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Els Mehuys, Koen Paemeleire, Geert Crombez, Els Adriaens ...+7 more authors

Institutions: Ghent University, Ghent University Hospital, University of Liège

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Authors: Mehuys, Els, Koen Paemeleire, Geert Crombez, Els Adriaens, Thierry Van Hees, Sofie Demarche, Thierry Christiaens, Lucas Van Bortel, Inge Van Tongelen, Jean Paul Remon

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THE HETEROGENEITY OF HEADACHE PATIENTS WHO SELF-MEDICATE: A CLUSTER ANALYSIS APPROACH

Els Mehuys[1], Koen Paemeleire[2], Geert Crombez[3], Els Adriaens[1], Thierry Van Hees[4], Sophie Demarche[4], Thierry Christiaens[5], Luc Van Bortel[6], Inge Van Tongelen[1], Jean-Paul Remon[1] and Koen Boussery[1]

[1] Pharmaceutical Care Unit, Ghent University, Belgium

[2] Department of Neurology, Ghent University Hospital, Belgium

[3] Department of Experimental-Clinical and Health Psychology, Ghent University, Belgium

[4] CIRM, Clinical Pharmacy Unit, University of Liege, Belgium

[5] Department of Family Medicine and Primary Health Care & Heymans Institute of Pharmacology, Ghent University, Belgium

[6] Heymans Institute of Pharmacology, Ghent University, Belgium

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Corresponding author:

E. Mehuys, Pharmaceutical Care Unit, Ghent University, Harelbekestraat 72, B-9000 Ghent, Belgium. Tel: +32 92648043. Fax: +32 92228236. E-mail: els.mehuys@ugent.be

INTRODUCTION

Headache is one of the most common health complaints. According to the Global Burden of Disease Study 2013, tension-type headache and migraine are the second and the seventh most prevalent chronic disorders in the world (with, respectively, 1.6 billion and 850 million incident cases in 2013) [35]. Headache can be associated with substantial morbidity and impaired quality of life [18]. For example, migraine is the 6th leading cause of disability worldwide [35].

There are medications available that effectively alleviate headaches [32], but these may be used incorrectly [10; 28]. In particular, both frequent and long-term use of acute headache medication may have a paradoxical effect, worsening headaches rather than relieving them. This condition, called medication-overuse headache (MOH), is a growing problem, with an estimated prevalence of at least 1% in the general population and up to 30-50% in tertiary headache centers [10; 28]. Detection of MOH is not easy: many patients rely solely on self-medication with over-the counter (OTC) analgesics, and have limited contact with physicians [19]. A study in community pharmacies found that about 25% of individuals who purchased OTC analgesics specifically for regular headaches overused that acute headache medication, and were thus at risk for developing MOH [27]. Community pharmacists may therefore be in a strategic position to identify and advise individuals who self-treat, particularly with respect to prevention and early detection of medication overuse (MO) in order to avoid development of MOH. To accurately assess the risk of MO, it is important to consider a broad profile of patients, as chronic headache is often associated with other pain complaints, such as musculoskeletal pain [15; 37]. In fact, there is evidence that the use of analgesics for other pain complaints, may also cause MOH in individuals with a primary headache syndrome, especially migraine [2; 36]. As yet, there is no clear picture of the types of individuals who self-medicate their headaches, and the prevalence of MO in these subtypes. This information is necessary to develop community pharmacist intervention programs for prevention of MOH.

This study aimed to identify subgroups of individuals with headache who self-medicate. A hierarchical cluster analysis was used to group patients as a function of sociodemographics, pain,

disability and medication use for pain. In addition, we compared attitudes about pain medication between the identified subgroups.

METHODS

Study design

This observational study was carried out from December 2012 till May 2013 in 202 community pharmacies in Belgium. Of note, in Belgium, the sale of OTC medicines is limited to pharmacies. Therefore, pharmacies are an ideal setting to recruit a representative sample of persons with intentions to self-medicate. Approval for the study was granted by the Ethics Committees of Ghent University Hospital (for Flanders) and CHU Liege (for Wallonia), and all patients gave written informed consent.

Participants

Pharmacy customers purchasing an OTC systemic analgesic were approached consecutively by the pharmacist and invited to participate in the study (OTC systemic analgesics available in Belgium: paracetamol, acetylsalicylic acid, ibuprofen 200-400 mg, naproxen 200 mg, and fixed dose combinations of simple analgesics with caffeine). They were eligible when meeting the following inclusion criteria: purchasing the analgesic for themselves, being aged ≥18 years, and suffering from pain during at least one full day in the last month. From each of the pharmacies, ten patients were planned to be recruited.

For the present analysis, only data of patients with headache were included. A headache patient was defined as a patient marking the head on a full body manikin (see section 'Data collection – pain characteristics').

Data collection

Pharmacy customers who agreed to participate completed a self-administered questionnaire, developed by the multidisciplinary research team (a neurologist, a pain psychologist, a general practitioner, a clinical pharmacologist and pharmacists) on the basis of literature and a previous study on this topic [27]. The questionnaire was piloted, before use, by one community pharmacist. It

comprised 33 items grouped into five domains: (1) sociodemographics and self-rated health, (2) pain characteristics, (3) pain disability, (4) use of pain medication and (5) attitudes about pain medication.

Sociodemographics and self-rated health

Respondents reported their gender, age, marital status, employment status and education level. Self-rated health was measured by the question "How in general would you rate your health?'' with response options of "excellent, very good, good, fair, or poor" [5].

Pain characteristics

Participants were asked to mark the location(s) of their current pain on a full body manikin (front and back views; separated into 45 mutually exclusive areas). Respondents also reported whether they had a medical diagnosis for their pain complaints. Those without migraine diagnosis completed the ID Migraine Screener (ID-M), a valid and reliable screening instrument for migraine in primary care [23]. In addition, the questionnaire assessed pain duration and pain frequency (number of days with pain in the past 3 months).

