What Contributes To Quality Of Life In Patients With Episodic And Chronic Cluster Headache?

Davide Cappon
The National Hospital for Neurology and Neurosurgery
Norazah Abu Bakar
Headache and Facial Pain Group
Mariam Asma Torkamani
The National Hospital for Neurology and Neurosurgery
Manjit Matharu
Headache and Facial Pain Group
Marjan Jahanshahi (m.jahanshahi@ucl.ac.uk)
The National Hospital for Neurology and Neurosurgery

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Abstract

Background: Cluster headache (CH) limits daily activities as well as social and family life, worsening quality of life (QoL). There is a paucity of research on what factors, other than pain and disability, influence QoL in Chronic CH (CCH) and Episodic CH (ECH). This study compares the potential contribution of several psychosocial variables to QoL in CCH and ECH and investigates the association of QoL with measures of pain, disability, psychiatric symptoms, psychological health, and functional well-being.

Methods: 167 patients with CCH and 239 with ECH were assessed. QoL was measured with the CH-QoL, a reliable and valid disease-specific measure of QoL in CH. Measures of psychological health (self-esteem, perceived stigma, acceptance of illness), functional well-being (in professional, social, and private life), and psychiatric symptoms (Hospital Anxiety and Depression Scale, General Health Questionnaire-28, Beck Hopelessness Scale, Starkstein Apathy Scale) as well as pain (McGill Pain Questionnaire, Pain Behaviour Checklist), and disability (HDI, HIT-6, MIDAS) were obtained.

Results: Individuals with CCH reported poorer QoL than those with ECH in terms of “restrictions of activities of daily living” and “mood and interpersonal relationships”. Patients with CCH and ECH who had a higher level of disability had significantly worse QoL. Patients with low self-esteem and those who reported less acceptance of their disease and reported higher perceived stigma had significantly worse QoL. Additionally, CCH and ECH patients with psychiatric comorbidities, such as anxiety, depression, hopelessness, and apathy had poorer QoL. QoL was correlated with measures of psychosocial functioning, disability, and psychiatric comorbidity.

Conclusions: CH has a greater psychosocial impact on CCH patients than on ECH patients, as evidenced by significantly worse ratings for the former on all disability, mood, psychological health, functional well-being and QoL measures. In addition to managing physical pain, treating the psychiatric, psychological, and social factors associated with cluster headaches may be useful in preventing and lessening the long-term impact of CH on QoL. Our findings highlight additional factors to consider in the clinical management of CH and to incorporate in cognitive behavioral therapy with CH patients to reduce disability and the psychosocial impact of CH on daily life.

Introduction:

Cluster headache (CH) is a trigeminal autonomic cephalalgia (TAC) characterized by attacks that generate excruciating pain associated with prominent cranial autonomic features and restlessness or agitation (1,2). Two subtypes of CH, episodic (ECH) and chronic (CCH), are clinically distinguished primarily on the basis of the frequency of the attacks, while the nature and severity of pain experienced by the two subtypes is comparable. Previous studies have shown that complications such as depression, anxiety, and daily functioning restrictions are common in CH sufferers, causing highly disabling headache that negatively impacts quality of life (3,4).

The disability associated with pain plays a significant role in worsening quality of life in CH (4,5). Nevertheless, evidence is lacking about what, besides pain and disability, contributes to quality of life in CCH and ECH. This paper seeks to examine how CH triggers a cascade of changes on a range of life domains, including physical, psychological, emotional, social, and functional well-being, contributing to poor quality of life in CH.

Quality of life (QoL) is accepted as a critical measure in health care as it includes the patients' perspective of their health. We previously developed and validated the cluster headache quality of life scale (CH-QoL), the first disease-specific patient-reported outcome measure to monitor QoL in patients with CH in clinical care and research (6). We also assessed and demonstrated that the CH-QoL has good internal consistency, test-retest reliability, validity, responsiveness, and sensitivity to change to assess treatment effectiveness (7).

In this study, we aim to identify the potential contribution of several factors that may influence QoL in CH sufferers. We hypothesized that besides disability due to pain, a cluster of relevant variables such as psychological health (self-esteem, perceived stigma, acceptance of illness) functional well-being (in professional, social and private life) psychiatric symptoms (depression, hopelessness, anxiety, apathy) contribute to QoL for people with CH. More specifically, the first aim was to evaluate and compare the impact of ECH and CCH on pain-related, psychiatric, psychological health, functional wellbeing measures and QoL assessed with the CH-QoL. Second, we aimed to determine the association of CH-QoL with measures of pain, disability, psychiatric symptoms, psychological health, and functional well-being.

Methods:

Patients

Data were collected as part of the development and validation of the cluster headache quality of life scale (CH-QoL) study (6). Four hundred and six patients with CH (ECH=239, CCH=167) participated (please see Table 1). They completed a booklet of questionnaires, including measures of quality of life, headache-specific disability scales, psychiatric symptoms scales, psychological health and functioning in life. This study was approved by the Local Ethics Committee. All participants gave written informed consent.

