

Incidence of migraine and tension-type headache in three different 'populations at risk' within the German DMKG headache study

German DMKG headache study Laura Khil, Volker Pfaffenrath, Andreas Straube, Stefan Evers and Klaus Berger *Cephalalgia* published online 24 November 2011 DOI: 10.1177/0333102411428953

The online version of this article can be found at: http://cep.sagepub.com/content/early/2011/11/22/0333102411428953

> Published by: SAGE http://www.sagepublications.com



International Headache Society

Additional services and information for *Cephalalgia* can be found at:

Email Alerts: http://cep.sagepub.com/cgi/alerts

Subscriptions: http://cep.sagepub.com/subscriptions

Reprints: http://www.sagepub.com/journalsReprints.nav

Permissions: http://www.sagepub.com/journalsPermissions.nav

>> Proof - Nov 24, 2011

What is This?



International Headache Society

Incidence of migraine and tension-type headache in three different populations at risk within the German DMKG headache study

Cephalalgia 0(0) 1–9 © International Headache Society 2011 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav DOI: 10.1177/0333102411428953 cep.sagepub.com



Laura Khil¹, Volker Pfaffenrath², Andreas Straube³, Stefan Evers¹ and Klaus Berger¹

Abstract

Background: Unlike the prevalence, the incidence of headache disorders has attracted only little attention in epidemiological research. Different definitions of the 'population at risk' among the few published migraine and tension-type headache incidence studies limit their comparability and warrant further research. Therefore, we analysed data from the German Migraine and Headache Society (DMKG).

Methods: Incidences were assessed in the general population in Germany via standardized headache questions using the International Classification of Headache Disorders, 2nd Edition (ICHD-2). The population was drawn from a 5-year agegroup- stratified and gender-stratified random sample from the population register.

Results: Of the 1312 baseline participants examined between 2003 and 2004, 1122 (85.5%) participated in the follow-up in 2006 and were the basis for three different populations at risk. We found that the three populations differed in size, age, gender and incidence estimate. The total sample incidence of migraine ranged between 0% and 3.3% and of tension-type headache between 5.3% and 9.2% depending on the definition of 'at risk'.

Conclusion: We concluded that one significant problem in headache incidence estimation is the definition of 'at risk', limiting comparability. Thus, this study supports the need for a common definition for prospective headache incidence estimations.

Keywords

Migraine, tension-type headache, prospective study, classification criteria, population at risk, change in headache phenomenology

Date received: 3 June 2011; revised: 15 September 2011; accepted: 8 October 2011

Introduction

Primary headache disorders are frequent in the general population. Close to 50% of the world's adult population actively suffers from headache (1). Many affected individuals do not consult a doctor, although headache disorders are often disabling and painful (2).

The two most frequent types of primary headaches are tension-type headache (TTH) and migraine. The many available studies on migraine and TTH prevalences (1,3–7) estimated that on average 14% of the adult population are affected by migraine and 46% by TTH, worldwide (lifetime prevalence) (1). However, the size of the studies and the applied methodology varied considerably among these studies. In contrast to the large number of reports on headache prevalence, there has so far been only one published prospective study on TTH incidence (8) and seven studies on migraine incidences (8–14) in the general population. Only five of the latter are prospective

¹University of Münster, Germany.

²Neurology Practice Leopoldstrasse, Germany. ³University of Munich, Germany.

Corresponding author:

Laura Khil Dipl.-Biol., Westfälische Wilhelms-University Münster, Institute of Epidemiology and Social Medicine, Domagkstraße 3, 48149 Münster, Germany Email: khil@uni-muenster.de

(8–10,13–14) and two (11,12) are cross-sectional studies with retrospective incidence estimations. Whereas in retrospective studies incidences of migraine are assessed in migraineurs using current age and age of onset, in prospective studies a group of disease-free individuals, called the 'population at risk', is followed for a specific period of time. Different definitions of the population at risk and variable lengths of the follow-up period among the published prospective studies on migraine incidence limit the comparability of the reported incidence estimates. In the past, little attention has been given to the problem of the population at risk definition. In case of headache incidence estimation the definition of 'at risk' is crucial, because the many headache types and subtypes offer various definitions of the 'disease-free status'. It is reasonable to believe that the risk for a new onset of migraine differs among those who never had any headache, compared with those who report previous unspecific, non-classifiable headaches. Furthermore, most incidence studies on primary headache types were published before 2004 and used the first edition of the International Classification of Headache Disorders (ICHD-1) (15) of the International Headache Society. The ICHD was revised in 2004 (ICHD-2) (16). One of the major changes in the second edition was the introduction of the categories 'probable' migraine and 'probable' TTH into the classification for patients with headaches who do not fulfil all criteria of migraine or TTH, respectively. There has so far been no prospective study on migraine or TTH incidence applying the new ICDH-2 criteria.

The aim of the present study was to estimate the incidence of migraine and TTH in a population based sample in Germany and in three different populations at risk within the study.

