Observational Studies

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Health-related quality of life in tension-type headache: a population-based study

<https://doi.org/10.1515/sjpain-2020-0166>

Received October 27, 2020; accepted December 9, 2020;
published online January 25, 2021

Abstract

Objectives: Tension-type headache (TTH) is the most prevalent primary headache disorder. We assessed the cross-sectional impact of TTH on health related quality of life (HRQoL) in a general population. We also examined the association of HRQoL scores with headache frequency, disability, medication overuse, poor self-rated health, psychiatric comorbidity, and pain sensitivity in individuals with TTH.

Methods: A sample of 547 subjects completed a headache diagnostic interview, the SF-12 to calculate physical (PCS) and mental (MCS) health component scores, depression (major depression inventory [MDI]) and neuroticism (Eysenck Personality Questionnaire) measures. We defined the following headache diagnosis categories: pure TTH, pure migraine, and coexistent headache (TTH + migraine). Cases were further classified into chronic (≥ 15) or episodic (< 15 headache days/month).

Results: Using generalized linear models (GLM) adjusted for age, sex and education, both PCS-12 and MCS-12 scores varied in groups distinguished by migraine and TTH status; scores were lower for individuals with coexistent headache (TTH + migraine; $n=83$), followed by pure TTH ($n=97$) and pure migraine ($n=43$) compared to the no headache group ($n=324$) ($p \leq 0.001$). In analyses considering chronicity, PCS-12 scores were lower in chronic coexistent headache followed by pure chronic TTH (CTTH), episodic migraine +/- episodic TTH (ETTH) and pure ETTH than in the no headache group ($p \leq 0.001$). MCS-12 scores were lower in pure CTTH, followed by chronic coexistent headache, episodic migraine +/- ETTH and pure ETTH compared to the no headache group ($p \leq 0.001$). Multiple regression models showed that in TTH, lower PCS-12 scores were associated with age ($p=0.04$), female sex ($p=0.02$), and poor self-rated health ($p \leq 0.001$). Lower MCS-12 scores in TTH were associated with depression ($p \leq 0.001$).

Conclusions: In a population sample, TTH, and to higher degree CTTH, are associated with decreased HRQoL.

Keywords: depression; migraine; pain sensitivity; quality of life; tension-type headache.

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Introduction

Tension-type headache (TTH) is the most common primary headache disorder in the general population [1]. One-year period prevalence estimates range from 38 to 78%, depending on frequency [2, 3]. Despite its high prevalence and substantial disability, TTH is poorly recognized and less studied than other primary headaches, particularly migraine [4]. Infrequent episodic TTH (ETTH; with ≤ 1 attack per month) may be minimally disabling. However, frequent ETTH and chronic TTH (CTTH) are associated with substantial disability and have enormous negative impacts on individuals and the society [5–7].

Health related quality of life (HRQoL) provides an important measure of burden of illness. Generic HRQoL

measures, such as the SF-12 Health Survey, provide a common metric for measuring the health burdens of disorders and health benefits of treatments, and have been used in studies of TTH. Studies of HRQoL can be conducted in clinic based or population samples. Because people with migraine seek care much more often than people with TTH, and severity of illness is a driver of consulting behavior, comparisons of the HRQoL burden of TTH and migraine are best made in population samples, to minimize the effects of referral or consultation bias.

Few studies have compared the HRQoL burden of TTH and migraine in population samples. We chose the SF-12, a well validated, widely used generic HRQoL measure [8, 9]. We ascertained headache type in a Danish population sample. The primary aim of this cross-sectional study was to assess the impact of TTH on HRQoL. Secondly we aimed to study the association of HRQoL scores with headache frequency, disability, impact, medication overuse, self-rated health status, psychiatric comorbidities, and pain sensitivity in individuals with TTH.

Methods

Study population

These data are from the Danish population study performed at the Research Center for Prevention and Health and the Danish Headache Center, University of Copenhagen, Glostrup Hospital. The methods of this study are described in detail elsewhere [2, 10]. In 1989, 1,000 residents from the County of Copenhagen aged 25–65 years, were randomly selected from the Danish Civil Registration System. In 2001, a combined cross-sectional and follow-up study designed to replicate the 1989 study was conducted. All individuals originally sampled from the 1989 study, aged 37–76 years, were identified from Danish Civil Registration System. In addition, 300 new individuals aged 25–36 years were selected by the same research criteria as in 1989 to participate in the 2001 cross-sectional study. Thus, a total of 1,300 individuals were selected for the 2001 cross-sectional study and were invited to participate in a headache interview and a clinical examination conducted by a physician. The sample was representative of the Danish population with respect to age, sex and employment status with the exception of self-employment such as fishing and farming that was underrepresented [2]. The study was approved by the Ethical Committee for Copenhagen County and by the Danish Data Protection Agency. Informed consent was obtained from individuals before participation.

