TIME TRADE-OFF UTILITIES FOR HEREDITARY ANGIOEDEMA HEALTH AND CAREGIVER STATES

PHARMACOECONOMICS – OPEN

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Funding: This study was funded by BioCryst Pharmaceuticals, Inc. Medical writing assistance was provided by Emma Conran, Porterhouse Medical Group, and funded by BioCryst Pharmaceuticals, Inc., in line with GPP3 guidelines.

Conflicts of Interest / Competing Interests: Siu Hing Lo is an employee of Acaster Lloyd Consulting Ltd. Acaster Andrew Lloyd is an employee and shareholder of Acaster Lloyd Consulting Ltd. Acaster Lloyd Consulting Ltd were commissioned to conduct the study by BioCryst Pharmaceuticals, Inc. the study sponsor. Shuayb Elkhalifa has previously received consulting fees from BioCryst Pharmaceuticals, Inc that were not related to this manuscript. Zlatko Sisic is an employee and shareholder of BioCryst Pharmaceuticals, Inc. Floortje E. van Nooten was an employee and shareholder of BioCryst Pharmaceuticals, Inc. during the conduct of this study.

Online Resource 1 – Qualitative interview guide

MODERATOR INSTRUCTIONS – DO NOT READ TO PARTICIPANT

All moderator instructions in the interview guide are in red.

All probes in the interview guide are in grey. Only use probes once the participant has had an opportunity to answer your questions unprompted.

There are four subgroups of participants:

1. **ADULT PATIENTS: adult HAE patients aged 18+ who are not caregivers**
2. **ADOLESCENT PATIENTS: adolescent HAE patients aged between 12–17 who are not caregivers**
3. **CAREGIVERS: caregivers of someone with HAE who are not HAE patients themselves**
4. **PATIENT-CAREGIVERS: HAE patients who also care for someone else with HAE (aged 18+ or 12–17)**

Each participant subgroup has some probes and questions specific to their subgroup.

Throughout the interview, only ask questions / use probes where appropriate, considering what has already been discussed.

If the participant has reported use of berotralstat (in the background questionnaire), make notes on any adverse events or product complaints and collect further detail at the end of the interview.

Introduction – all subgroups

Good (morning/afternoon/evening), introduce yourself.

Thank you for taking the time to participate in this interview. The purpose of this study is to better understand the impact of hereditary angioedema (HAE) on people's lives.

The interview will last approximately **[ALL EXCEPT PATIENT-CAREGIVERS:** one hour / **[PATIENT-CAREGIVERS:** 75 minutes**]**. Everything you say will be kept confidential, and only de-identified data will be shared or published beyond the study team.

Some questions may also seem repetitive, but we want to make sure that we do not miss anything important. In the interest of time, I may need to interrupt you sometimes to move on to the next question. This is not because we are not interested in what you are saying.

Our conversation will be recorded so that we can accurately represent what you are saying during the discussion in our research report. We will now begin recording. OK? Once the recording starts, I will repeat this question for the recording.

If the participant does not wish for the interview to be recorded, the interviewer should not proceed with the interview.

START RECORDING

Today is [DATE]. This is participant ID [INSERT ID NUMBER].

I would like to clarify a few points before we begin:

- I am not a medical doctor, so I am not qualified to give medical advice. If you have any questions about HAE as a result of our conversation today, I advise you to follow up with your regular doctor.
- There are no right or wrong answers; we understand that everyone has different experiences and we are interested in what you have to say.

- Please speak loudly enough to be heard for the recording.
- Do you have any questions before we begin?

[ADULT AND ADOLESCENT PATIENTS] This interview is divided into two sections. In the first section, I will ask you a few background questions. I will then ask about your HAE symptoms and treatment and how your HAE impacts your life.

[CAREGIVERS] This interview is divided into three sections. In the first section, I will ask you a few background questions. I will then ask about the HAE symptoms and treatment of the person(s) you care for. Finally, I will be asking about how HAE impacts your own life.

[PATIENT-CAREGIVERS] This interview is divided into four sections. In the first section, I will ask you a few background questions. I will then ask about your HAE symptoms and treatment and briefly about the HAE symptoms and treatment of the person(s) you care for. Next, I will ask how your HAE impacts your own life. Finally, I would like to learn more about your experience of caring for someone with the same condition.

Section A: Background – all subgroups

To start off, I would like to get an idea about who you are and your life.

- Please could you tell us about yourself?
  Age, work/education, hobbies, family
- *If not mentioned*, can you tell me who else is in your family?
  ADULT PATIENTS: caregivers, children / other dependants, partner
  ADOLESCENT PATIENTS: caregivers, (other) parent, siblings
  CAREGIVERS: relationship to HAE patient, children, partner
  PATIENT-CAREGIVERS: relationship to HAE patient, children, partner
- Can you tell me a bit about your / the person(s) you care for's diagnosis?
  First symptoms; time to diagnosis; misdiagnosis and unnecessary treatments; family history of HAE

Section B.1: Patient symptoms and treatment I – adult patients, adolescent patients and patient-caregivers

- Tell me about a typical day for you with an attack.
  Tell me about a typical day for you without an attack.
  What is a good/bad day like, day from morning to evening, how do they feel?
- How often do you experience an attack?
  On average, how many attacks in the last 3 months?
- How long did your two most recent attacks last? Does it vary?
- Did you need to: a) stay at home; b) are you bedbound; c) spend time in hospital?
- How long did it take for you to recover?
  Variations between mild/moderate/severe attacks
- How typical were these two attacks of the attacks you have experienced in the last year?
- Tell me about your symptoms when you have an attack.
- Tell me about any symptoms just before an attack.
  Locations: abdomen, back, face, neck, throat, lower/upper extremities, genitals, skin; movement between sites
  Severity: asymptomatic, mild, moderate, severe or extremely severe
  Why do you rate it as 'X'?
  Temporal factors: how often, how long at the start, during, when recovering from an attack

IF ABDOMINAL SYMPTOMS:
  - Pain/cramping/discomfort, swelling/bloating/tightness
  - Vomiting/nausea, diarrhoea/bloating
  - Dehydration, constipation, loss of appetite

IF SKIN SYMPTOMS:
  - Pain/discomfort
  - Skin swelling, itching/burning/irritation, redness / tender skin / rash

IF RESPIRATORY SYMPTOMS:
  - Throat, tongue swelling
  - Voice change, difficulties breathing, swallowing

- Other symptoms?
- Tell me about anything that can trigger an attack.
  - **Emotional:** stress, anxiety, worry
  - **Physical:** increased activity/tiredness, difficulties sleeping, physical trauma/injury, illness/infection, surgery, change in medication, hormonal changes, genetics, pregnancy
  - **Other:** change in weather, limit food and drinks choices, unknown
- Tell me about anything you do to cope with the attack symptoms.
  Drinking fluids, medication, creams, loose clothes, sleep
- *If using medication*: do you always use medication when you have an attack?
- Tell me about any treatment you have or anything you do to manage your HAE.
  Self-treatment or hospital visit, type of medication, long-term/short-term use of prophylaxis: effectiveness, side effects, feelings: anxiety about medication, feeling in control of HAE
- **[ADULT PATIENTS ONLY]** If you can remember, what were your main symptoms in adolescence?
  Changes in symptom type, severity or duration: adolescence vs. adulthood