Methods

Baseline data acquisition

The data for this study were collected in the Dortmunder Health Study (DHS), which is part of the DMKG Headache Study. The overall goal of the DHS was to assess the frequency of headache types, cardiovascular and other chronic diseases, and their consequences on daily life among those affected in an urban German population. In addition, sociodemographic data, comorbidities (self-reported) and various health-related lifestyle factors were collected. Migrational background was classified by own and parental place of birth and nationality and included first- and second-generation migrants. Depressive symptoms were assessed by the Center for Epidemiologic Studies Depression Scale (17). The detailed study procedure is described elsewhere (5). In brief, a 5-year age-group-stratified and gender-stratified random sample of 3,820 people was drawn from the population register from a total population of 591,000 living in Dortmund. The baseline data acquisition took place from October 2003 to September 2004. Participation was restricted to the age groups 25 to 75 years. Of the 3,820 people, 395 were not eligible because of moving from the study area, lack of sufficient knowledge of the German language, or death. Thus, 3,425 people were invited to an interview and standardized examination in the central study centre. Participants were interviewed face-to-face by trained interviewers who were supervised for interview quality. If personal participation was not possible, a standardized questionnaire with a shortened but otherwise identical set of questions was sent to the participant. Where there was no response, two additional invitation letters were sent out and up to five phone calls were made. Finally, all addresses of non-responders were again checked for movements out of the study region and home visits were made to the remaining addresses.

The overall response rate was 66.9%, yielding 2,291 participants (1312 interview and 979 questionnaire participants). For the purposes of this analysis, only interview participants were considered (n = 1312), because not all criteria of the IHS classification were implemented in the questionnaire. The interview and questionnaire groups did not differ in mean age and gender (52.1 vs. 53.0 years) but 12-month headache reports were significantly different (52.8% vs. 68.8%, p < 0.001).

Follow-up assessment

In 2006, a follow-up of the Dortmund Health Study data was conducted via mailed questionnaire to all participants of the baseline survey. This questionnaire included a headache question module, which was identical to the headache questions of the baseline interview. Participants were asked to return the completed questionnaire using an included prepaid envelope. Where there was no response, identical procedures were used as in the baseline sampling.

Headache assessment

The standardized headache question module was designed on the basis of the second edition of the International Headache Society's (IHS) classification criteria to assess the 6- and 12-month prevalence of headache in general and of migraine and TTH in particular. In addition, the design of this headache module allowed assessment and classification of the presence of any second headache type (5).

The IHS classification provides an algorithm that classifies headache disorders into major groups. Each group is then subdivided into headache subtypes.

In the present analysis, we focused on the two most common major groups of primary headache, migraine and tension-type headache (TTH). The IHS defines six subtypes of migraine and four subtypes of TTH. When referring to definite migraine, we classified headache according to IHS code 1.1 and 1.2 (migraine without and with aura) and definite TTH according to IHS code 2.1 to 2.3 (infrequent episodic, frequent episodic and chronic TTH). Probable migraine (PM, IHS code 1.6) was recorded when one criterion was missing to fulfil definite migraine, and probable TTH (PTTH, IHS code 2.4) when one was missing to fulfil definite TTH. PM and PTTH criteria are not mutually exclusive, so it is not always possible to distinguish between PM and PTTH. Participants who fulfilled both classifications were allocated to a group called 'PM plus PTTH'. If no classification criteria were fulfilled but headache was present, the headache type was recorded as 'unspecific headache'.

Definition of incidence and population at risk

In epidemiological studies the term incidence refers to the onset of a new condition (typically a specific disease). Cumulative incidences are estimated by the number of individuals that became diseased during a specific period of time divided by the number of all people initially free of the disease. The incidence rate is calculated by using the person-time instead of the number of people. Typically, incidences are estimated from prospective studies in which disease-free individuals are observed. These disease-free individuals are labelled 'population at risk' because they are potentially prone to an incident event. The population at risk determines the denominator for incidence calculations and poses a particular challenge in population-based headache incidence estimations because the different headache types offer various possible definitions of being disease-free and therefore various definitions of the population at risk.

To identify migraine-free individuals in the present study we assessed the presence of migraine during a period of 1 year before baseline (1 year prevalence). The same was true for the other headache types. Information on whether migraine-free individuals had suffered from migraine earlier in their life was not available. Thus, incident migraine (or other headache types mentioned in this study) is defined as a new onset migraine compared with the baseline condition, not excluding participants with a recurrent event after a symptom-free period of at least 1 year. We estimated incidences of migraine and of TTH in three different populations at risk: (a) participants with no headache 1 year before baseline (population A), (b) participants without definite and PM (for incidence of definite migraine, population B.1), or without definite TTH (for incidence of definite TTH, population B.2) 1 year before baseline, and (c) participants without definite migraine, PM and definite TTH 1 year before baseline (population C). Thus, the different populations at risk varied in the number of participants with 12-month headache prevalences (Table 2).