Table.1: Patient demographics for the groups with episodic or chronic cluster headache

Quality of life

Cluster headache quality of life scale

	Episodic cluster headache (ECH) N=239	Chronic cluster headache (CCH) N=167
Age (years)	52.7 (12.7)	52.0 (11.9)
Gender	78F 161M	51F 116M
	33%F 67%M	30%F 70%M
Gender M/F ratio * 100	206.5	227.5
Education (years)	14.7 (3.4)	13.7 (2.8)
Age at onset (years)	31.5 (13.2)	35.1 (12.8)
Employment status n (%)		
Employed	159 (67.4)	69 (41.8)
Retired	55 (23.3)	30 (18.2)
Unemployed	12 (5.1)	57 (34.5)
Unemployed due to disability	8 (3.4)	53 (32.1)
Never employed	10 (4.2)	9 (5.5)

The CH-QoL scale consists of 28 items that are answered on a four points scale (Never = 0 to Always = 4). In addition to a total score, 4 sub-scores are derived: Restrictions of activities of daily living items 1–9; Impact on mood and interpersonal relationships items 10–21; Pain and anxiety items 22–23; Lack of vitality items 24–28. The total scores range from 0-112 with higher scores indicating poorer health related quality of life (6).

Psychiatric comorbidities

Hospital Anxiety and Depression Scale (HADS)

HADS is a self-report scale to detect depression and anxiety (8). It is composed of a 7-item subscale for depression and a 7-item subscale for anxiety. The individual items for each subscale are added to give a total score indicating overall anxiety (HADS-A) and depression (HADS-D). For both subtests, the total score range is 0-24, with scores above 8 and 11 indicating “possible” and “definite” cases for anxiety/depression, respectively.

The General Health Questionnaire (GHQ28): The GHQ-28 is a 28-item self-report measure of the common symptoms of mental health, specifically anxiety, depression, social withdrawal and somatic symptoms, which is used to screen for those who are at risk of or likely to have psychiatric disorders (9). The items are scored using a binary scoring method, with the first two available response options having a score of

0 and the last two responses having a score of 1. The total possible score ranges from 0 to 84, with scores ³ 24 indicating psychiatric cases.

Starkstein apathy scale (SAS): The Apathy scale (SAS) has 14 items for screening and assessing the degree of apathy, with possible scores ranging from 0 to 42, and a cut-off score of 14 defining presence of low and high apathy (10).

The Beck hopelessness scale (BHS): The BHS provides a measure of hopelessness or pessimism about the future (11). It consists of twenty items scored either true or false, thus having a possible total score ranging from 0 to 20, with higher scores reflecting greater hopelessness. Based on the scores, three levels of hopelessness can be ascertained: normal (0 – 3), mild hopelessness (4 – 8), moderate hopelessness (9 – 14) and severe hopelessness (15 – 20).

Psychological Health

The Rosenberg Self-Esteem Scale (RSES): is a widely used measure of self-esteem that includes both positive and negative feelings about ones 'self (12). The questionnaire consists of ten items, each with a 4-point Likert response scale. Five items measure self-deprecation and another five assesses positive self-esteem. The scores range from 0 to 30, with scores below 15 indicating low self-esteem.

The stigma scale: The Stigma Scale contains six affirmations scored from 0 (not at all) to 4 (definitely), which assesses how their headache affects their interaction with others, such as avoidance of others, avoidance by others, feelings of self-consciousness, feeling apologetic, unattractiveness and being different compared to others. A total stigma score ranges from 6–24, with score 6 indicatives of negligible stigma, score 7–18 indicative of some stigma, and 18–24 as severe stigma.

The Acceptance of Illness Scale: The level of participants' acceptance of and ability to adjust to their CH was measured using the Acceptance of Illness scale. This is an 8-item questionnaire describing the negative feelings associated with chronic disorders, with higher scores reflecting greater acceptance and better adjustment to their headaches.

Functional well-being

Impact on patients social, professional, and private functioning: A ten-point scale to evaluate how much CH has changed participants life in social (such as friends), professional (such as work) and private (such as family) domains.

Pain and pain behaviour:

The McGill Pain Questionnaire (MPQ): The MPQ is a measure of the subjective pain experience that includes 78 items describing the quality of pain, divided across four domains, namely sensory, affective, evaluative and miscellaneous aspects of pain. The scores can be treated statistically and the total possible score ranges from 0 to 78, with higher scores indicating worse pain (13).

The Pain Behaviour Checklist (PBC): The PBC is a 54-item scale that has been validated to measure the behavioural response of chronic pain patients. It is divided across three domains: help-seeking, avoidance and complaint behaviour ((14)).

Disability

The Henry Ford Hospital Headache Disability Inventory (HDI): the HDI is a 25-item questionnaire, divided into emotional and functional subscales, which is used to quantify the impact of headache on daily living, with higher scores reflecting greater disability caused by their headache (15).