Pain disability

Disability was assessed by the Von Korff Pain Grading Scale [34]. This 7-item questionnaire measures the degree of pain intensity and activity-related disability in the past three months. Six of the items are scored on 11-point Likert scales (0 = "no pain/disability" and 10 = "worst pain/total disability"). The one remaining item requires filling in the number of days that pain has kept respondents from their typical activities. Total scores classify respondents into one of 4 levels of pain intensity and activity interference (grade 1: low disability and low pain intensity, grade 2: low disability and high pain intensity, grade 3: high disability and moderate limitation of activities, grade 4: high disability and severe limitation of activities).

Use of pain medication

Respondents reported their current pain medication (OTC and prescribed) with frequency of use during the prior three months, and they also indicated the pain location(s) they used the drug for.

From the perspective of risk of MOH, MO was defined as overusing acute headache medication in terms of treatment days per month (≥10 days/month for ergotamine, triptans, opioids, and combination analgesics; ≥15 days/month for paracetamol, acetylsalicylic acid, and NSAIDs) during the previous three months, according to the criteria of the International Classification of Headache Disorders Third Edition (ICHD-III beta version) for MOH [31]. First, we assessed whether participants met the definition of MO for pain medication used for treatment of headache. For patients not meeting the definition, we subsequently evaluated whether they met the definition of MO for pain medication used to treat their pain at other locations.

Attitudes about pain medication

Participants' attitudes about pain medication were assessed using items from the Pain Medication Attitude Questionnaire (PMAQ) [26]. The PMAQ examines concerns held by patients regarding their medication use. It consists of 47 items grouped into seven domains (addiction, need, scrutiny, side effects, tolerance, mistrust and withdrawal). Each item is scored on a 6-point Likert scale ranging from 0 ("never true") to 5 ("always true"). In this study, we did not use the complete PMAQ but selected a number of items that were considered of relevance to our study. This item selection was done by a multidisciplinary consensus panel comprising a neurologist (KP), pain psychologist (GC) and pharmacist (EM). Firstly, each member of the panel independently selected one or more items from each PMAQ domain, based on their own expertise and experience. Secondly, the panel developed a consensus on item selection during a face-to-face meeting (psychometric properties of the items from the original PMAQ [26] were used to support the discussion). This resulted in a final selection of ten PMAQ items which are displayed in Table 2. We grouped the selected items according to the domains used in the original PMAQ [26].

Statistical analysis

Cluster analysis was performed on complete cases using the following variables:

- sociodemographics and self-rated health: sex, age, marital status, employment status, education level, and self-rated health (which was considered as a continuous scale ranging from 1 ('excellent') to 5 ('poor'))
- pain characteristics: presence of migraine (i.e. self-reported physician-diagnosis of migraine), number of concomitant pain locations, location of concomitant pain (only pain locations present in ≥15% of the study population were included), pain frequency and pain duration
- pain disability: Von Korff Pain Grading Scale, individual items as well as pain grade (which was considered as a continuous scale ranging from 1 to 4)
- use of pain medication: number, prescription status (only OTC or OTC + prescription medication), type (only drug classes used by ≥15% of the study population were included), meeting definition of MO for pain medication used for treatment of headache and meeting definition of MO for pain medication used for treatment of pain other than headache.

These variables were subjected to Hierarchical Clustering on Principal Components [17]. We started with a factor analysis for mixed data (FAMD) as pre-step before clustering. FAMD balances the influence of both continuous and categorical variables and as a consequence, they are compared on an equal footing [29]. Next, we performed agglomerative hierarchical clustering on the results of the FAMD, using the Euclidean distance, and Ward's criterion as aggregation criterion. As clusters can be difficult to interpret through an eyeball procedure, we used a v-test to characterize them [9]. For continuous variables this test investigates whether the mean of the cluster is equal to the mean of the total sample. For categorical variables, the v-test evaluates whether a cluster is characterized by the categories of the categorical variable.

One-way ANOVA combined with a Scheffé post hoc test was used to compare mean PMAQ scores across the clusters.

All statistical analyses were performed with R version 2.15.3 (R Development Core Team, Vienna, Austria) and SPSS version 22 (SPSS Inc., Chicago, USA). P values <0.05 were considered significant.

RESULTS

In the 202 participating pharmacies, 10423 patients were contacted and pre-screened, of which 3580 (34%) matched our inclusion criteria. About 53% (n=1889) of them agreed to participate and were included in the main study. More than half of them reported to suffer from headache (N=1107) and were thus eligible for inclusion in the present analysis. After exclusion of incomplete cases (N=86), we obtained a final sample of 1021 patients (Figure 1). The characteristics of the study population are displayed in Table 1 (see column 'Total sample').

Clustering outcome

Hierarchical clustering was performed on the first two dimensions of the FAMD and suggested three patient clusters (Figure 2). Sociodemographics and self-rated health, pain characteristics, disability and pain medication use according to cluster are detailed in Table 1. The main features of each patient cluster were as follows.

Cluster 1

This cluster contained the largest number of participants (n=498, 48.8%). This was the youngest group (mean age: 39 years) and included an overrepresentation of highly educated singles, employees and students. Individuals in this group were more likely to have a physician-diagnosis of migraine. They had a low number of concomitant pain locations and a low pain frequency. This group was also characterized by low disability and high pain intensity (pain grade = 2). Overall, individuals in this cluster only used OTC analgesics. Medication overusers were less likely in this cluster.

