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Original Research

A qualitative study to explore the patient experience of hypertriglyceridemia-related acute pancreatitis

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KEYWORDS
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Severe hypertriglyceridemia;
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FCS;
Qualitative;
Symptoms;
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Conceptual model

BACKGROUND: Hypertriglyceridemia (HTG) is a common cause of acute pancreatitis (AP) and can be exacerbated by acquired metabolic conditions or rare inherited disorders (eg, familial chylomicronemia syndrome [FCS]), leading to HTG-induced AP (HTG-AP). HTG-AP is associated with severe abdominal pain typically requiring hospitalization and significantly impacts health-related quality of life (HRQoL).
OBJECTIVE: To understand patients' perspectives on the HRQoL impacts of HTG-AP.
METHODS: Interviews were conducted with adults with severe/very severe HTG and/or FCS, experiencing ≥1 HTG-AP episode in the past 2 years requiring an overnight hospitalization. An interview guide, developed with patient and clinical expert input, explored symptoms, long-term HRQoL impacts, and management of HTG-AP. Participants completed a background questionnaire, the EQ-5D-5L and select items from the *PROMIS Profile v1.0-FCS 28* prior to interview. Interview transcripts were analyzed using thematic and content analysis.
RESULTS: Twelve participants completed the study (aged 32-66 years), 3 with genetically confirmed FCS. Participants described a sudden onset of HTG-AP episodes and a gradual recovery following medical intervention (up to several weeks). Participants described substantial symptomatic burden during episodes, including severe abdominal pain, fatigue, gastrointestinal symptoms, fever, and appetite loss. These impacted psychological wellbeing, relationships, and daily activities. Many of the symptoms and impacts on HRQoL (eg, pain, work impacts) persisted between episodes and had long-term effects. Participants reported substantial lifestyle restrictions (eg, dietary) to manage symptoms.
CONCLUSION: HTG-AP has a substantial symptomatic and HRQoL burden during episodes, which can persist postrecovery. Treatments that reduce the incidence of HTG-AP have potential to improve HRQoL.

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Introduction

Severe hypertriglyceridemia (sHTG) is a condition characterized by severely elevated serum triglyceride (TGs) levels (>500 mg/dL), affecting ~1.4% of the United States (US) population.[1-3] sHTG can have serious clinical manifestations and is a known etiology of HTG-induced acute pancreatitis (HTG-AP).[4] sHTG can be caused or exacerbated by acquired metabolic conditions, such as diabetes and obesity, or inherited monogenic conditions, such as familial chylomicronemia syndrome (FCS) a very rare (~1-13:1,000,000 in the US) autosomal recessive disorder.[5-8]

Long-term management of sHTG and very severe HTG (elevated TG levels >2000 mg/dL) involves following a strict very low-fat diet and life-long avoidance of alcohol.[9] Individuals may also receive TG lowering drugs such as fibrates, high dose omega-3 fatty acids, statins and less frequently, niacin, or orlistat.[9,10] However, the majority of conventional therapies have limited efficacy in decreasing TGs or reducing HTG-AP events, particularly among those with FCS[9-12] and niacin is particularly poorly-tolerated.[13,14] A novel treatment in FCS has recently been approved by the Food and Drug Administration (FDA)[15] and other treatments are in development that may also address the need for a more effective therapy in sHTG.[10,16]

Several studies have demonstrated the extensive physical and psychological impacts of AP,[17–20] including sHTG-induced AP.[21] The onset of AP episodes is associated with acute onset of persistent, severe abdominal pain,[22] but can include other symptoms, such as gastrointestinal symptoms, fever, and dizziness.[23] Approximately 80% of patients with AP in the US are initially treated with opioids for the acute pain, with 9.6% having persistent opioid use after discharge.[24] Effective treatments for HTG-AP may prevent episodes of severe pain and have the additional benefit of minimizing prescription of opioids in this population. Key psychological impacts of AP relate to the unpredictability of the disease, fear of recurrence, and stress associated with hospitalization and disease management.[25] These health-related quality of life (HRQoL) impacts can persist beyond the episode itself, continuing into the recovery phase.[18-21,23,26] It is possible that HTG causes more severe AP than other etiologies[26,27] so prevention is the best option. However, little is known about the experience of living with this form of AP and its long-term impacts.

Capturing the patient voice is an important part of drug development and can facilitate shared decision making between patients and clinicians. To date, no qualitative studies have explored the long-term symptoms and HRQoL impacts associated with HTG-AP and the interrelationships between them. Qualitative research provides the opportunity for an in-depth exploration of the disease impact from the patient perspective, highlighting the disease burden and unmet need for effective treatment. The aim of this study was to explore patient perspectives on the experience and long-term impact of HTG-AP, as well as the experience of managing the condition and unmet treatment needs.

Materials and methods

Study design and participants

A cross-sectional, noninterventional, qualitative interview study was conducted with individuals with HTG-AP from the US, UK, and Germany. Inclusion criteria across countries were (1) diagnosis of sHTG (fasting plasma TG concentration: ≥ 500 mg/dL), or a self-reported diagnosis of FCS or multifactorial chylomicronemia syndrome (MCS), (2) confirmation of having fasting TG levels of ≥ 500 mg/dL within the past 2 years (eg, letter from clinician or documentation of medical record showing TG levels), (3) confirmation of ≥ 1 HTG-AP episode in the past 2 years that resulted in an overnight stay in hospital (eg, hospital record or physician letter), (4) sufficient level of literacy and spoken English or German to take part in a 60-minute interview, (5) aged ≥ 18 years, (6) resident of US, UK, or Germany, (7) willing and able to provide consent to take part in the study. Individuals were excluded if their AP was not caused by sHTG (eg, gallstones, excess alcohol consumption) or they had been treated with volanesorsen, investigational therapies for the reduction of TGs or participated in any clinical trial in the past 3 years.

Study materials

A semistructured interview guide was developed based on a targeted literature review and input from a patient advocate and clinical experts. The interview guide comprised open-ended questions on the patient experience with their most recent HTG-AP episode (which could have been any time in the past 2 years, so relied on retrospective recall), symptoms and HRQoL impacts associated with HTG-AP, the long-term HRQoL impacts, long-term treatment/management, and perceived benefits of reducing the risk of HTG-AP.