The Migraine Disability Assessment Scale (MIDAS): the MIDAS measures the number of days of disability due to headaches within the past three months, in terms of missed days and reduced productivity by 50% or more in various aspects of daily living (16). The areas covered are paid work or schoolwork, household duties and social, leisure or family activities. Scores are categorized into four disability grades, little or no disability (0-5 days), mild (6-10), moderate (11-20) and severe disability (>21) ().

The Headache Impact Test (HIT-6): the HIT-6 is a six-item questionnaire used to measure the adverse impact of headaches in various domains; role and social functioning, cognitive functioning, vitality and psychological distress, as well as an item on pain severity (17). The scores range from 36 to 78, and functional impact due to headaches can then be categorized into four groups: little or no impact (< 49), some impact (50 – 55), substantial impact (56 – 59) and severe impact (60 – 78).

Statistical analysis:

All data were analyzed using the computing environment R (18). Wilcoxon signed rank tests were used to examine whether there is a significant difference in measures of co-morbid psychiatric symptoms, disability, pain and social function had occurred between chronic vs. episodic CH. Spearman correlational analyses, corrected for multiple comparisons, were performed to explore the relationship between measures of comorbid psychiatric symptoms, disability, pain, and social function and the CH-QoL total scores. We calculated and reported 95 % confidence intervals for all analyses.

Results:

Cluster Headache Quality of Life scale (CH-QoL) in CCH and ECH.

CH-QoL total score and the 4 sub-domains scores for patients with CCH and ECH are presented in Table 2 and Figure 1. Patients with CCH had a significantly higher CH-QoL total score (Mdn= 71, IQR = 31) than ECH patients (Mdn= 65, IQR = 28, $p < 0.01$), indicating poorer health related QoL reported by CCH patients. The CH-QoL ‘restriction of daily activities’ score (Mdn = 25, IQR = 11) than ECH (Mdn = 23, IQR = 10.25), p = 0.03) and the CH-QoL ‘mood and interpersonal relationships’ score were also significantly higher for CCH (Mdn = 26, IQR = 17.5) than ECH (Mdn = 20, IQR = 17), p = 0.01). The median scores on the other two subscales ‘pain and anxiety’ and ‘lack of vitality’ subscales of CH-QoL were similar for patients with CCH (Mdn = 7, IQR = 2; Mdn = 15, IQR = 4) or ECH (Mdn = 7, IQR = 2; Mdn = 15, IQR = 6).

Table 2
Impact of chronic (CCH) and episodic (ECH) cluster headache on quality of life assessed on the Cluster Headache Quality of Life scale (CH-QoL).

CH-QoL subscale	CCH (SD)	ECH (SD)	Mdn Diff	Wilcoxon (95% CI)	p-values	r
ADL Restriction	25 (19-30)	23 (17-28)	-2	1.99 (0.1, 3.0)	0.03*	0.2
Mood & interpersonal relations	26 (16-33)	20 (11-28)	-4.8	5.01 (2.9, 7.9)	0.01*	0.5
Pain and anxiety	7 (6-8)	7 (6-8)	0	0.00 (-0.1, 0.0)	0.67	0.1
Lack of vitality	15 (13-17)	15 (11-17)	0	0.00 (-0.1,1.1)	0.20	0.2
CH-QoL total score	71 (55-86)	65 (49-77)	-6	- 2.97 (2.9,12)	0.01*	0.4

ADL=Activities of daily living, CCH= chronic cluster headache, ECH= episodic cluster headache, Mdn= Median, SD= Standard Deviation.

[insert Figure.1 here]

Figure.1: Box plots depicting the distribution of CH-QoL scale total score and 4 sub-scores for chronic and episodic cluster headache. Black dots represent individual patients. Note: Higher scores on CH-QoL indicate poorer health related quality of life. CH-QoL cluster headache quality of life scale, F1 restriction of activities of daily living; F2 mood & interpersonal relations; F3 pain and anxiety; F4 lack of vitality.

Comparison of patients with CCH or ECH in terms of pain-related and psychosocial variables

The median and standard deviation values of the measures of pain, disability, co-morbid psychiatric symptoms, psychological health and functional well-being for the patients with chronic (CCH) and episodic cluster headache (ECH) are presented in Table 3.

Psychiatric Comorbidities

CCH had significantly higher scores than ECH patients on both HADS anxiety (CCH Mdn=12.0, IQR=7; ECH Mdn = 8.0, IQR= 6.5, Mdn diff = 4.00, $p < 0.001$) and depression (CCH Mdn =11.0, IQR=7; ECH Mdn = 6.0, IQR= 8, Mdn diff = 5.00, $p < 0.001$). More than half of CCH patients (56.4%) had anxiety scores of ≥11 on the HADS compared to 33.9% of ECH patients, while 50.9% of the former had HADS depression scores of ≥ 11 compared to 19.3% of the latter. On the SAS, CCH patients had higher apathy scores than ECH patients (CCH Mdn=16.0, IQR=12.0; ECH Mdn= 11.0, IQR= 9.0, Mdn diff = 5.00, $p < 0.001$), with 56.5% of CCH and 38.4% of ECH patients having clinically significant levels of apathy. CCH patients also had significantly higher BHS scores (CCH Mdn=9.5, IQR=13.0; ECH Mdn= 4.0, IQR= 6.0, Mdn diff = 5.50, $p < 0.001$). Based on the BHS standardized cutoffs ≥ 9, 52.1% of CCH patients reported moderate-severe

