



# The evolving classifications and epidemiological challenges surrounding chronic migraine and medication overuse headache: a review

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Received July 16, 2021

Accepted October 15, 2021

Handling Editor: Jeong-Gill Leem

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Changes in diagnostic criteria, for example, the various International Classification of Headache Disorders criteria, would lead to changes in the outcomes of epidemiological studies. International Classification of Headache Disorders-1 was based mainly on expert opinion, yet most of the diagnostic criteria were reliable and valid, but it did not include chronic migraine. In its second version, the classification introduced chronic migraine, but this diagnosis resembled more a high-frequency migraine rather than the actual migraine transformation process. It also introduced medication overuse headache, but it necessitated analgesic withdrawal and subsequent headache improvement to be diagnosed as such. Hence patients having medication overuse headache could only be diagnosed in retrospect, which was an awkward situation. Such restrictive criteria for chronic migraine and medication overuse headache omitted a high proportion of patients. International Classification of Headache Disorders-3 allows a diagnosis of medication overuse headache due to combination analgesics if taken for at least 10 days per month for more than three months. Hence the prevalence rate of medication overuse headache and chronic migraine can increase compared to the previous version of the headache classification. Different criteria have been used across studies to identify chronic migraine and medication overuse headache, and therefore the information acquired from previous studies using earlier criteria becomes uncertain. Hence much epidemiological research would need to be interpreted cautiously or repeated with the most updated criteria, since the subjects in studies that apply the latest criteria may be phenotypically different from those in older studies.

**Key Words:** Analgesics; Brain Diseases; Classification; Headache; Headache Disorders; Headache Disorders, Primary; Headache Disorders, Secondary; Migraine Disorders.

## INTRODUCTION

Headache disorders have been the second leading cause of years lived with disability for nearly three decades [1].

Globally, in 2016, almost three billion individuals suffered from either a tension-type headache (1.89 billion, 95% confidence interval [CI] 1.71-2.10) or migraine (1.04 billion, 95% CI 1.00-1.09) [2]. Chronic migraine was the sixth high-

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**Author contributions:** Emanuel Schembri: Writing/manuscript preparation; Michelle Barrow: Writing/manuscript preparation; Christopher McKenzie: Writing/manuscript preparation; Andrew Dawson: Writing/manuscript preparation.

est cause of disability worldwide, but in the presence of a medication overuse headache, it became the third leading cause of worldwide disability [3]. More recently, migraine was the number one cause of years lived with disability in those between age 15 to 50 years, predominantly affecting females, and overall, second only to low back pain in years lived with disability [4]. Stovner et al. [2] attribute this steep rise in migraine disability to medication overuse headache and postulate that medication overuse headache should be seen as a sequela or a complication to migraine and not as a separate entity.

Chronic migraine and medication overuse headache sufferers comprise a subgroup of patients with a lower health-related quality of life than episodic headache sufferers [5]. Chronic migraine most frequently co-exists with medication overuse headache, with the latter headache developing in at least 50% of those with chronic migraine [6]. Moreover, the Eurolight project found medication overuse headache to be the costliest among headache disorders [7], and although it is not as prevalent as migraine, medication overuse headache is more expensive to health services as well as to the individual [8].

Outcomes of epidemiological studies can be affected by various factors, including study design, the population of interest, avoidance of bias, sample size estimation, diagnostic criteria [9], and classification changes. Up to date, epidemiological studies are crucial due to the changing International Classification of Headache Disorders [10-13].

## MAIN BODY

### 1. The evolving headache classifications

#### 1) International Classification of Headache Disorders-1

International Classification of Headache Disorders-1 [10], was based mainly on expert opinion. However, subsequent studies demonstrated that most of these criteria were reliable and valid [14]. Patients with chronic daily headaches could be classified into chronic tension-type headache, headache induced by chronic substance use or exposure, and chronic trigeminal autonomic cephalalgias, but not into chronic migraine.

#### 2) Silberstein-Lipton's classifications

Silberstein et al. [15] and the revised classification by Silberstein et al. [16] both necessitated at least a 6-month history of chronic tension-type headache, hence being similar to the International Classification of Headache Disorders-1, but more restrictive compared to the recent

International Classification of Headache Disorders versions, which necessitate a 3-month headache history. However, both Silberstein's versions account for transformed migraine (which was not included in International Classification of Headache Disorders-1) and are more inclusive compared to International Classification of Headache Disorders-2 [11] for chronic migraine, but still have substantial differences compared to International Classification of Headache Disorders-3 [13]. Silberstein's criteria [16] for transformed migraine require a headache history of at least one month only, and they do not necessitate a minimum number of migraine days per month, contrary to the International Classification of Headache Disorders-2 and International Classification of Headache Disorders-3 versions.