A background questionnaire, screener questionnaire, and informed consent form were developed. The background questionnaire included questions on socio-demographic and clinical characteristics, and selected pain and fatigue items from the *Patient-Reported Outcomes Measurement Information System (PROMIS) Profile v1.0-FCS 28*.[28-30] This included 5 items on pain symptoms in the last 7 days, asking about overall pain (on an 11-point numeric rating scale from 0 = no pain to 10 = worst pain imaginable), pain interference with daily activities, frequency of belly pain, belly pain severity, and belly pain interference with daily activities (scored on a 5-point Likert scale from not at all/never to very much/very bad/>1 a day). Participants were asked to complete the EQ-5D-5L[31–33] twice; once based upon how they felt at the time of completing the questionnaire and once thinking about how they felt during their most recent HTG-AP episode that resulted in an overnight stay in hospital. Participants were also asked to complete an optional line drawing exercise prior to interview. This involved drawing and annotating a single continuous line on a timeline to represent the changes in their HRQoL during their most recent episode of HTG-AP. Drawings were used as prompts during interviews. All study materials were developed in English and translated into German.

Recruitment and interviews

Participants were recruited by a specialist recruitment agency, who contacted individuals using purposive sampling via recruitment adverts. Recruitment aimed to include patients with a range of clinical characteristics. The agency confirmed patient eligibility using a screening questionnaire and obtained the evidence to meet the inclusion criteria (eg, clinician letter, medical/hospital records). All participants provided written informed consent prior to taking part, which was reconfirmed verbally at the start of their interview. Participants completed the background questionnaire, including the items from the *PROMIS Profile v1.0-FCS 28*, EQ-5D-5L task, and line drawing tasks prior to their interview.

Interviews were conducted between June and October 2023 via videoconference by 3 experienced qualitative researchers (including 2 study authors, DA and EH) who were native language speakers for each country. All 3 interviewers had a PhD in Psychology or related field, and more than 15 years combined qualitative research experience. None of the participants were known to the interviewers.

Interviews followed the semistructured interview guide, lasted around 1 hour, and were audio recorded. Recordings were transcribed verbatim for analysis. German transcripts were translated into English. All transcripts were deidentified using participant ID numbers. Participants were reimbursed for their time in line with fair market value rates.

Analysis

Quantitative data from the socio-demographic questionnaire were summarized using descriptive statistics. Means and SDs described continuous variables and frequencies and proportions described categorical data, including the *PROMIS Profile v1.0-FCS 28*. EQ-5D utility scores were calculated for (1) the patient's most recent HTG-AP episode resulting in an overnight stay in hospital, and (2) at the time of the background questionnaire completion using UK values from the National Institute for Health and Care Excellence (NICE) recommended Decision Support Unit (DSU) mapping algorithm.[30]

Interviews were analyzed by 2 study authors (DA, EH) using thematic and content analysis, assisted by MAXQDA, a software tool that does not automate any of the analysis process. Initially, 2 authors read and re-read the transcripts and developed an initial coding framework. They then independently coded 2 interview transcripts based on this coding framework. A postcoding comparison occurred, with all codes compared and reconciled. The coding framework was updated iteratively throughout the analysis. The codes were organized into themes and sub-themes that describe the experience of living with HTG-AP. Where possible, segments were also coded to indicate whether symptoms and impacts were experienced during or between episodes. A final quality review of the coding framework and all transcripts was conducted by a further study author (KW). Concept saturation was monitored during the analysis and documented in a saturation matrix to establish the point at which no new relevant concepts were elicited.[34,35]

Once the important concepts had been identified, a conceptual model was developed (EH, DA, KW) to illustrate the interrelationships between symptoms, impacts and the treatment/management strategies described by participants.

Table 1. Sociodemographic characteristics.

Characteristic	N = 12
	Mean (SD), Min-Max
Age, years	43.8 (10.8), *32.0-66.0*
Self-reported identity	**n (%)**
Female	8 (67)
Male	4 (33)
Employment	
Full time	5 (42)
Part time	1 (8)
Retired	1 (8)
Unable to work due to health	2 (17)
Other	3 (25)
Highest level of education	
Secondary education or equivalent	4 (33)
University/college degree or equivalent	5 (42)
Postgraduate degree or equivalent	2 (17)
Other	1 (8)
Ethnicity[a]	
White	8 (89)
Other	1 (11)
Country	
Germany	3 (25)
United Kingdom	5 (42)
United States	4 (33)

Abbreviations: Max, maximum; Min, minimum.
[a]Ethnicity not asked in Germany, total n = 9.

Results

Sample characteristics

Twelve individuals took part in the study. In the sample, the age of first AP episode ranged from 1- to 63-years-old, the total number of AP episodes experienced ranged from 1 to 30, over half were overweight or obese (58%), and half had type 2 diabetes. Full sociodemographic and clinical characteristics are shown in Tables 1 and 2, respectively.

Table 3 provides a summary of the EQ-5D-5L index and visual analogue scale (VAS) scores. At the time of background questionnaire completion, mean EQ-5D-5L index scores were 0.673, which are lower than population norms in the UK (0.856), US (0.825), and Germany (0.902).[36] Mean EQ-5D-5L index scores were -0.115 (SD = 0.329) during participants' most recent episode. Mean VAS ratings showed a similar pattern to the EQ-5D utility values.

Table 2. Clinical characteristics.

Characteristic	N = 12
HTG-AP episodes	**Mean (SD), *Min-Max***
Age of first HTG-AP episode (years)	32.2 (17.0), *1.0-63.0*
Total number of AP episodes in lifetime	9.0 (11.3), *1.0-30.0*
Days since last episode	319.4 (253.0), *18.0-703.0*
Number of hospital admissions due to AP	9.2 (10.2), *1.0-30.0*
Number of nights in hospital due to HTG-AP	64.3 (73.6), *2.0-200.0*
Number of nights in intensive care due to HTG-AP	13.2 (19.6), *0.0-60.0*
Body mass index (BMI) categories	**n (%)**
Underweight (<18.5)	0 (0)
Normal weight (18.5 to <25)	5 (42)
Overweight (25 to <30)	4 (33)
Obese (30+)	3 (25)
Triglyceride levels	
Severe HTG (fasting triglyceride levels 500-1999 mg/dL)	10 (83)
Very severe HTG (fasting triglyceride levels ≥ 2000 mg/dL)	2 (17)
Diagnoses[a]	
FCS	3 (35)
Type 2 diabetes	6[b] (50)
Management and medications	
Management of HTG-AP with diet	11 (92)
Insulin	4 (33)
Pancreatic enzymes	5 (42)
Other[c]	6 (50)

Abbreviations: AP, acute pancreatitis; BMI, body mass index; HTG, hypertriglyceridemia; HTG-AP, hypertriglyceridemia-induced acute pancreatitis; FCS, familial chylomicronemia syndrome; Max, maximum; Min, minimum.
[a]Participants could report multiple diagnoses, so total could be more than 100%.
[b]Count includes 2 participants who reported taking insulin but did not report a diagnosis of diabetes.
[c]Other medications include antidepressants, anti-inflammatories, testosterone, diabetes medication, cholesterol-lowering medication, lipid-lowering medication, heartburn medication, and painkillers.

