Chronic frequent headache in the general population

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Chapter 2

Chronic frequent headache in the general population - prevalence and associated factors –

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Abstract

We studied the prevalence and short-term natural course of chronic frequent headache (CFH) in the general population and identified risk factors. In the Netherlands everyone is registered at a single General Practice (GP). We sent questionnaires to all persons (n = 21,440) aged 25-55 years, registered at 16 GPs. We compared characteristics of 177 participants with CFH (> 14 headache days/month for > 3 months) to 141 participants with infrequent headache (1-4 days/month) and 526 without headache (<1 day/month). The prevalence of CFH was 3.7% (95% CI 3.4-4.0%). In five months, 12% showed a clinically relevant decrease to < 7days/month. In both headache groups 70% were women vs. 41% in the group without headache. Compared to the group with infrequent headache, the CFH group had more subjects with low educational level (35% vs. 11%; OR=4.3, 95% CI 2.3-7.8), medication overuse (62% vs. 3%; OR=38.4, 95% CI 13.8-106.9), sleeping problems (44% vs. 8%; OR=8.1, 95% CI 3.6-18.1), a history of head/neck trauma (36% vs. 14%; OR=4.0, 95% CI 2.2-7.1), high scores on the General Health Questionnaire (62% vs. 34%; OR=2.7, 95% CI 1.3-3.6), and more smokers (45% vs. 19%; (OR=3.1, 95% CI 1.9-5.3). We conclude that headache frequency fluctuates. Chronic frequent headache is common and associated with overuse of analgesics, psychopathology, smoking, sleeping problems, a history of head/neck trauma, and low educational level. Female sex is a risk factor for headache, not for chronification of headache.

Introduction

Chronic frequent headache (CFH), also known as chronic daily headache, is a collective term for primary headaches occurring on more than 14 days per month for at least three months. The prevalence of CFH in the general population is around 4% worldwide.[1-4] Many patients start with an infrequent episodic headache type (migraine or tension-type) that gradually becomes more frequent over time until their headaches are almost daily. The cause of this chronification process is unknown.

Clinical experience suggests a causal relationship with overuse of acute headache medication because withdrawal of medication often results in a dramatic improvement of headache frequency.[5] Several cross-sectional studies have reported an association between overuse and chronic headache. Two population-based studies in Spain and Taiwan reported that 25% and 34% of subjects with CFH overused acute headache medication.[1,4] These percentages were however not compared to control groups. In a community-based study conducted among Chinese elderly (> 64 years) CFH was associated with analgesic overuse (OR=79, 95% CI 19-321) and overuse was a predictor of persistent CFH at follow-up four years later.[6] Other factors that have been associated with CFH in the general population include female sex, low educational level, previously married status, arthritis, habitual snoring, and a history of migraine.[6-8] Because the control groups in these studies included subjects who rarely had headaches (only two headaches a year), these factors could be associated with having headaches regularly, rather than with chronic headache in particular.

There are limited data on the incidence and natural course of CFH. It is estimated that in a specialized headache centre 14% of patients with episodic migraine develop chronic headache during one year of follow-up.[9] In a general population sample in the USA with a headache frequency of 2-104 days/year, the one-year cumulative incidence of CFH was 3%.[8]
We studied the prevalence and short-term natural course of CFH in the Dutch general population. To identify risk factors for chronification of headache we compared subjects with CFH to subjects with infrequent headaches. Details on clinical features, comorbidity, personality profile, and impact on quality of life will be reported separately.

Methods

We studied the prevalence of CFH in the Dutch general population by sending a postal questionnaire (Q1) between January 2002 and September 2003 to all persons, aged 25-55, registered at 16 General Practitioners (GP), located in the regions of Leiden and The Hague. In the Netherlands almost everyone is registered at a single GP, which makes GPs' registers suitable for population-based studies. Leiden and The Hague are cities of 117,000 and 457,000 inhabitants respectively, located in the province of South-Holland, a mixed area with both urbanisation and agriculture. To minimise selective response, the primary objective (assessment of headache) was not explained, but a more general objective, namely evaluation of common health problems and self-treatment, was stated in a standard letter, signed by the GP. The questionnaire contained a number of headache-unrelated questions for masking reasons. We assessed headache frequency and medication use by the following questions: "On how many days per month on average did you suffer from headache in the past three months?" and "On how many days per month on average did you take medication to treat your headache?" We sent two reminders. Answers were given on a five-point frequency scale: on > 14 days/month (chronic frequent), on 8-14 days/month (very frequent), on 5-7 days/month (frequent), on 1-4 days/month (infrequent), and on < 1 day/month (none). Respondents were allocated into five groups according to headache frequency: Chronic Frequent Headache (CFH), Very Frequent Headache (VFH), Frequent Headache (FH), Infrequent Headache (IH) and No Headache (NH).