Hence a subject can have episodic migraine, with less than eight migraine days per month, and chronic tension-type headache, and still fulfil criteria A, B, C 1, and C 2 for transformed migraine by Silberstein et al. [16]. Furthermore, Silberstein's criteria include migraine with aura as a possible cause of transformed migraine, contrary to International Classification of Headache Disorders-2 and International Classification of Headache Disorders-2-revised [17], since the former includes a history of episodic migraine meeting any International Classification of Headache Disorders-1 criteria 1.1 to 1.6. Therefore, a higher prevalence of transformed migraine would be expected using Silberstein's criteria compared to the criteria of chronic migraine in the International Classification of Headache Disorders-2 and possibly in the International Classification of Headache Disorders-3. Moreover, Silberstein's criteria for medication overuse headache are also different since they necessitate an analgesic intake for at least one month, while in the International Classification of Headache Disorders-2 onwards, an analgesic intake duration of at least three months is required. Also, the criteria for medication overuse headache according to the individual analgesic classes are slightly different, as shown in **Table 1**. Hence the one-month duration inflates the prevalence of medication overuse headache, according to Silberstein's criteria.

#### 3) International Classification of Headache Disorders-2

The International Classification of Headache Disorders-2 [11] introduced other primary headache disorders, including hypnic headache, new daily persistent headache, hemicrania continua, and primary thunderclap headache [14]. The diagnostic criteria for migraine with aura were not profoundly changed but were instead made more easily understood, while the criteria for migraine without aura were unchanged. The most crucial change was the intro-

**Table 1.** Differences in medication overuse criteria between Silberstein's criteria and International Classification of Headache Disorders-3

Type of analgesic drug	Number of days of analgesic consumption	
	Silberstein's criteria [15] for medication overuse <sup>a</sup>	ICHD-3 criteria for MOH
Simple analgesic	> 5 d/wk (> 20 d/4 wk for TM with MOH) > 6 d/wk (> 24 d/4 wk for CTTH with MOH)	≥ 15 d/mo
Combination analgesics	> 3 tablets/d > 3 d/wk (> 12 d/4 wk)	≥ 10 d/mo
Narcotics	> 1 tablet/d: > 2 d/wk (> 8 d/4 wk for TM with MOH) > 3 d/wk (> 8 d/4 wk for CTTH with MOH)	≥ 10 d/mo
Ergotamine	> 2 d/wk (total 8 d/4 wk)	≥ 10 d/mo

ICHD-3: International Classification of Headache Disorders, third version, MOH: medication overuse headache, TM: transformed migraine, CTTH: chronic tension-type headache.

<sup>a</sup>Equivalent for four weeks: calculated as consumption per week multiplied for four weeks.

duction of the term chronic migraine, which was meant to include most of the patients seen in tertiary headache clinics, and it required the sufferer to have at least 15 migraine days per month for at least three months. The criteria for chronic migraine was “pain and associated symptoms of migraine without aura for 15 days or more per month over 3 months or longer, without medication overuse”.

However, this definition of chronic migraine resembled more a high-frequency migraine rather than the actual migraine transformation process, which usually results in the migraine losing some or many of its typical features. This definition restricted patients from being diagnosed with chronic migraine [18]. In fact, Katsarava et al. [19] field-tested various definitions and found the lowest prevalence of chronic migraine in those studies that adhered to the International Classification of Headache Disorders-2 classification of chronic migraine. Hence the criteria for chronic migraine in the International Classification of Headache Disorders-2 classification was deemed to be of little use for clinical practice, clinical trials, or population-based studies.

To diagnose a headache subtype, both the International Classification of Headache Disorders-1 and International Classification of Headache Disorders-2 required that the attacks must be untreated or unsuccessfully treated since early treatment, *e.g.*, triptans, can obscure the unfolding of migraine characteristics. Early intake of triptans would yield an excellent response, evidencing that the initial tension-type headache was, in fact, a mild migraine. This contrasts with pure tension-type headache, where triptans have a weak effect [20]. It is easier to avoid treatment for a few attacks in episodic cases to collect the headache characteristics for diagnostic purposes. However, the patient with a high headache frequency will find it more challenging to avoid analgesics, portraying the restrictive criteria for chronic migraine [21].

The International Classification of Headache Disor-

ders-2 introduced medication overuse headache, being an extremely important entity since previously it was classified in International Classification of Headache Disorders-1 under the heading of “headache associated with chronic use of a substance.” However, in the International Classification of Headache Disorders-2, if medication overuse was found to be present, it was directed to diagnose the patient as having a probable medication overuse headache and a probable chronic migraine. The International Classification of Headache Disorders-2 necessitated analgesic withdrawal and subsequent headache improvement for diagnosing medication overuse headache, meaning that patients having medication overuse headache cannot be diagnosed as such, and the condition can only be diagnosed once the patient does not suffer from it anymore. This was considered an awkward situation. In the absence of such improvement, the diagnosis would have been chronic migraine [14]. If the person suffered from both chronic migraine and medication overuse headache, then a dual diagnosis of probable chronic migraine and probable medication overuse headache is given [21]. Such a restrictive and unpractical approach for chronic migraine and medication overuse headache omitted a high proportion of patients [22].