Section B.2: Patient symptoms and treatment II – caregivers and patient-caregivers

REPEAT SECTION FOR EVERY PERSON WITH HAE IN IMMEDIATE FAMILY THEY REGULARLY CARE FOR

- How often does the person you care for experience an attack?
  On average, how many attacks in the last 6 months?
- How long did their two most recent attacks last? Does it vary?
- Did they need to: a) stay at home; b) are they bedbound; c) spend time in hospital?
- How long did it take for them to recover?
  Variations between mild/moderate/severe attacks
- Tell me about the location and severity of their HAE attack symptoms.
- Tell me about any symptoms just before an attack.
  Locations: abdomen, back, face, neck, throat, lower/upper extremities, genitals, skin; movement between sites
  Severity: asymptomatic, mild, moderate, severe or extremely severe
- Please describe their life when they do not have an attack.
  Emotional well-being **– EXPLORE CHANGES IN WORRY OVER TIME WHEN ATTACK-FREE**
  If on prophylaxis: changes on vs. off prophylaxis when between attacks

Section C: Patient impacts – adult patients, adolescent patients, patient-caregivers only

I would now like to try to understand how living with HAE impacts your life: a) during an attack; b) between attacks / when you do not have an attack.

- Tell me about how HAE impacts you physically during an attack.

- Does it vary depending on how severe the attack is? Or where the attack is?
- Does HAE impact you physically when you do not have an attack? How?
    - Incapacitated/bedridden/hospitalised
    - **Mobility:** less active; can't walk, sit or stand; limited use of hands/feet
    - **Fatigue:** tiredness, difficulties concentrating
    - Difficulties eating and speaking
    - *If on prophylaxis*: changes in HAE impacts when between attacks; on vs. off prophylaxis
- Does HAE impact your daily activities when you have an attack? How?
- Does it vary depending on how severe the attack is? Or where the attack is?
- Does HAE impact your daily activities when you do not have an attack? How?
- How does your daily life compare to that of people without HAE?
    - Grooming/self-care
    - Education/work, days off school/work, limited productivity, limitations on career
    - *If adult*: driving
    - Housework: cooking, cleaning; *if applicable*: caring for children
    - Diet: limitations in food
    - Doing or not doing things to avoid attacks
    - *If on prophylaxis*: changes in HAE impacts when between attacks; on vs. off prophylaxis
- Does HAE impact your social life and relationships when you have an attack? How?
- Does it vary depending on how severe the attack is? Or where the attack is?
- Does HAE impact your social life and relationships when you do not have an attack? How?
- How does your social life compare to that of people without HAE?
    - **Activities:** travelling, sports, leisure, going out
    - **Relationships:** friends, family, romantic relationships; *if adult*: partner, having children
    - Doing or not doing things to avoid attacks
    - *If on prophylaxis*: changes in HAE impacts when between attacks; on vs. off prophylaxis
- Does HAE impact your emotional well-being when you have an attack? How? To what extent?
- Does it vary depending on how severe the attack is? Or where the attack is?
- Does HAE impact your emotional well-being when you do not have an attack? How? To what extent?
    - Fear/anxiety/stress/worry due to uncertainty of HAE or use of medication – **EXPLORE CHANGES OVER TIME WHEN ATTACK-FREE**
    - Feeling helpless
    - Anger/frustration
    - Depression / low mood
    - Confidence/self-esteem/ashamed/embarrassed
    - Hereditary nature of HAE
    - Lack of understanding
    - Being dependent
    - Impact of avoiding attacks on emotional well-being
    - No / mild / moderate / severe / extremely severe impact **– PROBE FOR SEVERITY OF IMPACT**
    - *If on prophylaxis*: changes in HAE impacts when between attacks; on vs. off prophylaxis
- Does HAE impact your physical appearance when you have an attack? How?
- Does it vary depending on how severe the attack is? Or where the attack is?
- Does HAE impact your physical appearance when you do not have an attack? How?

    - Swelling of face, abdomen, or upper and lower extremities
    - Not being able to wear regular clothes, jewellery, shoes
    - Limiting activities/going out because of physical appearance
    - *If receiving androgens*: changes in appearance due to androgen therapy
- Does/has your treatment for HAE affect(ed) your daily life? How?
  Treatment administration burden: poor veins, subcutaneous administration, skills for using IV
  Side effects: short-term vs. long-term, impact of changes due to treatment
- Has having HAE had any impact on your education, career or financial situation? If so, how?
  Level of educational attainment, career progression, travel expenses / out-of-pocket costs, days off work / loss of income, redundancy due to HAE
- *If applicable*: does HAE impact your family? If so, how?
  Overall burden of HAE on family, impact on those who have HAE vs. impact on those in caregiver role vs. impact on those who do not have HAE and do not have a caregiver role
- Are there any other impacts of HAE that we haven't discussed yet?
- How would you rate the overall impact of having HAE on your life on a scale from 0 to 10? Why?
- What would your life have been if you did not have HAE?
- **[ADULT PATIENTS]** If you can remember, what were the main impacts of HAE when you were an adolescent? What has changed?
  School/education; relationships with friends, romantic partners, family; social and leisure activities; self-care
- **[ADULT AND ADOLESCENT PATIENTS]** Do you have people who care for you when you have an attack? *IF YES*: what is your relationship to them?
  Do you feel they understand your needs?
  Caregiver has HAE themselves or not
  And does them caring for you have any impact on your relationship with them?
  How does caring for you impact their life, do you think?
  Work/school, housework, leisure, social life/activities, time for self, self-care

Section D.1: Caregiver impacts – caregivers and patient-caregivers only

I would now like to try to understand how caring for someone with HAE impacts your life: a) during an attack; b) between attacks / when they do not have an attack.

- Could you describe a typical day when you need to care for them when they have an attack?
- Could you describe a typical day for you when they do not have an attack?
- Does caring for them impact your daily life when they have an attack? How?
- Does it vary depending on how severe the attack is? Or where the attack is?
- Does caring for them impact your daily life when they do not have an attack? How?
- How does your daily life compare to that of people who do not care for someone with HAE?
  Work/school, housework, leisure, social life/activities, time for self, self-care
- Does caring for them impact your emotional well-being when they have an attack? How? To what extent?
- Does it vary depending on how severe the attack is? Or where the attack is?
- Does caring for them impact your emotional well-being when they do not have an attack? How? To what extent?
    - Fear/anxiety/stress/worry
    - Anger/frustration
    - Depression / low mood
    - Emotional impact of hereditary nature of HAE
    - *If patient is under 18*: issues with independence and supervision

    - No / mild / moderate / severe / extremely severe impact – **PROBE FOR SEVERITY OF IMPACT**
- Does their treatment for HAE impact on you as a caregiver? How?
  Treatment administration burden, side effects
- Has caring for them had any impact on your career or financial situation? If so, how?
  Travel expenses / out-of-pocket costs, days off work / loss of income, redundancy due to HAE
- **[CAREGIVERS ONLY]** *If applicable*: does HAE impact your family? If so, how?
  Overall burden of HAE on family, impact on those who have HAE, impact on those in caregiver role, impact on those who do not have HAE and do not have a caregiver role
- If any, what are the main positive aspects of caring for someone with HAE?
- If any, what are the main negative aspects of caring for someone with HAE?
- How would you rate the overall impact of caring for someone with HAE on your life on a scale from 0 to 10? Why?
- Are there any other impacts of caring for someone with HAE that we haven't discussed yet?