Table 3. EQ-5D-5L index and VAS scores for participants during an episode and at time of background questionnaire completion (N = 12).

EQ-5D-5L scores	Recall period	
	During most recent episode of HTG-AP[a]	Today[b]
Index score		
Mean (SD)	-0.115 (0.329)	0.673 (0.208)
Median	-0.131	0.684
Min-Max	-0.524 to 0.503	0.243-0.985
VAS score		
Mean (SD)	19.1 (14.3)	64.1 (22.4)
Median	14.5	70.0
Min, Max	0.0-50.0	20.0-90.0

Abbreviations: HTG-AP, hypertriglyceridemia-induced acute pancreatitis; Max, maximum; Min, minimum; VAS, visual analogue scale.
[a]Based on retrospective recall of most recent episode within the last 2 years.
[b]At the time of background questionnaire completion.

Table 4 presents a summary of responses to the pain and fatigue items from the *PROMIS Profile v1.0-FCS 28*. At the time of completion, 11 (92%) participants had experienced some form of pain and 12 (100%) had experienced fatigue in the previous 7 days. Among those experiencing any pain, 10 (91%) reported that it interfered with their day-to-day activities. Among those experiencing fatigue, 11 (92%) reported that it affected their ability to initiate tasks. These results indicate the severity of pain and fatigue experienced between HTG-AP episodes still greatly affects an individual's day-to-day life.

The saturation matrix indicated that saturation was reached after 7 interviews, with no new concepts emerging in the last 5 interviews (Supplementary File 1).

Overview of the experience of HTG-AP episodes

The symptoms and impacts of HTG-AP and relationships between them are illustrated in a conceptual model in Figure 1. Abdominal pain, gastrointestinal symptoms, and fatigue were the core symptoms reported. Pain and fatigue had the most significant impact on daily activities, social activities, family life/relationships, and emotional wellbeing. The impact on emotional wellbeing affected participants' ability to carry out their usual daily and social activities, as well as their relationships.

The nature of experience of HTG-AP episodes was broadly similar across participants, but there was some variation in the speed of onset, severity of symptoms, and rate

Table 4. ***PROMIS Profile v1.0-FCS 28*** **items relating to abdominal pain, fatigue, and daily activities.**

In the past 7 days...[2]	Overall N = 12
1. How would you rate your pain on average? (scale 0-10, 0 = no pain, 10 = worst pain imaginable)	
Mean (SD)	4.0 (2.3)
[Median]	[4.0]
Min, Max	0.0-7.0
2. How much did pain interfere with your day-to-day activities? n (%)[1]	
Not at all	1 (9)
A little bit	4 (36)
Somewhat	3 (27)
Quite a bit	2 (18)
Very much	1 (9)
Not asked[1]	1
3.How often did you have belly pain? n (%)	
Never	2 (17)
One day	2 (17)
2-6 days	3 (25)
Once a day	0 (0)
More than once a day	5 (42)
4. At its worst, how would you rate your belly pain? n (%)[a]	
Not bad at all	0 (0)
A little bad	3 (30)
Somewhat bad	2 (20)
Quite bad	5 (50)
Very bad	0 (0)
Not asked[1]	2
5. How much did belly pain interfere with your day-to-day activities? n (%)[b]	
Not at all	1 (10)
A little bit	5 (50)
Somewhat	1 (10)
Quite a bit	3 (30)
Very much	0 (0)
Not asked[1]	2
6. I feel fatigued... n (%)	
Not at all	0 (0)
A little bit	2 (17)
Somewhat	4 (33)
Quite a bit	4 (33)
Very much	2 (17)
7. I have trouble starting things because I am tired... n (%)	
Not at all	1 (8)
A little bit	5 (42)
Somewhat	3 (25)
Quite a bit	3 (25)
Very much	0 (0)

[a]Items 2, 4, and 5 were conditionally displayed depending on answers to items 1 and 3, therefore not all participants were asked all items. Only response levels that were endorsed are displayed here.
[b]Recall period relates to the previous 7 days prior to questionnaire completion.

of recovery. Five participants described a rapid onset of episodes, with symptoms starting and intensifying within a matter of hours. Others reported experiencing less severe symptoms in the days preceding episode onset. Episodes often resulted in hospitalization, in some cases for up to 10 days. Ten participants reported experiencing health complications during episodes (eg, fluid retention, blood clots, refeeding syndrome, necrosis of the pancreas, pneumonia, cardiac episode). Two participants reported experiencing organ failure during a past episode, resulting in a month-long coma for 1 participant. Recovery time varied from a few days to 2 to 3 weeks, with participants describing being able to slowly reintroduce eating and drinking. From onset to recovery, some episodes were described as lasting up to 6 weeks. After episodes were perceived to be over, it often took individuals several more weeks to regain their health. Examples of the patient experience throughout an episode of HTG-AP, as illustrated in patient line drawings, are provided in the Supplementary File 2.

Symptoms and functional issues associated with HTG-AP

Abdominal pain

All participants (N = 12) reported experiencing abdominal pain during episodes of HTG-AP (Fig 2), which was often triggered by high fat, spicy or sugary foods, and strenuous movement. Most participants reported abdominal pain at the onset of HTG-AP episodes and described it as the first indicator of an episode. Six participants described the onset of abdominal pain as sudden and rapidly escalating, while three reported experiencing less severe abdominal pain in the days preceding an episode.

Participants recalled the pain during an episode as "unbearable" (n = 2), "intensively horrifying" (n = 1), "agonizing" (n = 1), and "stabbing" (n = 3).