To identify factors associated with chronification of headache, we compared subjects with CFH (headache on > 14 days/month) to subjects with infrequent headaches (1-4 days/month). We also compared the CFH group to the No Headache group (< 1 day/month) to discern chronification factors from factors associated with headache in general. After about five months (range three to seven), all individuals who reported CFH and two random samples of the Infrequent Headache group and No Headache group (each twice as large as the case group), received a second, more detailed questionnaire (Q2) containing questions on demographics, lifestyle factors, and headache characteristics. We re-assessed headache frequency with the following question: "On how many days per month on average did you suffer from headache in the past six months?" For further analyses we selected subjects who had the same headache frequency in both Q1 and Q2 (i.e. the stable frequency group). The following additional risk factors were recorded: age of onset of headache, a family history

(first degree relatives) positive for headache, a history of head or neck trauma prior to the onset of headache, sleeping problems, tranquillizer use, use of acute headache medication and caffeine intake. Overuse was defined as: use of analgesics on ≥ 3 days/week, use of triptans on ≥ 2 days/week, use of ergots on ≥ 1 day/week, use of narcotics on ≥ 10 days/month, and use of > 5 caffeine units a day. A caffeine unit is one cup of tea, coffee, or caffeine containing soda. We also asked subjects whether they had consulted their GP for headache in the past six months.

The General Health Questionnaire (GHQ-28) was used to screen for psychopathology.[10] It includes four subscales: somatic physical illness and distress, anxiety/insomnia, social dysfunction, and severe depression, each consisting of 7 items. Answers are given on a 4-point Likert scale, ranging from 0 "better than normally" to 3 "much worse than normally", with scores ranging from 0 to 21 for each subscale. Scores can be recoded into (0,0,1,1) with a total scoring range of 0 to 28 (the GHQ scoring method). We used a cut-off score of 4/5 to define a GHQ case.[10] The GHQ-28 has a sensitivity of 0.84 and a specificity of 0.82 in detecting psychopathology.[10]

Q2 also contained other questions on clinical features of headache, comorbidity, quality of life, coping strategies, and personality profile. These results will be published separately. Subjects in the CFH group received one reminder. Non-respondent CFH subjects received a short questionnaire to assess possible selection bias and included main items such as demographic variables, headache frequency, and medication and caffeine use. The Very Frequent Headache (8-14 days/month) group were to be followed over time to study the incidence of and risk factors for CFH. The Frequent Headache group did not receive Q2 and was not further analysed.

Statistical analysis was performed with SPSS, version 11.0. Prevalences and differences between groups are presented with 95% confidence intervals (95% CI). We evaluated factors associated with chronification by comparing the CFH group to the Infrequent Headache group. Odds ratios are given for putative risk factors. We used the Mantel-Heanszel procedure to adjust for potential confounders.

The Medical Ethics Committee of Leiden University Medical Center approved the study.

Results

Sixteen GP practices participated in the study; seven located in the cities of Leiden and The Hague, five in urban areas and four in villages in rural areas. All GPs estimated the percentage of immigrants in their practice to be less than 10%, except for one practice, where 50% of patients were non-western immigrants, mainly from Turkey, Morocco, the Dutch Antilles and Suriname. In total 21,440 subjects received Q1, 16,232 (76%) completed Q1 and 1160 (5%) refused to participate or had moved (Figure 1). The response per practice varied between 69% and 84%, except for the practice with the high number of immigrants, where only 53% of subjects completed Q1.