Survey

The headache interviews were designed to assess International Classification of Headache Disorders (ICHD-1) criteria [11] for migraine and TTH. The interviewer in 2001 had no knowledge of the headache diagnoses from 1989. Telephone interviews were conducted with the same interviewer, data collection period, questions, and sequence as

the face-to-face interviews. As in 1989, information about socio-demographic, psychological, and lifestyle factors, mental health, HRQoL, as well as education and self-rated health was obtained through self-reported questionnaires completed independently. For the assessment of self-rated health, the participant was asked how he or she would say his/her overall health was: excellent, very good, good, fair, and poor. The last two categories were coded as poor self-rated health. Headache-related daily disability was assessed during the headache interview by asking the participant if he/she felt disabled in their daily life because of headache (migraine and TTH). The daily use of acute headache medication was self-reported.

Headache definitions

For these analyses, headache diagnoses were assigned according to the third edition of the International Classification of Headache Disorders (ICHD-3). ICHD-1 criteria for TTH and migraine are fundamentally the same as ICHD-3. No differences in classifications would be expected at the first digit level [12]. Study participants were asked about the number of days with TTH and migraine per year in the past year with seven response categories: “0 days”, “1–7 days”, “8–14 days”, “15–30 days”, “31–100 days”, “101–179 days”, “180 days or more”. We categorized study participants using two classification systems (groupings). Grouping I, the diagnostic group, is based on headache type: pure migraine, pure TTH, coexistent headache (migraine and TTH) and no primary headache. Grouping II considers headache frequency: episodic migraine +/- ETTH (<15 headache days per month), episodic migraine coexistent with CTTH (chronic coexistent headache) (≥15 any headache days per month), pure frequent episodic ETTH (between 1 and 14 headache days per month), pure CTTH (≥15 headache days per month), vs. no primary headache. No subjects had ICHD-classified chronic migraine in 1989 or in 2001. The no headache group consisted of individuals with no headache or only infrequent TTH (0–14 days/year).

Health-related quality of life: SF-12 health survey

HRQoL was measured with the Danish version of the SF-12 Health Survey, a subset of the SF-36 health survey [13, 14]. It has two subscales the PCS-12 (physical component summary) and MCS-12 (mental component summary). Higher summary scores indicate better HRQoL with a mean of 50 and standard deviation of 10 in the US general population. The SF-12 has been shown to be reliable in headache populations [15, 16].

Mental health variables

Depression was assessed with the 10-item Major Depression Inventory (MDI), which assesses DSM-IV and ICD-10 symptoms of depression for the past two weeks [10, 17]. The total score assesses the severity of the depressive symptoms and is calculated by summing up 10 items. Score ranges from 0 (no depression) to 50 (extreme depression).

Neuroticism was assessed by the Eysenck Personality Questionnaire (EPQ) [10, 18]. We used two of the four EPQ scales: the 23-item neuroticism scale (N-scale) and the 21-item lie scale (L-scale). The N-scale is summed for a total neuroticism score of 0–23 with higher scores indicating higher level of neuroticism. The L-scale assesses dissimulation or a tendency toward social conformity with a range of 0–21.

Quantitative sensory testing

Individuals who participated in the general and neurological examination were included in the Quantitative Sensory Testing study [19]. Local pericranial tenderness was examined by use of the palpometer to train the examiner to exert a palpation pressure of moderate intensity (140 U) [20]. Total tenderness score (TTS) was calculated by summation of the scores from the eight right- and left-sided locations with maximum possible score of 48. Pressure pain thresholds (PPTs) at the anterior part of the temporal muscle were assessed by an electronic pressure algometer (Somedic AB, Stockholm, Sweden) with a circular stimulation probe (0.5 cm²). A pressure loading rate of 0.68 N/s (Newtons/second) was used [19, 21].

Data analysis

Data were summarized for each diagnostic grouping using descriptive statistics such as means and standard deviations (SD), and frequency counts with percentages. Cross-sectional analysis included chi-square test for comparison of proportions. For continuous variables, we used the Shapiro-Wilk test to determine whether the data were normally distributed. For variables that were not normally distributed (e.g., age), a Mann-Whitney test was used to test for comparisons of two continuous variables. Outcome variables of interest such as PCS-12 and MCS-12 scores were compared using Generalized Linear Models (GLM) controlling for the effect of age groups, sex, education. The daily use of acute headache medications was additionally entered as a covariate to account for potential influence on PCS-12 and MCS-12 scores. Pairwise comparisons with Bonferroni correction were performed to compare outcome variables between headache diagnostic categories in groupings.