> *“It is like somebody has wedged a knitting needle right through your sternum, all the way through the back and you can feel all your insides touching your ribs and every movement makes it rub and hurt! The pain is like a 10 out of 10, can’t think, can’t speak, can’t do anything.” (P 114, UK)*

Eleven participants reported that their abdominal pain persisted after the episode was over. Some reported that their back (n = 5) and shoulder pain (n = 2) also persisted. Although the pain between episodes was less severe than during an episode, 2 participants reported that they experience daily pain, and 4 participants described it as long-term.

> *“There’s always something, 24 hours a day, 7 days a week, it’s always like a dull pain...because it’s become such the norm [pain], I’ve just learned to cope.” (P 113, UK)*

Gastrointestinal symptoms

Gastrointestinal symptoms reportedly experienced during HTG-AP episodes included nausea or vomiting (n = 9), diarrhea (n = 7), bloating (n = 5), and heartburn (n = 5), as shown in Figure 2.

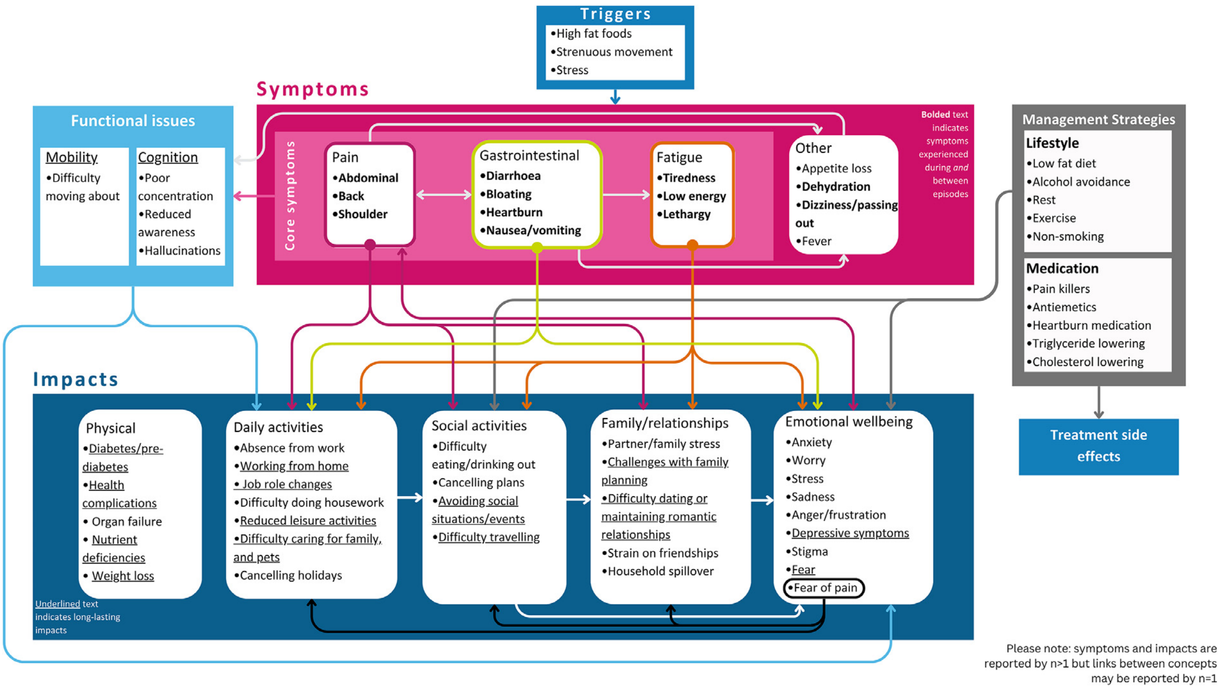

Figure 1. **Conceptual model on the relationship between key symptoms and impacts of acute pancreatitis.**

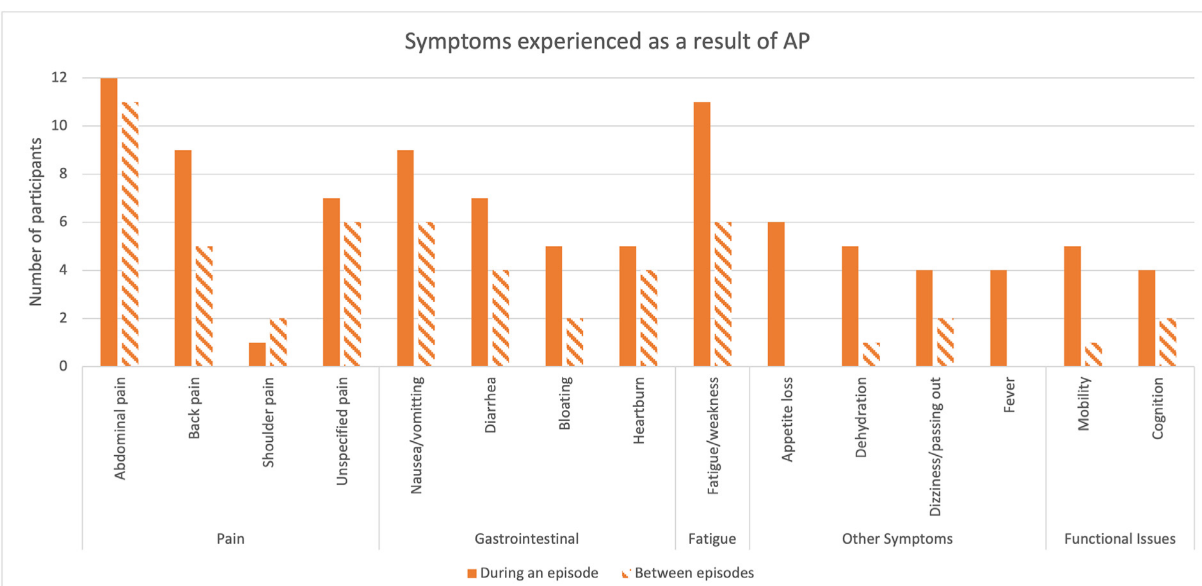

Figure 2. **Symptoms experienced during and between episodes of acute pancreatitis (AP).**

"A normal day with pancreatitis I can't keep anything down. It's though it's severe enough to lead to really bad dehydration." (P 202, US)

Five participants reported that the nausea persisted between episodes but was less severe and could be triggered by food consumption.

"Even when there is not an episode. It's like if I forget to take the [gastroesophageal reflux treatment]…then I end up getting really sick after I eat" (P 202, US)

Three participants described experiencing severe diarrhea during an episode, with 1 participant unable to leave the bathroom for sustained periods of time. Four participants reported that the diarrhea persisted between episodes, although it was less severe.

