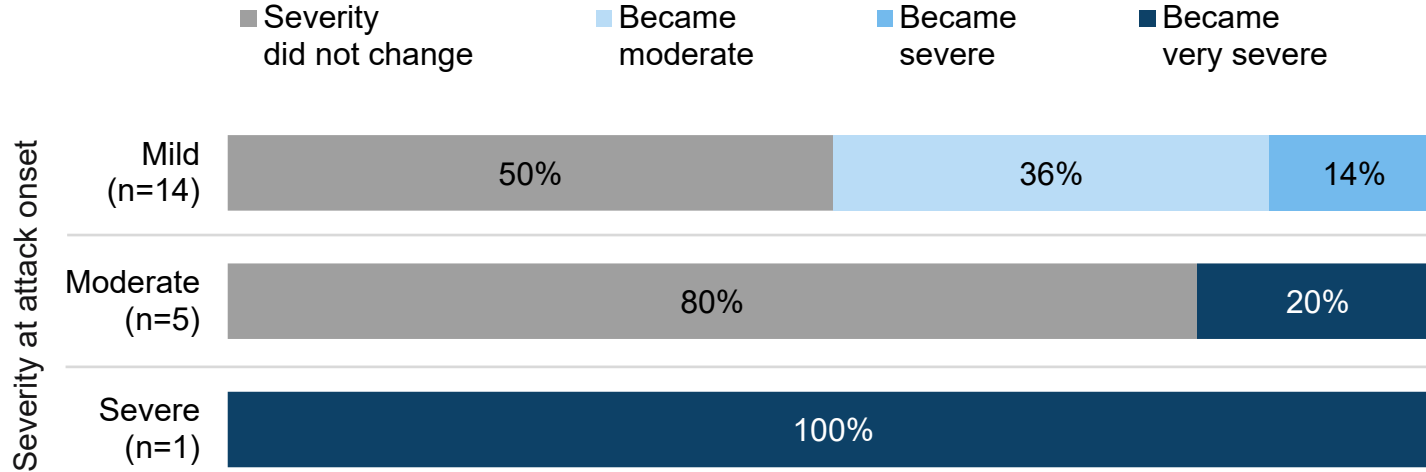
- 55% reported self-administering on-demand treatment for their attacks

Long-Term Prophylaxis at Time of Last Untreated Attack



^an = 11

Progression of Untreated Attack Severity



Q: When the attack was at its most severe, how would you describe it?

- 14 participants (70%) described their last untreated attack as mild at treatment and of these, 7 participants (50%) progressed to moderate/severe
- Severity progressed for 45% of all attacks, either becoming moderate, severe, or very severe

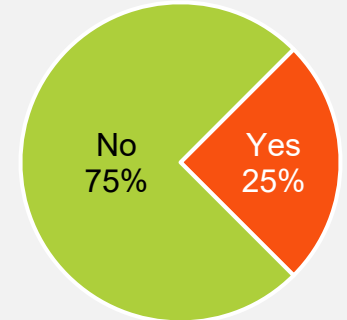
Initial Site of Attack and Symptom Spread

Initial Site of Attack

On-Demand Treatment Only (n=9) On-Demand Treatment + LTP (n=11)

Initial Site of Attack	Percentage	On-Demand Treatment Only (n=9)	On-Demand Treatment + LTP (n=11)
Peripheral / Trunk (net)	55%	78%	36%
Peripheral (e.g., hands, legs, feet, etc.)	45%	67%	27%
Trunk	10%	11%	9%
Abdominal/stomach	20%	11%	27%
Face/tongue	15%	11%	18%
Throat	5%	--	9%
Other	5%	--	9%

Symptoms Spread to Another Site (n=20)