Multiple linear regression models were run to further assess the influence of selected variables on PCS-12 and MCS-12 scores, respectively, in individuals with pure TTH, assuming normal distribution of SF-12 data. Variables of interest included age, sex, education, daily use of acute headache medication, TTH frequency, migraine frequency, self-reported disability due to TTH in the past year, poor self-rated health, TTS, PPT, depression scores, EPQ N-scales scores. For both dependent variables, PCS-12 and MCS-12, a series of models were run to create final trimmed models for each variable. The first model included demographic predictor variables: age (continuous variable), sex and education. Each subsequent model included sex, age, and significant predictors from the previous model. The second model added TTH frequency and daily use of acute headache medication. The third model added self-reported disability due to TTH in the past year and poor self-rated health. The fourth model added mean TTS, and the fifth model added mean temporal PPT. The final trimmed model added MDI scores and EPQ N-scale scores.

Individuals with missing data were excluded from analyses. Two-tailed p-values were calculated, and five percent was accepted as the level of significance. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.

Results

Study population

A total of 551 of 848 potentially eligible participants who were interviewed in 2001 completed the SF-12 questionnaire.

Complete data were available on 547 participants (64.5%) on variables of interest such as demographics (age, sex and education), MDI, N-scale and SF-12 data. Individuals who provided data and were included in the analysis did not differ significantly from individuals excluded for missing data in terms of sex ($p=0.37$), and presence of migraine ($p=0.69$) or TTH ($p=0.06$). Eligible participants were older than those excluded for missing data (50.2 ± 13.8 vs. 46.9 ± 13.9 ; $p=0.001$). A total of 281 study participants (51.4%) were women.

In Grouping I, 43 (7.9%) participants had pure migraine, 97 (17.7%) had pure TTH, 83 (15.2%) had coexistent headache (migraine and TTH), and 324 (59.2%) had no diagnosed headache disorder. The no headache was identical for Grouping I and Grouping II. In Grouping II, 105 (19.2%) had episodic migraine +/- ETTH, 21 (3.8%) had chronic coexistent headache, 87 (15.9%) had pure frequent ETTH, and 10 (1.8%) had pure CTTH.

Of 547 study participants, 515 (94.1%) also participated in Quantitative Sensory Testing. Participants did not differ significantly from non-participants by sex ($p=0.87$) or presence of primary headache (migraine and/or TTH) ($p=0.14$). The mean age of Quantitative Sensory Testing participants was higher than non-participants, 50.8 ± 13.7 vs. 41.4 ± 12.1 ($p<0.001$).

SF12 physical and mental health scores by headache categories

PCS-12 and MCS-12 scores (mean $\pm$ SD) by primary headache status are presented in Table 1. For Grouping I, both PCS-12 and MCS-12 scores were lower for participants with coexistent headache, followed by pure TTH and pure migraine compared to the no headache group (Table 1, overall $p \leq 0.001$). For Grouping II, PCS-12 scores were lower in chronic coexistent headache followed by pure CTTH, episodic migraine +/- ETTH and pure ETTH than in the no headache group (Table 1, overall $p \leq 0.001$). MCS-12 scores were lower in pure CTTH, followed by chronic coexistent headache, episodic migraine +/- ETTH and pure ETTH compared to the no headache group (Table 1, overall $p \leq 0.001$). Additional adjustment for daily use of acute headache medication did not change the overall statistical significance among categories for Groupings I and II.

In pairwise comparisons of Grouping I diagnostic categories adjusting for age, sex, and education, PCS-12 scores were significantly lower, indicating worse HRQoL, for the pure migraine, coexistent headache and the pure TTH groups compared with the no headache group (Table 2A, Model 1). The coexistent headache group had significant decrements in PCS-12 in comparison with the pure

Table 1: SF-12 physical and mental health summary scores by primary headache status in the general population (N=547).