hopelessness, while only 23.6% of ECH reported clinically significant levels of hopelessness. Patients with CCH also had significantly higher scores on the GHQ-28 than ECH patients (CCH Mdn=10.0, IQR=16.0; ECH Mdn= 5.0, IQR= 11.0, Mdn diff = 5.00, $p < 0.001$), considerably exceeding the cut-off score > 4 for this scale. Scores above the cut-off had been reported by 73.2% of CCH and 56.1% of ECH patients, suggesting a high proportion of CCH patients experienced distress due to their headaches.

Disability

Patients with CCH had significantly higher scores on the MIDAS than ECH patients (CCH Mdn=83.0, IQR=139.5; ECH Mdn= 13.0, IQR= 50.0, Mdn diff = 70.00, $p < 0.001$). Based on the MIDAS disability grades, over half of the total sample of patients reported being severely disabled (56.8%), 8.1% were moderately disabled, 5.3% were mildly disabled, and 29.8% reported minimal disability. Patients with CCH had a significantly higher HIT-6 score than ECH patients (CCH Mdn=65.0, IQR=9.0; ECH Mdn= 62.0, IQR= 12.0, Mdn diff = 3.00, $p < 0.001$). The HIT-6 classification shows that the cluster headache severely impacts most patients (70.5%), 10.6% reported substantial impact, 11.9% had some impact, while only 7.0% had little or no impact. Patients with CCH had a significantly higher HDI total score than ECH patients (CCH Mdn=76.0, IQR=24.0; ECH Mdn= 64.0, IQR= 24.5, Mdn diff = 12.00, $p < 0.001$). The HDI total ranges from 4 – 100, indicating profound disability due to their headaches for both CCH and ECH groups.

Functional Well-being

We evaluated how much CH changes the life of sufferers in the professional, social or private domains. In all three domains patients with CCH reported significantly greater impact than patients with ECH (professional, CCH Mdn=10.0, ECH Mdn= 8.0; private, CCH Mdn=9.0, ECH Mdn= 8.0; social, CCH Mdn=9.0, ECH Mdn= 7.0, $p < 0.001$).

Psychological Health

The degree of perceived stigma associated with CH is also significantly greater in CCH patients than ECH (CCH Mdn=12.0, IQR=5.0; ECH Mdn= 8.0, IQR= 4.0, Mdn diff = 7.00, $p < 0.001$). Patients with CCH had significantly lower scores than ECH patients on the Rosenberg Self-Esteem scale (CCH Mdn=15.0, IQR=10.0; ECH Mdn= 20.0, IQR= 8.3, Mdn diff = 5.00, $p < 0.001$), with a higher proportion of CCH patients reporting low self-esteem on the Rosenberg Self-Esteem scale (CCH 44.8% vs. ECH 19.1%, $p < 0.001$) compared to the group with ECH. Low scores on the Acceptance of Illness scale reflect a lack of acceptance and poor adjustment to their CH. CCH reported significantly lower scores than ECH patients on the Acceptance of Illness scale (CCH Mdn=17.0, IQR=11.0; ECH Mdn= 24.0, IQR= 11.0, Mdn diff = 7.00, $p < 0.001$) indicating that CCH had poorer adjustment to their CH.

Pain And Pain-related Behaviours

We found no significant difference on the McGill Pain Questionnaire, CCH patients and ECH reported similar pain severity ratings (CCH Mdn=48.0, IQR=21.0; ECH Mdn= 43.0, IQR= 22.5, Mdn diff = 4.00)), suggesting that CCH and ECH experience similar levels of pain.

The PBC total score revealed significant differences in the patients' pain-related coping behaviours, with the CCH patients having higher total scores (CCH Mdn=34.0, IQR=12.0; ECH Mdn= 27.0, IQR= 23.0, Mdn diff = 7.00, $p < 0.001$), as well as on the helpseeking (CCH Mdn=3.0, IQR=2.0; ECH Mdn= 2.0, IQR= 3.0, Mdn diff = 1.00, $p < 0.001$) and avoidance (CCH Mdn=19.0, IQR=12.0; ECH Mdn= 13.0, IQR= 16.0, Mdn diff = 6.00, $p < 0.001$) subscales.

[insert Table.3 here]

Table3. Measures of co-morbid psychiatric symptoms, disability, pain and social function for patients with chronic and episodic cluster headache.