Cluster 2

Participants in Cluster 2 (n=301, 29.5%) were the oldest, with a mean age of 59 years. Men, married/cohabiting persons, widowers, retired individuals, househusbands/wives and persons with lower education levels were more present in this group. Patients had an intermediate number of concomitant pain locations, intermediate pain frequency, as well as low disability and high pain intensity (pain grade = 2). Individuals only using OTC analgesics (without prescription pain

medication) and users of paracetamol were overrepresented in this group. This cluster also showed a slight overrepresentation of persons meeting the definition of MO for analgesics for treatment of pain other than headache.

Cluster 3

Cluster 3 comprised 21.7% of the total sample (n=222) and had a mean age of 52 years. Individuals in this group were more likely to be divorced, unemployed, househusband/housewife or not working due to ill health. Also patients with lower levels of education were overrepresented in this cluster. Their self-rated health was low. Prevalence of physician-diagnosed migraine was high. They reported a high number of concomitant pain locations, high pain frequency, as well as high disability and severe limitation of activities (pain grade = 4). Finally, individuals in this group used a high number of pain medications, and were more likely to use prescription pain medication in addition to their OTC purchased analgesics and to be medication overusers.

Figure 3 summarizes the key characteristics of the three patient clusters.

Attitudes about pain medication

Attitudes about pain medication differed significantly between clusters (Table 2). For all but one item (i.e., “I would be unwilling to reduce my pain medication(s)”), cluster 3 held significantly higher levels of concern about their medication than clusters 1 and 2.

DISCUSSION

This study aimed to identify subgroups of individuals with headache who present to the pharmacy to self-medicate. The cluster analysis resulted in the identification of three subgroups, varying considerably with respect to sociodemographics, self-rated health, headache type, concomitant pain, disability and pain medication use. The clusters can be conveniently characterized as follows: the young uncomplicated migraine patient (cluster 1), the older headache patient with some age-related concomitant pain (cluster 2) and the middle-aged migraine patient with complex pain comorbidity (cluster 3).

A remarkable difference between the three clusters concerns the extent of pain problems beyond headache. Indeed, the number of concomitant pain locations increases from cluster 1 to 2, and from 2 to 3. The same is true for the frequency of days in pain. It may well be that the pain comorbidity contributes to a more frequent analgesic use, and a higher risk for MO. Of further note is that the difference between the clusters cannot be easily explained by a simple difference in the duration of the pain, or by a simple difference in the age of the participants. Indeed, there was no difference in pain duration between the three clusters. Also, age did not vary linearly with the pain complexity of the clusters. Cluster 1 had the lowest number of other pain locations, and consisted of the youngest individuals. However, cluster 2 consisted of the oldest participants, but had only half the number of other pain locations of cluster 3, which is on average 7 years younger.

The observed prevalence of MO differed substantially between clusters. The first cluster represented the largest number of patients and showed the lowest prevalence of MO (16%). These patients were relatively young and most of them suffered from migraine. They had the lowest number of other pain locations, and their disability was low. These results suggest that this cluster mainly includes rather “uncomplicated” migraine patients who seem to be able to self-treat. For these patients, evidence-based guidelines on self-medication are available [14].

Patients from cluster 2 (the older headache patient with some age-related concomitant pain) reported a medium prevalence of MO (40%). It seems that this cluster consists of the oldest patients

with mainly non-migraine headache, with on average two other pain locations and an overall low disability. Intriguingly, in cluster 3 (the middle-aged migraine patient with complex pain comorbidity) most patients suffered from migraine, and reported MO (73%), in particular overuse of medication to relieve their headaches. These patients also had the highest number of concomitant pain locations, and were most disabled by pain. It may well be that this subgroup is particularly at risk of developing MOH: they report a high prevalence of migraine (which is a risk factor for MOH [6; 7]) and a high rate of MO. Overall, the patients from cluster 3 seem to consist of patients at risk. Indeed, a closer examination of their specific profile reveals that it consists of some well-established risk factors for chronic pain problems. Patients do report multiple pain problems, which is a well-known risk factor for chronic pain [33]. Furthermore, patients have on average a more vulnerable socio-economic status. About 30 % of patients were either unemployed, or not working due to ill health, and 15 % of the patients were divorced. As yet we do not know what is cause and effect in this patient group. It may well be that the relationship between socio-economic status and pain problems is reciprocal, potentially fuelling a vicious circle of more pain and suffering. Notwithstanding, guidance and treatment of these patients may be more intense than for the patients from other clusters.

This study also assessed the patients' concerns regarding their use of pain medications. In line with the previous results, patients from cluster 3 displayed the largest concerns about their pain medication. They had a higher perceived need for pain medication, were more afraid of being prescribed the wrong medication, and had more concerns about unfavorable scrutiny by others, side effects, addiction, tolerance and withdrawal. We may easily interpret these concerns as sign of addictive behaviour to medication. However, we believe that more is at stake [22]. The worries and concerns reported may be better framed within a context of repeated but frustrating attempts to get control over their pain and suffering by use of pain medication. As there is no simple solution to their problem, patients may start to ruminate and worry about possible solutions [8], and about the pros and cons of these possible solutions. A result may be that patients start to self-experiment with pain medication, leading to poor adherence, including overuse, underuse or irregular use [26]. Evidently,

further research about the reported concerns about pain medication is warranted. A further elucidation and specification of these concerns may provide an avenue for interventions. Indeed, being concerned about something, is often a reason for seeking help. Being able to recognize and address concerns in patients, is a key feature of patient-centered care. In the context of this study, concerns about pain and medication use may be addressed by general practitioners and/or medical specialists. However, when community pharmacists have the necessary communication and counselling skills, the pharmacy may also prove to be an effective and efficient setting to deliver adequate information about headache and its management.