#### 4) International Classification of Headache Disorders-2-revised

Following the restrictive criteria for chronic migraine in the International Classification of Headache Disorders-2, there were multiple revisions, and a revised version was published [17] for chronic migraine. The revised diagnostic criteria for chronic migraine necessitated at least 15 headache days (tension-type headache and/or migraine) per month, of which at least eight days had to be migraine or headaches that responded to migraine medications for at least three months [21]. The reduction in the number of

migraine days encapsulates the main clinical features of migraine transformation.

Therefore, the International Classification of Headache Disorders-2-revised criteria for chronic migraine were more relevant and less restrictive to actual clinical practice [21] and epidemiological studies, whereby the prevalence of chronic migraine patients was found to be up to threefold higher [23]. Similarly, Bigal et al. [21] found that amongst patients with transformed migraine, without medication overuse, attending a headache specialty clinic, only 5.6% met the International Classification of Headache Disorders-2 criteria for chronic migraine. In comparison, 92.4% of the cases met the International Classification of Headache Disorders-2-revised criteria for chronic migraine criteria. Nonetheless, the new criteria for chronic migraine were criticized as being too wide-ranging. Hence heterogeneous cases, with different needs and prognoses could be clustered within the chronic migraine group.

International Classification of Headache Disorders-2-revised also revised the criteria for medication overuse headache. If medication overuse headache was present, the person was diagnosed with medication overuse headache, not chronic migraine, and it no longer necessitated headache resolution or reversion to its previous pattern within two months after discontinuation of the overused analgesic [24]. The International Classification of Headache Disorders-2-revised allowed a higher proportion of subjects to be correctly diagnosed with medication overuse headache [21], possibly increasing its prevalence rates in epidemiological studies. However, difficulty was still found when applying the criteria in patients with medication overuse headache [25]. Many patients with more than 15 days of headache per month were likely to take analgesia for more than ten days per month, and medication overuse headache was seen as a separate diagnosis and precluded a diagnosis of chronic migraine. It is evident that these revisions led to confusion, tension, and a lack of agreement in diagnosis and clinical trials.

### **5) International Classification of Headache Disorders-3beta and International Classification of Headache Disorders-3**

The International Classification of Headache Disorders-3beta [12], and the International Classification of Headache Disorders-3 [13], provide identical diagnostic criteria for chronic migraine and medication overuse headache. The main two differences in the diagnostic criteria for chronic migraine between the International Classification of Headache Disorders-2-revised and the last two versions is that the newer versions include the possibility

of chronic migraine having an aura component, while the International Classification of Headache Disorders-2-revised mentions solely migraine without aura. They also allow the diagnosis of chronic migraine with and without medication overuse headache. This improved definition of chronic migraine recognizes the varying severity of migraine attacks that the features of migraine can lessen, thus resembling tension-like headache, potentially allowing the chronic migraine diagnosis to be given to many more patients than previously. May and Schulte [26] raise a valid question about whether these latest changes in migraine classification and criteria would lead to contradictory results between new and older studies on chronic migraine.

The criteria for medication overuse headache have very similar meanings except that International Classification of Headache Disorders-2-revised necessitates the intake of combination medications for at least 15 days per month, while the later versions diagnose medication overuse headache due to combination analgesics if taken for at least 10 days per month for more than three months. This lower threshold can also increase the prevalence rate of medication overuse headache due to combination-analgesic overuse and including medication overuse headache due to multiple drug classes not individually overused. However, the third criterion in the current classification, the International Classification of Headache Disorders-3 [13], requires excluding other headaches. This poses a challenge in gathering data on the prevalence of medication overuse headache, particularly in surveys of the general population with large samples. A diagnosis of a secondary headache requires a specialist interview and neurological examination. Therefore, it is highly recommended that future epidemiology studies should focus on the general population with direct interviews conducted by headache specialists. This would serve to minimize selection bias and increase diagnostic precision [27].

Interestingly, the transition in epidemiology reporting suggests that those studies in chronic migraine that apply the International Classification of Headache Disorders-3beta [12] criteria to their subjects may be clinically and pathophysiologically different from those in older studies [26]. Clinical and functional magnetic resonance imaging studies in chronic migraine have demonstrated complex brain alterations compared to the intermittent changes seen in episodic migraine [28].

## **2. Controversy surrounding chronic migraine and medication overuse headache**

There have been different case definitions of chronic migraine over the last couple of decades and as these defini-

tions have evolved, so has the epidemiology of migraine evolved. However, the diagnostic criteria for chronic migraine remain controversial [25]. The term *chronic migraine* is itself considered to be ambiguous, and the demarcation between the definition of chronic migraine and that of episodic migraine is deemed arbitrary. The current definition for chronic migraine is headaches occurring more than 15 days per month of which 8 days at least have the features of a migraine [13]. Torres-Ferrús et al. [29] argue that there is little difference in those patients that have high-frequency episodic migraine (that is up to or equal to 14 days headache per month) and chronic migraine, and that according to the current criteria for chronic migraine, these high-frequency episodic migraine patients could potentially miss out on treatment options that might otherwise provide benefit. In summary, and as highlighted by Manzoni and Torelli [30], “the diagnostic criteria for chronic migraine fail to distinguish between patients with very different degrees of severity”.

