Exploring the Quality of Life Benefits of Subcutaneous C1-Inhibitor (C1-INH) Replacement Therapy Using Qualitative Research Methods

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INTRODUCTION

- With the advent of highly effective therapies for the management of hereditary angioedema (HAE), treatment guidelines increasingly emphasize improved health-related quality of life (HRQoL) as an important aspect of disease management[1-3]
- Accordingly, there have been numerous studies evaluating HRQoL quantitatively in patients with HAE using validated HRQoL questionnaires[4]
- In contrast, qualitative research is designed to elicit information from patients using one-on-one interviews in a semi-structured, open-ended question format to understand patient experiences and gain insights on the "why" of these experiences, eg, "Why was an experience positive or negative? Why do you feel this way?"
- Prior qualitative research in a European HAE population[5] evaluated issues related to the burden of illness; however, there have been no qualitative studies addressing the impact of routine prophylaxis on HRQoL
- Routine prevention with subcutaneous C1-inhibitor (C1-INH[SC]; HAEGARDA®; CSL Behring) has been shown in clinical trials to produce measurable improvements in HRQoL as compared to placebo using existing HRQoL instruments (EQ-5D, Hospital Anxiety and Depression Scale, and Work Productivity and Activity Impairment)[6]
- We conducted a qualitative research study to explore in-depth with patients the reasons for improvements in HRQoL while using C1-INH(SC) replacement therapy and to develop a better understanding of treatment attributes and benefits most important to patients

METHODS

Design
- Non-interventional, qualitative research study conducted at four US sites
- The study was exempted from ethics approval (Chesapeake IRB)
- Written informed consent was given by all patients

Study population
- Patients were recruited by clinicians treating patients with C1-INH(SC) for HAE
- Eligibility criteria:
  - ≥18 years of age
  - Diagnosis of HAE
  - Native English speaker
  - Current use of C1-INH(SC) replacement therapy for ≥3 consecutive months
- Key exclusion criteria:
  - Physical/mental conditions or substance abuse problems that might limit or impede the patient's ability to participate in the study
  - Patients currently enrolled in a clinical trial or an interventional study

Data collection
- Each telephone interview (approximately 60 minutes) was conducted by an interviewer from ICON plc trained in qualitative interviewing
- Semi-structured interview techniques were used to collect spontaneously reported information and information prompted by probing if not spontaneously reported but nonetheless relevant to study objectives
- The interviews were audio recorded with participants' permission, transcribed and anonymized

Data analysis
- Qualitative analyses were conducted on all transcripts by sorting quotes into concepts using thematic analysis methods based on grounded theory principles[7]
- Concept coding was carried out using Atlas.ti software, version 8.0
- Concepts expressed by ≥5 patients were retained for the conceptual models
- Two conceptual models were developed:
  - Concepts and themes pertaining to impact of HAE symptom relief on HRQoL
  - Opinions about C1-INH(SC), compared to past HAE treatments

RESULTS

Demographics
- The study sample included 14 patients (**Table 1**)