Section D.2: Being a patient-caregiver – patient-caregivers only

- Does having HAE yourself impact on you caring for someone else with HAE? If so, how?
  Easier or more difficult
- If any, what are the positive aspects of having HAE yourself and caring for someone with HAE?
  Familiarity with HAE, knowledge of the condition and treatment, mutual emotional support
- If any, what are the negative aspects or challenges of having HAE yourself and caring for someone with HAE?
  Impact of own condition on ability to care; timing of own attacks and attacks of person(s) they care for

Section E: Conclusion

We are soon coming to the end of this interview.

- What are your hopes and wishes for future HAE treatment?
  Attack severity, frequency, duration, control; mode of treatment administration: preference for oral vs. injection
- How would you summarise the impact of HAE on your life?
- Are there any other ways in which your quality of life is impacted by HAE that we have not discussed?

If the participant has reported use of berotralstat and reported adverse events and/or product complaints, please collect further details now.

Thank you for your help with this research.

We really appreciate the time you have taken to participate in this study.

Online Resource 2 – Vignette development: Draft vignettes

HAE – Adult – Between attacks

- You have a lifelong incurable condition that sometimes causes swelling. Swelling most commonly affects the arms, legs, face or tummy and can last for hours or days. It can be brought on by known triggers or come on suddenly without an identifiable trigger.
- Currently, you do not have any swelling.
- Your mobility and physical function are normal for someone your age.
- You are able to wash and dress normally.
- You are able to go about daily activities, such as work/school, housework and childcare.
- You have some soreness and scars from injections you need to have because of your condition.
- You need to remember to take your injection device with you wherever you go. You need to plan ahead to make sure there is a suitable space for you to take the medication if you have swelling. You may also need to plan where you could get emergency hospital care if you cannot control your swelling.
- You avoid activities that could trigger swelling, such as carrying heavy objects, strenuous sports or repetitive movements. Stressful situations can also trigger a swelling.
- You sometimes feel tired and sometimes have poor sleep.
- You sometimes feel down or depressed. You often feel afraid or anxious about experiencing sudden swelling.

HAE – Adult – Abdominal attack

- You have a lifelong incurable condition that sometimes causes swelling. It can be brought on by known triggers or come on suddenly without an identifiable trigger.
- You ***currently have*** swelling in your tummy causing you to experience severe pain. You have diarrhoea, feel nauseous and sometimes vomit.
- Your mobility and physical function are limited by your swelling and the severe pain you experience.
- You find it difficult to wash and dress yourself because of the severe pain.
- You are unable to leave your home and need to rest in bed most of the time because of your swelling.
- You are unable to go about daily activities, such as work/school, housework and childcare.
- You feel dependent on your partner for help around the house and care for your child(ren).
- You feel very tired and unwell. You have poor sleep.
- You feel distressed and down because of the swelling.

HAE – Adult – Peripheral attack – face

- You have a lifelong incurable condition that sometimes causes swelling. It can be brought on by known triggers or come on suddenly without an identifiable trigger.
- You ***currently have*** swelling in your face (e.g. lips, cheeks, eyes) causing you some discomfort.
- Your mobility and physical functioning are unaffected.
- You can wash and dress normally.
- You feel embarrassed about the appearance of your face, as you may get unwanted attention from other people in public spaces.
- You may have some problems working, doing housework and caring for your child(ren) normally. You don't feel comfortable leaving the house.
- You feel dependent on your partner for help.
- You feel unwell. You have poor sleep.

- You feel distressed and down because of the swelling and feel anxious about the possibility of swelling spreading to your throat.

HAE – Adult – Peripheral attack – hand

- You have a lifelong incurable condition that sometimes causes swelling. It can be brought on by known triggers or come on suddenly without an identifiable trigger.
- You ***currently have*** swelling in your hand causing you some discomfort.
- You are unable to use your hand normally, which affects your physical functioning, specifically any task that requires use of your hand.
- It is difficult for you to wash and dress normally, so you rely on your partner for help.
- You do not want to leave your home, because of your swelling. You feel embarrassed about the appearance of your hand.
- Your ability to work, do housework and care for your child(ren) is affected because you are unable to use your hand normally.
- You feel dependent on your partner for help around the house and childcare.
- You feel unwell. You have poor sleep.
- You feel distressed and down because of the swelling.

HAE – Adult – Laryngeal attack with hospitalisation

- You have a lifelong incurable condition that sometimes causes swelling. It can be brought on by known triggers or come on suddenly without an identifiable trigger.
- You ***currently have*** swelling in your throat and face causing you considerable discomfort. You have been admitted to hospital and require emergency care to keep your airways open.
- You are currently resting in bed. Your voice is hoarse.
- You are unable to do any normal daily activities, such as working, housework or childcare.
- You are completely dependent on your partner for help around the house and childcare.
- You feel unwell. You have poor sleep.
- You feel very distressed, very anxious and down because your ability to breathe is affected by the swelling.

HAE – Carer while patient is experiencing an attack

- A member of your family has a lifelong incurable condition that sometimes causes swelling in different body parts. It can be brought on by known triggers or come on suddenly without an identifiable trigger.
- They are currently experiencing swelling, and you are caring for them.
- You help them to administer injections to treat their swelling. You also provide emotional support. You sometimes may need to assist them to wash or dress themselves.
- Your normal daily activities, such as working, housework and childcare, may be interrupted. You may need to take on more household tasks (e.g. cooking).
- You feel distressed because your family member is unwell. You feel frustrated that the condition affects your family life so much. Administering treatment can be stressful for you.

Online Resource 3 – Vignette development: Interview guides

Patient interview guide

Good (morning/afternoon/evening), my name is [insert name] and I am a researcher at Acaster Lloyd Consulting Ltd. Thank you for taking the time to participate in this interview. The purpose of this conversation is to understand the impact that hereditary angioedema (HAE) has on individuals with this condition.

More specifically, we are looking to develop descriptions of people with HAE for the general public. These descriptions should describe what might be typical and will vary by whether a person with HAE has an attack and, if they have an attack, which body parts are affected.

The purpose of today's interview is to help us develop these descriptions. The severity of each description is supposed to be fair, typical and representative.

The results will be anonymous; your identity will not be disclosed and all information you provide will remain confidential. Your participation is voluntary, so you can stop participating at any time without giving us a reason.

We will be recording this interview, so we don't miss any of your comments. Can I check that this is OK with you? [If yes] OK, thank you. I'll start recording now.

Background questions

First, a few background questions about your experiences with different types of HAE attacks.