We argue for an increased role of community pharmacists in the management of headache. To prevent MO and limit the risk of developing MOH, a possible recommendation is that pharmacists routinely provide advice on the maximum intake frequency of acute headache medication, keep records of OTC analgesic dispensing (for headache and other pain conditions), encourage patients to report any self-medication to their treating physician, and inform patients about the potential link between regular analgesic intake and headache chronification. There is a need for such advice as previous research has indicated that most patients are unaware of this association [27]. Moreover, this simple advice has proven its effectiveness in both prevention and treatment of MOH in other settings, i.e. general practice [21] and hospital [13; 30]. In addition, pharmacists should be vigilant for risk factors for pain chronification and could proactively identify and address concerns about pain medication, which may help to enhance adherence and detect (fear of) addiction. In case of suspicion of MOH, referral to a general practitioner should be made to discuss strategies to reduce the intake of acute pain medication including non-drug treatment options [4], preventative drug treatment (e.g. for neuropathic pain or migraine) [11; 24] and targeted interventional pain management [25]. Increased pharmacist involvement in headache management requires adequate knowledge of headache and MOH. Recently, a Swedish study found that current knowledge on MOH is insufficient among pharmacy staff [16]. Increased educational efforts about headache disorders will thus be necessary to allow pharmacists to take up their extended role.

A strength of this study is the large number of participants in a yet largely unstudied patient population (i.e. individuals who self-treat their headaches). Another strength is that, to our knowledge, this is the first application of cluster analysis to patients with headache in order to identify clinically relevant patient subgroups in an unbiased way and not based on any a priori assumptions. Some limitations also have to be taken into account when interpreting the results. First, the present analysis aimed to be hypothesis-generating and further research is required to confirm our findings. Second, this study only screened for MO but we did not make a diagnosis of MOH. It should be kept in mind that the current ICHD-criteria for MO are based on expert opinion, rather than on formal evidence. However, from a community pharmacist's point of view, the conceptual difficulties in dealing with MO and MOH are not relevant as the pharmacist's role is to prevent MO in order to avoid development of MOH. Third, because we used a body manikin to assess pain locations, we were not able to determine whether neck pain reported by migraineurs was a concomitant site of pain with the migraine attacks [3; 12; 20] or chronic neck pain as comorbid condition [1]. Fourth, we used self-reported data, which may be subject to recall bias (e.g. regarding physician diagnosis or medication use). Fifth, the number of potential participants refusing study participation was relatively high (47%). Potential bias caused by those who refused participation could not be assessed as our Ethics Committee prohibits data collection in study refusers, but we have recorded reasons for refusal (mainly 'no time' and 'no interest').

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REFERENCES

[1] Ashina S, Bendtsen L, Lyngberg AC, Lipton RB, Hajiyeva N, Jensen R. Prevalence of neck pain in migraine and tension-type headache: A population study. Cephalalgia : an international journal of headache 2015;35(3):211-219.

[2] Bahra A, Walsh M, Menon S, Goadsby PJ. Does chronic daily headache arise de novo in association with regular use of analgesics? Headache 2003;43(3):179-190.

[3] Calhoun AH, Ford S, Millen C, Finkel AG, Truong Y, Nie Y. The prevalence of neck pain in migraine. Headache 2010;50(8):1273-1277.

[4] Cunningham NR, Kashikar-Zuck S. Nonpharmacological treatment of pain in rheumatic diseases and other musculoskeletal pain conditions. Current rheumatology reports 2013;15(2):306.

[5] DeSalvo KB, Bloser N, Reynolds K, He J, Muntner P. Mortality prediction with a single general self-rated health question. A meta-analysis. Journal of general internal medicine 2006;21(3):267-275.

[6] Diener HC, Dählof CGH. Headache associated with chronic use of substances. Olesen J, Tfelt-Hansen P, WelchKMA, editors. The headaches. 2nd ed. Philadelphia: Lippincott,Williams & Wilkins, 1999: 871-8.

[7] Diener HC, Limmroth V. Medication-overuse headache: a worldwide problem. The Lancet Neurology 2004;3(8):475-483.

[8] Eccleston C, Crombez G. Worry and chronic pain: a misdirected problem solving model. Pain 2007;132(3):233-236.

[9] Escofier B, Pagès J. Analyses factorielles simples et multiples, Objectifs, méthodes et interprétation. Dunaod, Paris 2008.

[10] Evers S, Marziniak M. Clinical features, pathophysiology, and treatment of medication-overuse headache. The Lancet Neurology 2010;9(4):391-401.

[11] Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, Gilron I, Haanpaa M, Hansson P, Jensen TS, Kamerman PR, Lund K, Moore A, Raja SN, Rice AS, Rowbotham M, Sena E, Siddall P, Smith BH, Wallace M. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. The Lancet Neurology 2015;14(2):162-173.

[12] Giffin NJ, Ruggiero L, Lipton RB, Silberstein SD, Tvedskov JF, Olesen J, Altman J, Goadsby PJ, Macrae A. Premonitory symptoms in migraine: an electronic diary study. Neurology 2003;60(6):935-940.

[13] Grande RB, Aaseth K, Benth JS, Lundqvist C, Russell MB. Reduction in medication-overuse headache after short information. The Akershus study of chronic headache. European journal of neurology : the official journal of the European Federation of Neurological Societies 2011;18(1):129-137.

[14] Haag G, Diener HC, May A, Meyer C, Morck H, Straube A, Wessely P, Evers S. Self-medication of migraine and tension-type headache: summary of the evidence-based recommendations of the Deutsche Migrane und Kopfschmerzgesellschaft (DMKG), the Deutsche Gesellschaft fur Neurologie (DGN), the Osterreichische Kopfschmerzgesellschaft (OKSG) and the Schweizerische Kopfwehgesellschaft (SKG). The journal of headache and pain 2011;12(2):201-217.