Prevalence

Of all 16,232 participants, 679 reported to have CFH (4.2%, 95% CI 3.9-4.5). In the practice with the high number of immigrants the prevalence of CFH was 12.3% (95% CI 10.1–14.5). Without this practice, the prevalence of CFH was 3.7% (95% CI 3.4-4.0). Prevalences of the other headache frequency groups are shown in Figure 1. Of 679 CFH subjects, 430 (63%) used headache medication on more than 14 days/month, compared to 32 (4%) in the Very Frequent Headache group, 33 (2%) in the Frequent Headache group, 15 (0%) in the Infrequent Headache group, and 1 (0%) in the No Headache group.

Follow-up

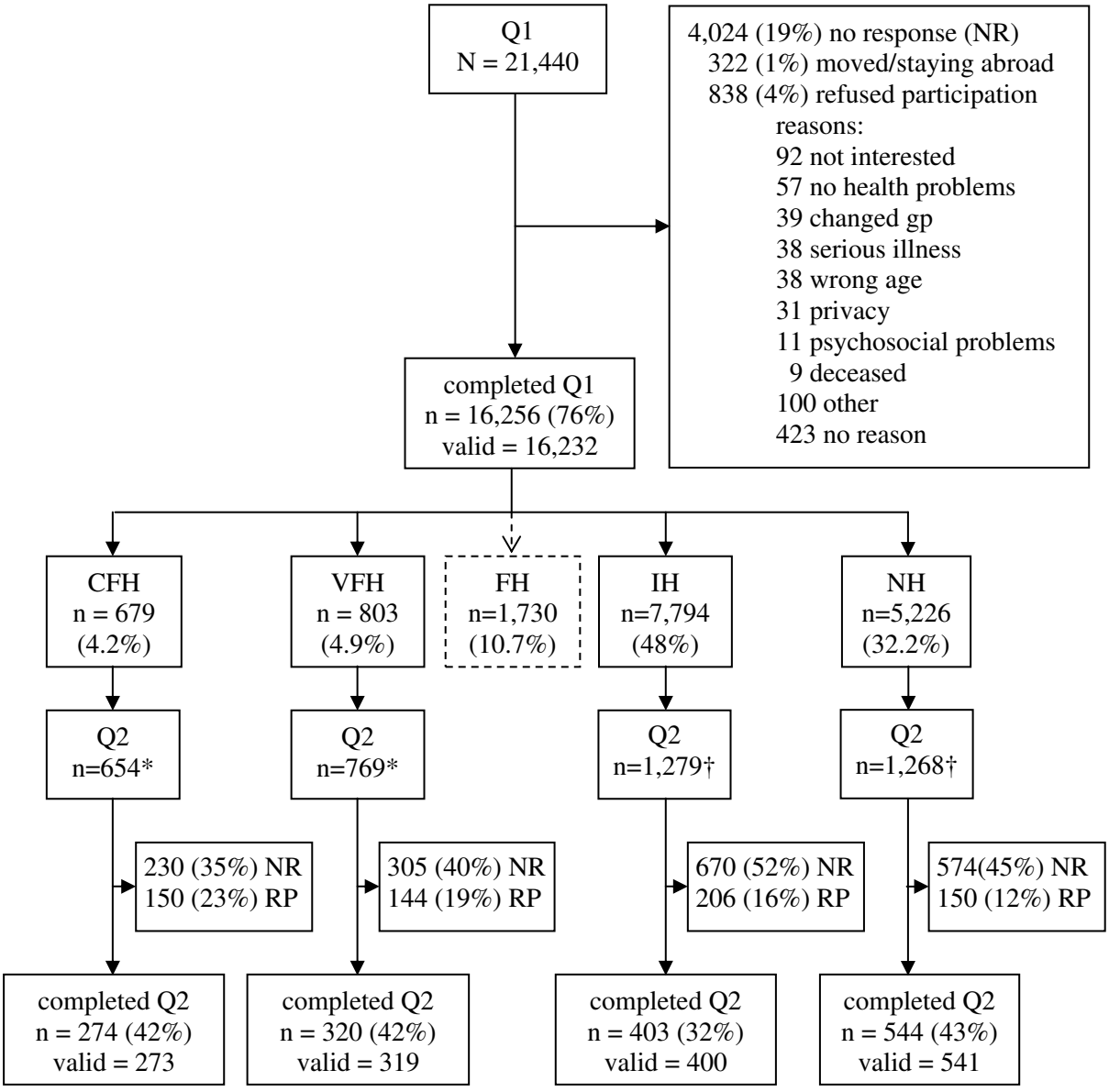
Q2 was sent to 3970 subjects. Time between Q1 and Q2 was five months on average (range three to seven months). A total of 1541 subjects (39%) completed Q2, 650 (16%) subjects refused to participate, and 1779 subjects (45%) did not respond. We excluded five subjects from analysis because they proved to be older than their registered age. Three subjects didn't complete Q2 properly and were excluded. Figure 1 shows the response per headache frequency group. Participants who had reported Infrequent Headache in the first survey (Q1) completed Q2 less often than the others.