- On average, how often have you had an HAE attack in the past year?
- How often have you had an attack that affected your abdomen?
- How often have you had an attack that affected your hands?
- How often have you had an attack that affected your face?
- How often have you had an attack that affected your throat? Have you been to the hospital because of a throat attack?

General feedback on the vignettes

I am now going to move on to the next part of the interview, where I would like to find out your views about draft descriptions of life with HAE. I am interested in hearing your feedback on the accuracy of the descriptions that we have sent to you in an email.

- Do you have this description in front of you?

I would like to go over the descriptions in great detail.

GO OVER HEALTH STATES LINE BY LINE. PROBE FOR THINK-ALOUD FEEDBACK.

- What are your overall impressions of the descriptions of someone with HAE?
- How do these descriptions of someone with HAE fit with your experience?
- Are the descriptions too severe or extreme? Alternatively, does it understate what people with HAE experience?
- In our description of the impact of HAE, we have a number of bullet points. Could we review each bullet in turn? Too severe/extreme or understated? Fair representation overall? Appropriate? What is missing?
- We also describe the psychological and social impact on people with HAE. Do you think this is a fair description from your experience?

- Comparing the health state descriptions, do you think the differences in the descriptions accurately reflect the differences between a) having an attack vs. not having an attack; b) attacks in different body parts?
- Are there any other impacts that we have missed?
- Is there anything else that seems incorrect?

Close of interview

We have now come to the end of the interview.

Before I stop the recorder, do you have any further comments about the description or your experience of having HAE?

OK, great. Thank you very much for your participation.

If the participant has reported use of berotralstat and reported adverse events and/or product complaints, please collect further details now.

STOP RECORDING

Caregiver interview guide

Good (morning/afternoon/evening), my name is [insert name] and I am a researcher at Acaster Lloyd Consulting Ltd. Thank you for taking the time to participate in this interview. The purpose of this conversation is to understand the impact that hereditary angioedema (HAE) has on people who provide informal care for people with this condition.

More specifically, we are looking to develop descriptions of people who care for someone with HAE for the general public. These descriptions should describe what might be typical when caring for someone with HAE

The purpose of today's interview is to help us develop these descriptions. The severity of each description is supposed to be fair, typical and representative.

The results will be anonymous; your identity will not be disclosed and all information you provide will remain confidential. Your participation is voluntary, so you can stop participating at any time without giving us a reason.

We will be recording this interview, so we don't miss any of your comments. Can I check that this is OK with you? [If yes] OK, thank you. I'll start recording now.

General feedback on the vignettes

I am now going to move on to the next part of the interview, where I would like to find out your views about a draft description of caring for someone with HAE. I am interested in hearing your feedback on the accuracy of the description that we have sent to you in an email.

- Do you have this description in front of you?

I would like to go over the description in great detail.

GO OVER HEALTH STATES LINE BY LINE. PROBE FOR THINK-ALOUD FEEDBACK.

Questions for health state

- What are your overall impressions of the descriptions of caring for someone with HAE?
- How do these descriptions of caring for someone with HAE fit with your experience?

- Are the descriptions too severe or extreme? Alternatively, does it understate what caring for someone with HAE is like?
- In our description of the impact of caring for someone HAE, we have a number of bullet points. Could we review each bullet in turn? Too severe/extreme or understated? Fair representation overall? Appropriate? What is missing?
- We also describe the psychological and social impact of caring for someone with HAE. Do you think this is a fair description from your experience?
- Are there any other carer impacts that we have missed?
- Is there anything else that seems incorrect?

Close of interview

We have now come to the end of the interview.

Before I stop the recorder, do you have any further comments about the descriptions or your experience of caring for someone with HAE?

OK, great. Thank you very much for your participation.

If the participant has reported the HAE patient using berotralstat and reported adverse events and/or product complaints, please collect further details now.

STOP RECORDING

HCP interview guide

Good (morning/afternoon/evening), my name is [insert name] and I am a researcher at Acaster Lloyd Consulting Ltd. Thank you for taking the time to participate in this interview. The purpose of this conversation is to understand the impact that hereditary angioedema (HAE) has on individuals with this condition.

More specifically, we are looking to develop descriptions of people with HAE for the general public. These descriptions should describe what might be typical and will vary by whether a person with HAE has an attack and, if they have an attack, which body parts are affected.

The purpose of today's interview is to help us develop these descriptions. The severity of each description is supposed to be fair, typical and representative.

The results will be anonymous; your identity will not be disclosed and all information you provide will remain confidential. Your participation is voluntary, so you can stop participating at any time without giving us a reason.

We will be recording this interview, so we don't miss any of your comments. Can I check that this is OK with you? [If yes] OK, thank you. I'll start recording now.

Background questions

First, a few background questions about your professional experience with HAE.

- Please tell us a bit about your role.
- How long have you been working with patients with HAE?
- How many patients with HAE do you have under your care?
- How often do you typically see a patient with HAE?

General feedback on the vignettes

We will discuss descriptions of HAE patients with you, although we do not mention the condition in the text for methodological reasons.

I am now going to move on to the next part of the interview, where I would like to find out your views about draft descriptions of someone with HAE. I am interested in hearing your feedback on the accuracy of the descriptions that we have sent to you in an email.

Do you have this description in front of you?

GO OVER HEALTH STATES LINE BY LINE. PROBE FOR THINK-ALOUD FEEDBACK.

- What are your overall impressions of the descriptions of someone with HAE?
- How do these descriptions of someone with HAE fit with your experience?
- Are the descriptions too severe or extreme? Alternatively, does it understate what people with HAE experience?
- In our description of the impact of HAE, we have a number of bullet points. Could we review each bullet in turn? Too severe/extreme or understated? Fair representation overall? Appropriate? What is missing?
- We also describe the psychological and social impact on people with HAE. Do you think this is a fair description from your experience?
- Comparing the health state descriptions, do you think the differences in the descriptions accurately reflect the differences between a) having an attack vs. not having an attack; b) attacks in different body parts?
- Are there any other impacts that we have missed?
- Is there anything else that seems incorrect?

Close of interview

We have now come to the end of the interview.

Before I stop the recorder, do you have any further comments about the description or your experience of providing care for a patient with HAE?

OK, great. Thank you very much for your participation.

If the participant has reported a patient's use of berotralstat and reported adverse events and/or product complaints, please collect further details now.

STOP RECORDING

Online Resource 4 – TTO valuation: Interview script

Instructions for the interviewer are shown using **CAPITALISED TEXT**. These should **not** be read to the participant.

Instructions for the participant are shown using plain text. These should be read aloud to the participant.

POINTS TO MENTION WHEN STARTING AN INTERVIEW

Thank you for taking the time to participate in this study. The purpose of this study is to gain an understanding of the impact of a condition that causes swelling in different body parts, and to estimate the value that you would place on a treatment for their condition.

During the interview I will ask you to choose between different descriptions. These all describe the experiences of [an adult with this condition / caring for someone with this condition]. I will provide you with different patient and carer descriptions and ask you to think about how good or bad they are.

Before we begin, I would like to tell you a few things about the interview.

1. All the information you provide us will remain **confidential**. We only know your first name and, in our records, that name will be replaced with an ID number.