[15] Hagen K, Einarsen C, Zwart JA, Svebak S, Bovim G. The co-occurrence of headache and musculoskeletal symptoms amongst 51 050 adults in Norway. European journal of neurology : the official journal of the European Federation of Neurological Societies 2002;9(5):527-533.

[16] Hedenrud T, Babic N, Jonsson P. Medication overuse headache: self-perceived and actual knowledge among pharmacy staff. Headache 2014;54(6):1019-1025.

[17] Husson F, Josse J, Pagès J. Principal component methods - hierarchical clustering - partitional clustering: why would we need to choose for visualizing data? Technical report (2010).

Available from: http://factominer.free.fr/docs/HCPC_husson_josse.pdf (last accessed May 26, 2015).
[18] Jensen R, Stovner LJ. Epidemiology and comorbidity of headache. The Lancet Neurology 2008;7(4):354-361.
[19] Jonsson P, Linde M, Hensing G, Hedenrud T. Sociodemographic differences in medication use, health-care contacts and sickness absence among individuals with medication-overuse headache. The journal of headache and pain 2012;13(4):281-290.
[20] Kelman L. Migraine pain location: a tertiary care study of 1283 migraineurs. Headache 2005;45(8):1038-1047.
[21] Kristoffersen ES, Straand J, Vetvik KG, Benth JS, Russell MB, Lundqvist C. Brief intervention for medication-overuse headache in primary care. The BIMOH study: a double-blind pragmatic cluster randomised parallel controlled trial. Journal of neurology, neurosurgery, and psychiatry 2014.
[22] Lauwerier E, Paemeleire K, Van Damme S, Goubert L, Crombez G. Medication use in patients with migraine and medication-overuse headache: the role of problem-solving and attitudes about pain medication. Pain 2011;152(6):1334-1339.
[23] Lipton RB, Dodick D, Sadovsky R, Kolodner K, Endicott J, Hettiarachchi J, Harrison W. A self-administered screener for migraine in primary care: The ID Migraine validation study. Neurology 2003;61(3):375-382.
[24] Lipton RB, Silberstein SD. Episodic and chronic migraine headache: breaking down barriers to optimal treatment and prevention. Headache 2015;55 Suppl 2:103-122; quiz 123-106.
[25] Manchikanti L, Helm Ii S, Singh V, Hirsch JA. Accountable interventional pain management: a collaboration among practitioners, patients, payers, and government. Pain physician 2013;16(6):E635-670.
[26] McCracken LM, Hoskins J, Eccleston C. Concerns about medication and medication use in chronic pain. The journal of pain : official journal of the American Pain Society 2006;7(10):726-734.
[27] Mehuys E, Paemeleire K, Van Hees T, Christiaens T, Van Bortel LM, Van Tongelen I, De Bolle L, Remon JP, Boussery K. Self-medication of regular headache: a community pharmacy-based survey. European journal of neurology : the official journal of the European Federation of Neurological Societies 2012;19(8):1093-1099.
[28] Munksgaard SB, Jensen RH. Medication overuse headache. Headache 2014;54(7):1251-1257.
[29] Pagès J. Analyse factorielle de données mixtes. Revue de Statistique Appliquée 2004;52:93-111.
[30] Rossi P, Faroni JV, Nappi G. Short-term effectiveness of simple advice as a withdrawal strategy in simple and complicated medication overuse headache. European journal of neurology : the official journal of the European Federation of Neurological Societies 2011;18(3):396-401.
[31] Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia : an international journal of headache 2013;33(9):629-808.
[32] Steiner TJ, Martelletti P. Aids for management of common headache disorders in primary care. The journal of headache and pain 2007;8 Suppl 1:S2.
[33] van Hecke O, Torrance N, Smith BH. Chronic pain epidemiology and its clinical relevance. British journal of anaesthesia 2013;111(1):13-18.
[34] Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. Pain 1992;50(2):133-149.
[35] Vos T BR, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, and others. 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(9995):743-800.
[36] Wilkinson SM, Becker WJ, Heine JA. Opiate use to control bowel motility may induce chronic daily headache in patients with migraine. Headache 2001;41(3):303-309.

[37] Yoon MS, Manack A, Schramm S, Fritsche G, Obermann M, Diener HC, Moebus S, Katsarava Z. Chronic migraine and chronic tension-type headache are associated with concomitant low back pain: results of the German Headache Consortium study. Pain 2013;154(3):484-492.