Four participants reported experiencing bloating and 5 experienced heartburn during episodes, with the latter reportedly lasting up to 2 or 3 days.

"It feels like I eat food and have the feeling that it is not digested quickly, is not digested well and I get bloating.

That is actually there every day, even without pain." (P 302, DE)

Fatigue

Most participants (n = 11) described experiencing fatigue due to HTG-AP. Three participants described experiencing it during episode onset, progressing to "severe" (n = 1), "debilitating" (n = 1), and "mind-blowing" (n = 1) levels by the peak of the episode. Several participants reported that they needed to sleep more than usual.

> *"It took me half an hour to brush my hair, and then I fell asleep for two hours. It was literally that, [I] would be wake up and manage to do something for about 30/40 minutes, and then sleep for another two hours." (P 109, UK)*

Three participants described their experience of fatigue as varying from 1 episode to the next. Another reported experiencing the same level of fatigue during every episode. Four participants described how it took a long time (ie, several weeks) to recover from fatigue symptoms. Six participants described experiencing fatigue between episodes, but it was less severe than during episodes.

> *"I'm exhausted and there's no reason why…I know when people say, "You can be tired," but pancreatitis lethargic is just a different type of tiredness. It's so hard to explain that you just feel hungover but you're not hungover." (P 111, UK)*

One participant indicated that they believed they were experiencing "chronic" fatigue due to nutrient deficiencies caused by HTG-AP.

Functional limitations

Five participants reported experiencing difficulties with their mobility during episodes. Mobility issues were caused by various symptoms, including pain (n = 3), dizziness (n = 1), nausea (n = 1), and fatigue (n = 3).

> *"My bathroom is like 20 feet away from my couch and in an episode it's hard to get from my couch to my bathroom." (P 202, US)*

Four participants described experiencing cognitive difficulties during episodes, including difficulties concentrating (n = 2), difficulties verbalizing thoughts (n = 1), hallucinations (n = 1), and confusion and disorientation (n = 1).

> *"I have in the past become confused and disoriented so that's why it is really important to get to the hospital right away so that doesn't happen." (P 216, US)*

Two participants reported that they experienced cognitive difficulties between episodes, including problems with concentration (n = 1) and information processing (n = 1). One of these participants suggested that they had long-lasting difficulties with concentration.

Other symptoms

Other symptoms reported during HTG-AP episodes included appetite loss (n = 6), dizziness or passing out (n = 5), dehydration (n = 4), and fever (n = 4). Four participants described having a loss of appetite. Dehydration (n = 2) and dizziness or passing out (n = 1) were also experienced between episodes. Long-term physical impacts related to HTG-AP included weight loss (n = 5) and nutrient deficiencies (n = 3), as shown in the saturation matrix (Supplementary File 1).

HRQoL impact of HTG-AP

Daily activities

All participants reported that HTG-AP had a negative impact during episodes on their ability to perform their daily activities (see Supplementary File 1), including work (n = 9), leisure activities (n = 8), housework (n = 6), and caregiving responsibilities (ie, caring for children, family, pets; n = 5) (Fig 3). Most (n = 10) also reported impact to their daily activities between episodes.

> *"I couldn't go for a walk, I couldn't go to work, couldn't do any housework, couldn't do anything that I like doing, I didn't have the concentration span to be able to read." (P 114, UK)*

Nine participants reported being unable to work during episodes because they were hospitalized or because of impaired physical and cognitive functioning. Between episodes, 4 participants reported impacts on work, including finding work more challenging and having to reduce time spent working. Some participants described long-term work impacts, including switching to remote employment, taking extended time off work, changing job roles/tasks, and adapting the way they work to avoid stress. One participant described taking extended leave from work following an episode.

> *"Normally, I bounce back quite quickly after pancreatitis attack but this just seems to have…stopped me doing a lot of things… I can't go back to work today because I can't even walk two feet in front of me." (P 111, UK)*

Six participants reported substantial difficulties or being unable to carry out housework during episodes, including cleaning, laundry, shopping, and cooking, and 2 also reported difficulties between episodes because of persisting symptoms. Others (n = 4) recalled how they were unable to care for their children, family members, or pets during an episode because of the time spent in hospital and loss of mobility. Two participants described ongoing impacts on caregiving between episodes, with 1 individual having to put a plan in place for childcare in case an episode is triggered.

Two participants reported being unable to carry out leisure activities during episodes, including reading, watching tv, holidays, and exercise. Seven participants described limiting leisure activities (eg, exercise/sport) between episodes

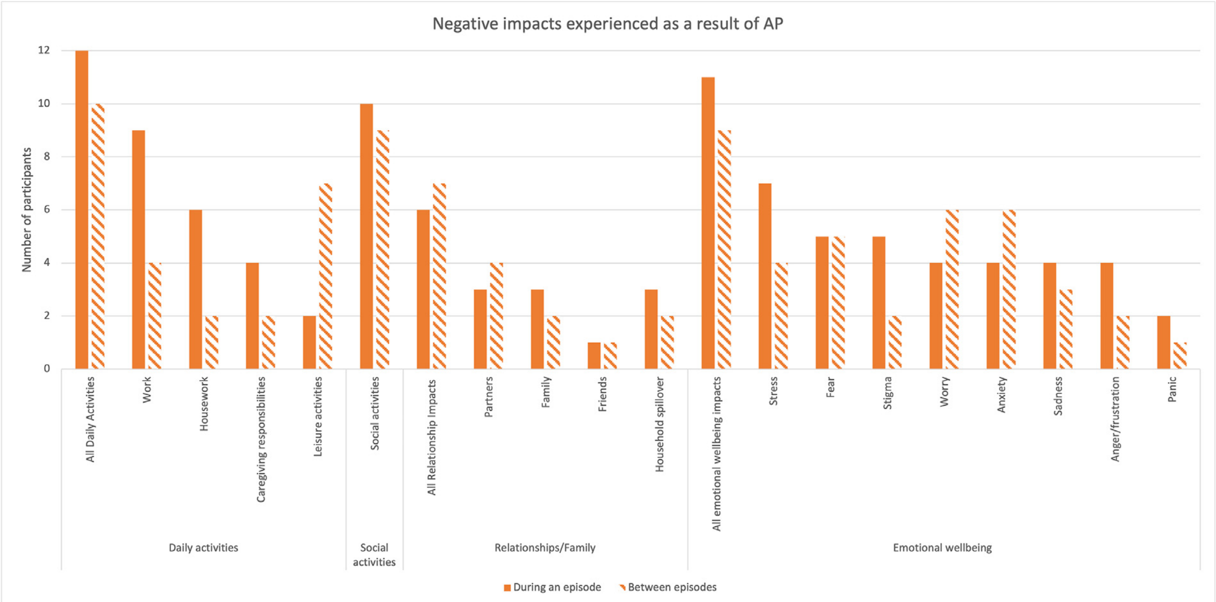

Figure 3. Impact of acute pancreatitis (AP) during and between episodes.

because of persisting symptoms or concerns over triggering an episode.

