

Supplementary material

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Supplementary eTable 1

Supplementary eTable 1. Response frequency on variables with missing data.

| Variable | Response frequency (%) | | |
|----------------------------------|------------------------|--------------|----------------|
| | All (n=874) | Male (n=575) | Female (n=299) |
| Age at onset | 89,4 | 89,2 | 89,6 |
| Heredity | 95,3 | 95,8 | 94,3 |
| Attacks per day | 97,8 | 97,6 | 98,3 |
| Attack duration | 97,6 | 97,4 | 96,6 |
| Bout length | 96,2 | 96,3 | 96,0 |
| Pain intensity ^{*a} | 100 | 100 | 100 |
| Associated symptoms | 93,7 | 92,7 | 95,7 |
| Migraine | 96,6 | 92,3 | 97,2 |
| Tension-type headache | 97,8 | 98,1 | 97,3 |
| Diurnal rhythmicity | 96,9 | 97,7 | 96,5 |
| Annual rhythmicity ^{*b} | 96,0 | 96,7 | 94,9 |
| Chronotype | 99,0 | 99,1 | 99,0 |
| Hours of night sleep | 98,3 | 98,6 | 97,7 |
| Use of acute treatment | 100 | 100 | 100 |
| Use of prophylactic treatment | 100 | 100 | 100 |
| Triggers | 96,0 | 96,5 | 95,0 |
| Body Mass Index | 95,9 | 96,2 | 95,3 |

Heredity includes first- and second-degree relatives with cluster headache. Pain intensity was rated on a scale from 0-10 with 0 = no pain to 10 = worst imaginable pain. * Only asked to study participants collected after 2016 based on ^a302 individuals (184 males/118 females) and ^b290 individuals (178 males/112 females) for whom detailed information was available.

Supplementary eTable 2

Supplementary eTable 2. Chronotype by age group in cluster headache participants.

| Age (years) | Sex group | Chronotype (%) | | | p-value | |
|-------------|----------------|----------------|---------|---------|---------|-------|
| | | Morning | Neither | Evening | | |
| <35 | Male (n=73) | 14.7 | 29.3 | 56.0 | 0.46 | 0.001 |
| | Female (n= 60) | 23.3 | 26.7 | 50.0 | | |
| 35-49 | Male (n=176) | 29.0 | 23.3 | 47.7 | 0.029 | |
| | Female (n=79) | 38.3 | 30.9 | 30.9 | | |
| 50-64 | Male (n=210) | 34.4 | 29.7 | 35.9 | 0.21 | |
| | Female (n=104) | 40.4 | 33.7 | 26.0 | | |
| ≥65 | Male (n=111) | 34.8 | 29.5 | 35.7 | 0.60 | |
| | Female (n=53) | 29.6 | 37.0 | 33.3 | | |

Data on chronotype was available from 866 cluster headache (CH) participants (570 males/296 females). Groups were compared using Chi-squared test.

Supplementary eTable 3

Supplementary eTable 3. Tobacco habits in cluster headache participants and the Swedish general population.

| | Cluster headache participants (%) | | General population (%) | | CH males vs CH females <i>p</i> -value | CH males vs males <i>p</i> -value | CH females vs females <i>p</i> -value |
|-------------|-----------------------------------|--------|------------------------|--------|---|--------------------------------------|--|
| | Male | Female | Male | Female | | | |
| Smoking Yes | 26.8 | 25.1 | 11.0 | 9.2 | 0.63 | <0.0001 | <0.0001 |
| Tobacco Yes | 44.9 | 30.1 | 31.3 | 13.4 | <0.0001 | <0.0001 | <0.0001 |

Data for tobacco habits was available from 874 cluster headache (CH) participants (575 males/299 females). Data for general Swedish population (16 years and older) retrieved from Statistics Sweden (<https://www.scb.se>) Living Conditions Surveys (ULF/SILC) – Health 2018. Tobacco habits were available for 8,305K controls (4,150K males/4,155K females). Tobacco includes both smoking and the use of snus/snuff. Numbers were compared using Fisher's exact test.