Non-respondents analysis

In the CFH group 230 (35%) did not respond to Q2. Mean age of the non-respondents was 40 (SD 8), and 140 (61%) were female. Ninety-two (40%) non-respondents had a non-Dutch name indicating a foreign nationality. Sixty-eight (30%) non-respondents completed the short

non-response questionnaire, of which 24 (35%) had a low educational level and 37 (54%) did not have CFH anymore.

Figure 1. Flowchart of response.



* Some subjects didn't receive Q2 because they returned Q1 after the Q2 mailing date, † random sample (twice as large as the CFH group), Q1 = general health survey, Q2 = second detailed questionnaire, CFH = chronic frequent headache (>14 days/month), VFH = very frequent headache (8-14 days/month), FH = frequent headache (5-7 days/month), IH = infrequent headache (1-4 days/month), NH = no headache (<1 day/month), NR = no response, RP = refused to participate.

Frequency changes

Re-assessment of headache frequency in Q2 showed that of 273 subjects with CFH in Q1, 177 (65%) had a stable headache frequency of > 14 days/month, 62 (23%) had changed to Very Frequent Headache (8-14 days/month) and 34 (12%) now reported a headache frequency of less than 8 days/month (Table 1).

Table 1 Changes in headache frequency between Q1 and Q2

Headache frequency group Q1		Headache frequency group Q2 n (% of Q1 frequency group)				
Group	N	CFH (>14 d/m)	VFH (8-14 d/m)	FH (5-7 d/m)	IH (1-4 d/m)	NH (<1 d/m)
CFH (>14 d/m)	273	**177 (65%)**	62 (23%)	20 (7%)	12 (4%)	2 (1%)
VFH (8-14 d/m)	319	65 (20%)	**115 (36%)**	80 (25%)	41 (13%)	18 (6%)
IH (1-4 d/m)	400	3 (1%)	14 (4%)	45 (11%)	**141 (35%)**	197 (49%)
NH (<1 d/m)	540	1 (0%)	1 (0%)	1 (0%)	11 (2%)	**526 (97%)**
Q1 missing data	1					1 (100%)
Total Q2	1533	246	192	146	205	744

Q1 = general health survey, Q2 = second detailed questionnaire, CFH = chronic frequent headache (>14 days/month), VFH = very frequent headache (8-14 days/month), FH = frequent headache (5-7 days/month), IH = infrequent headache (1-4 days/month), NH = no headache (< 1 day/month). Numbers in bold are stable headache frequency groups (Q1 = Q2), in total 959 of 1533 subjects (63%). Time between Q1 and Q2 ranged from 3 – 7 months.

Overuse at baseline (Q1) was not a predictor for persistent CFH at Q2 (OR: 1.5, 95% CI 0.9 to 2.5). Vice versa, 65 (20%) subjects who had Very Frequent Headache (8-14 days/month) in Q1, changed to CFH over five months. Overuse at baseline (Q1) in this group was not a predictor for CFH in Q2 either (OR: 2.4 , 95% CI 0.9 to 6.5). In Q2, 109 (62%) of the stable CFH group still reported overuse of acute headache medication, compared to 26 (27%) of

those who had changed to lower headache frequencies, a difference of 35% (95% CI 23 to 46%). So, in the group who changed to lower frequencies, the percentage of overusing subjects decreased from 51% at baseline to 27% in Q2, while in the stable CFH group there was no change. To assess whether the subjects who changed to lower frequencies had received specific headache treatment we looked at GP consultation and prophylactic use. Remission was not attributable to treatment; only 20 (22%) subjects had consulted their GP for headache in the past six months compared to 56 (33%) in the stable CFH group (difference -11%, 95% CI –23 to 0%), and there was only a 3% difference in the use of prophylactic medication between both groups (95% CI –10 to 3%).