Fortunately, global research has improved knowledge on the complexity of medication overuse headache [31,32], and hence medication overuse headache was included in the rewrite of the global burden of disease study [33]. However, today there is still debate whether medication overuse headache is “a distinct entity, a complication, or an epiphenomenon in the natural course of headache disorders” [34]. May and Schulte [26] maintain that medication overuse can be seen as a potential cause of migraine transformation. They acknowledge that with improved research methodology and global collaborative efforts, these questions will be answered, thereby improving care and helping clinicians make the right treatment decisions for patients with chronic migraine.

It is recommended that more researchers should analyze medication overuse headache, as the majority of randomized trials have excluded medication overuse. All the phase III studies carried out on the anti-calcitonin gene-related peptide monoclonal antibodies in migraine excluded medication overuse in their population [6]. In contrast, there was a high prevalence of acute medication overuse in the patient population with chronic migraine in the Phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) trials [35,36]. These studies were undertaken to evaluate the efficacy and safety of botulinum toxin A as a headache prophylaxis in people with chronic migraine. These were large global, multicenter, double-blinded, placebo-controlled studies. The primary endpoints at 24 weeks differed in the two studies. The PREEMPT-1 used the frequency of headache episodes, and the results were negative. The PREEMPT-2, therefore, amended their primary endpoint and used frequency of headache days per 28 days. However, selecting appropriate

primary efficacy endpoints should be done beforehand. A pooled analysis (n = 1,384) demonstrated 8.4 fewer headache days on botulinum toxin A compared with 6.6 on a placebo, but this was deemed to be clinically meaningful for patients with chronic migraine [37]. However, a major criticism was the high placebo effect seen in both studies. Moreover, the level of unblinding was not documented in these studies.

The inclusion of medication overuse in the PREEMPT studies was not in agreement with the International Classification of Headache Disorders criteria at the time. However, the researchers justified this because, at the time of enrolment, there was considerable debate regarding the criteria, and it was deemed that the population with medication overuse was more reflective of the clinic population. These patients (64%) were stratified according to the frequency of acute medication use during the 28-day baseline period and in line with International Headache Society clinical trial guidelines. However, medication overuse headache can improve following treatment, and the high proportion of participants with medication overuse could have been partly the reason for the improvement seen in both arms of the trials. Moreover, many of the participants had not previously trialed prophylactic drugs, which is not reflective of real-life patients. Following efficacy, safety, and cost-analysis, botulinum toxin A is now a recommended treatment for chronic migraine in the UK, provided that patients have been trialed with three prophylactic agents, and where medication overuse has been addressed [38].

Russell [27] highlights that the epidemiology of medication overuse headache is affected by the change of diagnostic criteria. The medication overuse headache population is not necessarily the same in different settings. Many of the older studies have been focused in the specialist clinic setting, such as headache centres and neurology clinics, using a wide variety of definitions. Studies based on selected populations such as clinic-based studies and workplace and university studies are limited as they are very different population samples [27]. Data collected from such populations are likely to be biased. For example, samples derived from the specialized clinic setting will be reversed when recounting their chronic migraine and medication history, and doubts are cast on the generalizability of results from such specialized settings to primary care. Westergaard et al. [39] found that while diagnostic criteria are useful in the clinic setting, they are not always applicable in general population-based research.

### 3. The impact of the changing the International Headache Society classifications on certain studies

Studies in migraine epidemiology to assess prevalence and incidence are essential, particularly to highlight to the public and policy-makers that migraine, particularly chronic migraine, is a major health problem. It is also important to conduct such studies to determine other factors and data on pain characteristics, co-morbidities, as well as impact on quality of life, on family, and the risk factors for migraine. Therefore, below we will critically evaluate some epidemiological studies.

The American Migraine Study by Stewart et al. [40] and another methodologically identical survey conducted by Lipton et al. [41], being the American Migraine Study II, both used a representative sample of the US population in terms of age, sex, household size and geographic location. This aided direct comparison despite the studies having been conducted ten years apart. Each household member with a severe headache was asked to fill in the questionnaire, hence aiding inclusion. Both had similar response rates (63.4% vs. 68.3%, respectively), and both used the International Classification of Headache Disorders-1 for diagnosing migraine. Their results were very similar in terms of migraine prevalence being 17.6% in females and 5.7% in males in Stewart et al. [40] and 18.2% in females and 6.5% in males [41].

However, the results do not portray the incidence of chronic migraine, since the International Classification of Headache Disorders-1 was used; hence chronic migraine was not evaluated. Besides, in the American Migraine Study, subjects with severe daily headaches were not categorized as suffering from migraine since it stated, "migraine is an episodic disorder" [41]. Therefore, migraine prevalence could potentially be higher. Furthermore, their definition of migraine did not include "aggravation by walking stairs or similar routine physical activity," as stated in the International Classification of Headache Disorders-1, which could have led to the misdiagnosis of some migraineurs to a class termed "other severe headache." The self-administered nature of the questionnaire could lead to recall bias. Furthermore, the overrepresentation of upper-income white households in their sample could lower migraine prevalence since a lower socioeconomic status is associated with a higher migraine prevalence [42].