2. The interview will take **approximately 60 minutes** in total to complete. We will ask you to complete some forms as well as answer questions in the interview.

3. Please **take your time** answering the questions.

4. Please remember that there are **no right or wrong answers**. We are interested in your opinion and that is what is important to us. Do not worry about being consistent with previous answers and **feel free to change your mind** if you want to.

5. If you have **any questions throughout the interview**, please feel free to ask. We may have to wait until the end of the interview to answer some questions.

6. Your participation in this study is **voluntary**, so if at any time you would like to stop the interview please let me know.

7. Do you have **any questions** before we start?

INTRODUCTION TO HEALTH STATES:

The descriptions you are about to be shown relate to someone with a condition that causes swelling of different body parts.

OVERVIEW:

START WITH THE FEELING THERMOMETER, THEN COMPLETE THE TTO EXERCISE. FOR EACH ONE, START WITH THE PRACTICE HEALTH STATES (AFTER FULL HEALTH AND DEAD).

Practice health states

We are going to go through two different tasks which we will use to get your views on these descriptions. We will explain these tasks with two practice descriptions. The purpose of this is to make sure you understand the tasks so please ask me if you have any questions as we go through.

Feeling thermometer

The first method uses this scale.

DISPLAY THERMOMETER

We are going to use this scale to find out **how good or bad** you think each description is.

1. The scale runs from 0 to 100.

2. Down towards 0 are the very worst or the least preferred descriptions. The further down the scale that you place a description, the worse you believe it would be.

3. As you go up the scale the descriptions get better until you approach 100 where the very best descriptions could be located. The further up the scale you place a description, the better you believe it would be to experience.

4. I am going to ask you to read each description vignette and **then rate it on the scale to indicate how good or bad you think it is.**

This is the first description that I would like you to read.

REFER RESPONDENT TO "FULL HEALTH" VIGNETTE

LET RESPONDENT READ VIGNETTE

This vignette describes full health.

Full health is equal to 100 on the scale and so we place it at 100. This is as good as your health can be.

This next vignette describes the state of being immediately dead.

REFER RESPONDENT TO "DEAD" VIGNETTE

LET RESPONDENT READ VIGNETTE

Looking at the scale, where would you place the dead vignette? Should you decide that you want to move this at any point, you are free to do so.

REFER RESPONDENT THE INTRODUCTORY TEXT

Please read this text and imagine you are the individual described. This text relates to all of the following descriptions which I am about to give you.

START WITH PRACTICE HEALTH STATES (PRACTICE 1 AND PRACTICE 2)

I will refer you to the descriptions one at a time and I would like you to read each vignette carefully and think about **how good or bad it is**. Then I would like you to rate it on the scale. You may decide that a description is worse than dead and decide to place it lower down the scale.

When you read the vignettes imagine living as the person in the description for the **rest of your life.**

REFER RESPONDENT TO VIGNETTE (PRESENT IN ORDER AS ASSIGNED FOR EACH PARTICIPANT)

WAIT FOR RESPONDENT TO COMPLETE RATING

GET NEXT VIGNETTE READY

Now read this vignette and again **rate how good or bad** it is on the scale.

After you have rated a few vignettes you may wish to **move some of the ratings around on the scale**.

Please feel free to adjust the ratings if you need to.

CONTINUE TO REFER TO VIGNETTES ONE BY ONE TO RESPONDENT- MAKE SURE THEY RATE ALL HEALTH STATE VIGNETTES

BE AWARE THAT SOME PARTICIPANTS WILL INTERPRET THE SCALE THE WRONG WAY ROUND- PLACING THE WORST STATES TOWARDS 100. IF YOU SUSPECT THEY ARE DOING THIS THEN CHECK (**HAVE THEM CONFIRM THAT THEY BELIEVE THE STATES ARE CLOSER TO 'FULL HEALTH' OR 'DEAD' AS APPROPRIATE**).

IF THEY DON'T REALISE THEIR MISTAKE THEN CONTINUE TO THE END OF THE FEELING THERMOMETER TASK AND TERMINATE THE INTERVIEW. BE VERY WARY OF GUIDING PARTICIPANTS OR SUGGESTING TO THEM THAT THEIR ANSWERS ARE IN ANY WAY INCORRECT.

Now that you have rated all the vignettes on the scale, are there any changes you would like to make?

PAUSE UNTIL RESPONDENT INDICATES SATISFACTORY COMPLETION OF ANY REVISIONS

IF THERE ARE ANY STATES RATED AS WORSE THAN DEAD THEN ASK PARTICIPANTS TO CONFIRM THAT THEY ARE WORSE THAN DEAD:

- Now I would like to record your values for each vignette on the scale.
- Starting at the bottom of the scale, please refer to each vignette in turn and read off the value on the scale that you have given to that vignette.
- I will write down your answers.

Now we are ready to move onto the next stage in the interview.

Here we will ask you to rate the same description vignettes, but this time we will use a different method.

REMOVE FEELING THERMOMETER

Health State Valuation Task

In this task we are going to use the same descriptions but using a different method.

In each question I will present you with a series of two choices and ask you to choose the one that you would prefer. If you think the **two choices are about the same tell me** and I will write this down. In order to make the task easier to understand we will use an aid similar to a game board.

PLACE THE TTO BOARD NEXT TO YOU ON SCREEN.

SET SCALES TO BOTH SHOW ALIVE FOR 10 YEARS

PLACE FULL HEALTH STATE VIGNETTE ON LIFE A

REFER TO A HEALTH STATE VIGNETTE ON LIFE B

The top part of the board is labelled Life A and the bottom part of the board is labelled Life B. These are two choices and we want to know which Life you would prefer. The vignettes describe the health status of each Life – or what each Life would be like the whole time.

REFER TO THE LIFE A AND LIFE B VIGNETTES

The scale besides each vignette represents the period of time you can expect to live in this state for. For the purposes of this exercise please imagine that the longest that you can expect to live is 10 years.

Each scale will also show the number of years of life lost due to an early death.

POINT TO SCALE A

The pink colour on the scale shows the number years of Full Health.

RUN FINGER ALONG PINK PART OF SCALE A

You can expect to live 10 years, from today, after that you would die.

POINT TO SCALE A

The years of life lost due to an early death are shown by the black colour.

MOVE THE SLIDER TO DEMONSTRATE A CHANGE IN DURATION.

POINT TO SCALE B

The blue colour here in Life B represents the time you will live in Life B. Think about how good or bad Life B would be for you. In Life B you can expect to live a life as described on the vignette and you will live for 10 years, from today, followed by death.

Do you understand these ideas?

YES- SET BOTH SCALES TO SHOW ALIVE FOR 10 YEARS AND CONTINUE BELOW

NO- REPEAT PREVIOUS PAGE.

Please read the Full Health vignette again

ALLOW RESPONDENT TIME TO READ FULL HEALTH VIGNETTE

So the duration of Full Health is represented by the pink on the scale.

START WITH THE TWO PRACTICE HEALTH STATES.