Ethics

The Study was approved by the local ethics committee of the medical faculty at the University of Münster. All participants gave their written informed consent before inclusion in the study.

Statistical methods

Continuous variables were described with means and standard deviations and compared using Student's t-test. Differences in categorical variables were compared using the chi-square test or Fisher's exact test (if cell number was 5 or less). Age effects were analysed by grouping into 5-year age groups. Because the true time point of an incident event was unknown, our data were interval-censored. Thus, annual incidence rates in person-years and their corresponding confidence intervals were calculated with parametric survival models fitting an exponential distribution using the SAS LIFEREG procedure (18). Because traditional methods for confidence interval calculations do not perform well when the estimate is zero or based on small numbers (less than 5), confidence intervals for the cumulative incidences were calculated using an alternative approach (19). The effect of age on migraine and TTH incidences was analysed using a linear trend test with age as a continuous variable. Participants who were lost to follow-up were excluded from the analysis (n = 190). All data analyses were carried out using SPSS statistical software, version 18.0, and SAS statistical software, version 9.2.

Results

Follow-up response was 85.5% after a mean time of 2.2 years and yielded 1,122 participants. Those who participated in the follow-up assessment were significantly older than participants who did not participate (52.9 vs. 47.5 years, p < 0.001). Furthermore, participants differed significantly from non-participants in the number of people with a migrational background (13.7% vs. 29.5%, p < 0.001), the distribution of social class with more non-participants in the lower

social-class (15.3% vs. 8.4%, p = 0.008) and the number of smokers, with more current smokers in non-participants (24.3% vs. 32.6%, p = 0.026). At baseline more non-participants than participants were suffering from current headache (12-month baseline prevalence, 62.6% vs. 51.2%, p = 0.003). Other baseline characteristics were not significantly different.

Baseline characteristics of the sample population are summarized in Table 1. The mean age of the 1,122 participants was 52.9 (SD 13.5) years, with a slightly higher proportion of women (53.3%) than men. Approximately 14% had a migrational background and about a quarter had a body mass index (BMI) of 30 or higher. More than 24% were current smokers and 7.8% reported an alcohol consumption of more than 40 g per day. The prevalence of severe depressive symptoms (Center for Epidemiologic Studies Depression Scale-Revised (CESD) \geq 16) in this sample population was 15.8%. Almost 4% had a history of heart attack, 2% a history of stroke and 7.8% had been diagnosed with diabetes. At baseline, 51.2% of the participants had experienced headache during the preceding 12 months. Based on the ICDH-2, definite migraine and definite TTH prevalences at baseline were 8.5% and 20.1%, respectively (definite TTH prevalence was 18.0% for TTH as a first and 2.1% as a second (additional) hedache type; second headache type means that more than one headache type was present). Of those with migraine 14 participants (14.7%) had TTH as a second headache. Prevalence of PM was 3.9%, of PTTH 11.1%, and of PM plus PTTH 6.7%. In total, 9 (4.3%) participants with one of the probable headache types had TTH as a second headache. However, migraine was never indicated as a second headache.

Incidences were estimated in three different populations at risk (populations A to C). The size, mean age and gender varied among the three risk populations (Table 2). Population A (including all participants without headache during 12 months before baseline), yielded 48.8% (n=548) of the sample population. The proportion of women and the mean age differed considerably from the other two populations. 87.6% (n=983) of the sample population was included in population B.1 (all participants without definite and probable migraine) and 79.9% (n=897) in population B.2 (all participants without definite TTH). In population C (participants free of definite and probable migraine and free of definite TTH at baseline) 772 participants (68.8% of the sample population) remained for the analysis.

The cumulative headache incidence was estimated within population A. There were 145 new cases of headache resulting in an overall cumulative headache incidence of 26.5% (95% CI 24.6–28.7%). In this population no incident headache case was classified into definite migraine, but the cumulative incidence of

Table	۱.	Baseline	characteristics	of the	study p	opulation
(n =	22))				

Characteristics	
Sociodemographic factors	
Mean age (SD), years	52.9 (13.5)
Women (%)	53.3
Migrational background (%)	13.7
Social class (%)*	
Low	8.4
Middle	49.6
High	42.1
Risk factors (%)	
$BMI \ge 30$	25.9
Smoker	
Never	44.2
Ex	31.5
Current	24.2
Alcohol consumption (%)	
Non-drinker	38.3
I–39 g/day	52.5
>40 g/day	7.8
Co-morbidities (%)	
Severe depressive symptoms†	15.8
History of diabetes	7.8
History of heart attack	3.8
History of stroke	2.1
12-month headache prevalences	
Any headache	51.2
Migraine	8.5
Probable migraine	3.9
Tension-type headache (TTH)	20.1
Probable tension-type headache TTH	11.0
Probable migraine plus probable tension-type headache	6.3

*According to the Winkler-Schicht-Index.

 $^\dagger Summary$ Score of the Center of Epidemiologic Studies Depression Scale $\geq 16.$

BMI: body mass index, SD: standard deviation.