FIGURES and TABLES

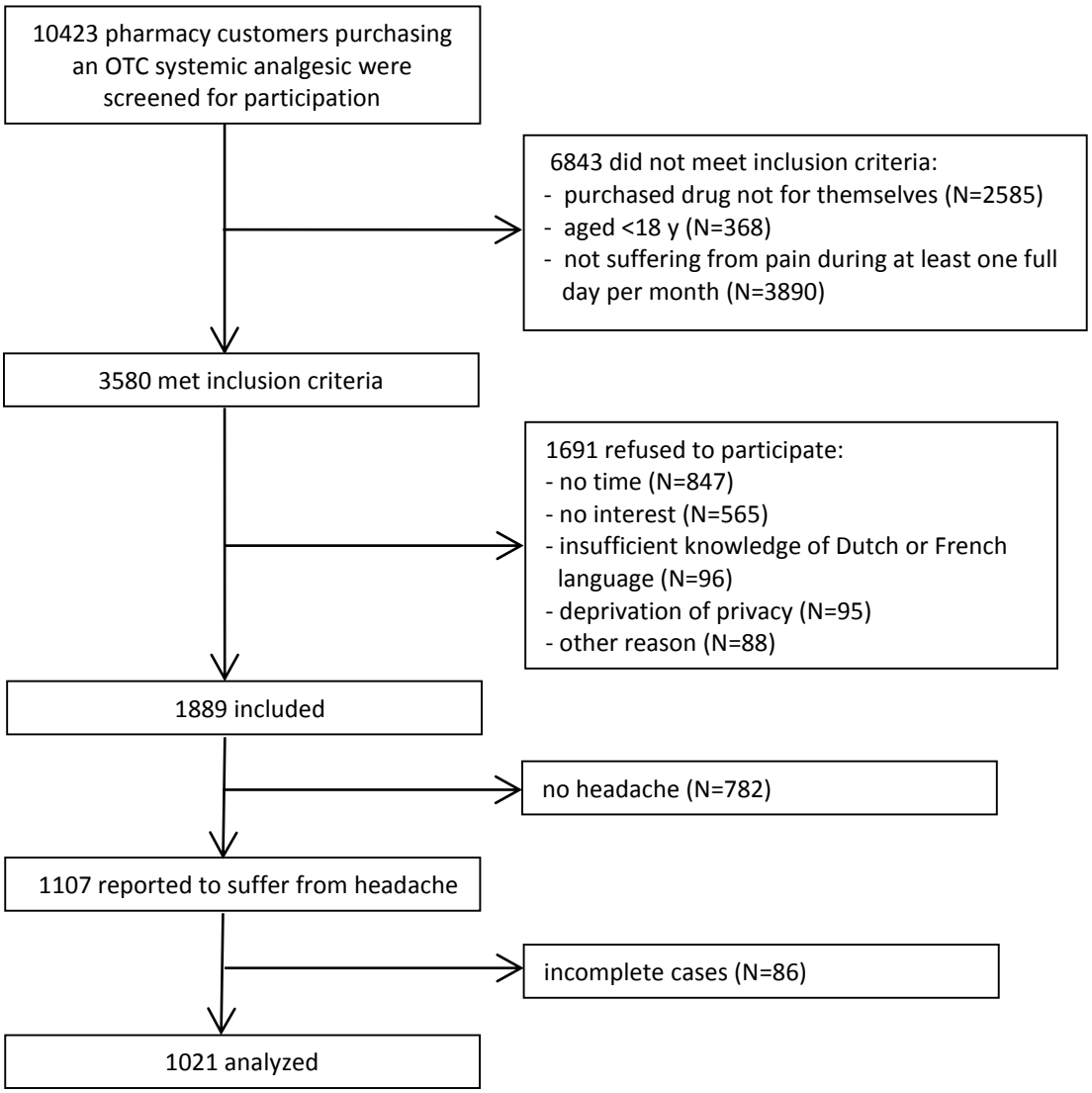

Figure 1: Flow scheme of participant recruitment and data analysis.