BHS= Beck Hopelessness Scale, CCH= chronic cluster headache, ECH= episodic cluster headache, HADS-A & D= Hospital Anxiety and Depression Scale, HDI= The Henry Ford Hospital Headache Disability Inventory, HIT-6= The Headache Impact Test, MIDAS= The Migraine Disability Assessment Scale, SAS= Starkstein apathy scale, Mdn= Median, IQR= Interquartile range, % percent above cut-offs.

Relationship of pain, disability, psychiatric symptoms, and psychological health, with Cluster Headache Quality of Life questionnaire (CH-QoL) total score in CCH and ECH.

Spearman correlational analyses, corrected for multiple comparisons, were performed to explore the relationship between measures of comorbid psychiatric symptoms, disability, pain, and social function and the CH-QoL total scores. The results are presented in Table 4 and Figure 2, 3 and 4.

[insert Table.4 here]

Table.4: Correlations of comorbid psychiatric symptoms, disability, pain, and social function with the cluster headache quality of life scale (CH-QoL) total score in CCH and ECH

BHS= Beck Hopelessness Scale, CCH= chronic cluster headache, ECH= episodic cluster headache, HADS-A & D= Hospital Anxiety and Depression Scale, HDI= The Henry Ford Hospital Headache Disability Inventory, HIT-6= The Headache Impact Test, MIDAS= The Migraine Disability Assessment Scale, SAS= Starkstein apathy scale.

Psychiatric symptoms

For both CCH and ECH there was a significant positive correlation between CH-QoL total score and HAD anxiety ($r = 0.68$, $p < 0.01$; $r = 0.58$, $p <0.01$), HAD depression ($r = 0.64$, $p < 0.01$; $r = 0.52$, $p <0.01$), Starkstein apathy scale ($r = 0.59$, $p < 0.01$; $r = 0.57$, $p <0.01$), GHQ 28 ($r = 0.60$, $p < 0.01$; $r = 0.34$, $p <0.01$),

Variable	CCH (IQR)	Cases %	ECH (IQR)	Cases %	Mdn Diff	Wilcoxon test (95% CI)	p-values
Mood							
HADS-A (cut-off ≥11)	12 (8-15)	56.4	8 (5-11)	33.9	-4	3.01 (2.0, 4.0)	0.01*
HADS-D (cut-off ≥11)	11 (7-14)	50.9	6 (2-10)	19.3	-5	4.99 (4.0, 6.0)	0.01*
SAS (cut-off ≥14)	16 (10-22)	56.5	11 (7-16)	38.4	-5	3.99 (2.0,5.0)	0.01*
BHS (cut-off ≥ 9)	9.5 (4-17)	52.1	4 (2-8)	23.6	-5.5	4.00 (3.0, 6.0)	0.01*
Minimal (0-3)		21.3		47.6			
Mild (4-8)		25.6		28.8			
Moderate (9-14)		17.7		12.7			
Severe (15-20)		35.4		10.9			
Disability							
MIDAS	84 (28-168)		13 (0-50)		-71	49.99 (34.0,67.0)	0.01*
HIT-6	65 (61-70)		62 (55-67)		-3	3.99 (2.0, 6.0)	0.01*
HDI total score	76 (64-88)		64 (52-76)		-12	11.99 (7.9, 15.9)	0.01*
Pain							
McGill Pain Questionnaire							
Total	48 (37-58)		43 (34-56)		-5	3.99 (0.1, 7.0)	0.02
Evaluative	5 (4-5)		5 (4-5)		0	0.01 (-0.1, 0.1)	0.49
Affective	9 (6-11)		9 (5-11)		0	0.99 (-0.01,1.0)	0.08
Sensory	25 (17-31)		21 (14-28)		-4	2.99 (0.0, 4.9)	0.02
Miscellaneous	10 (7-13)		9 (7-13)		-1	0.01 (-0.01, 1.0)	0.45
Pain report behaviour							

PBC Total	34 (26-38)	27 (13-36)	-7	6.01 (3.9,9.0)	0.01*
Help Seeking	3 (2-4)	2 (1-4)	-1	1 (0.1, 1.1)	0.01*
Avoidance	19 (12-24)	13 (4-20)	-6	5.0 (3.0,7.0)	0.01*
Complaint	7 (6-9)	7 (3-8)	0	0.9 (0.1, 1.1)	0.07
Psychological Health					
Stigma scale	12 (9-14)	8 (6-11)	-4	3.01 (2.0,4.0)	0.01*
Life Satisfaction Rate	2.6 (1.1-5.1)	5.5 (2.2-7.8)	2.9	-1.8 (-2.4, -1.1)	0.01*
Rosenberg Self-Esteem scale	15 (10-20)	20 (16-24)	5	-5.01 (-6.9, -3.9)	0.01*
Acceptance of illness scale	17 (12-23)	24 (19-30)	7	-6.01 (-8.0, -4.9)	0.01*
Functional well-being					
Social Affected	9 (8-10)	7 (5-8)	-2	1.99 (1.0, 2.0)	0.01*
Professional Affected	10 (8-10)	8 (6-9)	-2	1.0 (1.0, 2.0)	0.01*
Private Affected	9 (7-10)	8 (5-9)	-1	1.0 (1.0, 2.0)	0.01*

and BHS ($r = 0.62$, $p < 0.01$; $r = 0.42$, $p < 0.01$), indicating that an increase of symptoms of anxiety, depression, apathy and hopelessness are associated with higher scores on the CH-QoL, indicating poorer QoL with increased psychiatric morbidity.