PM was 1.5% (95% CI 1.1–2.5%). The cumulative incidence of definite TTH was 5.3% (95% CI 4.5–6.7%), of PTTH 10.8% (95% CI 9.5–12.5%) and of PM plus PTTH 0.4% (95% CI 0.2–1.2%).

Age- and gender-specific cumulative incidences and incidence rates of definite migraine are shown in Table 3 for populations B.1 and C. We found 32 new cases in population B.1 and 22 in population C, resulting in an overall cumulative incidence of 3.3% and 2.9%, respectively. The incidence rates per 1000 person years were 15.1 and 13.2. In both populations the incidence was markedly higher in women than in

Population at risk	n	Mean age, years (SD)	Female, %	l2-month headache prevalence, N (%)	
Population A: no headache at baseline	548	57.9 (12.5)	42.7	0	
Population B.1: no migraine at baseline	983	53.5 (13.5)	49.0	479 (44.3)	
Population B.2: no TTH at baseline	897	54.2 (13.4)	52.7	350 (39%)	
Population C: no migraine and no TTH at baseline	772	55.4 (13.3)	48.2	225 (29.2)	

Table 2. Characteristics of the three different populations at risk within the study

SD: standard deviation, TTH: tension-type headache.

Table 3. Age and gender specific incidences of definite migraine in population B.I and C

Age group	Population at risk B.I					Population at risk C			
	n	е	Cumul-inc.% (95%Cl)	Rate per 1000 PY (95%Cl)	n	е	Cumul-inc.% (95%Cl)	Rate per 1000 PY (95%Cl)	
All									
25–34	115	4	3.5(2.3–7.7)	16.0 (5.9–42.5)	73	3	4.1 (2.6–10.2)	19.0 (6.1–58.6)	
35-44	148	6	4.1 (2.9–7.6)	18.8 (8.5-42.0)	102	2	1.9(1.2-6.2)	9.1 (2.3–36.2)	
45–54	208	9	4.3 (3.2–7.1)	20.4 (10.6–39.2)	149	6	4.0 (2.8–7.5)	19.0 (8.5-42.2)	
55–64	270	10	3.7 (2.8–5.9)	17.2 (9.3–32.0)	229	8	3.5 (2.6–5.9)	16.2 (8.1–32.4)	
65–75	242	3	1.2 (0.8–3.2)	5.7 (1.8–17.6)	219	3	1.4 (0.9–3.5)	6.3 (2.2–19.4)	
25–75	983	32	3.3 (2.8–4.1)	15.1 (10.7–21.3)	772	22	2.9 (2.3-3.8)	13.2 (8.7–20.0)	
Women									
25–34	61	4	6.6 (4.3–14.0)	30.3 (11.4-80.7)	38	3	7.9 (4.8–18.7)	37.0 (12.0–114.8)	
35–44	76	4	5.3 (3.5–11.4)	24.5 (9.2–65.4)	54	2	3.7 (2.1–11.4)	17.2 (4.3–68.8)	
45–54	106	8	7.6 (5.5–12.6)	33.8 (17.9–71.7)	73	6	8.2 (5.7–14.9)	39.2 (17.6–87.3)	
55–64	130	10	7.7 (5.8–12.0)	36.2 (19.5-67.4)	109	8	7.3 (5.4–12.2)	34.6 (17.3–69.2)	
65–75	111	3	2.7 (1.7–6.9)	12.5 (4.0-38.7)	98	3	3.1 (1.9–7.7)	4. (4.6–43.8)	
25–75	484	29	6.0 (5.0–7.6)	28.0 (19.5-40.3)	372	22	5.9 (4.9–7.9)	27.7 (18.2–42.1)	
Men									
25–34	54	0	0.0 (0-6.7)	0.0	35	0	0.0 (0-10.0)	0.0	
35–44	72	2	2.8 (1.6-8.7)	12.8 (3.2–51.3)	48	0	0.0 (0-7.5)	0.0	
45–54	102	I	1.0 (0.5–5.0)	4.5 (0.7–32.6)	76	0	0.0 (0-4.9)	0.0	
55–64	140	0	0.0 (0-2.7)	0.0	120	0	0.0 (0-3.1)	0.0	
65–75	131	0	0.0 (0-2.9)	0.0	121	0	0.0 (0-3.1)	0.0	
25–75	499	3	0.6 (0.4–1.6)	2.8 (0.9-8.6)	400	0	0.0 (0-1.0)	0.0	

Cumul-inc.: cumulative incidence, PY: person years; CI: confidence interval; e: events.

men ($p \le 0.001$). However, no significant difference was found between age groups (p > 0.1).

Table 4 shows age- and gender-specific cumulative incidences and incidence rates of definite TTH. The overall cumulative incidence in population B.2 was 9.3% with 83 incident cases, whereas 69 incident cases were observed in population C, resulting in an overall cumulative incidence of 8.9%. The overall incidence rates per 1000 person years for populations B.2 and C were 44.3 and 42.7, respectively. The incidence was higher among women ($p \le 0.006$) and decreased

markedly with increasing age ($p \le 0.001$). However, differences in incidences between age groups were not significant in men (p > 0.2).