	PCS-12	MCS-12	N
Grouping I			
No primary headache (reference)	52.8 ± 5.9	53.9 ± 6.8	324
Pure migraine	49.6 ± 8.5	50.3 ± 9.3	43
Pure TTH	49.3 ± 8.4	50.3 ± 9.4	97
Coexistent headache	45.6 ± 10.3	49.9 ± 7.9	83
	<0.001	<0.001	
Grouping II			
No primary headache (reference)	52.8 ± 5.9	53.9 ± 6.8	324
Episodic migraine +/- ETTH	48.5 ± 8.7	50.4 ± 8.0	105
Chronic coexistent headache	39.2 ± 12.1	48.1 ± 10.1	21
Pure ETTH	49.5 ± 8.3	51.2 ± 8.8	87
Pure CTTH	47.7 ± 9.0	43.0 ± 11.6	10
	<0.001	<0.001	

Values are means ± SD; SD, standard deviation; PSC, Physical Component Summary; MSC, Mental Component Summary; TTH, tension-type headache; Coexistent headache, migraine and TTH; ETTH, frequent episodic TTH; CTTH, chronic TTH. Overall p-values were obtained from Generalized Linear Models (GLM) analysis with mean scores adjusted for sex, two age groups (<50 yrs, ≥50 yrs), and education level. Additional adjustment for daily use of acute headache medication did not change the overall statistical significance in Groupings I and II (N=476).

migraine and pure TTH groups. Except for the comparison of the coexistent headache and pure migraine groups, these patterns generally held after further adjustment for daily medication use (Model 2). MCS-12 scores were significantly lower for the pure migraine, the coexistent headache and the pure TTH groups (Table 2B, Model 1). The coexistent headache group and the pure migraine and pure

TTH groups did not differ in MCS-12 scores. Adjustment for daily use of acute headache medication attenuated differences between the coexistent headache and no headache groups (Model 2).

For Grouping II, after adjusting for age, sex and education, PCS-12 scores were significantly lower for the chronic coexistent headache, episodic migraine +/- ETTH, and pure ETTH compared to the no headache group (Table 3A, Model 1). Chronic coexistent headache had significant decrements in PCS-12 relative to the other headache groups. Adjustment for daily use of acute headache medication did not change the significance among categories (Model 2). In comparison with the no headache group, MCS-12 scores are significantly lower for the episodic migraine +/- ETTH, chronic coexistent headache, and pure CTTH groups (Table 3B, Model 1). The Pure CTTH group did have lower scores compared to episodic migraine +/- ETTH and pure ETTH groups. After adjusting for daily use of acute headache medication, only MCS-12 scores in pure CTTH, remained significantly lower compared to episodic migraine +/- ETTH, pure ETTH and no headache groups (Model 2).

SF12 physical and mental health scores: influencing factors in tension-type headache

Table 4A and 4B shows results of multiple linear regression models assessing the influence of selected variables on PCS-12 and MCS-12 scores in pure TTH. In the final trimmed multiple regression model, lower PCS-12 scores were significantly associated with age (p=0.04), female sex

Table 2A: GLM parameter estimates and pairwise group comparisons of SF-12 Physical (PCS-12) health summary scores (physical health) with Bonferroni corrections in Grouping I.

	Parameter estimates		Pairwise group comparisons (p-Values)		
	Est.	95% CI	Vs. 1. No headache	Vs. 2. Pure migraine	Vs. 3. Coexistent headache
Model 1					
Intercept	56.6	(54.3; 59.0)			
1. No headache	0				
2. Pure migraine	-3.9	(-6.1; -1.6)	**		
3. Coexistent headache	-7.9	(-9.7; -6.1)	***	*	
4. Pure TTH	-3.9	(-5.5; -2.3)	***	NS	**
Model 2					
Intercept	56.7	(54.2; 59.2)			
1. No headache	0				
2. Pure migraine	-3.9	(-6.3; -1.5)	**		
3. Coexistent headache	-6.4	(-8.3; -4.5)	***	NS	
4. Pure TTH	-3.5	(-5.2; -1.8)	***	NS	*

Model 1: Adjusted for two age groups (<50 yrs, ≥50 yrs), sex and education level (N=547); Model 2: Model 1 plus adjusted for daily medication use (N=476); TTH, tension-type headache; Coexistent headache, migraine and TTH; NS, non-significant; *p<0.05, **p<0.01, ***p<0.001. All p-values corrected for multiple comparisons (Bonferroni).

Table 2B: GLM parameter estimates and pairwise group comparisons of SF-12 Mental (MCS-12) health summary scores (mental health) with Bonferroni corrections in Grouping I.