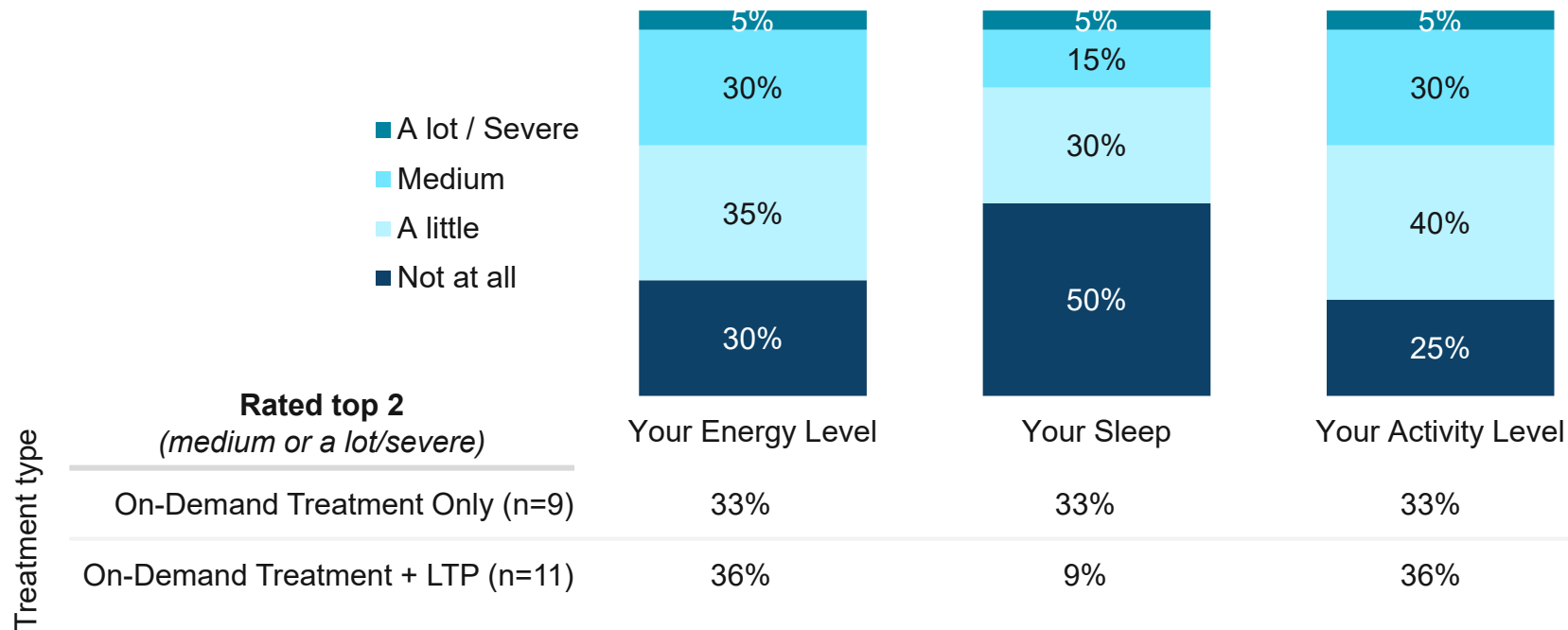


% yes

On-Demand Treatment (n=9)	22%
Long-Term Prophylaxis (n=11)	27%

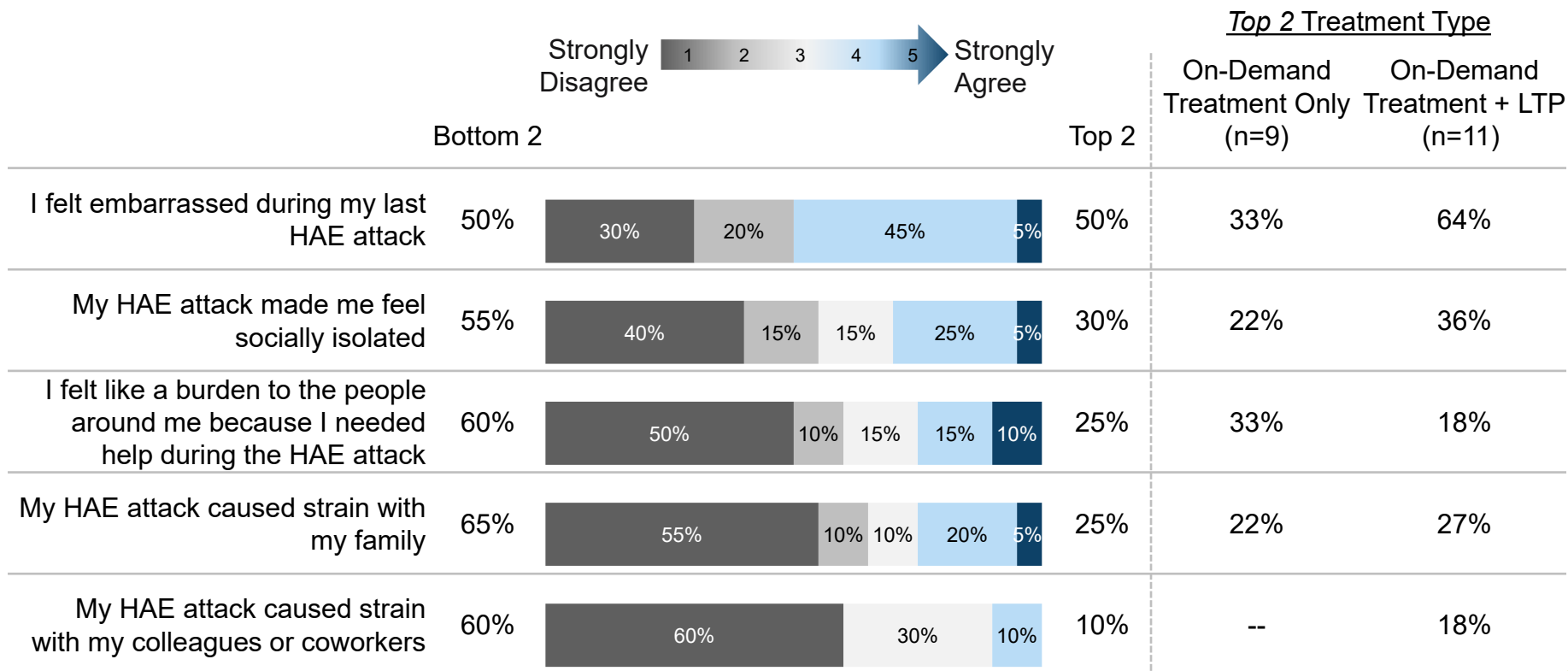
- One in five patients reported that their last untreated attack affected their face/tongue (15%) or throat (5%)
- Five attacks (25%) spread to other locations, including 1 to the larynx and 1 to the face