"Long walks I can't do because I'm too scared in case it sets it off" (P 108, UK)

Social activities

All participants (N = 12) reported an impact on social activities (see Supplementary File 1), with impacts experienced during and between episodes (Fig 3).

During episodes, several participants reported being unable to socialize (n = 8) or avoiding social situations.

"In an acute phase I avoid all people I know…because you leave a bad impression when you appear so weak." (P 302, DE)

Some participants (n = 3) described avoiding or restricting their social activities between episodes because of their persisting symptoms or fear of experiencing another episode. Others described ongoing difficulties socializing between episodes, as most activities involved food and alcohol.

"Family gatherings are tough because I don't want them to see me that way…We used to hang out with family four, five, six hours. Now it's an hour and a half, I can handle an hour and a half." (P 204, US)

Relationships and family

Seven participants reported that HTG-AP had an impact on their relationships both during and between episodes (as shown in Fig 3).

"I would say that some relationships were impacted…-maybe friends who were younger and at the time didn't really care to understand why I was sick" (P 216, US)

Seven participants reported how their HTG-AP also affected relationships between episodes, including relationships with partners or prospective partners.

"Pancreatitis has cost me my business, my house, my marriage, nearly cost me my life so I should be grateful for that. It's cost me everything." (P 113, UK)

Four participants reported that HTG-AP, experienced both during and between episodes, had spill-over effects on their household/family, including family/partners having to take time off work, additional caregiving burden for family/partners, restrictions on activities and holidays. Two participants reported an impact on family planning due to their poor health and potential complications of pregnancy, while another 2 participants described experiencing financial burden related to HTG-AP.

Emotional wellbeing

All participants reported a negative emotional impact of HTG-AP. The most frequently reported emotional impacts included stress (n = 9), worry (n = 8), anxiety (n = 8), fear (n = 8), sadness (n = 6), stigma (n = 6), anger/frustration (n = 5), and panic (n = 3), all of which were experienced both during and between episodes (see Fig 3).

"I was scared and stressed and worried and thinking, 'Am I actually going to make it out of here upright or feet first?" (P 109, UK)

Four participants reported feeling frustrated or angry during episodes, attributed to a lack of understanding from the medical profession and not being properly informed about their prognosis, triggers, and prevention.

"That's that level of frustration at not being able to know what's going on, what the prognosis is, how long it's

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going to take, nobody actually knew anything" (P 114, UK)

Four participants reported sadness or depressive symptoms during episodes because of the restrictions on daily activities and social activities. Two participants also described an emotional trauma attached to their experience of HTG-AP and feelings of panic.

"You're naturally afraid or panic that something might be going on again." (P 308, DE)

Nine participants reported experiencing significant emotional impacts between episodes, including feelings of worry, anxiety, fear, panic, and stress. These feelings were related to the possibility of another episode, as well as how possible episodes could impact health and daily activities (eg, missing an important event, such as their child's graduation).

Six participants reported experiencing stigma from colleagues and health care workers because of the perceived cause of AP (ie, alcohol induced). Stigma was reported by individuals in all 3 countries, suggesting that it may be present across different healthcare systems and regions.

"So many medical people still believe alcohol is the main cause of pancreatitis, as soon as you say pancreatitis, they automatically assume you're an alcoholic and you get mistreated from that point onwards." (P 113, UK)

Management of AP

Although AP episodes often resulted in hospitalization, some participants (n = 4) described how they tried to manage their AP episodes at home (eg, with painkillers). Only when the symptoms became unmanageable did they seek hospital care.

"*I try to deal with at home, but then it gets to that point when you know you can't deal with it at home" (P 108, UK)*

Participants reported long-term lifestyle changes to manage HTG-AP, including following a strict diet (n = 11), avoiding alcohol (n = 8), exercising (n = 6), and not smoking (n = 3). Dietary restrictions were often described as burdensome (n = 10). Participants described requiring strong pain relief, such as morphine (n = 4), while in hospital to manage their pain. Three participants reported taking pain medication between episodes, but this did not guarantee a life without pain.

"It's [abdominal pain] dull but it's agony and it's always there. It doesn't matter what you try to take for it." (P 202, US)

Most participants (n = 10) described pain as one of the most important symptoms to improve because of the current lack of effective pain relief and the impact it has on many areas of daily life. Participants emphasized a desire for prospective effective treatments that would allow them to eat what they want and eliminate worries about dietary triggers and return to their usual social activities. Six participants described a preference for novel treatments that could prevent future episodes, and 3 participants described a need for treatments that can better manage symptoms during episodes.

Discussion

This is the first qualitative study to explore the experience of HTG-AP from the patient perspective and illustrate the findings in a conceptual model. The reported symptomatic and HRQoL burden was most significant during episodes, with the abdominal pain, gastrointestinal symptoms, and fatigue debilitating participants' ability to function and carry out usual activities. These symptoms had an impact on participants' emotional wellbeing, relationships, and family life. The severity of HTG-AP episodes often resulted in hospitalization, serious health complications, and a gradual recovery, taking several weeks to regain health. The qualitative findings were supported by quantitative data from the EQ-5D-5L index scores, which showed participants considered the experience of their most recent episode of AP to be worse than death. In addition, data from the *PROMIS Profile v1.0-FCS 28* indicated that most participants had experienced pain and fatigue in the past 7 days, and this impacted their ability to perform their daily activities. These findings are consistent with previous studies that have demonstrated the extensive physical and psychological impacts of AP experienced during and after AP episodes.[18-21,23,26,27]

A novel finding of this study is that the symptoms and impacts of an HTG-AP episode persisted postrecovery, often having long-lasting effects. These qualitative findings were also supported by quantitative data from the EQ-5D-5L, which showed that although index and VAS scores were worst when participants recalled their experience during an episode of AP, they also remained below population norms for the UK, US, and Germany at the point of questionnaire completion.[28] These findings are in line with previous studies that have highlighted some ongoing HRQoL burden experienced between episodes and recovery.[18,37] However, the present study extends on previous literature by demonstrating the full extent of the symptomatic and HRQoL burden experienced throughout the AP journey including episode onset, during and between episodes, as well as the long-term impacts.