Demographics

Further analyses were limited to the groups in which the reported headache frequency did not change over the two surveys (i.e. the stable frequency groups). Table 2 shows the differences in demographic variables between subjects with CFH, Infrequent Headache and No Headache. In both headache groups the majority were women in contrast to the No Headache group where the majority were men.

Table 2 Demographic variables in stable CFH group vs. stable IH and NH groups

	NH N = 526	IH N = 141	CFH N = 177	difference CFH-IH (95%CI)	difference CFH-NH (95%CI)
Mean age, y (SD)	45 (9)	42 (8)	43 (8)	0.5 (-1.5 to 2.4)	-1.9 (-3.4 to -0.4)
Female, n (%)	215 (41)	97 (70)	125 (72)	2% (-8 to 12)	31% (22 to 39)
Educational level					
Low, n (%)	87 (17)	16 (11)	62 (35)	24% (15 to 33)	19% (12 to 26)
Medium, n (%)	180 (34)	47 (34)	70 (40)	6% (-4 to 17)	6% (-3 to 14)
High, n (%)	257 (49)	77 (55)	43 (25)	-30% (-41 to -20)	-24% (-33 to -17)

NH = no headache (< 1 day/month), IH = infrequent headache (1-4 days/month), CFH = chronic frequent headache (>14 days/month).

Risk factors

Mean age at onset of headache was 19 (SD 11) for the CFH group and 18 (SD 9) for the Infrequent Headache group. In both headache groups 62% of subjects had a family history positive for headache. Table 3 summarizes the prevalence and odds ratios for putative risk factors for chronification of headache.

Overuse of acute headache medication was strongly associated with CFH. Of the 109 subjects in the CFH group overusing acute headache medication, 90 (83%) subjects overused one class of medication, 16 (15%) and three (3%) subjects overused two and three different classes respectively. The percentage of smokers was similar in medication over-users (43%) and non-over-users (46%), mean difference 3% (95% CI -19 to 12%). Caffeine overuse was not associated with CFH. The average intake of caffeine in each group was seven units a day, including coffee, tea, ice-tea, and cola.

CFH subjects reported sleeping problems more frequently than subjects with Infrequent Headache. Sleeping problems were not related to caffeine use. In the CFH group 74 of 170 (44%) reported sleeping problems on > 3 nights/week; 66 (39%) had problems falling asleep and 26 (15%) awoke at night with headache. In contrast, 11 of 139 (8%) subjects with Infrequent Headache had sleeping problems on > 3 nights/week; all had problems falling asleep, none awoke at night with headache. Tranquillizer use was higher in the CFH group than in both control groups but was no longer associated with CFH after adjusting for frequent sleeping problems.

In the CFH group, 62% of subjects screen positive for psychopathology. This percentage was the same for the new CFH group (those who changed to CFH). With a sensitivity and specificity of 0.84 and 0.82 respectively, the true prevalence of psychiatric comorbidity in CFH is estimated to be 66%. Results of the GHQ-28 are presented in Table 4.

Table 3 Prevalence and odds ratios of putative risk factors for chronification of headache