AFTER PRACTICE HEALTH STATES:

ASK PARTICIPANT IF THEY HAVE HAD ANY DIFFICULTY WITH THE PRACTICE TASK AND IF NOT IF THEY ARE HAPPY TO MOVE ON TO THE MAIN TASK.

IF THEY CONFIRM THEIR UNDERSTANDING AND YOU FEEL THEY HAVE UNDERSTOOD, RETURN TO TTO BOARD AND GO THROUGH THE STUDY HEALTH STATES.

IF PARTICIPANT IS UNSURE, OR IF YOU ARE NOT SURE THEY UNDERSTAND, EXPLAIN THE TASK AGAIN AND REPEAT THE PRACTICE EXERCISE, CONFIRMING THEIR UNDERSTANDING THROUGHOUT.

IF AFTER REPEATING THE PRACTICE EXERCISE, THE PARTICIPANT DOES NOT UNDERSTAND OR IS NOT ENGAGED IN THE EXERCISE, TERMINATE THE INTERVIEW.

FOR FIRST HEALTH STATE PLEASE READ OUT ADDITIONAL TEXT BELOW, FOR OTHER HEALTH STATES SET SCALE A TO 10 YEARS, REFER TO THE NEXT HEALTH STATE VIGNETTE AND READ TEXT

This is the first description. Please read this vignette carefully.

Life B is represented by this description.

Let's start the first question by working through it together. The top part of the board represents Life A. The vignette describes Full Health. The duration of Life A is shown by the pink part of the scale.

POINT TO LIFE A

The scale shows that Full Health will last for 10 years followed by death.

The bottom vignette and time scale describe Life B. This is the description that you have just read. The bottom time scale, marked in blue, shows that this state will last for 10 years followed by death.

POINT TO THE SLIDER ON LIFE A SHOWING THE DURATION

1. Which Life would you prefer, 10 years in Life A or 10 years in Life B, or are they about the same?

IF PARTICIPANT IS UNSURE AT ANY STAGE:

Would you like me to explain this again?

A- MOVE LIFE A SCALE TO 0 YEARS (ALL BLACK) AND CONTINUE

B - ASK "WHY?" MARK RESPONSE (Prefer B: 1.0, and note reason given)

SAME - MARK RESPONSE (Equal: 1.00)

---

2. Now I've changed the Life A time scale to 0 which can be considered as 'dead'. Which Life would you prefer now? 10 years in Life B or being 'dead'?

A or SAME – <u>GO TO LT-TTO INTERVIEW GUIDE (page 11)</u>

B - MOVE SCALE A TO 9.5 YEARS AND CONTINUE

---

3. Now Life A represents 9 years and 6 months of Full Health in total. Which Life would you prefer now? Or are they about the same?

A – MOVE SCALE A TO 0.5 YEARS,

B - MARK RESPONSE (Prefer B: 0.975) GO TO THE NEXT HEALTH STATE

SAME - MARK RESPONSE (Equal: 0.950)

---

4. Now you have 6 months of Full Health followed by death in Life A. Which Life would you prefer? Or are they about the same?

A – MARK RESPONSE (Prefer A: 0.025), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 9 YEARS AND CONTINUE

SAME - MARK RESPONSE (Equal: 0.050)

---

5. Now you have 9 years of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 1 YEARS AND CONTINUE

B - MARK RESPONSE (Prefer B: 0.925) GO TO THE NEXT HEALTH STATE

SAME – MARK RESPONSE (Equal: 0.900)

---

6. Now you have 1 year of Full Health followed by death in Life A which Life would you prefer? Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.075), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 8.5 YEARS AND CONTINUE

SAME - MARK RESPONSE (Equal: 0.100)

---

7. Now you have 8 years and 6 months of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 1.5 YEARS AND CONTINUE

B- MARK RESPONSE (Prefer B: 0.875) GO TO THE NEXT HEALTH STATE

SAME - MARK RESPONSE (Equal: 0.850)

---

8. Now you have 1 year and 6 months of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.125), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 8 YEARS AND CONTINUE

SAME – MARK RESPONSE (Equal: 0.150)

---

9. Now you have 8 years of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 2 YEARS,

B - MARK RESPONSE (Prefer B: 0.825) GO TO THE NEXT HEALTH STATE

SAME – MARK RESPONSE (Equal: 0.800)

---

10. Now you have 2 of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.175), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 7.5 YEARS AND CONTINUE

SAME – MARK RESPONSE (Equal: 0.200)

---

11. Now you have 7 years and 6 months of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 2.5 YEARS,

B - MARK RESPONSE (Prefer B: 0.775) GO TO THE NEXT HEALTH STATE

IF HEALTH STATES SAME – MARK RESPONSE (Equal: 0.750)

---

12. Now you have 2 years and 6 months of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MARK RESPONSE (Prefer A: 0.225), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 7 YEARS AND CONTINUE

SAME – MARK RESPONSE (Equal: 0.250)

---

13. Now you have 7 years of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 3 YEARS

B - MARK RESPONSE (Prefer B: 0.725) GO TO THE NEXT HEALTH STATE

SAME – MARK RESPONSE (Equal: 0.700)

---

14. Now you have 3 years of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.275), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 6.5 YEARS AND CONTINUE

SAME – MARK RESPONSE (Equal: 0.300)

---

15. Now you have 6 years and 6 months of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 3.5 YEARS AND CONTINUE

B- MARK RESPONSE (Prefer B: 0.675) GO TO THE NEXT HEALTH STATE

SAME – MARK RESPONSE (Equal: 0.650)

---

16. Now you have 3 years and 6 months of Full Health followed by death in Life A , which Life would you prefer? Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.325), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 6 YEARS AND CONTINUE

SAME – MARK RESPONSE (Equal: 0.350)

---

17. Now you have 6 years of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 4 YEARS,

B - MARK RESPONSE (Prefer B: 0.625) GO TO THE NEXT HEALTH STATE

SAME – MARK RESPONSE (Equal: 0.600)

---

18. Now you have 4 years of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.375), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 5.5 YEARS AND CONTINUE

SAME – MARK RESPONSE (Equal: 0.400)

---

19. Now you have 5 years and 6 months of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A – MOVE SCALE A TO 4.5 YEARS,

B - MARK RESPONSE (Prefer B: 0.575) GO TO THE NEXT HEALTH STATE

SAME – MARK RESPONSE (Equal: 0.550)

---

20. Now you have 4 years and 6 months of Full Health followed by death in Life A, which Life would you prefer? Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.425), GO TO THE NEXT HEALTH STATE.

B - MOVE SCALE A TO 5 YEARS AND CONTINUE

SAME – MARK RESPONSE (Equal: 0.450)

---

21. Now you have 5 years of Full Health followed by death in Life A, which Life would you prefer?

Or are they about the same?

A - MARK RESPONSE (Prefer A: 0.475) GO TO THE NEXT HEALTH STATE

B – MARK RESPONSE (Prefer B: 0.525), GO TO THE NEXT HEALTH STATE.

SAME - MARK RESPONSE (Equal: 0.500)

LEAD-TIME TTO INTERVIEW GUIDE

Given that this is how you feel about this description I am going to ask you a bit more about it using a slightly different method

SHOW THE LT-TTO BOARD (OTHER SIDE OF BOARD).