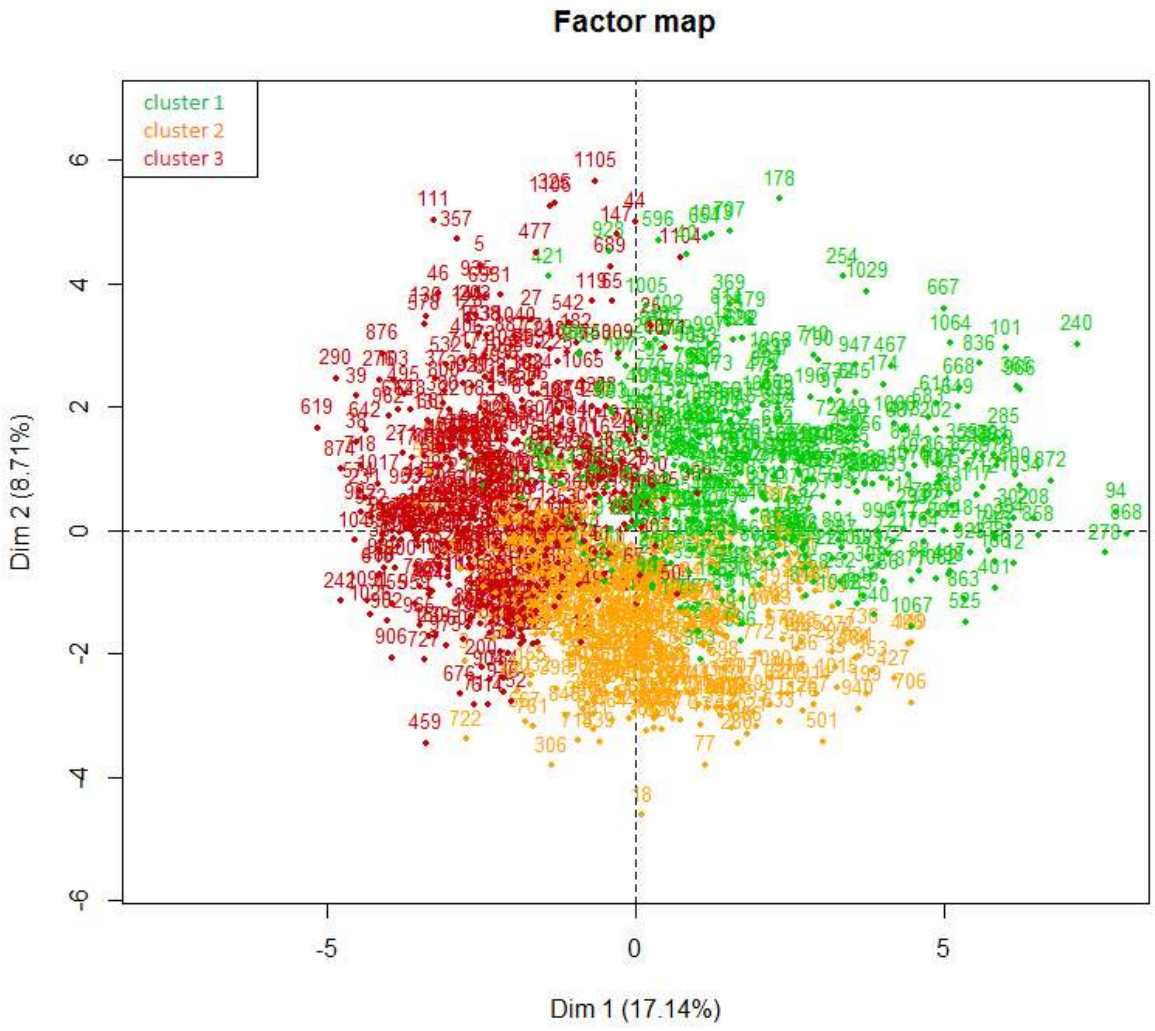

Figure 2: Graphical results of the factor analysis for mixed data (FAMD). X and Y axis represent the two first dimensions of the FAMD (these two dimensions explain 25.9% of the point variability). Individuals are subdivided into three separated clusters (green, orange and red dots).

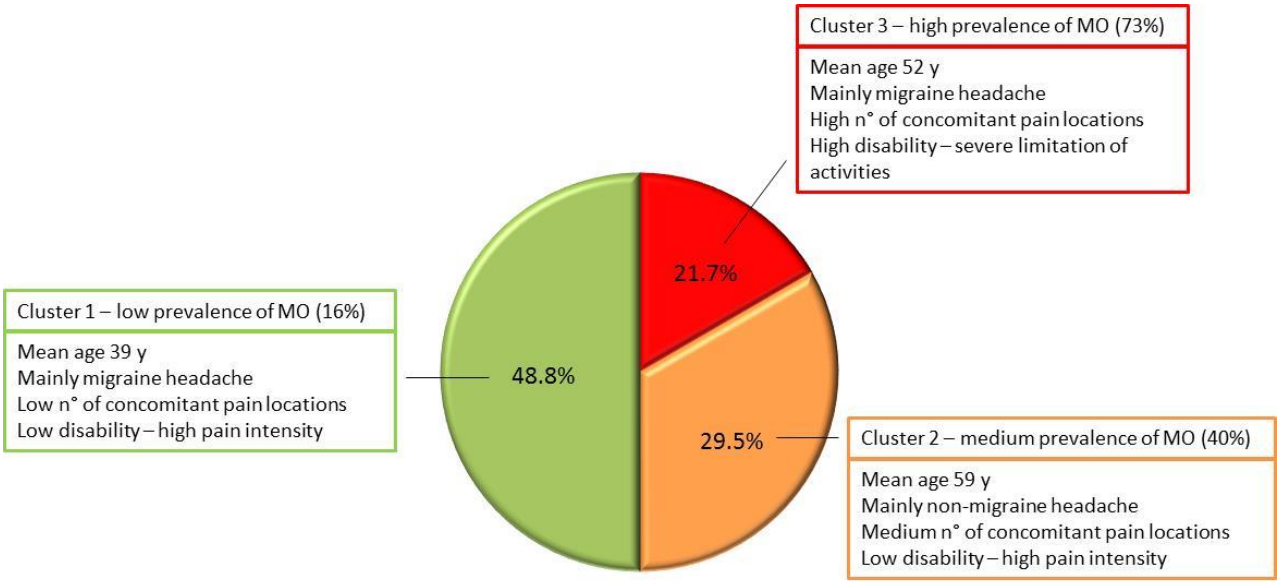

Figure 3: Summary of main features of the patient clusters.

Table 1: Characteristics of the three subgroups of patients identified by cluster analysis.

	Cluster 1 (N=498)	Cluster 2 (N=301)	Cluster 3 (N=222)	Total sample (N=1021)
SOCIODEMOGRAPHICS AND SELF-RATED HEALTH				
Male sex	18.7%	**25.9%****	16.7%	20.4%
Age, years	**38.9±11.5*****	**59.1±12.5*****	**51.9±12.3*****	47.7±14.9
Marital status				
Alone	**31.3%*****	**7.3%*****	17.6%	21.3%
Married or cohabiting	62.4%	**71.4%****	59.5%	64.4%
Divorced	**6.2%***	6.6%	**14.9%*****	8.2%
Widowed	**0.0%*****	**14.6%*****	8.1%	6.1%
Employment status				
Employed	**81.7%*****	**40.2%*****	**37.8%*****	59.9%
Unemployed	**3.0%***	3.7%	**9.5%*****	4.6%
Retired	**2.2%*****	**39.9%*****	18.5%	16.8%
Househusband/housewife	**3.0%*****	**13.6%*****	**13.5%****	8.4%
Not working due to ill health	**1.2%*****	**2.7%****	**20.3%*****	5.8%
Student	**8.8%*****	**0.0%*****	**0.5%*****	4.4%
Education level				
Primary education	**1.8%*****	**17.3%*****	**18.9%*****	10.1%
Secondary education	**47.2%*****	**62.1%****	**64.4%****	55.3%
Higher education	**51.0%*****	**20.6%*****	**16.7%*****	34.6%
Self-rated health[a]	**2.9±0.8*****	3.3±0.7	**4.2±0.7*****	3.3±0.9
PAIN CHARACTERISTICS				
Migraine				
Physician-diagnosed	**47.4%*****	**21.9%*****	43.2%	39.0%
[Suspected (based on ID-M[b])	24.7%	19.9%	25.2%	23.4%]
N° of concomitant pain locations	**1.1±1.3*****	2.1±1.6	**4.3±2.9*****	2.1±2.2
Location of concomitant pain				
Low back	**25.7%*****	**42.9%***	**59.5%*****	38.1%
Neck	**24.7%*****	33.6%	**56.8%*****	34.3%
Shoulder	**8.4%*****	26.6%	**50.0%*****	22.8%
Upper leg/knee	**5.0%*****	**22.6%****	**39.2%*****	17.6%
Pain duration, years	14.2±11.8	15.4±14.8	14.6±12.5	14.6±12.9
Pain frequency (days with pain in past 3 months)	**19.7±21.4*****	**45.8±35.8*****	**73.9±26.4*****	39.1±34.8
PAIN DISABILITY				
Pain Grading Scale, pain grade[c]	**2.1±0.8*****	**1.7±0.8*****	**3.6±0.6*****	2.3±1.0
Pain Grading Scale, individual items				
Pain right now, 0-10 Likert scale	**3.5±2.9*****	**3.4±2.3*****	**6.4±2.5*****	4.1±2.9
Worst pain, 0-10 Likert scale	7.7±1.6	**6.4±2.1*****	**9.0±1.1*****	7.6±1.9
Average pain, 0-10 Likert scale	5.5±1.8	**4.4±1.6*****	**7.1±1.6*****	5.5±2.0
Disability days[d] (in past 3 months)	**3.6±7.6*****	**3.6±10.0*****	**34.4±32.8*****	10.3±21.3
Daily activities, 0-10 Likert scale	4.7±2.3	**2.7±2.1*****	**7.2±1.8*****	4.6±2.7
Social activities, 0-10 Likert scale	4.4±2.6	**2.2±2.1*****	**6.9±2.1*****	4.3±2.9
Work activities, 0-10 Likert scale	4.4±2.5	**2.6±2.2*****	**7.5±1.9*****	4.6±2.8
PAIN MEDICATION				