Participants reported making long-term lifestyle changes to avoid HTG-AP episodes, including strict dietary restrictions and alcohol avoidance. These restrictions had a wider impact on emotional wellbeing and participation in daily activities and social activities. They also reported taking a range of medications to manage symptoms and to prevent episodes, but these were often perceived as lacking efficacy. When asked about their perceptions of a successful treatment, participants described the importance of both preventions of episodes and management of specific symptoms. These findings highlight an unmet need for new treatments that can reduce the number of HTG-AP episodes and reduce the symptom burden associated with experiencing episodes. New and emerging therapies, such as those which inhibit apolipoprotein CIII (ApoCIII), have demonstrated significant reductions in TG levels.[15,38] These advancements underscore the potential to improve long-term HRQoL for individuals with HTG-AP. Together with the current study, these innovations highlight how improved care for HTG-AP patients requires the development of treatments that incorporate and prioritize the patient experience.

A strength of this study is that the sample consisted of patients with a variety of clinical and background characteristics, including different etiologies of HTG-AP (ie, FCS and sHTG). The results did not suggest there were any notable differences between those with FCS and those without FCS across the qualitative data, EQ-5D or PROMIS FCS, however the FCS subsample was small ($n = 3$) making subgroup comparisons challenging. The exclusion criteria also reduced any potential bias through participant exposure to clinical trial protocols or new treatments. A limitation that should be considered is that the small sample size may not be representative of all patients experiencing HTG-AP (eg, those eligible for participation in clinical trials), however this study's design is consistent with best practice qualitative research guidelines; qualitative research is not designed to be representative. Further, the presence of comorbidities (eg, diabetes) among the sample may impact the certainty that the reported burden is exclusively a result of HTG-AP. Although study inclusion required the experience of an HTG-AP episode within last 2 years, this still required participants to rely on retrospective recall, so some participants may not have accurately recalled their experience. It is also possible that there may be some overlap in the reporting and interpretation of experiences during and between episodes. Another limitation of the study is that it does not explore the relative impact on family members of those who experience HTG-AP. In addition to the disruption in life and worry during episodes, the long-term dietary/lifestyle changes required by the affected family member has the potential to disrupt family, cultural, and even societal norms to accommodate the strict requirements of living with this condition.

Conclusions

In conclusion, HTG-AP is associated with substantial symptomatic and HRQoL burden, which was at its worst during episodes. Many symptoms and impacts persisted post recovery, having long-lasting effects on health and daily life. Long-term management with a restrictive diet is particularly burdensome and has a negative impact on HRQoL. Treatments which prevent episodes, and reduce the symptom burden, have the potential to have acute and long-lasting benefit.

CRediT authorship contribution statement

Asia Sikora Kessler: Writing – review & editing, Methodology, Conceptualization. **Daniel Aggio:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis. **Ellen M. Howard:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis. **Daniel E. Soffer:** Writing – review & editing, Methodology. **Jordi Alonso:** Writing – review & editing, Methodology. **Sarah Acaster:** Writing – review & editing, Methodology, Conceptualization. **Kate Williams:** Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Conceptualization.

Ethical approval

This study was reviewed and approved by Western Institutional Review Board (WIRB) – Copernicus Group Independent Review Board (IRB tracking number: 20231351). All participants provided their written informed consent to participate in the study. All participants provided their informed consent for their de-identified data to be published.

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Declaration of competing interest

Asia Sikora Kessler is an employee of, and holds stock and stock options in, Ionis Pharmaceuticals Inc. Daniel Aggio, Ellen Howard and Kate Williams are employees of Acaster Lloyd Consulting Ltd and may hold stock or stock options in the company. Daniel Soffer's institution has contracts for research with Ionis Pharmaceuticals Inc, and he has served as consultant for Ionis Pharmaceuticals Inc. Sarah Acaster is a shareholder and the co-owner of Acaster Lloyd Consulting Ltd. Jordi Alonso's institution received consultancy fees from Ionis Pharmaceuticals Inc.

Data statement

Raw data (interview transcripts) are not publicly available to protect participant privacy due to the rare nature of FCS.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jacl.2025.04.190.