[insert Figure.2 here]

Figure.2: Scatter plots representing significant Spearman correlations between CH-QoL total score and measures of psychiatric comorbidities, anxiety (HADS-A), depression (HADS-D), hopelessness (BHS) and apathy (Starkstein apathy scale). Note: CH-QoL total higher scores indicate poorer health related quality of life. HADS-A, HADS-D, BHS, Starkstein higher scores indicate poorer functioning. Individual observation, correlation lines, R values and p-values are showed for chronic cluster headache (CCH, purple circles) and episodic cluster headache (ECH, orange triangles).

	CCH		ECH	
	Spearman r	p-value adjusted <0.001	Spearman r	p-value adjusted <0.001
Mood				
HADS anxiety	0.68	<0.001*	0.58	<0.001*
HADS depression	0.64	<0.001*	0.52	<0.001*
SAS	0.59	<0.001*	0.57	<0.001*
GHQ28 total score	0.60	<0.001*	0.34	<0.001*
BHS	0.62	<0.001*	0.42	<0.001*
Disability				
MIDAS	0.45	<0.001*	0.28	<0.001*
HIT 6	0.48	<0.001*	0.40	<0.001*
HDI total	0.76	<0.001*	0.72	<0.001*
Pain				
McGill Pain Questionnaire				
Total	0.36	<0.001*	0.24	0.002
Evaluative	0.29	<0.001*	0.20	0.008
Affective	0.47	<0.001*	0.28	<0.001*
Sensory	0.22	0.01	0.16	0.04
Miscellaneous	0.33	<0.001*	0.31	<0.001*
Pain Behavior Checklist				
PBC Total	0.46	<0.001*	0.25	<0.001*
Help Seeking	0.03	0.71	0.15	0.03
Avoidance	0,49	<0.001*	0.28	<0.001*
Complaint	0,22	0,02	0.13	0.06
Psychological Health				
Stigma total score	0.74	<0.001*	0.57	<0.01*
Life Satisfaction Rate	-0.69	<0.001*	-0.49	<0.01*
Rosenberg Self-Esteem scale	-0.71	<0.001*	-0.54	<0.01*

Acceptance of illness	-0.76	<0.001*	-0.70	<0.01*
Functioning in life				
Social Life	0.59	<0.001*	0.44	<0.01*
Professional Life	0.54	<0.001*	0.57	<0.01*
Private Life	0.47	<0.001*	0.44	<0.01*

Disability

For both CCH and ECH we found a significant positive correlation between the CH-QoL total score and the MIDAS ($r = 0.45$, $p < 0.01$; $r = 0.28$, $p <0.01$), HIT-6 ($r = 0.48$, $p < 0.01$; $r = 0.40$, $p <0.01$), and HDI ($r = 0.76$, $p < 0.01$; $r = 0.72$, $p <0.01$), suggesting that an increase of disability as a result of CH is associated with higher CH-QoL scores and poorer QoL.

[insert Figure.3 here]

Figure.3: Scatter plots representing significant Spearman correlations between CH-QoL total score and measures of disability (MIDAS, HIT-6, HDI). Note: CH-QoL total higher scores indicate poorer health related quality of life. MIDAS, HIT-6 and HDI higher scores indicate higher disability. Individual observation, correlation lines, R values and p-values are showed for chronic cluster headache (CCH, purple circles) and episodic cluster headache (ECH, orange triangles).

Psychological health

For both CCH and ECH, there was a significant negative correlation between CH-QoL total score and Life satisfaction rate (respectively $r = -0.69$, $p < 0.01$; $r = -0.49$, $p <0.01$), indicating that lower ratings of life satisfaction is associated with poorer quality of life.

For both CCH and ECH, there was a significant negative correlation between CH-QoL total score and the Rosenberg Self-Esteem scale (respectively $r = -0.71$, $p < 0.01$; $r = -0.54$, $p <0.01$); suggesting that lower self-esteem is associated with poorer QoL.

For both CCH and ECH, there was also a significant negative correlation between CH-QoL total and Acceptance of the Illness (respectively $r = -0.76$, $p < 0.01$; $r = -0.70$, $p <0.01$), suggesting that lower acceptance of CH is associated with poorer QoL.

Pain behavior

For both CCH and ECH, there was a significant positive correlation between CH-QoL total and PBC total (respectively $r = 0.46$, $p < 0.01$; $r = 0.25$, $p <0.01$) and also PBC avoidance (respectively $r = 0.49$, $p < 0.01$; $r = 0.28$, $p <0.01$), suggesting that more pain-related behaviours and particularly engaging in pain avoidance behaviours are associated with lower QoL.