SET LIFE A TO SHOW ALIVE FOR 10 YEARS

REFER TO FULL HEALTH STATE VIGNETTE ON PLACEHOLDER TO THE LEFT

REFER TO HEALTH STATE VIGNETTE ON PLACEHOLDER TO THE BOTTOM RIGHT

On the board you can see two scales both showing 20 years. The top scale is labelled Life A and the bottom scale is labelled Life B. As before, we want to know which you prefer, imagining that you are the individual described.

Please imagine that in the top scale, Life A, you would live for 10 years, from today, in the pink Full Health state described on the left, and then you would die. In the bottom scale, Life B, you would live for 10 years, from today, in the pink Full Health state described on the left, followed by 10 years as the person described on the bottom, and then you would die.

Do you understand these ideas?

WITH THE MARKER FOR LIFE A SET TO 10 YEARS

3. Now, do you prefer Life A, Life B, or are they about the same?

A – MOVE SCALE A TO 0 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: 0.0) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME – MARK RESPONSE (Equal: 0.0)

---

4. Now I've changed Life A to 0 which can be considered as 'dead'. Which Life do you prefer now or are they about the same?

A – MARK RESPONSE (Prefer A: -1.0) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B- MOVE SCALE A TO 9.5 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -1.000)

---

5. Now you have 9 years and 6 months of Full Health followed by death in Life A, which Life would you prefer or are they about the same?

A - MOVE SCALE A TO 0.5 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.025) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME – MARK RESPONSE (Equal: -0.050)

---

6. Now you have 6 months of Full Health followed by death in Life A, which Life would do you prefer or are they about the same?

A – MARK RESPONSE (Prefer A: -0.975) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 9 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.950)

---

7. Now you have 9 years of Full Health followed by death in Life A, which Life would you prefer or are they about the same?

A - MOVE SCALE A TO 1 YEAR AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.075) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME – MARK RESPONSE (Equal: -0.100)

---

8. Now you have 1 year of Full Health followed by death in Life A, which Life do you prefer or are they about the same?

A – MARK RESPONSE (Prefer A: -0.925) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 8.5 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.900)

---

9. Now you have 8 years and 6 months of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A - MOVE SCALE A TO 1.5 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.125) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME LIFE – MARK RESPONSE (Equal: -0.150)

---

10. Now you have 1 year and 6 months of Full Health followed by death in Life A, which Life do you prefer, or are they about the same?

A – MARK RESPONSE (Prefer A: -0.875) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 8 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.850)

---

11. Now you have 8 years of Full Health followed by death in Life A, which Life would you prefer or are they about the same?

A - MOVE SCALE A TO 2 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.175) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME – MARK RESPONSE (Equal: -0.200)

---

12. Now you have 2 years of Full Health followed by death in Life A, which Life would you prefer or are they about the same?

A – MARK RESPONSE (Prefer A: -0.825) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 7.5 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.800)

---

13. Now you have 7 years and 6 months of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A - MOVE SCALE A TO 2.5 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.225) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

IF HEALTH STATES SAME – MARK RESPONSE (Equal: -0.250)

---

14. Now you have 2 years and 6 months of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A – MARK RESPONSE (Prefer A: -0.775) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 7 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.750)

---

15. Now you have 7 years of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A - MOVE SCALE A TO 3 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.275) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME- MARK RESPONSE (Equal: -0.300)

---

16. Now you have 3 years of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A – MARK RESPONSE (Prefer A: -0.725) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 6.5 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.700)

---

17. Now you have 6 years and 6 months of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A - MOVE SCALE A TO 3.5 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.325) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME – MARK RESPONSE (Equal: -0.350)

---

18. Now imagine you have 3 years and 6 months of Full Health followed by death in Life A, which Life would you prefer or are they about the same?

A – MARK RESPONSE (Prefer A: -0.675) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 6 YEARS AND CONTINUE.

IF HEALTH STATES SAME – MARK RESPONSE (Equal: -0.650)

---

19. Now you have 6 years of Full Health followed by death in Life A, which Life would you prefer or are they about the same?

A - MOVE SCALE A TO 4 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.375) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME – MARK RESPONSE (Equal: -0.400)

---

20. Now you have 4 years of Full Health followed by death in Life A, which Life would you prefer or are they about the same?

A – MARK RESPONSE (Prefer A: -0.625) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 5.5 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.600)

---

21. Now you have 5 years and 6 months of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A - MOVE SCALE A TO 4.5 YEARS AND CONTINUE.

B - MARK RESPONSE (Prefer B: -0.425) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

SAME – MARK RESPONSE (Equal: -0.450)

---

22. Now you have 4 years and 6 months of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A – MARK RESPONSE (Prefer A: -0.575) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B-MOVE SCALE A TO 5 YEARS AND CONTINUE.

SAME – MARK RESPONSE (Equal: -0.550)

---

23. Now you have 5 years of Full Health followed by death in Life A, which Life would you prefer, or are they about the same?

A - MARK RESPONSE (Prefer A: -0.525) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

B – MARK RESPONSE (Prefer B: -0.475), GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

IF HEALTH STATES SAME - MARK RESPONSE (Equal: -0.500) GO TO THE NEXT HEALTH STATE (TTO PROCEDURE, PAGE 4)

<u>AT THE END OF THE INTERVIEW</u>, ASK THE FOLLOWING QUESTIONS ABOUT ANY HEALTH STATES VALUED AS WORSE THAN DEAD (LT-TTO PROCEDURE)

- Are you aware that answer you gave for this description suggests that being the person in this description is worse than being dead?
- Knowing this now, would you change how you evaluated this description?

NOTE RESPONSES IN THE NOTES COLUMN ON THE SCORE SHEET FOR THE RELEVANT HEALTH STATE.