References

1. Saadatagah S, Pasha AK, Alhalabi L, et al. Coronary heart disease risk associated with primary isolated hypertriglyceridemia; a population-based study. *J Am Heart Assoc*. 2021;10(11):e019343.
2. Nelson J, Vemuri D, L'Italien G, et al. Unique discordance of LDL-C levels and apo A1/remnant ratios in South Asians: implications for risk stratification for prevalent diabetes mellitus. *J Clin Lipidol*. 2016;10(3):665–666.
3. Nichols GA, Arondekar B, Garrison LP. Patient characteristics and medical care costs associated with hypertriglyceridemia. *Am J Cardiol*. 2011;107(2):225–229.
4. Christian JB, Bourgeois N, Snipes R, Lowe KA. Prevalence of severe (500 to 2,000 mg/dl) hypertriglyceridemia in United States adults. *Am J Cardiol*. 2011;107(6):891–897.
5. Pallazola VA, Sajja A, Derenbecker R, et al. Prevalence of familial chylomicronemia syndrome in a quaternary care center. *Eur J Prevent Cardiol*. 2020;27:2276–2278.
6. Gaudet D, Méthot J, Déry S, et al. Efficacy and long-term safety of alipogene tiparvovec (AAV1-LPLS447X) gene therapy for lipoprotein lipase deficiency: an open-label trial. *Gene Ther*. 2013;20(4):361–369.
7. Hegele RA, Berberich AJ, Ban MR, et al. Clinical and biochemical features of different molecular etiologies of familial chylomicronemia. *J Clin Lipidol*. 2018;12(4):920–927 e4.
8. Valdivielso P, Sánchez-Chaparro MÁ, Calvo-Bonacho E, et al. Association of moderate and severe hypertriglyceridemia with obesity, diabetes mellitus and vascular disease in the Spanish working population: results of the ICARIA study. *Atherosclerosis*. 2009;207(2):573–578.
9. Garg R, Rustagi T. Management of hypertriglyceridemia induced acute pancreatitis. *Biomed Res Int*. 2018;2018:1–12.
10. Gouni-Berthold I, Schwarz J, Berthold HK. Updates in drug treatment of severe hypertriglyceridemia. *Curr Atheroscler Rep*. 2023;25(10):701–709.
11. Paquette M, Amyot J, Fantino M, Baass A, Bernard S. Rare variants in triglycerides-related genes increase pancreatitis risk in multifactorial chylomicronemia syndrome. *J Clin Endocrinol Metab*. 2021;106(9):e3473–e3482.
12. Brahm AJ, Hegele RA. Chylomicronaemia—current diagnosis and future therapies. *Nat Rev Endocrinol*. 2015;11(6):352–362.
13. Hernandez P, Passi N, Modarressi T, et al. Clinical management of hypertriglyceridemia in the prevention of cardiovascular disease and pancreatitis. *Curr Atherosclerosis Rep*. 2021;23.
14. Jacobson TA. A "Hot" topic in dyslipidemia management—"how to beat a flush": optimizing niacin tolerability to promote long-term treatment adherence and coronary disease prevention. *Mayo Clin Proc*. 2010;85(4):365–379.
15. US Food and Drug Administration. *FDA approves drug to reduce triglycerides in adult patients with familial chylomicronemia syndrome*. FDA; 2024. Available from: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-drug-reduce-triglycerides-adult-patients-familial-chylomicronemia-syndrome#:~:text=The%20U.S.%20Food%20and%20Drug,familial%20chylomicronemia%20syndrome%20(FCS)
16. Stroes ESG, Alexander VJ, Karwatowska-Prokopczuk E, et al. Olezarsen, acute pancreatitis, and familial chylomicronemia syndrome. *New Engl J Med*. 2024;390(19):1781–1792.
17. Coté GA, Yadav D, Abberbock JA, et al. Recurrent acute pancreatitis significantly reduces quality of life even in the absence of overt chronic pancreatitis. *Am J Gastroenterol*. 2018;113(6):906–912.
18. Chen L, Zhou X, Tu X, et al. People's perceptions and experience of managing life after recurrent pancreatitis: a qualitative study in eastern China. *Sci Rep*. 2022;12(1):18749.
19. Liu J, Zhang B. The lived experience of inpatients with acute recurrent pancreatitis. *Gastroenterol Nursing*. 2020;43(3):249–257.
20. Ma S, Yang X, He H, et al. Psychological experience of inpatients with acute pancreatitis: a qualitative study. *BMJ Open*. 2022;12(6):e060107.
21. Burbridge C, Randall JA, Sanchez RJ, et al. Symptoms and dietary impact in hypertriglyceridemia-associated pancreatitis: development and content validity of two new measures. *PharmacoEconomics - Open,*. 2020;4(1):191–201.
22. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis - 2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102–111.
23. Williams K, Tickler G, Valdivielso P, et al. Symptoms and impacts of familial chylomicronemia syndrome: a qualitative study of the patient experience. *Orphanet J Rare Dis*. 2023;18(1):316.
24. Wu B.U., Butler R.K., Chen W. Factors associated with opioid use in patients hospitalized for acute pancreatitis. JAMA Netw Open. 2019;2(4). [cited 2024 Aug 14]e191827–e191827. Available from: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2730469. Accessed August 14, 2024.
25. Ma S, Yang X, He H, Gao Y, Chen Y, Qin J, et al. Psychological experience of inpatients with acute pancreatitis: a qualitative study. *BMJ Open*. 2022;12(6):e060107.
26. Gupta R, Rajani R, Primrose JN, Johnson CD. Body composition, physiological function and psychological changes in patients with predicted severe acute pancreatitis. *Pancreatology*. 2001;1(1):58–62.
27. Carr RA, Rejowski BJ, Cote GA, Pitt HA, Zyromski NJ. Systematic review of hypertriglyceridemia-induced acute pancreatitis: a more virulent etiology? *Pancreatology*. 2016;16(4):469–476.
28. Janssen B, Szende A. Population Norms for the EQ-5D. 2013 Sep 26. In: Szende A, Janssen B, Cabases J, editors. Self-Reported Population Health: An International Perspective based on EQ-5D [Internet]. Dordrecht (NL): Springer; 2014. Chapter 3.
29. Kaiser K, Fox RS, Perschon C, et al. Qualitative development of the PROMIS profile v1.0-familial chylomicronemia Syndrome (FCS) 28. *Quality Life Res*. 2023;32(2):605–614.
30. Obbarius A, Klapproth CP, Liegl G, et al. Measuring PROMIS pain interference in German patients with chronic conditions: calibration, validation, and cross-cultural use of item parameters. *Quality Life Res*. 2023;32(10):2839–2852.
31. Hernández Alava M, Pudney S, Wailoo A. Estimating the relationship between EQ-5D-5L and EQ-5D-3L: results from a UK population study. *Pharmacoeconomics*. 2022;41(2):199–207.
32. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality Life Res*. 2011;20(10):1727–1736.
33. Boczor S, Daubmann A, Eisele M, Blozik E, Scherer M. Quality of life assessment in patients with heart failure: validity of the German version of the generic EQ-5D-5LTM. *BMC Public Health*. 2019;19(1):1464.
34. Patrick DL, Burke LB, Gwaltney CJ, et al. Content validity—establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO Good Research Practices Task Force report: part 1—Eliciting concepts for a new PRO instrument. *Value in Health*. 2011;14(8):967–977.
35. Hennink M, Kaiser BN. Sample sizes for saturation in qualitative research: a systematic review of empirical tests. *Soc Sci Med*. 2022 Jan;292:114523.
36. Janssen B, Szende A. Population norms for the EQ-5D. *Self-reported population health: An international perspective based on EQ-5D* Springer; 2014:19–30.
37. Boije K, Drocic A, Engström M, Bjerså K. Patients' Perceptions of experiences of recovering from acute pancreatitis. *Gastroenterol Nursing*. 2019;42(3):233–241.
38. Filtz A, Parihar S, Greenberg GS, et al. New approaches to triglyceride reduction: is there any hope left? *Am J Prevent Cardiol*. 2024;18:e100648.