To compare the incidence of definite migraine in our study with previously published migraine incidences in other prospective studies, we plotted cumulative migraine incidences of the few population-based cohort studies against follow-up time. Figure 1 shows the total and gender-specific cumulative incidence by length of the follow-up period. For a better comparison the *x*-axis (time) was transformed into a logarithmic scale.

Age group		Population at risk B.2					Population at risk C				
	n	e	Cumul-inc.% (95%Cl)	Rate per 1000 PY (95%CI)	n	e	Cumul-inc.% (95%Cl)	Rate per 1000 PY (95%Cl)			
All											
25–34	89	16	18.0 (14.2–24.4)	90.2 (55.2–147.3)	73	14	19.2 (14.9–26.6)	96.3 (57.0-162.7)			
35–44	150	19	12.7 (10.2–17.0)	61.9 (39.5–97.0)	102	12	11.8 (9.0–17.3)	57.3 (32.5–101.0)			
45–54	179	21	.7 (9.6– 5.5)	57.4 (37.4–88.0)	149	18	2. (9.7– 6.4)	59.4 (37.4–94.4)			
55–64	253	16	6.3 (5.0-8.9)	29.8 (18.3-48.6)	229	14	6.1 (4.8–8.9)	28.2 (17.1–48.6)			
65–75	226	11	4.9 (3.7–7.5)	22.7 (12.8-41.0)	219	11	5.0 (3.8–7.8)	23.4 (13.0-42.3)			
25–75	897	83	9.3 (8.3–10.5)	44.3 (35.8–55.0)	772	69	8.9 (8.0–10.3)	42.7 (33.7–54.1)			
Women								· · · ·			
25–34	53	14	26.4 (20.4–35.6)	139.5(82.4–236.0)	38	12	31.6 (23.7-42.9)	171.0 (96.8–302.0)			
35-44	92	14	15.2 (11.9–21.4)	75.4 (44.6–127.4)	54	8	14.8 (10.6–23.7)	73.2 (36.6–146.5)			
45–54	98	15	15.3 (12.0-21.2)	76.1 (45.8–126.2)	73	12	16.4 (12.5–23.7)	82.4 (46.8–145.2)			
55–64	128	11	8.6 (6.5–13.1)	40.9 (22.6–73.8)	109	10	9.2 (6.9–14.2)	43.7 (23.5-81.3)			
65–75	102	5	4.9 (3.4–9.7)	22.8 (9.5–54.9)	98	5	5.1 (3.5–10.1)	23.8 (10.0–57.2)			
25–75	473	59	12.5 (11.0–14.5)	60.7 (47.0–78.4)	372	47	12.6 (11.0–15.0)	61.5 (46.2-81.8)			
Men											
25–34	36	2	5.6 (3.1–16.5)	26.0 (65.1–104.1)	35	2	5.7 (3.2–17.0)	26.7 (6.7–106.7)			
35-44	58	5	8.6 (5.8–16.6)	41.2 (17.1–99.0)	48	4	8.3 (5.4–17.5)	40.0 (15.0–106.6)			
45–54	81	6	7.4 (5.2–13.5)	35.6 (16.0–79.2)	76	6	7.9 (5.5–14.3)	38.2 (17.1–85.1)			
55–64	125	5	4.0 (2.7-8.0)	18.7 (7.8–44.9)	120	4	3.3 (2.2–7.3)	15.6 (5.8-41.4)			
65–75	124	6	4.8 (3.4–9.0)	22.6 (10.2–50.3)	121	6	5.0 (3.5–9.2)	23.1 (10.4–51.5)			
25–75	424	24	5.7 (4.7–7.4)	26.7 (17.8–39.8)	400	23	5.5 (4.8–7.6)	25.9 (17.1–39.4)			

Table 4. Age and gender specific incidences of definite tension-type headache (TTH) in Population B.2 and C

Cumul-inc.: cumulative incidence, PY: person years; CI: confidence interval; e: events.

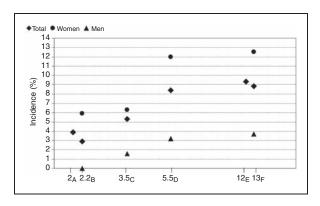


Figure 1. Comparison of migraine incidences in published studies with different follow-up periods. The follow-up period was transformed into a logarithmic scale. Two studies did not separate incidences by gender, so this information was left out for those studies. (A) Breslau et al. 2003 (10), (B) Dortmunder Health Study, (C) Breslau et al. 1994 (9), (D) Breslau et al. 1996 (14), (E) Lyngberg et al. 2005 (8), (F) Swartz et al. 2000 (13).