	Parameter estimates		Pairwise group comparisons (p-Values)		
	Est.	95% CI	Vs. 1. No headache	Vs. 2. Pure migraine	Vs. 3. Coexistent headache
Model 1					
Intercept	52.4	(49.9; 54.9)			
1. No headache	0				
2. Pure migraine	−3.4	(−5.9; −0.9)	*		
3. Coexistent headache	−3.9	(−5.9; −2.0)	**	NS	
4. Pure TTH	−3.5	(−5.3; −1.7)	**	NS	NS
Model 2					
Intercept	52.8	(50.1; 55.6)			
1. No headache	0				
2. Pure migraine	−2.6	(−5.3; 0.0)	NS		
3. Coexistent headache	−2.8	(−4.9; −0.7)	NS	NS	
4. Pure TTH	−2.9	(−4.8; −1.0)	*	NS	NS

Model 1: Adjusted for two age groups (<50 yrs, ≥50 yrs), sex and education level (N=547); Model 2: Model 1 plus adjusted for daily medication use (N=476); TTH, tension-type headache; Coexistent headache, migraine and TTH; NS, non-significant; *p<0.05, **p<0.01, ***p<0.001. All p-values corrected for multiple comparisons (Bonferroni).

Table 3A: GLM parameter estimates and pairwise group comparisons of SF-12 Physical (PCS-12) health summary scores (physical health) with Bonferroni corrections in Grouping II.

	Parameter estimates		Pairwise group comparisons (p-Values)			
	B	95% CI	Vs. 1. No headache	Vs. 2. Episodic migraine +/- TTH	Vs. 3. Chronic coexistent headache	Vs. 4. Pure ETTH
Model 1						
Intercept	56.5	(54.2; 58.8)				
1. No headache	0					
2. Episodic migraine +/- ETTH	−5.0	(−6.6; −3.4)	***			
3. Chronic coexistent headache	−13.4	(−16.5; −10.3)	***	***		
4. Pure ETTH	−3.8	(−5.5; −2.1)	***	NS	***	
5. Pure CTTH	−4.3	(−8.7; 0.1)	NS	NS	**	NS
Model 2						
Intercept	56.5	(54.1; 59.0)				
1. No headache	0					
2. Episodic migraine +/- ETTH	−4.6	(−6.3; −2.9)	***			
3. Chronic coexistent headache	−10.4	(−13.7; −7.2)	***	**		
4. Pure ETTH	−3.6	(−5.4; −1.9)	**	NS	**	
5. Pure CTTH	−2.2	(−6.7; 2.2)	NS	NS	*	NS

Model 1: Adjusted for two age groups (<50 yrs, ≥50 yrs), sex and education level (N=547); Model 2: Model 1 plus adjusted for daily medication use (N=476); ETTH, frequent episodic tension-type headache; CTTH, chronic tension-type headache; Coexistent headache, migraine and TTH; NS, non-significant; *p<0.05, **p<0.01, ***p<0.001. All p-values corrected for multiple comparisons (Bonferroni).

(p=0.02), poor self-rated health (p≤0.001). Lower MCS-12 scores were significantly associated with depression scores (p≤0.001) in final model.

Discussion

The present study demonstrates that HRQoL is reduced in the pure TTH group relative to headache-free controls on

both the PCS and MCS subscales of the SF-12. We observed similar decrements for the pure migraine group and even greater decrements in the coexistent headache group. The findings are consistent with prior reports indicating that migraine and other pain disorders are associated with decreased health-related quality of life [15, 22–25]. In contrast to the coexisting disorder group, SF-12 scores did not differ between individuals with pure TTH and those with pure migraine suggesting that in a population sample,

Table 3B: GLM parameter estimates and pairwise group comparisons of SF-12 Mental (MCS-12) health summary scores (physical health) with Bonferroni corrections in Grouping II.

	Parameter estimates		Pairwise group comparisons (p-Values)			
	B	95% CI	Vs. 1. No headache	Vs. 2. Episodic migraine +/- TTH	Vs. 3. Chronic coexistent headache	Vs. 4. Pure ETTH
Model 1						
Intercept	52.4	(49.9; 54.9)				
1. No headache	0					
2. Episodic migraine +/- ETTH	-3.2	(-5.0; -1.5)	**			
3. Chronic coexistent headache	-5.9	(-9.2; -2.5)	**	NS		
4. Pure ETTH	-2.5	(-4.4; -0.7)	NS	NS	NS	
5. Pure CTTH	-11.1	(-15.9; -6.4)	***	*	NS	**
Model 2						
Intercept	52.8	(50.1; 55.5)				
1. No headache	0					
2. Episodic migraine +/- ETTH	-2.5	(-4.4; -0.7)	NS			
3. Chronic coexistent headache	-3.9	(-7.5; -0.3)	NS	NS		
4. Pure ETTH	-2.0	(-4.0; -0.1)	NS	NS	NS	
5. Pure CTTH	-9.8	(-14.6; -4.9)	**	*	NS	*

Model 1: Adjusted for two age groups (<50 yrs, ≥50 yrs), sex and education level (N=547); Model 2: Model 1 plus adjusted for daily medication use (N=476); ETTH, frequent episodic tension-type headache; CTTH, chronic tension-type headache; Coexistent headache, migraine and TTH; NS, non-significant; *p<0.05, **p<0.01, ***p<0.001. All p-values corrected for multiple comparisons (Bonferroni).