Castillo et al. [43] evaluated the prevalence of chronic daily headaches using a representative sample of the Spanish population ( $n = 2,252$ ) by distributing a questionnaire. They had a high response rate (83.5%). Those subjects who had at least ten headache days per month were provided with a headache diary for one month. Afterwards, these were seen by a neurologist, who classified them into the

chronic daily headaches subtypes according to the criteria of Silberstein et al. [15] and revised by Silberstein et al. [16], instead of using the International Classification of Headache Disorders-1. One hundred thirty-five participants had headache on ten or more days per month, while 89 individuals (4.7%) had chronic daily headache, eighty of whom were females. Eight participants (17%) had analgesic overuse, while transformed migraine was diagnosed in 45 individuals, of which 14 (31.1%) individuals overused ergots or analgesics.

Bigal et al. [44] conducted a longitudinal population-based study to assess the role of specific classes of acute medications in the development of transformed migraine in those with episodic migraine. The population, derived from the American Migraine Prevalence and Prevention Study, was a representative sample of the general US population. For epidemiological purposes, diagnostic criteria were built into a questionnaire. Those with episodic migraine from the study population were classified according to the International Classification of Headache Disorders-2, but individuals with more than 15 headaches daily were classified according to the Silberstein et al.'s criteria [15]. Bigal et al. [44] justified using the Silberstein and Lipton criteria because the International Classification of Headache Disorders-2 chronic migraine criteria were too restrictive to implement in a large population study and excluded most patients with transformed migraine. The researchers found that out of 8,219 people with episodic migraine, the annual incidence of transformed migraine was 2.5% (209 patients) and that both frequency of headaches and medication overuse were independently associated with transformed migraine. Medications such as opioids and barbiturates were associated with increased risk of transformation, while triptans and nonsteroidal anti-inflammatory drugs were not associated with transformation. Adjustment analyses were carried out for headache frequency, severity, headaches days, prophylactic medication use and sex.

Buse et al. [45] aimed to estimate the prevalence of chronic migraine in the US population, older than 12 years of age, using a stratified random sample. To aid comparison, they used the same questionnaire which was used in the American Migraine Study II [41], with the headache diagnostic module based on the International Classification of Headache Disorders-2, having a sensitivity of 93% and a specificity of 85% for detecting chronic migraine compared to expert diagnosis. They found that 11.79% (17.27% of females; 5.72% of males) of the sample met the criteria for migraine according to the International Classification of Headache Disorders-2, while 0.91% (1.29% of females; 0.48% of males) met the criteria for chronic migraine. Furthermore, chronic migraine represented 7.68% of migraine

cases overall, and the proportion generally increased with age.

However, this study had several shortcomings. It did not abide entirely by the International Classification of Headache Disorders-2 definition of chronic migraine; instead, it was “more closely aligned with Silberstein et al. [16] criteria for chronic migraine.” However, we are not told which of Silberstein’s criteria were used. Therefore, it is not mentioned if the  $\geq 15$  headache days per month were all migraine or could have had tension-type headache characteristics, significantly affecting chronic migraine prevalence. Also, despite assessing for migraine with aura, we are not told about the presence of aura in chronic migraine sufferers. Notwithstanding medication overuse headache being commonly encountered in chronic migraine, the authors did not assess for its prevalence due to the awkward criteria in the International Classification of Headache Disorders-2. The self-administered questionnaire and the need to self-identify as suffering from severe headaches could lead to underreporting of chronic migraine due to recall bias. The study also restricted the number of respondents from each household to three, contrary to Lipton et al. [41]. Therefore, the prevalence rates could be higher if more persons within the same household who suffered from migraine could complete the questionnaire. The prevalence rates for chronic migraine could be lower if the original International Classification of Headache Disorders-2 criteria were strictly adhered to, while if the International Classification of Headache Disorders-3 criteria were used, the prevalence of chronic migraine sufferers could have been higher since migraine with aura would be included.

Steiner et al. [8] evaluated the personal impact of headache across ten European states using the translated version of the same questionnaire, hence aiding direct comparison. However, the diagnostic validation of each translation was not done. A modified cluster sample was used, yet samples varied in their representativeness of the respective general populations. It mentioned that the headache diagnostic questions were based on the International Classification of Headache Disorders-2. However, the questions were adopted from the HARSHIP (Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation) questionnaire [46], which was based on the International Classification of Headache Disorders-3beta. Hence it can get confusing. The algorithm differentiated chronic from episodic headache subtypes, and it provided a diagnosis of probable medication overuse headache, which trumped all other diagnoses. The participants were directed towards the most bothersome headache, possibly reducing the influence of tension-type headache days in cases of chronic migraine, probably de-

flating its overall prevalence.