Supplementary eTable 4

Supplementary eTable 4. Alcohol consumption in cluster headache participants and the Swedish general population.

| Alcohol consumption | Cluster headache participants (%) | | | | General population (%) | |
|---------------------|-----------------------------------|---------|------------|---------|------------------------|---------|
| | Episodic CH | | Chronic CH | | Male | Females |
| | Male | Females | Male | Females | | |
| None/seldom | 25 | 54 | 62 | 71 | 10 | 18 |
| Low | 27 | 23 | 17 | 22 | 55 | 50 |
| Intermediate | 39 | 22 | 19 | 6 | 19 | 24 |
| High | 9 | 2 | 2 | 2 | 15 | 8 |

The definition for the different categories of alcohol consumption differs between our questionnaire for cluster headache (CH) participants and the data obtained for the Swedish general population (GP; source: Statistics Sweden, Living Conditions, Report no 114: Use of alcohol and tobacco, 2007) and are therefore difficult to compare: No/seldom consumption (CH: <1 unit/week; GP: <1 unit/year), low consumption (CH: 1-2 units/week; GP: <4-5 units/week), intermediate consumption (CH: 3-4 units/week; GP: <7-8 units/week), high consumption (CH: >1 unit/day; GP: >1-2 units/day).

Supplementary eTable 5

Supplementary eTable 5. Body Mass Index (BMI) in cluster headache participants and the general Swedish population.

| BMI | All (%) | | | Males (%) | | | Females (%) | | |
|-----------|------------|------------|-------------------|------------|------------|--------------|-------------|------------|-------------|
| | CH | Controls | p-value | CH | Controls | p-value | CH | Controls | p-value |
| Mean ± SD | 26.0 ± 4.4 | 25.6 ± 2.3 | <0.0001 | 26.5 ± 4.1 | 26.1 ± 3.3 | 0.009 | 25.0 ± 4.9 | 25.2 ± 3.3 | 0.34 |
| <18.5 | 1.1 | 2.2 | 0.006 | 0.2 | 1.5 | 0.005 | 2.8 | 3.0 | 0.66 |
| 18.5-24.9 | 43.7 | 47.9 | | 37.1 | 41.9 | | 56.5 | 54.0 | |
| 25.0-29.9 | 38.8 | 35.8 | | 45.4 | 42.1 | | 26.0 | 29.3 | |
| ≥30 | 16.5 | 14.1 | | 17.4 | 14.6 | | 14.7 | 13.6 | |

Data for body mass index (BMI) was available from 838 cluster headache (CH) participants (553 males/285 females). Data for general Swedish population (16 years and older) retrieved from Statistics Sweden (<https://www.scb.se>) Living Conditions Surveys (ULF/SILC) – Health 2018. BMI categories were available for 8,305K controls (4,151K males/4,154K females). BMI presented as mean ± standard deviation (SD). BMI categories are defined as: underweight (<18.5), normal (18.5-24.9), overweight (25.0-29.9), obese (≥30). The mean of the three groups (all, males and females) were compared using multiple unpaired t tests. Chi-squared test was used to compare the different age groups with regard to sex.