N° of pain medications	**2.0±1.0***	**1.8±0.9*****	**2.6±1.3*****	2.1±1.1
Prescription status				
Only OTC pain medication	**70.9%*****	**73.4%*****	**34.7%*****	63.8%
OTC + prescription pain medication	**29.1%*****	**26.6%*****	**65.3%*****	36.2%
Type				
Paracetamol	**56.0%*****	**70.8%*****	68.0%	63.0%
NSAID	**50.4%****	**38.2%****	44.1%	45.4%
Fixed dose combinations of simple analgesics with caffeine	**30.9%***	**22.3%***	26.6%	27.4%
Meeting definition of medication overuse				
For pain medication used to treat headache	**14.9%*****	27.9%	**51.8%*****	26.7%
For pain medication used to treat other pain[e]	**1.0%*****	**11.6%***	**21.2%*****	8.5%
[Total	15.9%	39.5%	73.0%	35.2%][f]

Data are presented as mean±SD or % of patients. Bold values: significantly different from the total sample mean (continuous variables) or total sample % of patients (categorical variables). Asterisks indicate the level of statistical significance (* P<0.05, ** P<0.01,*** P<0.001).

[a] Self-rated health: 1 ('excellent'), 2 ('very good'), 3 ('good'), 4 ('fair'), 5 ('poor').

[b] The ID-Migraine Screener (ID-M) was only completed by patients *without* physician-based migraine diagnosis (N=623). Suspected migraine was not included in the cluster analysis (see Methods - statistical analysis).

[c] Pain grade: 1 ('low disability and low pain intensity'), 2 ('low disability and high pain intensity'), 3 ('high disability and moderate limitation of activities), 4 ('high disability and severe limitation of activities').

[d] Days kept from usual activities (work, school or housework)

[e] The number of patients meeting the definition of medication overuse for pain medication used to treat other pain was only determined for patients *not* meeting the definition of medication-overuse for pain medication used to treat headache.

[f] The total number of medication-overusers was not included in the cluster analysis.

Table 2: Attitudes about pain medication across the three patient clusters.

	Cluster 1 (N=498)	Cluster 2 (N=301)	Cluster 3 (N=222)	P value (ANOVA)
Addiction				
"I am concerned that taking medication for a long time will lead to addiction"	1.7±1.7[a]	1.7±1.7[a]	2.3±1.9[b]	<0.001
Need				
"I would be unwilling to reduce my pain medication(s)"	2.0±1.7[a]	2.1±1.7[a]	2.3±1.8[a]	>0.05
"I could cope without my pain medication(s)"	1.9±1.5[a]	2.0±1.5[a]	0.8±1.2[b]	<0.001
"I feel that I need more pain medication(s) than my doctor is giving me" [c]	1.2±1.4[a]	1.0±1.3[a]	1.7±1.6[b]	<0.001
Scrutiny				
"I worry what others think about my use of pain medication(s)"	0.7±1.1[a]	0.6±1.1[a]	1.1±1.5[b]	<0.001
Side effects				
"I have concerns about the side effects from my pain medication(s)"	1.5±1.3[a]	1.4±1.4[a]	2.0±1.6[b]	<0.001
"I am afraid that I do not know enough about side effects"	1.5±1.3[a]	1.5±1.3[a]	1.9±1.5[b]	<0.01
Tolerance				
"It worries me that I have to increase the dose to get the same pain relief"	1.8±1.4[a]	1.5±1.5[a]	2.6±1.6[b]	<0.001
Mistrust				
"I am afraid that I am being prescribed the wrong pain medication(s)" [c]	0.8±1.1[a]	0.8±1.1[a]	1.2±1.3[b]	<0.001
Withdrawal				
"I worry that I will have some withdrawal symptoms if I stop my medication"	0.8±1.3[a]	1.0±1.5[a]	1.7±1.7[b]	<0.001

Data are presented as mean±SD. Each item was answered on a 6-point Likert scale, ranging from 0 (''never true'') to 5 (''always true'').

[a,b] Mean values with the same superscript do not differ significantly from each other (Scheffé post hoc test)

[c] This item was only answered by patients taking prescription medicines.