HAE-related Quality of Life During Untreated Attacks: Physical Health Impact

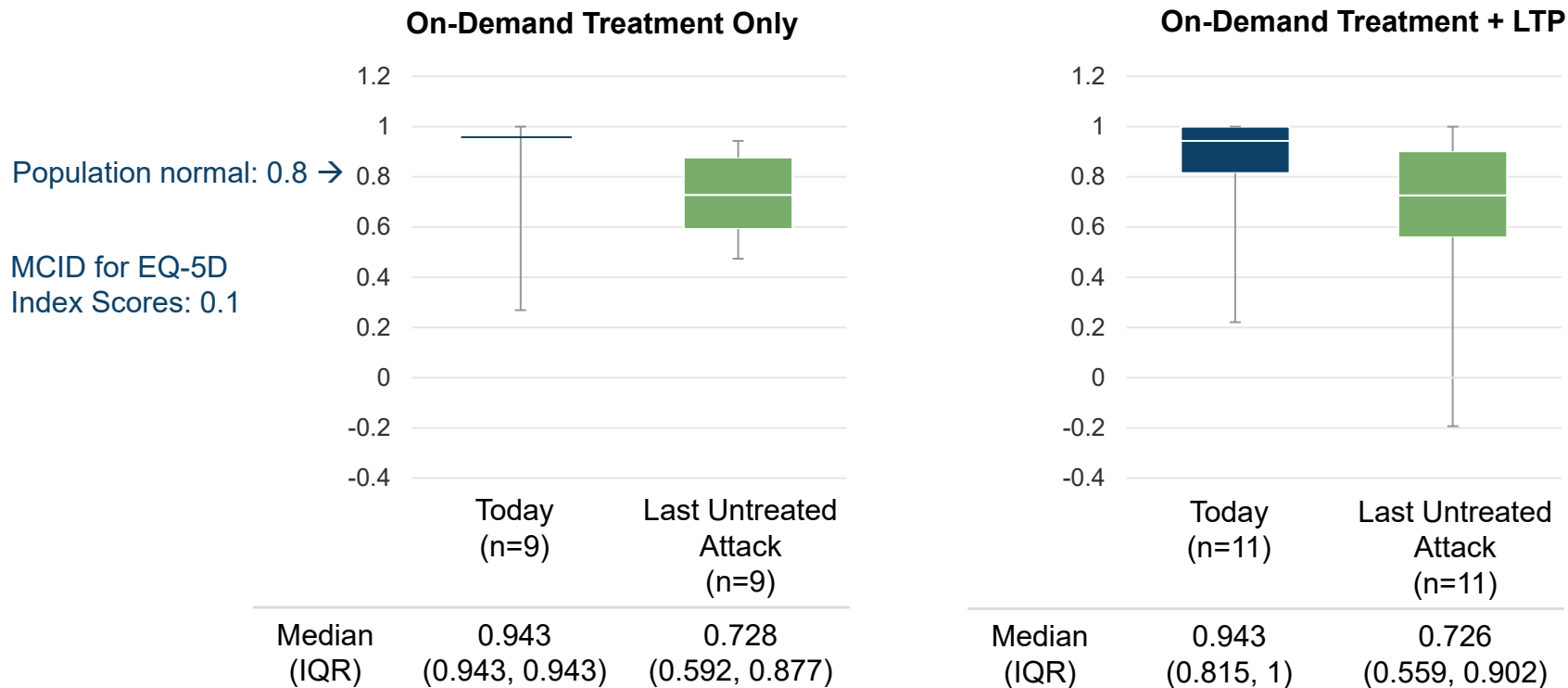


- At least 50% of participants reported that their last untreated attack impacted their energy levels, sleep, or activity levels at least “a little”