Participation rates were low, possibly leading to unrecognized biases. The unadjusted lifetime prevalence of any headache was 91.3%, while the sex-adjusted 1-year prevalences were: any headache 78.6%; migraine 35.3%; tension-type headache 38.2%, headache on  $\geq 15$  days per month 7.2%; and probable medication overuse headache 3.1%. The baseline sex distribution skew portrayed an interest bias. To estimate the magnitude of such a bias, non-responders were contacted and queried about the presence of any headaches. Interest bias could lead to an overestimation of 14% in the 1-year prevalence rates of migraine being outside the range obtained from other studies. Even if this bias was reduced by 14%, the 1-year prevalence of migraine would be 30.4%, which is still high. The high rates of chronic daily headaches and medication overuse headache reported were probably influenced by interest bias too. This article concluded that it should not be seen as a primary source of headache prevalence estimates due to some diagnostic uncertainties and moderate interest bias.

Streel et al. [47] assessed the one-year prevalence of migraine in the southern region of Belgium, using a translated and validated (into French) version of the ID Migraine questionnaire in a representative stratified random sample of 751 participants aged 20-69 years. It reported an overall one-year migraine prevalence of 25.8%, with 40.8% of migraineurs reporting visual aura. Migraine prevalence was higher in females than males (33.9% vs. 17.9%) and declined markedly after the age of 50.

However, there are issues when reporting findings using the French version of ID Migraine, which obtained a sensitivity of 87.5% and a specificity of 100% in a group of 67 subjects interviewed face to face by a neurologist [48]. Such a methodology, in the validation process of the tool, aids standardization of the assessment but can introduce bias. Also, 12.5% of subjects were misdiagnosed as non-migraine with the French ID Migraine, hence reducing the prevalence of migraine. The psychometric properties of the French ID Migraine version were confirmed using the International Classification of Headache Disorders-2, while in the original version of ID Migraine, these were validated against the International Classification of Headache Disorders-1 by a headache specialist [49]. The authors assessed for visual disturbances, even though these were not included in the 3-item ID Migraine. They reported that 40.8% of migraineurs experienced visual aura. However, the authors advocate caution when evaluating this high prevalence rate since migraine with aura is best identified in a face-to-face interview. Besides, chronic headaches were not mentioned in the text. Furthermore, ID Migraine could lead to meningitis being misdiagnosed as migraine.

It should be noted that such a tool would be useful for telephone screening, yet it may wrongly exclude some migraineurs.

In their systematic review, Westergaard et al. [39] highlight the variations in prevalence estimates in those with medication overuse headache across 27 population studies in 16 European countries and the US. They attribute the prevalence variations to the lack of consistency in the definitions of medication overuse headache used. Besides, they found only one study [50] that attempted to detoxify the patient before determining a firm diagnosis of medication overuse headache, a criterion determined by the International Classification of Headache Disorders-2. Furthermore, only one study presented an incidence rate (0.72 per 1,000 person-years) [51]. Overall, the systematic review found that the prevalence of medication overuse headache varied widely from 0.5% to 7.2% in all the studies that used the International Classification of Headache Disorders-2 criteria, and this variance is not in accordance with the generally quoted 1% to 2% global prevalence of medication overuse headache [52]. This leads to pondering whether the figures found in the review studies are grossly underestimated or even overestimated and whether the studies conducted within the time frame of these earlier classifications are still valid.

Interestingly, Serrano et al. [53], who assessed fluctuations in episodic and chronic migraine, found that almost three-quarters of their population with chronic migraine at baseline drop below the diagnostic boundary of more than 15 headache days per month at least once over a year. This suggests that headache days alone are not an adequate measure when considering headache classification and diagnosis, thus having implications for clinical trial design.

## CONCLUSIONS

It is evident that different criteria have been used across studies to identify migraine and the epidemiological data is conflicting. In addition, there is a need to account for cultural factors and the socioeconomic status of the population since a low socioeconomic status is a further risk factor for medication overuse headache [51]. Steiner and Stovner [54] highlight that the burden is not evenly distributed among cases and recommend that larger samples are required to estimate burden than to estimate prevalence. Most of the burden is accounted for by a minority of those with the disorders such as chronic migraine and medication overuse headache. Such consideration is crucial, especially in primary care, where most patients with headaches are managed, hence the need for improving

the knowledge of headaches and their management. Considering all the changes, even intricate ones, between the various classification systems, the information acquired from previous studies using earlier criteria becomes uncertain and may not even be applicable to newer studies using the revised International Classification of Headache Disorders criteria. Hence much epidemiological research would need to be interpreted cautiously or repeated with the most updated criteria.

## ACKNOWLEDGMENTS

This article was originally submitted as part of the MSc in the Clinical Management of Pain at the University of Edinburgh, Edinburgh, UK.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

## FUNDING

ES received funding from the Endeavor Scholarship Scheme (Malta). Scholarships are part financed by the European Union—European Social Fund (ESF)—Operational Program II—Cohesion Policy 2014-2020 - Investing in human capital to create more opportunities and promote the well-being of society.