	NH (n=526)	IH (n=141)	CFH (n=177)	difference CFH-IH (95%CI)	OR CFH-IH (95%CI)
Low educational level	87 (17)	16 (11)	62 (35)	24% (15, 33)	4.3 (2.3, 7.8)
Head/neck trauma prior to onset of headache	-	20 (14)	64 (36)	23% (14, 33)	4.0 (2.2, 7.1)*
Smoking	142 (27)	27 (19)	79 (45)	25% (15, 36)	3.1 (1.9, 5.3)*
Alcohol, glass/week	9	5	5	-0.5 (-2.4, 1.4)	-
Caffeine overuse	341 (65)	90 (64)	115 (65)	1% (-10, 12)	1.0 (0.6, 1.6)*
Acute headache medication overuse	19 (4)	4 (3)	109 (62)	59% (50, 67)	38.4 (13.8, 106.9)†
Paracetamol	4 (1)	1 (1)	79 (45)	44% (36, 52)	
NSAID's	14 (3)	3 (2)	41 (23)	21% (14, 28)	
Triptans	0	0	3 (2)	2% (-1, 4)	
Ergots	0	0	1 (1)	1% (-1, 2)	
Narcotics	1 (0)	0	7 (4)	4% (1, 7)	
Prophylactic medication	23 (4)	7 (5)	23 (13)	8% (2, 15)	2.3 (0.9, 5.9)*
Headache indication‖	1 (0)	0	15 (9)	8% (4, 13)	
Other indications	22 (4)	7 (5)	8 (5)	0% (-5, 4)	
Sleeping problems	-	11 (8)	74 (44)	36% (26, 45)	8.1 (3.6, 18.1)‡
Tranquillizer use	16 (3)	12 (9)	36 (20)	12% (4, 20)	1.7 (0.8, 3.7)§
Hypnotics	8 (2)	9 (6)	19 (11)	4% (–2, 11)	
Anxiolytics	9 (2)	4 (3)	20 (11)	8% (3, 14)	
GHQ-28 case	80 (16)	45 (34)	102 (62)	29% (18, 40)	2.7 (1.3, 3.6)§

Values are number of subjects (%) unless stated otherwise. * Adjusted for educational level, † adjusted for educational level and smoking, ‡ adjusted for educational level, smoking and medication overuse, § adjusted for sleeping problems. ‖ Subjects used medication which could have been prescribed for either headache or a

comorbid disorder (e.g. propanolol for migraine or hypertension). NH = no headache (< 1 day/month), IH = infrequent headache (1-4 days/month), CFH = chronic frequent headache (>14 days/month), NSAID = non-steroidal anti-inflammatory drugs, GHQ = General Health Questionnaire.

Table 4 General Health Questionnaire-28 scores

	NH (n=503)	IH (n =134)	CFH (n=164)	Mean difference CFH vs IH (95%CI)	Mean difference CFH vs NH (95%CI)
Total GHQ score	2.2 (4.0)	3.9 (4.8)	8.5 (7.4)	4.5 (3.1, 6.0)	6.3 (5.4, 7.2)
GHQ score > 4, n (%)	80 (16)	45 (34)	102 (62)	29% (18, 40)	46% (40, 53)
GHQ subscales:					
Somatic symptoms	3.2 (2.5)	5.8 (2.7)	9.7 (4.2)	3.9 (3.1, 4.7)	6.5 (6.0, 7.0)
Anxiety/insomnia	3.7 (3.7)	5.0 (4.2)	8.0 (5.1)	3.0 (1.9, 4.1)	4.3 (3.6, 5.0)
Social dysfunction	7.2 (1.9)	7.6 (2.4)	9.0 (3.4)	1.4 (0.7, 2.1)	1.8 (1.4, 2.2)
Severe depression	0.8 (2.4)	1.2 (2.2)	3.8 (4.9)	2.7 (1.8, 3.6)	3.0 (2.4, 3.5)

Values are means (SD) unless stated otherwise. NH = no headache (<1 day/month), IH = infrequent headache (1-4 days/month), CFH = chronic frequent headache (>14 days/month), GHQ = General Health Questionnaire.

Discussion

We found a prevalence of CFH in the Dutch general population of 3.7%. This is in accordance with previous population-based studies.[1-4] Although the prevalence worldwide is around 4%, we found a much higher prevalence in the practice with a high number of non-western immigrants. Even if we consider all non-respondents in this particular practice to have a low headache frequency, the prevalence would still be higher. In the Netherlands, prevalence of poor reported health is highest among Turks and Moroccans.[11] An adverse social and economic position may contribute to the poor health status of these ethnic minorities.