[insert Figure.4 here]

Figure.4: Scatter plots representing significant Spearman correlations between CH-QoL total score and measures of psychological health (Self-esteem, Acceptance of illness, Stigma), pain (McGill pain questionnaire) and pain behavior (PBC total). Note: CH-QoL total higher scores indicate poorer health related quality of life. Self-esteem and Acceptance of the illness higher scores indicate better functioning. Individual observation, correlation lines, R values and p-values are showed for chronic cluster headache (CCH, purple circles) and episodic cluster headache (ECH, orange triangles).

Discussion:

The first aim of this study was to compare the impact of ECH and CCH on QoL on the disease-specific and validated CH-QoL. Higher scores on the CH-QoL indicate a poorer health-related QoL. As expected, the CH-QoL total and the four subscale scores were worse for patients with CCH than ECH. The difference was significant for the total score and the subscales of "restrictions of ADL" and "mood & interpersonal relations". These results are in line with the other generic scales showing greater disability and more psychiatric symptoms in CCH (18–21). These results support the sensitivity of CH-QoL to discriminate between CCH and ECH.

The second aim of this study was to compare the impact of CCH and ECH on measures of pain, disability, psychiatric symptoms, psychological health, and functional well-being (see Table 5) and to determine the association of CH-QoL with these psychosocial and pain-related measures. We found that CCH and ECH patients with a higher level of disability on the MIDAS, HIT 6, and HDI had significantly poorer QoL measured with the CH-QoL. We also found patients who had low self-esteem and reported less acceptance of illness and higher perceived stigma had a significantly worse QoL (Figure 4). Furthermore, CCH and ECH patients with psychiatric comorbidities, such as anxiety, depression, hopelessness, and apathy had a significantly worse QoL (Figure 2). These findings corroborate evidence of the high prevalence of psychiatric illness among CH patients (18, 19) and the significant impact CH has on patients' QoL (4, 22). This impact is significantly greater in patients with CCH than those who suffer the episodic variant, which is as expected as their headaches are unremitting.

As expected, the results from this study demonstrate that the psychosocial impact of CH is greater for CCH patients compared to those with ECH, as shown by the significantly worse scores for the former in all disability, mood, psychological health, and functional well-being scales (see Table 3). Disability scores were significantly worse in CCH, with 76.3% reporting severe disability on the MIDAS. We found that 50.9% of CCH and 19.3% of ECH met criteria for depression on HADS-D, and 56.4% of CCH and 33.9% ECH reached the HADS-A cutoff for anxiety, indicating more ‘caseness’ for both depression and anxiety among CCH patients. In addition, 52.1% of CCH and 23.6% of ECH experienced severe levels of hopelessness that might be a ‘precursor’ to suicidal ideation and intention. Further, we found that 56.5% of CCH and 39.3% reported high levels of perceived stigma, indicating that CH sufferers are self-conscious and avoid other people as a result of their headaches. These findings corroborate evidence of

the significant disabling impact of CH on patients' lives, confirming the high prevalence of psychiatric comorbidities and showing that the impact is significantly greater in patients with CCH than ECH. Additionally, hopelessness levels were significantly higher for CCH, which correspond to the suicidal tendencies often described in CH patients (18, 23). Concerning psychological-health, CCH patients also have lower self-esteem and life satisfaction than those with ECH.

The correlational analysis confirmed the associations between the various measures of psychosocial functioning, disability and psychiatric comorbidity with QoL measured on the CH-QoL. In general, the pattern, direction and significance of these associations were similar for patients with CCH and ECH, but the magnitude of these associations were stronger for those with CCH than ECH (Figures 2 & 3). Differences in the pattern of associations between CCH and ECH emerged on the McGill Pain Questionnaire, on which the associations with CH-QoL were significant for the total, evaluative and miscellaneous categories for the CCH but not ECH patients (Table 4). These results are in line with our hypothesis that besides, pain and disability, a cluster of variables such as psychiatric symptoms, psychological health, and functional well-being contribute to QoL in CH.

To summarize, this study aimed to evaluate the relationship between pain, disability, and QoL in patients with CH, using a multitude of measures that incorporate the most important symptoms and signs in CH. We sought to assess the impact of CH on the individual's functioning associated with the underlying disease and influenced by personal and psychological factors. The ultimate goal was to identify some of the psychosocial factors contributing to QoL in CH, which may help future clinical management of CH in the long term.

Conclusions:

Besides treating physical pain, it might be useful to prevent and reduce the disease's long-term consequences considering specific psychiatric, psychological, and social factors associated with cluster headache. Our study may prove of value in identifying new factors to consider in cognitive behavioural interventions for CH sufferers.