HAE-related Quality of Life During Untreated Attacks: Social Health Impact

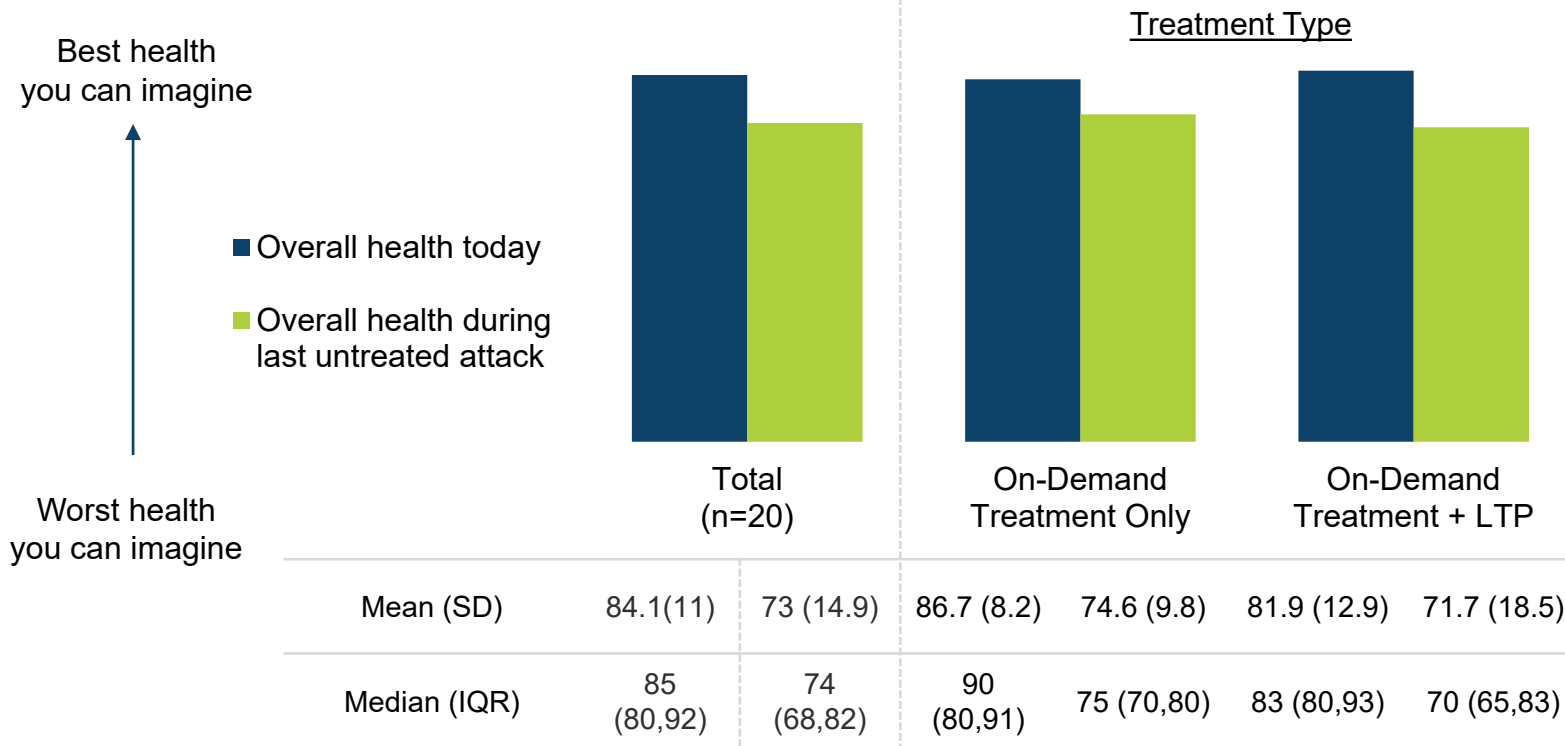


Physical and Mental Quality of Life (EQ-5D Index Scores) Today and During the Last Untreated Attack by Treatment



- QOL index scores decrease as attack severity increased from mild (median 0.736) to moderate (median 0.622)

EQ-5D-5L VAS (General Health) Scores for Current and Last Treated Attack



- General health scores were worse at the time of attack for both treatment groups

Conclusions

- HAE patients receiving on-demand only and those also taking LTP reported that untreated attacks:
 - often progressed in severity
 - migrated to other locations, including the larynx
 - were associated with negative impact on both social and physical health
- Decreased QOL and general health scores were reported during the untreated attacks
- Results emphasize the need for greater education on the implications of not treating HAE attacks and support guidelines that all attacks should be considered for treatment