Online Resource 5 – Revisions to patient vignettes

Content change	Source	Original text	Final text
Synopsis of HAE **Simplified synopsis to ensure general description is applicable to all HAE patients. Added description of lifestyle changes as a result of condition.**	P1, P2	You have a lifelong incurable condition which sometimes causes swelling. Swelling most commonly affect the arms, legs, face or tummy and can last for hours or days. It can be brought on by known triggers or come on suddenly without an identifiable trigger.	You have a lifelong incurable condition which sometimes causes swelling in different body parts. Swelling can be suddenly brought on by known or unknown triggers. You have adapted your lifestyle because of your condition.
HAE medication **Removed 'soreness' as a consequence of injections**	P1	You have some soreness and scars from injections you need to have because of your condition.	You have some scars from injections you need to have because of your condition.
HAE medication **Expanded description of HAE medication to accommodate for items other than the injection**		You need to remember to take your injection device with you wherever you go.	You need to remember to take your injection, various items to administer the injection, and other medication with you wherever you go.
Psychological impact of laryngeal attack risk **Expanded description of psychological impact of HAE to include details on risk of laryngeal attacks**	P1, P2, HCP	You often feel afraid or anxious about experiencing sudden swelling.	You often feel afraid or anxious about experiencing sudden swelling. If affecting your throat, it can obstruct your breathing, which could be fatal.
Abdominal attack **Expanded description of abdominal attack to include mention of cramps**	P2	You **currently have** swelling in your tummy causing you to experience severe pain.	You **currently have** swelling in your ***tummy*** causing you to experience cramps and severe pain.
Abdominal attack **Added sentence to explain that hospital visit could be needed if uncontrolled**	P1	–	You might need to go to hospital if the swelling is not controlled.
Facial attack **Added sentence to explain that speech and eyesight could be affected**	P1, P2	–	Your speech or your eyesight may be affected by the swelling.
Laryngeal attack **Amended description of the role of the hospital in dealing with a laryngeal attack**	P1, HCP	You have been admitted to hospital and require emergency care to keep your airways open.	You need to go to hospital immediately and may require emergency hospital admission for monitoring of your airways and breathing.
Laryngeal attack **Amended description of impact on voice and physical sensations**	P2	You are currently resting in bed. Your voice is hoarse.	You are currently resting. Your voice changes and your throat feels tight. You are experiencing difficulty swallowing and may find breathing more difficult.
Laryngeal attack **Amended description to make risk of dying explicit**	P1	You feel very distressed, very anxious and down because your ability to breathe is affected by the swelling.	You feel very distressed and down, and very afraid and anxious because your breathing is affected and because of the risk of dying.

Online Resource 6 – Revisions to caregiver vignette

Content change	Source	Original text	Final text
Caregiver responsibilities **Added sentence to explain that a caregiver might need to take the patient to hospital**	C1	–	You might need to take them to hospital if their swelling is not controlled.
Lifestyle adaptations **Added sentence on lifestyle changes as a result of caring for someone with HAE**	C1	–	You have adapted your lifestyle as a result of caring for someone with this condition.
Impact on family life **Deleted quantifier 'so much' from sentence on impact on family life**	C2	You feel frustrated that the condition affects your family life so much.	You feel frustrated that the condition affects your family life.

Online Resource 7 – Final vignettes

Final vignettes

State	Vignette
Patient state 1: **Attack-free**	• You have a lifelong incurable condition that sometimes causes swelling in different body parts. Swelling can be suddenly brought on by known or unknown triggers. • ***Currently***, you ***do not have any*** swelling. • Your mobility and physical function are normal for someone your age. • You are able to wash and dress normally. • You are able to go about daily activities, such as work/school, housework, childcare and social activities. • You have some scars from injections you need to have because of your condition. • You need to remember to take your injection, various items to administer the injection, and other medication with you wherever you go. You need to plan ahead to make sure there is a suitable space for you to take the medication if you have swelling. You may also need to plan where you could get emergency hospital care if necessary. • You avoid activities that could trigger swelling, such as carrying heavy objects, strenuous/contact sports or repetitive movements. Stressful situations can also trigger a swelling. • You have adapted your lifestyle because of your condition. • You sometimes feel tired and sometimes have difficulty sleeping. • You sometimes feel down or depressed. You often feel afraid or anxious about experiencing sudden swelling. If affecting your throat, it can obstruct your breathing, which could be fatal.

Patient state 2: **Abdominal attack**	• You have a lifelong incurable condition that sometimes causes swelling in different body parts. Swelling can be suddenly brought on by known or unknown triggers. • You ***currently have*** swelling in your ***tummy*** causing you to experience cramps and severe pain. Symptoms may also include diarrhoea, nausea and vomiting. • Your mobility and physical function are limited by your swelling and the severe pain you experience. • You find it difficult to wash and dress yourself because of pain and tiredness. • You have a lack of appetite. • You are unable to leave your home and need to rest in bed most of the time because of your swelling. You might need to go to hospital if the swelling is not controlled. • You are unable to go about daily activities, such as work/school, housework, childcare and social activities. • You feel dependent on your partner/family for help around the house and for care for your child(ren). • You feel very tired and unwell. You have difficulty sleeping. • You feel distressed and down. You feel afraid or anxious.
Patient state 3: Facial attack	• You have a lifelong incurable condition that sometimes causes swelling in different body parts. Swelling can be suddenly brought on by known or unknown triggers. • You ***currently have*** swelling in your ***face (e.g. lips, cheeks, eyes)*** causing you discomfort or pain. • Your general mobility and physical functioning are unaffected. • Your speech or your eyesight may be affected by the swelling. • You can wash and dress normally. • You feel embarrassed about the appearance of your face, as you may get unwanted attention from other people in public spaces.

	• You have some problems going about daily activities, such as work/school, housework, childcare and social activities. You do not feel comfortable leaving the house. • You feel dependent on your partner/family for help. • You feel very tired and unwell. You have difficulty sleeping. • You feel distressed and down. You feel afraid or anxious that the swelling could spread to your throat, which would mean that you need to go to hospital immediately and that you may require emergency hospital admission for monitoring of your airways and breathing.
Patient state 4: Hand attack	• You have a lifelong incurable condition that sometimes causes swelling in different body parts. Swelling can be suddenly brought on by known or unknown triggers. • You ***currently have*** swelling in your ***hand*** causing you discomfort or pain. • You are unable to use your hand normally, which affects your physical functioning (specifically any task that requires use of your hand). • It is difficult for you to wash and dress normally, so you rely on your partner/family for help. • You do not want to leave your home, because of your swelling. You feel embarrassed about the appearance of your hand. • You have some problems going about daily activities, such as work/school, housework, childcare and social activities. You are unable to use your hand normally. • You feel dependent on your partner/family for help around the house and childcare. • You feel very tired and unwell. You have difficulty sleeping. • You feel distressed and down. You feel anxious.

Patient state 5: **Laryngeal attack**	• You have a lifelong incurable condition that sometimes causes swelling in different body parts. Swelling can be suddenly brought on by known or unknown triggers. • You ***currently have*** swelling in your ***throat*** and ***face*** causing you considerable discomfort. You need to go to hospital immediately and may require emergency hospital admission for monitoring of your airways and breathing. • You are currently resting. Your voice changes and your throat feels tight. You are experiencing difficulty swallowing and may find breathing more difficult. • You cannot go about any normal daily activities, such as work/school, housework, childcare and social activities. • You are completely dependent on your partner/family for help around the house and childcare. • You feel very tired and unwell. You have difficulty sleeping, because you are afraid to sleep. • You feel very distressed and down, and very afraid and anxious because your breathing is affected and because of the risk of dying.
Caregiver state while caring for someone having an HAE attack	• A member of your family has a lifelong incurable condition that sometimes causes swelling in different body parts. Swelling can be suddenly brought on by known or unknown triggers. • They are currently experiencing swelling, and ***you are caring for them***. • You help them to administer injections to treat their swelling. You also provide emotional support. You sometimes may need to assist them to wash or dress themselves. You might need to take them to hospital if their swelling is not controlled. • Your normal daily activities, such as work, housework, childcare and social activities, may be interrupted. You may need to take on more household tasks (e.g. cooking).

	• You have adapted your lifestyle as a result of caring for someone with this condition. • You feel distressed because your family member is unwell. You feel frustrated that the condition affects your family life. Administering treatment can be stressful for you.

HAE hereditary angioedema