Abbreviations:

ADL: Activities of daily living

CCH: chronic cluster headache

CH-QoL: Cluster Headache Quality of Life scale

ECH: episodic cluster headache

BHS: Beck Hopelessness scale

HADS: Hospital Anxiety and Depression scale

HDI: The Henry Ford Hospital Headache Disability Inventory

HIT-6: The Headache Impact Test

MIDAS: The Migraine Disability Assessment scale

MPQ: The McGill Pain Questionnaire

PBC: Pain Behavior Checklist

RSES: The Rosenberg Self-esteem scale

SAS: Starkstein apathy scale

Declarations:

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Ethics approval and consent to participate

This study was approved by the Queen Square National Hospital for Neurology and Neurosurgery local ethics committee. All participants gave informed consent.

Consent for publication

Not applicable.

Competing interests: M.M. reports grants from Abbott, Medtronic and electroCore, honoraria for serving on advisory boards from AbbVie, Beckley Psytech, Eli Lilly, Lundbeck, Novartis and Salvia, and payment for presentations by Abbvie; in addition, M.M. has a patent WO2018051103A1 issued. All other authors report nothing to declare.

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Authors' Contributions:

D.C. was involved in the study's conceptualization, execution, data analysis and interpretation, writing of the first draft and review and critique of the manuscript. N.A.B. was involved in data collection, review and critique of the manuscript, M.A.T. was involved in data collection, review and critique of the manuscript, M.M. review and critique of the manuscript, M.J. was involved in conceptualization of the study, data

analysis and interpretation, drafting and review of the manuscript. The author(s) read and approved the final manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Table

Table 5 is not available with this version

Figures

Figure 1

Box plots depicting the distribution of CH-QoL scale total score and 4 sub-scores for chronic and episodic cluster headache. Black dots represent individual patients. Note: Higher scores on CH-QoL indicate poorer

health related quality of life. CH-QoL cluster headache quality of life scale, F1 restriction of activities of daily living; F2 mood & interpersonal relations; F3 pain and anxiety; F4 lack of vitality.

Figure 2

Scatter plots representing significant Spearman correlations between CH-QoL total score and measures of psychiatric comorbidities, anxiety (HADS-A), depression (HADS-D), hopelessness (BHS) and apathy (Starkstein apathy scale). Note: CH-QoL total higher scores indicate poorer health related quality of life. HADS-A, HADS-D, BHS, Starkstein higher scores indicate poorer functioning. Individual observation, correlation lines, R values and p-values are showed for chronic cluster headache (CCH, purple circles) and episodic cluster headache (ECH, orange triangles).

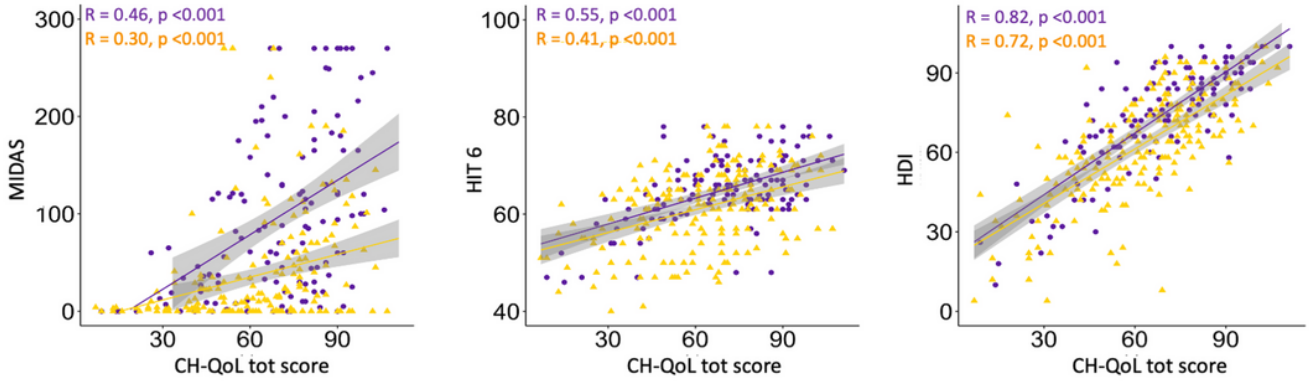

Figure 3

Scatter plots representing significant Spearman correlations between CH-QoL total score and measures of disability (MIDAS, HIT-6, HDI). Note: CH-QoL total higher scores indicate poorer health related quality of life. MIDAS, HIT-6 and HDI higher scores indicate higher disability. Individual observation, correlation lines, R values and p-values are showed for chronic cluster headache (CCH, purple circles) and episodic cluster headache (ECH, orange triangles).

Figure 4

Scatter plots representing significant Spearman correlations between CH-QoL total score and measures of psychological health (Self-esteem, Acceptance of illness, Stigma), pain (McGill pain questionnaire) and pain behavior (PBC total). Note: CH-QoL total higher scores indicate poorer health related quality of life. Self-esteem and Acceptance of the illness higher scores indicate better functioning. Individual

observation, correlation lines, R values and p-values are showed for chronic cluster headache (CCH, purple circles) and episodic cluster headache (ECH, orange triangles).