We used the estimated cumulative incidence of group C from our study for this comparison. With 2.2 years of follow-up, our study had a similar follow-up time to the study by Breslau and colleagues conducted in 2003 (10),

but our incidence was lower. Generally, the incidences presented in figure 1 followed a continous pattern until a follow-up time of 5.5 years. After that point, there was a nonlinear increase in the incidence. Furthermore, the incidence was consistently higher in women in all studies (Figure 1).

Discussion

In a population-based cohort study in Germany we assessed migraine and TTH incidences using the ICDH-2 published in 2004. Incidences were calculated in three different populations at risk within the study, addressing the methodological problem of adequately defining 'at risk' in prospective studies on migraine and TTH. We found that the three populations differed in size, age, gender and in estimated incidences, ranging from 0% to 3.3% (definite migraine) and 5.3% to 9.3% (definite TTH) depending on the definition of 'at risk'. In agreement with previous findings (8,13–14) incidences of definite migraine and TTH were higher in women than in men, and TTH incidence decreased with increasing age. In our study, we made the interesting observation that the subgroup with no headache

history at baseline did not present a single incident case of definite migraine. We assume that in the age group studied here, previous headache might be a risk factor for incident migraine.

Strengths of this study are the large sample size and the high follow-up response (85.5%). Furthermore, we were able to apply the ICDH-2 and had trained interviewers for standardized headache assessment. The incidence of migraine and TTH was based on a rather short follow-up time of 2.2 years, reducing recall bias. However, the short follow-up time could also be regarded as limitation. Another limitation of this study is that the follow-up assessment used self-completion questionnaires, whereas baseline assessment was done using face-to-face interviews. However, the number and wording of questions in the headache module was identical in both assessments. Thus, we do not expect significant response differences in headache prevalences due to the assessment technique. However, the precision of headache type classification (e.g. TTH or migraine) might be lower using questionnaires instead of interviews (20). Hence, misclassification of headache types could result in slight under- or overestimations of the specific incidences. The cohort was limited to an age span from 25 to 75 years and did not allow for incidence observations in younger age groups. Another limitation of this study is that we did not assess the lifetime prevalence of migraine at baseline, but the 12-month prevalence. Thus, we could not completely exclude participants who had definite migraine attacks longer ago than 1 year before baseline and were attack-free during that previous year. This may result in an overestimation of our migraine incidences owing to inclusion of recurrences. However, we consider such a disease course as rare and the probability of inclusion of recurrences as small. Therefore, the definition of incidence in our study is a mixture of incidence and recurrence as defined by the ICDH. Furthermore, we addressed the problem of migraine incidence overestimation due to recurrence by excluding PM from the population at risk, because it might be that participants who fulfilled definite migraine criteria years before had remitted to a PM (diminution of severe symptoms) at the baseline and relapsed back to a definite migraine (reoccurrence of more severe symptoms) at the follow-up assessment.

Finally, the sample population was limited to the baseline interview participants. Using questionnaires for headache classification is not considered as limitation. Schürks and colleagues reported a large agreement between self-reported migraine and ICDH-2 questionnaire-based migraine assessment (21).

We plotted the cumulative migraine incidence observed in our study and those of other prospective studies on follow-up time and found that incidences followed a continuous pattern until about 5.5 years. The rather slight increase might be explained by two factors. First, there were different age ranges in the 5.5 year study by Breslau (14) from the studies by Swartz (13) and Lyngberg (8), and second, different definitions of 'at risk' were applied. Whereas Breslau's population at risk was determined by all participants with no migraine at baseline, Swartz included only those without headache at baseline. This might result in a different susceptibility of the populations because a history of headache could influence the probability of a new migraine. The issue of different population at risk definitions has been given little attention in headache studies. However, the definition of at risk is crucial in headache incidence studies because the different headache types and subtypes can either be included in or excluded from the population at risk. For example, of the five prospective studies on migraine incidence published so far (8–10,13,14), two included all participants with no headache at baseline (10,13) and three with no migraine at baseline (8,9,14). We estimated migraine and TTH incidence in three different populations. Including only participants with no headache at baseline resulted in a population characterized by the lowest number of participants at risk, the highest age and a smaller proportion of women. In this population we observed a lower incidence of definite migraine and TTH. This is not a surprising result, but it highlights how the definition of the population at risk influences the incidence estimate. In detail, because the prevalence of migraine and TTH varies between age groups, gender, sociodemographic determinants and other risk factors (4-7,22), the population at risk is inversely defined by the characteristics of prevalent cases within the sampled study population. In our study, the overall headache prevalence at baseline was 51.2%. Excluding participants with any type of headache at baseline reduced the size of the population by about 50%. In addition, it is known that migraine and TTH are more common in women and in younger participants, yielding an older population at risk with fewer women. Thus, this definition of 'at risk' may result in a less susceptible population.