Table 4A: Multiple linear regression models of SF-12 Physical (PCS-12) health summary scores with variables of interest in individuals with pure TTH (n=97).

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
(Constant)	54.33 (4.64)***	49.90 (6.26)***	62.42 (4.18)***	61.22 (3.94)***	60.70 (4.97)***	59.80 (3.59)***
Age (years)	-0.15 (0.06)*	-0.11 (0.07)	-0.10 (0.06)	-0.11 (0.06)	-0.10 (0.06)	-0.11 (0.05)*
Sex (female/male)	-0.79 (1.69)	-1.17 (1.80)	-2.95 (1.59)	-2.47 (1.77)	-2.78 (1.74)	-3.40 (1.48)*
Education ^a	1.20 (0.52)*	1.01 (0.54)				
TTH frequency ^b		0.94 (0.97)				
Daily use of acute headache medication (yes/no)		-9.28 (4.09)*	-3.72 (3.50)			
Self-reported disability due to TTH in the past year (yes/no)			-2.32 (1.55)			
Poor self-rated health (yes/no)			-9.47 (1.99)***	-10.68 (1.89)***	-10.87 (1.85)***	-13.01 (1.90)***
TTS				-0.04 (0.08)		
Temporal PPT					0.00 (0.01)	
Depression (MDI) total score						0.06 (0.11)
Neuroticism scale (EPQ N-scale) total score						0.28 (0.17)
N	97	92	91	87	87	96
R squared	0.12	0.16	0.35	0.35	0.35	0.40
Adjusted R squared	0.09	0.11	0.32	0.32	0.32	0.36

Values are B (SE); B, unstandardized coefficient; SE, standard error; TTH, Tension-type headache; MDI, Major Depression Inventory; EPQ, Eysenck Personality Questionnaire. ^aEducation categories: general upper secondary school or lower (reference) vocational upper secondary school, vocational education, short-cycle higher education, medium-cycle higher education, long-cycle higher education, other education. ^bTTH frequency categories: 0, 1–7, 8–14, 15–30, 31–100, 101–179, 180 or more days per year. The first multiple linear regression model included demographic predictor variables: age (continuous variable), sex and education. Each subsequent model included sex, age, and significant predictors from the previous model. The second model added TTH frequency and daily use of acute headache medication. The third model added self-reported disability due to TTH in the past year and poor self-rated health. The fourth model added mean TTS, and the fifth model added mean temporal PPT. The final trimmed model added MDI scores and EPQ N-scale scores. *p≤0.05, **p≤0.01, ***p≤0.001.

Table 4B: Multiple linear regression models of SF-12 Mental (MCS-12) health summary scores with variables of interest in individuals with pure TTH (n=97).

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
(Constant)	46.03 (5.48)***	57.21 (6.95)***	50.49 (5.00)***	51.04 (5.00)***	49.24 (6.29)***	52.49 (3.17)***
Age (years)	0.05 (0.07)	0.11 (0.08)	0.08 (0.07)	0.06 (0.08)	0.06 (0.07)	0.08 (0.05)
Sex (female/male)	−0.17 (2.00)	−1.16 (2.09)	−1.53 (1.96)	−0.97 (2.24)	−0.59 (2.20)	1.65 (1.31)
Education ^a	0.78 (0.61)	−1.97 (1.14)				
TTH frequency ^b		−6.84 (4.73)				
Daily use of acute headache medication (yes/no)		57.21 (6.95)				
Self-reported disability due to TTH in the past year (yes/no)			−0.05 (1.95)			
Poor self-rated health (yes/no)			−7.30 (2.42)**	−7.54 (2.40)**	−7.41 (2.34)**	0.24 (1.67)
TTS				0.00 (0.11)		
Temporal PPT					0.01 (0.01)	
Depression (MDI) total score						−0.77 (0.10)***
Neuroticism scale (EPQ N-scale) total score						−0.28 (0.15)
N	97	92	96	87	87	96
R squared	0.02	0.09	0.10	0.12	0.12	0.62
Adjusted R squared	−0.01	0.04	0.06	0.07	0.07	0.60