Our prevalence number is a reliable estimate due to the high response to the first questionnaire. The response to the second detailed and extensive questionnaire was low, but yielded high enough numbers to compare risk factors. Demographic characteristics were similar in the respondent and non-respondent CFH subjects, except for the higher percentage of non-Dutch names in the latter. As this is an indication for a foreign ethnic origin, the language of the questionnaire might have been too difficult. The question is whether non-response introduced bias in the associations. If non-respondents are healthier than respondents, prevalence estimates of risk factors based on respondents could be overestimated. However, non-response does not necessarily cause bias in associations. In a large population-based study on risk factors for chronic disease conducted in the Netherlands (MORGEN-project) the response rate was 45%. Associations between lifestyle factors and health did not vary according to response status.[12]

In many subjects headache frequency changed over time without specific headache treatment. Twelve percent had a clinically relevant decrease from >14 days to <8 days/month. This could be an underestimation, because the time between questionnaires ranged from three to seven months, meaning that some participants were asked about overlapping time periods. This spontaneous change in headache frequency can be seen as regression towards the mean[13] and underscores the need for control groups when assessing efficacy of treatments for CFH. A decrease in headache frequency was associated with a decrease in headache medication overuse. However, medication use at baseline could not predict outcome in Q2. Our data correspond with two population-based follow-up studies in the US and Taiwan, where after

one and two years respectively, only 44% and 35% still had CFH.[4,8] Whether subjects had received treatment or whether this was a spontaneous remission was not described.

We found that the majority of CFH subjects overused analgesics. The cross-sectional design of this study makes it impossible to determine the direction of causality. Improvement after withdrawal would make a causal relationship between overuse and chronification of headache likely. Since analgesics are mostly Over-The-Counter (OTC) products, the GP may not be informed about the overuse. In fact, the majority did not consult their GP for headache in the past six months. Many CFH subjects however frequently suffer from sleeping problems as well, and a substantial percentage use tranquillizers. Sleeping problems could be a possible cue for GPs to ask about headaches and analgesic use. Only 9% of CFH subjects used prophylactic medication to reduce headache frequency. To prevent overuse physicians should inform the headache patient about restricting use of acute headache medication and the possibility of prophylactic therapy.

Smoking is associated with CFH. We assumed that medication over-users would show an overall tendency towards substance use; however, tobacco use did not differ between over-users and non-over-users. Nicotine induces dopamine release in the ventral striatum causing positive mood changes, which may relieve negative consequences of pain. Since we don't have information on the age of onset of smoking, we don't know whether smoking could be more than a secondary phenomenon.

As found in other studies, CFH subjects had a lower educational level than subjects without CFH.[2,14] A low educational level is an indication of low socio-economic status, which is associated with poor health status in general. We don't think that headache interfered with scholarly achievements, because the mean age at onset of headache was 19.

About one third of CFH subjects reported a history of head or neck trauma prior to the onset of headache. This may be partly due to recall bias. On the other hand, tissue injury might have triggered central sensitisation, a pathologic change in central pain processing observed in models of chronic pain.[15]

In headache clinics, the majority of patients with CFH have co-morbid psychiatric disorders.[16-18] The most commonly reported disorders are major depression and generalized anxiety disorder, panic disorder, and phobias. In our population-based study, 62% of subjects with CFH screened positive for psychopathology, twice as many as in the Infrequent Headache group. Breslau et al. found a bi-directional relationship between migraine and major depression, suggesting shared etiologic factors.[19] Alternatively, pain may exacerbate a pre-existing vulnerability to psychopathology, which in turn intensifies the pain and so on.[20] This would imply that either condition cannot be treated independently of the other.

The strength of our study is the large number of participants and the identification of associated factors by comparing the CFH group to control groups with infrequent headache and no headache. In both headache groups the majority were women, in contrast to the No Headache group. Female sex seems to be a risk factor for headache, not for the chronification of headache. A limitation of our study is that prevalence of risk factors is based on self-report, which is not as accurate as studies based on interviews by specialists and headache diaries. We conclude that headache frequency fluctuates spontaneously and chronification is common. In the Netherlands the prevalence of CFH in the general population, aged 25-55 years, is 3.7%. We identified several risk factors to be associated with CFH including overuse of analgesics, psychiatric comorbidity, smoking, sleeping problems, a history of head/neck trauma, and low educational level.

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