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## REFERENCES

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; 392: 1789-858.
2. GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990-



- 2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2018; 17: 954-76.
3. Steiner TJ, Birbeck GL, Jensen RH, Katsarava Z, Stovner LJ, Martelletti P. Headache disorders are third cause of disability worldwide. *J Headache Pain* 2015; 16: 58.
  4. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; 390: 1211-59.
  5. Silberstein SD, Dodick DW, Bigal ME, Yeung PP, Goadsby PJ, Blankenbiller T, et al. Fremanezumab for the preventive treatment of chronic migraine. *N Engl J Med* 2017; 377: 2113-22.
  6. Giamberardino MA, Affaitati G, Curto M, Negro A, Costantini R, Martelletti P. Anti-CGRP monoclonal antibodies in migraine: current perspectives. *Intern Emerg Med* 2016; 11: 1045-57.
  7. Linde M, Gustavsson A, Stovner LJ, Steiner TJ, Barré J, Katsarava Z, et al. The cost of headache disorders in Europe: the Eurolight project. *Eur J Neurol* 2012; 19: 703-11.
  8. Steiner TJ, Stovner LJ, Katsarava Z, Lainez JM, Lampl C, Lantéri-Minet M, et al. The impact of headache in Europe: principal results of the Eurolight project. *J Headache Pain* 2014; 15: 31.
  9. Steiner TJ, Stovner LJ, Al Jumah M, Birbeck GL, Gururaj G, Jensen R, et al. Improving quality in population surveys of headache prevalence, burden and cost: key methodological considerations. *J Headache Pain* 2013; 14: 87.
  10. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. *Cephalalgia* 1988; 8 Suppl 7: 1-96.
  11. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004; 24 Suppl 1: 9-160.
  12. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013; 33: 629-808.
  13. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018; 38: 1-211.
  14. Olesen J, Steiner TJ. The international classification of headache disorders, 2nd edn (ICDH-II). *J Neurol Neurosurg Psychiatry* 2004; 75: 808-11.
  15. Silberstein SD, Lipton RB, Solomon S, Mathew NT. Classification of daily and near-daily headaches: proposed revisions to the IHS criteria. *Headache* 1994; 34: 1-7.
  16. Silberstein SD, Lipton RB, Sliwinski M. Classification of daily and near-daily headaches: field trial of revised IHS criteria. *Neurology* 1996; 47: 871-5.
  17. Headache Classification Committee, Olesen J, Bousser MG, Diener HC, Dodick D, First M, et al. New appendix criteria open for a broader concept of chronic migraine. *Cephalalgia* 2006; 26: 742-6.
  18. Manzoni GC, Grisendi I, Torelli P. ICHD-3: what changes do we need regarding migraine? *Curr Pain Headache Rep* 2011; 15: 170-6.
  19. Katsarava Z, Manack A, Yoon MS, Obermann M, Becker H, Dommes P, et al. Chronic migraine: classification and comparisons. *Cephalalgia* 2011; 31: 520-9.
  20. Olesen J. International Classification of Headache Disorders, Second Edition (ICHD-2): current status and future revisions. *Cephalalgia* 2006; 26: 1409-10.
  21. Bigal ME, Rapoport AM, Sheftell FD, Tepper SJ, Lipton RB. The International Classification of Headache Disorders revised criteria for chronic migraine—field testing in a headache specialty clinic. *Cephalalgia* 2007; 27: 230-4.
  22. Bigal ME, Tepper SJ, Sheftell FD, Rapoport AM, Lipton RB. Field testing alternative criteria for chronic migraine. *Cephalalgia* 2006; 26: 477-82.
  23. Straube A, Pfaffenrath V, Ladwig KH, Meisinger C, Hoffmann W, Fendrich K, et al. Prevalence of chronic migraine and medication overuse headache in Germany--the German DMKG headache study. *Cephalalgia* 2010; 30: 207-13.
  24. Manzoni GC, Bonavita V, Bussoni G, Cortelli P, Narbone MC, Cevoli S, et al. Chronic migraine classification: current knowledge and future perspectives. *J Headache Pain* 2011; 12: 585-92.
  25. Jiang H, Deng Y, Zhang Y, Jin J, Kong X, Zhu Q, et al. Field testing of the ICHD-3 $\beta$  and expert opinion criteria for chronic migraine. *J Headache Pain* 2016; 17: 85.
  26. May A, Schulte LH. Chronic migraine: risk factors, mechanisms and treatment. *Nat Rev Neurol* 2016; 12: 455-64.
  27. Russell MB. Epidemiology and management of medication-overuse headache in the general population. *Neurol Sci* 2019; 40(Suppl 1): 23-6.
  28. Goadsby PJ, Hargreaves R. Refractory migraine and chronic migraine: pathophysiological mechanisms. *Headache* 2008; 48: 1399-405.
  29. Torres-Ferrús M, Quintana M, Fernandez-Morales J, Alvarez-Sabin J, Pozo-Rosich P. When does chronic migraine strike? A clinical comparison of migraine according to the headache days suffered per month. *Cephalalgia* 2017; 37: 104-13.
  30. Manzoni GC, Torelli P. Chronic headaches: a clinician's experience of ICHD-3 beta. *Neurol Sci* 2015; 36 Suppl 1: 51-5.
  31. Schwedt TJ, Chong CD. Medication overuse headache: pathophysiological insights from structural and functional brain MRI research. *Headache* 2017; 57: 1173-8.
  32. Martelletti P. The journey from genetic predisposition to medication overuse headache to its acquisition as sequela of