Values are B (SE); B, unstandardized coefficient; SE, standard error; TTH, Tension-type headache; MDI, Major Depression Inventory; EPQ, Eysenck Personality Questionnaire. ^aEducation categories: general upper secondary school or lower (reference) vocational upper secondary school, vocational education, short-cycle higher education, medium-cycle higher education, long-cycle higher education, other education. ^bTTH frequency categories: 0, 1–7, 8–14, 15–30, 31–100, 101–179, 180 or more days per year. The first multiple linear regression model included demographic predictor variables: age (continuous variable), sex and education. Each subsequent model included sex, age, and significant predictors from the previous model. The second model added TTH frequency and daily use of acute headache medication. The third model added self-reported disability due to TTH in the past year and poor self-rated health. The fourth model added mean TTS, and the fifth model added mean temporal PPT. The final trimmed model added MDI scores and EPQ N-scale scores. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$.

both primary headache disorders have similar effects on HRQoL. However, generic HRQoL measures may be insensitive to differences between diagnostic categories, though a migraine specific quality of life measure may not be appropriate for a sample with pure TTH. Since no one in our sample had chronic migraine, we may have underestimated the burden of migraine. Effects were larger for PCS-12 than MCS-12 suggesting that coexistent headache diseases may have greater impact on physical health than on mental health. Using Grouping II (frequency), we found that pure CTTH was associated with substantial decrements in HRQoL, which were greater for the MCS than the PCS. Thus, headache frequency may partially explain the low HRQoL in individuals with TTH. The frequency and intensity of the pain disorders have previously been found to relate to the magnitude of this impact [15, 26].

HRQoL in TTH was assessed in two previous population-based studies. In the Republic of Georgia [27], using the Short Form-36 (SF-36) Health Survey questionnaire, people without headache had higher scores, indicating better HRQoL in all sub-scales, including PSC and MSC, than those with episodic headache (coexistent migraine and TTH) or chronic headache (unspecified

headache ≥ 15 days/month). However, no differences were found between respondents with episodic headache and those with headache on ≥ 15 days/month or between individuals with migraine and TTH [27]. In a study from Spain [28] using SF-36 Health Survey, no difference in HRQoL between CTTH and transformed migraine was found but older age of the CTTH group might have confounded this finding.

There are several clinic-based studies on HRQoL in patients with TTH. In a large study in outpatient tertiary headache clinic [29], patients with CTTH had numerically lower SF-36 scores in six out of eight domains compared to those with migraine but higher than in patients with transformed migraine; patients who met the criteria for both CTTH and transformed migraine were classified as transformed migraine in the study. In another study of 209 patients from a tertiary headache clinic [30], using the SF-20 survey, HRQoL reductions was greater for TTH than for migraine in the domains of Social Functioning and Mental Health. However, lower HRQoL scores in clinic-based study samples as well as in patients in clinical trials are expected due to the possibility of selection for more severe disease [15, 16].

In our study, we also modeled both PCS-12 and MCS-12 as a function of demographic variables, clinical aspects of pure TTH, pain sensitivity and mental health constructs to better understand the factors that influence HRQoL in TTH. We found that age, female sex and poor self-rated health were associated with lower PCS-12 scores. Daily use of acute headache medication was associated with worse physical domain of HRQoL in one of the models, but the daily acute treatment may be a proxy for more severe disease, high frequency headache and/or medication overuse headache. The depression scores assessed by MDI predicted lower MCS-12 scores, indicating reductions in mental health quality of life. Education, TTH frequency, self-reported disability due to TTH in the past year, TTS, and PPTs did not significantly influence the SF-12 scores in the final models.

The lack of influence of TTH frequency on HRQoL in our sample contrasts with previous findings in population studies of migraine; headache frequency was a significant predictor of HRQoL for both MCS-12 and PCS-12 scores in these studies [15, 24, 31]. The influence of headache-related disability on PCS scores in TTH is similar to migraine.