In contrast to other studies (8–9,13), we did not find a higher migraine incidence (definite migraine) in younger age groups. This finding may be due to a much shorter follow-up time in this study than in Swartz's (13) and Lyngberg's (8) studies, in which a long follow-up time might cause misclassification of the true age of incident migraine. Additionally, Swartz's study (13) included participants aged 18 to over 45, with more participants younger than 45 than older than 45 (860 vs. 483). In our study, the opposite was true. We assume that in the present study the short follow-up time and the fewer participants in younger age groups could result in an underestimation of migraine incidence in younger age groups. Furthermore, we observed rather few incident cases, especially for men (the incidence of definite migraine in men was in fact zero in population C). Thus, when analysing age effects it should be noted that the low number of cases could result in statistical uncertainty.

It was previously mentioned that PM and PTTH are not mutually exclusive, requiring the IHS classification to integrate further information for a final diagnosis (5). In addition, difficulties in distinguishing migraine from TTH have been reported (23), leading to the conclusion that this problem could also apply to PM and PTTH. Furthermore, it was previously suggested that PM is a precursor of migraine and that participants with PM may develop definite migraine over time (24). We found that all participants with incident definite migraine in population at risk B.1 had a history of headache at baseline. Nine of them were initially classified into TTH. Thus, our data support the abovementioned suggestions and extend them to PTTH and unspecific headache (PM plus PTTH).

The change of the classification of initial headache over time is a known problem, especially in studies with children and adolescents (25,26). An interesting observation is that age-dependent incidences for migraine and TTH did not differ greatly, regardless of the basic population (B or C). In other words, the presence of headache at baseline increased the risk of developing a definite migraine or a definite TTH to the same extent. The fact that no patients with no headache at baseline developed a definite migraine in the follow-up period of 2.2 years but that some did develop TTH is unexplained and might be related to a 'progress' of headaches from initial mild to moderate headaches to severe headaches during the course of a headache disorder. In this respect it would be interesting how these 145 new patients would be classified today. The exclusion of all participants with any headache seems, therefore, not to be an adequate population at risk definition in population-based migraine or TTH incidence studies, because this definition might result in an underestimation of the incidences. Furthermore, the difficulty in distinguishing migraine from TTH is exacerbated by the fact that the coexistence of other headaches can complicate a precise separation between migraine and TTH in epidemiological studies (20,27). Keeping TTH in the population at risk for migraine incidence estimations and migraine for TTH incidence estimations might result in an overestimation of the incidences. Therefore, we recommend excluding both migraine and TTH from the population at risk for TTH as well as for migraine incidence estimations in population-based studies using interviews or questionnaires for headache classification. However, the issue of finding an adequate population at risk requires further discussion and a consensus.

In summary, we found an influence of the definition of 'at risk' on the sample characteristics and observed incidences of migraine and tension-type headache in this prospective 2.2 year follow-up study. Our results support the need for a consensus population at risk in future headache incidence studies.

Funding

This study was supported by the German Migraine and Headache Society (DMKG) and by unrestricted grants of equal share from Almirall, Astra Zeneca, Berlin Chemie, Boehringer, Boots Health Care, Glaxo-Smith-Kline, Janssen Cilag, McNeil Pharma, MSD Sharp & Dohme and Pfizer to the University of Münster.

Conflicts of interest

L.K. has nothing to disclose.

V.P. received honoraria for participation in clinical trials, contribution to advisory boards or oral presentations from: Addex Pharma, Allergan, Almirall, AstraZeneca, Bayer Vital, Berlin Chemie, Boehringer Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, Janssen-Cilag, Lilly, 3 M Medica, MSD, Novartis, Pfizer, Shaper and Bruemmer, SanoviAventis and Weber & Weber. Financial support for research projects was provided by Allergan, Almirall, AstraZeneca, Bayer, GSK, Janssen-Cilag, Pfizer. V.P. has no ownership interest and does not own stocks of any pharmaceutical company.

A.S. has received honoraria from Allergan, Berlin Chemie, Desitin, Boehringer Ingelheim, MSD and Pfizer and grants from the German Science Foundation, German Ministry of Research and Education and the Kröner-Fresenius Foundation.

S.E. has received unrestricted grants and honoraria in the past two years from Addex, Allergan, Berlin Chemie, Boehringer, Colucid, GSK, Ipsen, Merz, MSD, Pfizer, Eisai and UCB.

K.B. has received research support for the conduction of DMKG Headache Study unrestricted grants of equal share from the German Migraine and Headache Society and a consortium formed by Almirall, Astra-Zeneca, Berlin-Chemie, Boehringer Ingelheim Pharma, Boots Healthcare, GlaxoSmithKline, Janssen Cilag, McNeil Pharmaceuticals, MSD Sharp & Dohme and Pfizer to the University of Münster; for the 'Course of Restless Legs Syndrome Study' unrestricted grants from the German Restless Legs Society and a consortium formed by Boehringer Ingelheim Pharma, Mundipharma Research, Neurobiotec, UCB (Schwarz Pharma) and Roche Pharma to the University of Münster; and from the German Ministry of Research and Education for several research projects within the German Competence Net Stroke and an ongoing cohort study on depression and subclinical arteriosclerosis.