- chronic migraine. *J Headache Pain* 2018; 19: 2.
33. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388: 1545-602.
  34. Vandenburg N, Laterza D, Lisicki M, Lloyd J, Lupi C, Tischler H, et al. Medication-overuse headache: a widely recognized entity amidst ongoing debate. *J Headache Pain* 2018; 19: 50.
  35. Aurora SK, Dodick DW, Turkel CC, DeGryse RE, Silberstein SD, Lipton RB, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. *Cephalalgia* 2010; 30: 793-803.
  36. Diener HC, Dodick DW, Aurora SK, Turkel CC, DeGryse RE, Lipton RB, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. *Cephalalgia* 2010; 30: 804-14.
  37. Dodick DW, Turkel CC, DeGryse RE, Aurora SK, Silberstein SD, Lipton RB, et al. OnabotulinumtoxinA for treatment of chronic migraine: pooled results from the double-blind, randomized, placebo-controlled phases of the PREEMPT clinical program. *Headache* 2010; 50: 921-36.
  38. National Institute for Health and Care Excellence (NICE). Botulinum toxin type A for the prevention of headaches in adults with chronic migraine [Internet]. London: NICE; 2012. Available at: <https://www.nice.org.uk/guidance/ta260/resources/botulinum-toxin-type-a-for-the-prevention-of-headaches-in-adults-with-chronic-migraine-pdf-82600545273541>.
  39. Westergaard ML, Hansen EH, Glümer C, Olesen J, Jensen RH. Definitions of medication-overuse headache in population-based studies and their implications on prevalence estimates: a systematic review. *Cephalalgia* 2014; 34: 409-25.
  40. Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine headache in the United States. Relation to age, income, race, and other sociodemographic factors. *JAMA* 1992; 267: 64-9.
  41. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache* 2001; 41: 646-57.
  42. Winter AC, Berger K, Buring JE, Kurth T. Associations of socioeconomic status with migraine and non-migraine headache. *Cephalalgia* 2012; 32: 159-70.
  43. Castillo J, Muñoz P, Guitera V, Pascual J. Kaplan Award 1998. Epidemiology of chronic daily headache in the general population. *Headache* 1999; 39: 190-6.
  44. Bigal ME, Serrano D, Buse D, Scher A, Stewart WF, Lipton RB. Acute migraine medications and evolution from episodic to chronic migraine: a longitudinal population-based study. *Headache* 2008; 48: 1157-68.
  45. Buse DC, Manack AN, Fanning KM, Serrano D, Reed ML, Turkel CC, et al. Chronic migraine prevalence, disability, and sociodemographic factors: results from the American Migraine Prevalence and Prevention Study. *Headache* 2012; 52: 1456-70.
  46. Steiner TJ, Gururaj G, Andrée C, Katsarava Z, Ayzenberg I, Yu SY, et al. Diagnosis, prevalence estimation and burden measurement in population surveys of headache: presenting the HARSHIP questionnaire. *J Headache Pain* 2014; 15: 3.
  47. Streeel S, Donneau AF, Hoge A, Albert A, Schoenen J, Guillaume M. One-year prevalence of migraine using a validated extended French version of the ID Migraine™: a Belgian population-based study. *Rev Neurol (Paris)* 2015; 171: 707-14.
  48. Streeel S, Donneau AF, Dardenne N, Hoge A, Bruyère O, Albert A, et al. Validation of an extended French version of ID Migraine™ as a migraine-screening tool. *Cephalalgia* 2015; 35: 437-42.
  49. Lipton RB, Dodick D, Sadovsky R, Kolodner K, Endicott J, Hettiarachchi J, et al. A self-administered screener for migraine in primary care: the ID Migraine validation study. *Neurology* 2003; 61: 375-82.
  50. da Silva A Jr, Costa EC, Gomes JB, Leite FM, Gomez RS, Vasconcelos LP, et al. Chronic headache and comorbidities: a two-phase, population-based, cross-sectional study. *Headache* 2010; 50: 1306-12.
  51. Hagen K, Linde M, Steiner TJ, Stovner LJ, Zwart JA. Risk factors for medication-overuse headache: an 11-year follow-up study. *The Nord-Trøndelag Health Studies. Pain* 2012; 153: 56-61.
  52. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; 386: 743-800.
  53. Serrano D, Lipton RB, Scher AI, Reed ML, Stewart WBF, Adams AM, et al. Fluctuations in episodic and chronic migraine status over the course of 1 year: implications for diagnosis, treatment and clinical trial design. *J Headache Pain* 2017; 18: 101.
  54. Steiner TJ, Stovner LJ. Societal impact of headache: burden, costs and response. Cham, Springer. 2019, pp 83-104.