In one population study, headache related disability predicted only PCS-12 scores [15]. Depression has been reported to account for the low scores on most SF-36 scale scores [32]. Lipton et al. [15] demonstrated that after adjusting for sex, age, and education, migraine and depression were independently associated with decreased MCS-12 and PCS-12 scores. In multiple regression models adjusting for depression, migraine remained associated with HRQoL physical and mental scores [15]. We found that in a multiple regression model, in individuals with TTH, the MCS-12 scores were also influenced by depression scores. Influence of depression on HRQoL in TTH was previously studied only in clinic based studies. In a study of 25 clinic patients with CTTH anxiety exerts a mediating effect and depression exerts a modulating effect on the relationship of headache frequency and pain intensity on reduced quality of life in the mental health and social functioning domains, as measured by SF-36 [28]. Rollnik et al. [33] showed that depression scores correlated positively with poor quality of life in patients with CTTH. In addition, patients with CTTH scored lower on the Nottingham Health Profile (NHP) and the Everyday Life Questionnaire (ELQ), compared to patients with ETTH [33]. Age may confound this result.

The current study has methodological limitations. Due to the cross-sectional design, we do not know the causal direction of the associations between headache types and low HRQoL. Moreover, we cannot assess the influence of treatment of TTH on HRQoL. To address these questions

longitudinal observational studies and randomized trials are warranted. In addition, the sample size is modest by epidemiological standards and the data were collected in 2001. Recent studies on the burden of headache revealed that the burden of headache may change over time [5].

These weaknesses are offset by much strength. The sample was recruited through the nation-wide Danish Civil Registration System, which registers all residents in Denmark with a unique 10-digit code, facilitating the representative sampling of a general population. Participation rates are high for a population study. Diagnoses were assigned by a detailed clinical headache interviews conducted by a physician using ICHD criteria [11]. Participants completing the SF-12 did not differ from all participants with regard to migraine or TTH status, though they were older.

The present study is one of few to address HRQoL in TTH. One of the interesting findings in our study is the high impact of coexisting TTH and migraine on HRQoL. Careful distinction of headache disorders and recognition of coexisting headache types would be beneficial for future research concerning the magnitude, specificity and causes of low HRQoL. Our study highlights the point that cost-effective and compassionate headache treatment strategies should address psychiatric comorbidities, medication overuse, and coexisting headache types [34, 35].

Acknowledgments: We thank Birthe Krogh Rasmussen, MD, PhD, Torben Jørgensen, MD, PhD and Nurse Vibeke Thomsen for their assistance with the study.

Research funding: The study was supported by the East Denmark Health Science Research Forum, the Danish Medical Association Research Fund, the Danish Health Insurance Foundation, the Danish Hospital Foundation for Medical Research, the Danish Headache Society, the Cool Sorption Foundation, GlaxoSmithKline A/S, Merck Sharp Dohme A/S, Pfizer A/S, Lundbeck Pharma A/S and H. Lundbeck A/S. The funding sources have not been involved in the conduct of the study.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Sait Ashina, MD received honoraria for consulting from Allergan, Amgen, Eli Lilly, Impel NeuroPharma, Percept, Novartis, Satsuma, Supernus, Theranica. Dawn C Buse, PhD has received grant support and honoraria from Allergan, Amgen, Biohaven, Lilly, Novartis, and Promus/Dr. Reddys. She has not been paid by any company for work writing manuscripts, or writing or presenting abstracts, posters or platforms. She serves on the

editorial boards of Current Pain and Headache Reports, the Journal of Headache and Pain, Pain Medicine News, and Pain Pathways magazine. Jakob B. Bjorner works for QualityMetric, who licenses the SF-12[®] Health Survey. Lars Bendtsen, MD has received honoraria for lectures from MSD, Allergan and Pfizer and serves on the scientific advisory board for Berlin-Chemie. Ann C Lyngberg, MD has no disclosures. Rigmor H. Jensen, MD has received honoraria for lectures and patient leaflets from MSD, Berlin-Chemie Menarini, ATI, Novartis, Teva, Allergan and Pfizer and is conducting clinical trials for Eli-Lilly and Lundbeck. Richard B Lipton, MD receives research support from the NIH, the FDA, the S and L Marx Foundation, the Migraine Research Foundation, and the National Headache Foundation. He holds stock options in Biohaven Holdings and CtrlM Health. He serves as consultant, advisory board member, has received honoraria from or research support from: Abbvie (Allergan), American Academy of Neurology, American Headache Society, Amgen, Biohaven, Biovision, Boston Scientific, Dr. Reddy's (Promius), Electrocore, Eli Lilly, eNeura, Equinox, GlaxoSmithKline, Grifols, Lundbeck (Alder), Merck, Pernix, Pfizer, Teva, Vector and Vedanta.

Informed consent: Informed consent was obtained from individuals before participation.

Ethical approval: The study was approved by the Ethical Committee for Copenhagen County and by the Danish Data Protection Agency.

Data availability: Research data are not shared. The data are not publicly available due to privacy or ethical restriction.

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