Table 1. Patient demographics and HAE treatment characteristics

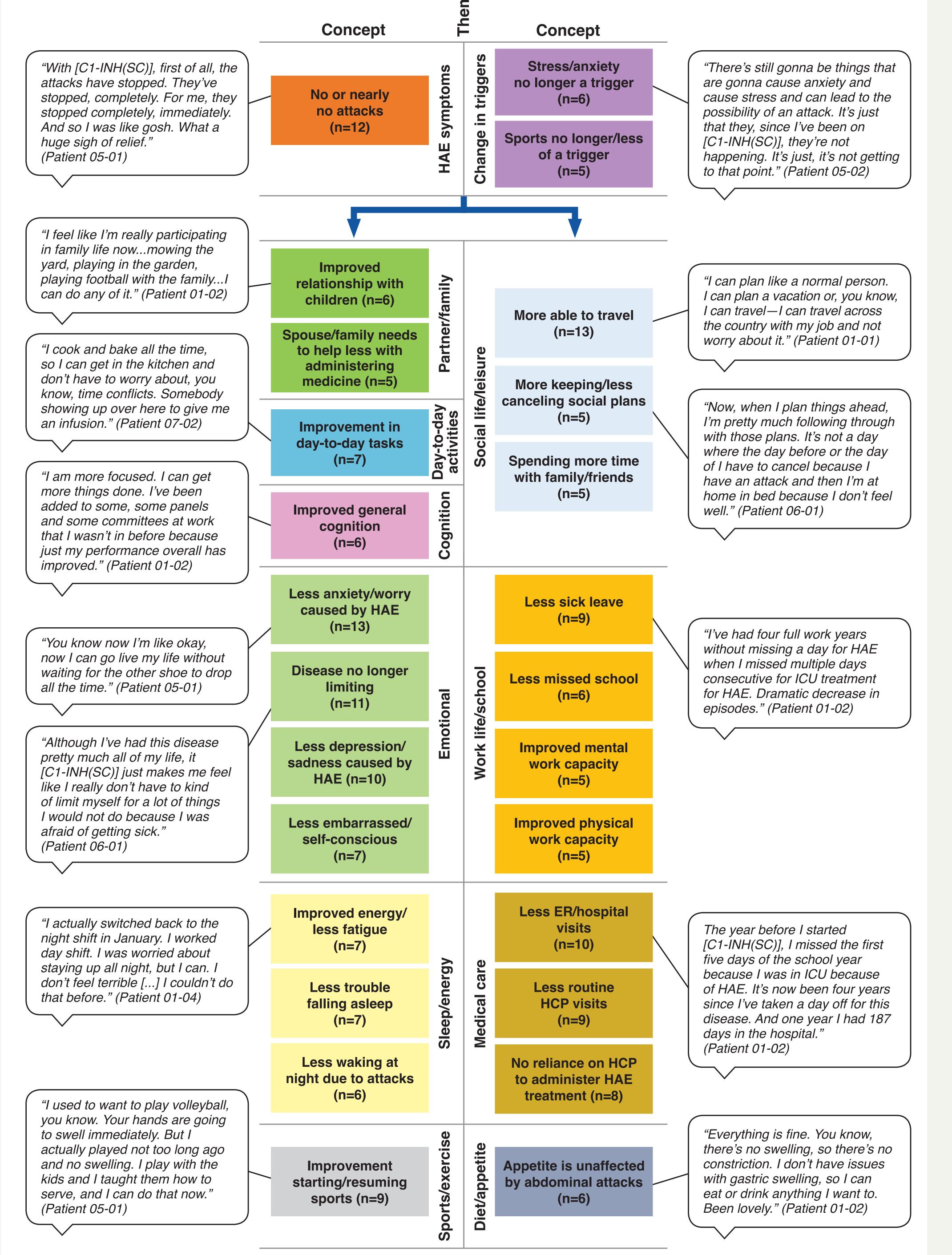|	N=14
Age, years, mean (range)	47.5 (28–72)
Gender, female, n (%)	9 (64.3)
Race, n (%)	
White	13 (92.9)
Black	1 (7.1)
Year of HAE diagnosis, mean (range)	1987 (1957-2012)
Employment status, n (%)	
Full time	8 (57.1)
Part time	2 (14.3)
Retired	2 (14.3)
Full-time parent	1 (7.1)
Unemployed due to HAE	1 (7.1)
Prior HAE prophylaxis, n (%)	
Plasma-derived C1-INH(IV)	9 (57.1)
Androgens	2[a] (14.3)
No long-term prophylaxis	2 (14.3)
Unknown	1 (7.1)
Current on-demand treatment, n (%)	
Icatibant only	9 (64.3)
Icatibant and plasma-derived C1-INH(IV)	2 (14.3)
Icatibant and recombinant C1-INH(IV)	1 (7.1)
Plasma-derived C1-INH(IV) only	1 (7.1)
Recombinant C1-INH(IV) only	1 (7.1)