Supplementary eTable 6

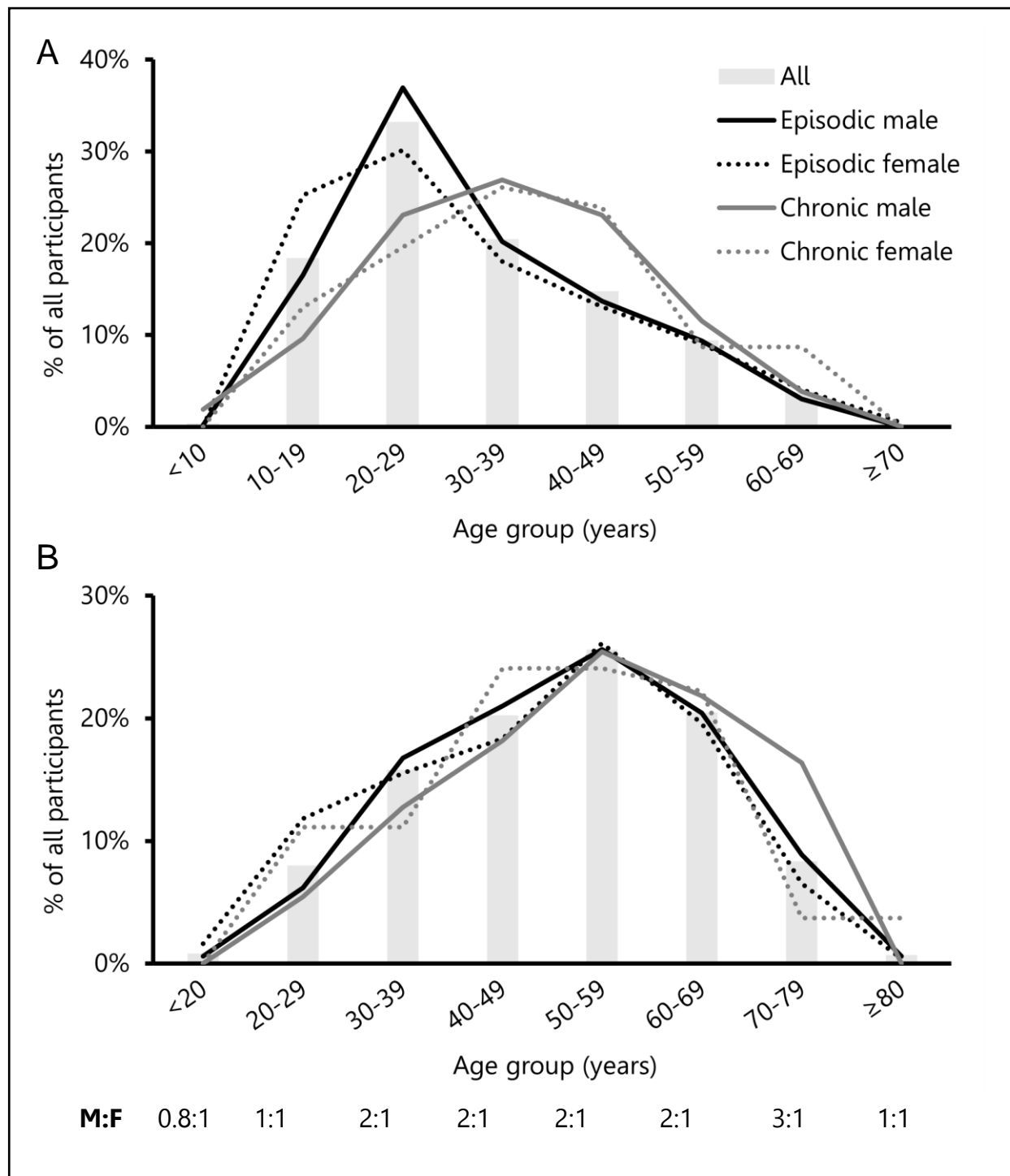
Supplementary eTable 6. Prevalence of migraine in cluster headache (CH) participants and the general Swedish population.

| Migraine | CH participants | PILOT study | OCTO-Twin study | GENDER study | CH vs PILOT p-value | CH vs OCTO p-value | CH vs GENDER p-value |
|-----------------|----------------------------|------------------------|----------------------------|-------------------------|------------------------------------|-----------------------------------|-------------------------------------|
| All | 160/874 (18.3) | 177/1284 | 127/702 | 84/498 | 0.005 | 0.95 | 0.56 |
| (%) | | (13.8) | (18.1) | (16.9) | | | |
| Males | 72/575 (12.5) | 50/588 | 28/234 | 21/249 | 0.028 | 0.91 | 0.09 |
| (%) | | (8.5) | (12.0) | (8.4) | | | |
| Females | 88/299 (29.4) | 127/696 | 99/468 | 63/249 | 0.0001 | 0.01 | 0.29 |
| (%) | | (18.3) | (21.2) | (25.3) | | | |

Data for general Swedish population retrieved from two different publications: Svensson et al. (PILOT)¹ and Nilsson et al. (OCTO-Twin, GENDER)². Numbers were compared using Fisher's exact test.

Supplementary eFigure 1

Supplementary eFigure 1. Distribution of age at onset and study inclusion age in cluster headache participants.



Age distribution in male and female cluster headache (CH) participants subdivided by CH subtype for (A) age at CH onset, and (B) age at study inclusion. Male to female (M:F) ratio is stated for each age group in B.

eReferences

1. Svensson DA, Ekbom K, Larsson B, Waldenlind E. Lifetime prevalence and characteristics of recurrent primary headaches in a population-based sample of Swedish twins. *Headache*. 2002;42(8):754-765. doi:10.1046/j.1526-4610.2002.02177.x
2. Nilsson S, Edvinsson L, Malmberg B, Johansson B, Linde M. *A Relationship between Migraine and Biliary Tract Disorders: Findings in Two Swedish Samples of Elderly Twins*. Vol 122.; 2010:286-294. doi:10.1111/j.1600-0404.2009.01310.x