References

- Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalalgia* 2007; 27(3): 193–210.
- Lipton RB, Stewart WF and Simon D. Medical consultation for migraine: results from the American Migraine Study. *Headache* 1998; 38(2): 87–96.
- Patel NV, Bigal ME, Kolodner KB, Leotta C, Lafata JE and Lipton RB. Prevalence and impact of migraine and probable migraine in a health plan. *Neurology* 2004; 63(8): 1432–1438.
- Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML and Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology* 2007; 68(5): 343–349.
- Pfaffenrath V, Fendrich K, Vennemann M, Meisinger C, Ladwig KH, Evers S, et al. Regional variations in the prevalence of migraine and tension-type headache applying the new IHS criteria: the German DMKG Headache Study. *Cephalalgia* 2009; 29(1): 48–57.
- 6. Gobel H, Petersen-Braun M and Soyka D. The epidemiology of headache in Germany: a nationwide survey of a representative sample on the basis of the headache classification of the International Headache Society. *Cephalalgia* 1994; 14(2): 97–106.
- Lipton RB and Bigal ME. The epidemiology of migraine. Am J Med 2005; 118(Suppl 1): 3S–10S.
- Lyngberg AC, Rasmussen BK, Jorgensen T and Jensen R. Incidence of primary headache: a Danish epidemiologic follow-up study. *Am J Epidemiol* 2005; 161(11): 1066–1073.
- Breslau N, Davis GC, Schultz LR and Peterson EL. Joint 1994 Wolff Award Presentation. Migraine and major depression: a longitudinal study. *Headache* 1994; 34(7): 387–393.
- Breslau N, Lipton RB, Stewart WF, Schultz LR and Welch KM. Comorbidity of migraine and depression: investigating potential etiology and prognosis. *Neurology* 2003; 60(8): 1308–1312.
- Stewart WF, Linet MS, Celentano DD, Van Natta M and Ziegler D. Age- and sex-specific incidence rates of migraine with and without visual aura. *Am J Epidemiol* 1991; 134(10): 1111–1120.
- Stewart WF, Wood C, Reed ML, Roy J and Lipton RB. Cumulative lifetime migraine incidence in women and men. *Cephalalgia* 2008; 28(11): 1170–1178.

- Swartz KL, Pratt LA, Armenian HK, Lee LC and Eaton WW. Mental disorders and the incidence of migraine headaches in a community sample: results from the Baltimore Epidemiologic Catchment area follow-up study. *Arch Gen Psychiatry* 2000; 57(10): 945–950.
- Breslau N, Chilcoat HD and Andreski P. Further evidence on the link between migraine and neuroticism. *Neurology* 1996; 47(3): 663–667.
- Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia* 1988; 8(Suppl 7): 1–96.
- The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004; 24 Suppl 1: 9–160.
- Van Dam NT and Earleywine M. Validation of the Center for Epidemiologic Studies Depression Scale-Revised (CESD-R): Pragmatic depression assessment in the general population. *Psychiatry Res* 2011; 186: 128–132.
- Allison PD. Survival analysis using the SAS[®] system: a practical guide, 2nd ed. Cary, NC: SAS Institute, 2010.
- Gardner MJ and Altman DG. Statistics with confidence. London: British Medical Journal, 1989, p.45–48.
- Rasmussen BK. Migraine and tension-type headache are separate disorders. *Cephalalgia* 1996; 16: 217–219.
- Schürks M, Buring J and Kurth T. Agreement of selfreported migraine with ICHD-II Criteria in the Women's Health Study. *Cephalalgia* 2009; 29: 1086–1090.
- Robbins MS and Lipton RB. The epidemiology of primary headache disorders. *Semin Neurol* 2010; 30(2): 107–119.
- Kaniecki RG. Migraine and tension-type headache: an assessment of challenges in diagnosis. *Neurology* 2002; 58(9 Suppl 6): S15–S20.
- Lanteri-Minet M, Valade D, Geraud G, Chautard MH and Lucas C. Migraine and probable migraine–results of FRAMIG 3, a French nationwide survey carried out according to the 2004 IHS classification. *Cephalalgia* 2005; 25: 1146–1158.
- Mazzotta G, Carboni F, Guidetti V, Sarchielli P, Feleppa M, Gallai V, et al. Outcome of juvenile headache in outpatients attending 23 Italian headache clinics. Italian Collaborative Study Group on Juvenile Headache (Societa Italiana Neuropsichiatria Infantile [SINPI]). *Headache* 1999; 39(10): 737–746.
- Camarda R, Monastero R, Santangelo G, Raimondo D, Puma D, Pipia C, et al. Migraine Headaches in Adolescents: A Five-Year Follow-Up Study. *Headache* 2002; 42: 1000–1005.
- Leston JA. Migraine and tension-type headache are not separate disorders. *Cephalalgia* 1996; 16: 220–223.