[a]1-stanozolol, 1-danazol

Interview findings
- **Figure 1** presents concepts and themes relating to the impact on HRQoL of HAE symptom relief that were identified within 5 or more of the 14 patient interviews
- **Figure 2** presents concepts and themes relating to feelings about C1-INH(SC) use specifically that were identified within 5 or more of the 14 patient interviews
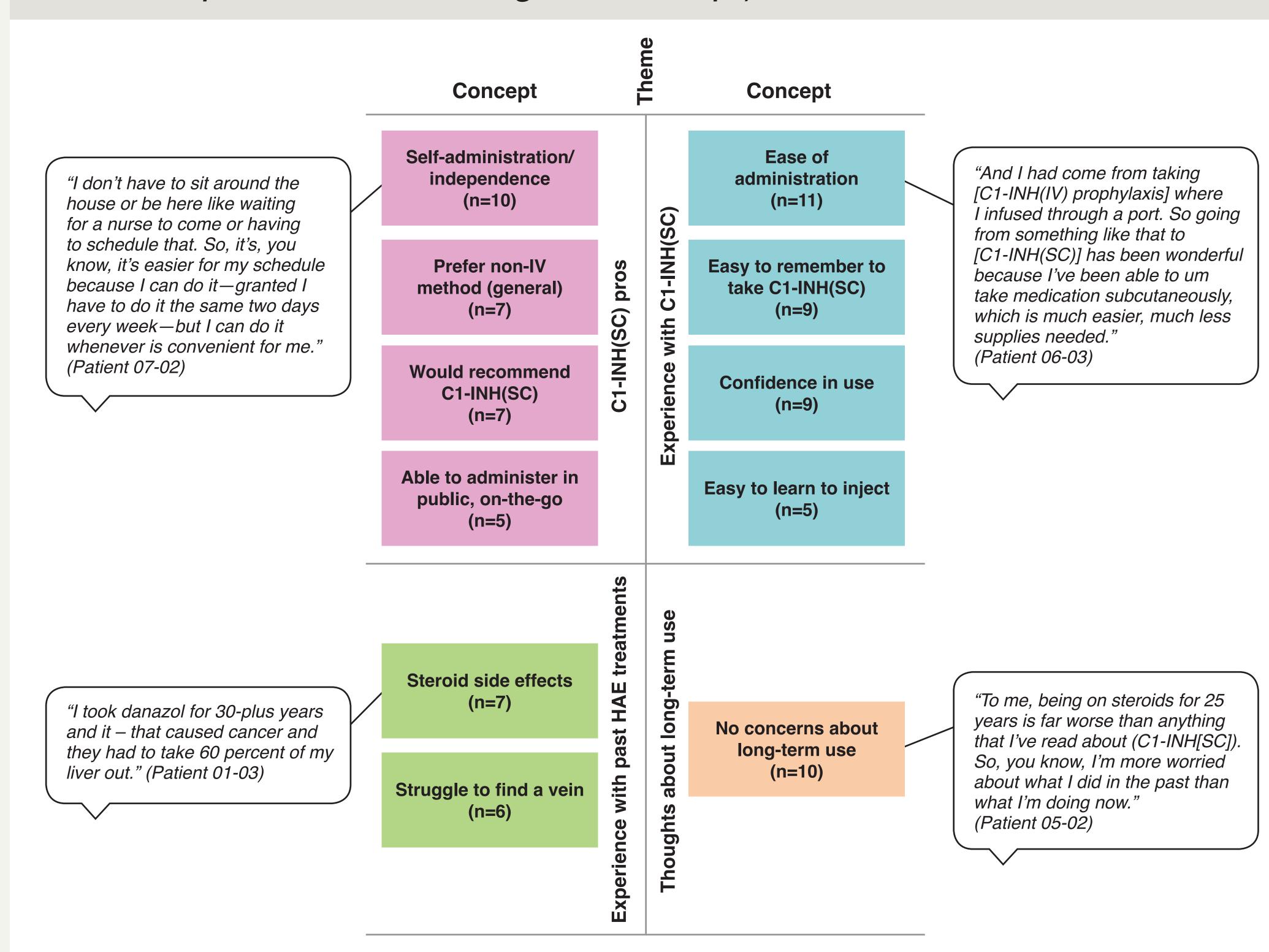

Figure 1. Concepts[a] and themes pertaining to impacts of HAE symptom relief on HRQoL identified from patient interviews and sample illustrative quotes (n=number of patients mentioning the concept)

[a]Concepts expressed in at least 5 patient interviews

Figure 2. Patient opinions and experience with C1-INH(SC) replacement therapy; concepts and themes that emerged from interviews and sample illustrative quotes (n=number of patients mentioning the concept)

STUDY LIMITATIONS
- Racially homogenous sample
- Patient invitation was at the discretion of the investigators rather than by random selection, but random selection is not typically used for qualitative research

SUMMARY AND CONCLUSIONS
- This study is the first qualitative research project to identify concepts important to patients with HAE when using routine C1-INH(SC) replacement
- The results complement prior HRQoL research and provide in-depth insight on reasons for improved HRQoL shown with HRQoL instruments in C1-INH(SC) clinical trials
- In the majority of interviews (>75%), patients mentioned benefits of ease of administration of C1-INH(SC), an improved ability to travel, a reduction in HAE-related anxiety/worry, and administration without the assistance of others
- 12 of 14 patients interviewed indicated having no or almost no HAE attacks while using C1-INH(SC)
- Patients expressed increased confidence and a sense of independence, optimism, and freedom to live their lives as they chose rather than having their lives limited by HAE

References: 1. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. Allergy. 2018;73(8):1575-1596. **2.** Craig T, Aygören-Pürsün E, Bork K, et al. WAO guideline for the management of hereditary angioedema. WAO Journal. 2012;5(12):182-199. **3.** Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. J Allergy Clin Immunol Pract. 2013;1(5):458-467. **4.** Caballero T, Prior N. Burden of illness and quality-of-life measures in angioedema conditions. Immunol Allergy Clin North Am. 2017;37(3):597-616. **5.** Bygum A, Aygören-Pürsün E, Beusterien K, et al. Burden of illness in hereditary angioedema: a conceptual model. Acta Derm Venereol. 2015;95(6):706-710. **6.** Lumry WR, Craig T, Zuraw B, et al. Health-related quality of life with subcutaneous C1-inhibitor for prevention of attacks of hereditary angioedema. J Allergy Clin Immunol Pract. 2018;6(5):1733-1741.e3. **7.** Charmaz K. Grounded Theory in the 21st century. 3rd ed. Thousand Oaks, CA: Sage; 2005.