

Medication use in patients with Migraine and Medication-Overuse

Headache: The role of problem solving and attitudes about pain medication

Lauwerier, E. ¹, Paemeleire, K. ², Van Damme, S. ¹, Goubert, L. ¹, Crombez, G. ¹

1 Department of Experimental-Clinical and Health Psychology, Ghent

University, Belgium

2 Department of Neurology, Ghent University Hospital, Belgium

* Corresponding author: Emelien Lauwerier, Department of Experimental-Clinical and Health Psychology, Ghent University, Henri Dunantlaan 2, B- 9000 Ghent, Belgium. Tel: +32 9 264 91 06, Fax: +32 9 264 64 89

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Abstract

Excessive medication intake is a risk factor for the development of Medication-Overuse Headache (MOH), a condition characterized by an increase of headache frequency to a daily or near-daily pattern. As yet, it is largely unknown why some patients overuse medication. In this study, we examined to what extent attitudes about pain medication, especially perceived need and concerns, and problem solving are related to MOH. Patients with migraine (N=133) and MOH with a history of migraine (N=42) were recruited from a tertiary headache referral center and completed questionnaires measuring problem solving and attitudes about pain medication. A problem solving mode aimed at solving pain was associated with a higher need for and concerns about medication intake. Interestingly, in a model accounting for demographic factors and pain intensity, attempts to control pain, need for medication and concerns about scrutiny by others because of medication intake all had a unique value in accounting for MOH. Results are discussed in terms of how repeated attempts to solve pain may trigger overuse of medication, even in the presence of clear negative consequences.

1. Introduction

Acute and preventive pharmacological treatment has proven effective in reducing the frequency, severity and duration of migraine attacks [47,48,51]. However, overuse of acute medication may bring along negative consequences, and eventually result in Medication-Overuse Headache (MOH) [12]. This is a disorder characterized by increased headache frequency up to a daily or almost daily pattern [47]. The prevalence rates of MOH across different European countries range from 0,7 to 1,7% [1,7,50,54,57]. In tertiary care, up to 30% of patients in Europe and more than 50% in the USA present with MOH [5,27,36,46]. MOH may have severe effects on quality of life [4,55].

To date, it remains unclear why some patients overuse medication. Functional and structural changes in the brain may be involved in the development of MOH [14,51], and explain why MOH occurs frequently in patients with episodic migraine [4,7,12]. However, a largely neglected issue relates to the psychological determinants of medication use. According to Horne and Weinman [26], medication intake depends upon a cost-benefit analysis of the need for medication against its perceived costs. In particular, increasing medication use may be beneficial in reducing the pain temporarily, but may also lead to obvious costs such as somatic, neurological and/or psychological complications [15,16,34,44]. When such negative effects prevail, Horne and Weinman [26] would predict a decrease of medication intake. However, this does not seem to be the case in patients with MOH. It seems that those patients are inclined to medication overuse despite being aware of its negative consequences [51]. Even after a successful treatment, most often consisting of psycho-education and a withdrawal protocol, the relapse rate is about 25-30% [19,30,31,40].

In an attempt to further our understanding of this apparently paradoxical behavior in MOH, we adopt a functional coping perspective [13,52] that is based upon the Dual Process Model of coping [6]. According to this model, there are two modes of coping with adversity, such as pain: assimilative and accommodative coping. When pain interferes with valued activities [28], patients in the assimilative mode focus their attention and efforts upon solving pain, such as by taking medication, in order to resume daily life. In the accommodative mode, patients disengage from persistent attempts to solve pain, and (re-) engage in the pursuit of valued life goals that are less affected by their pain. Often patients are then more willing to accept that there is no solution, and that pain will last for a longer duration. It has been proposed that many patients with chronic pain become stuck in the assimilative mode, and thus persevere in attempting to solve an insoluble problem [13,52]. Such ineffective problem solving fuels and exacerbates hypervigilance, distress and disability [8, 9].

Building upon these arguments, we expect that patients with MOH will more frequently adopt an assimilative coping mode than patients with episodic migraine. Related, we expect that, in comparison with patients with episodic migraine, MOH patients believe to be in more need for medication to control their pain, despite being aware and concerned about its negative consequences.

2. Method

2.1. Participants

The study was approved by the Medical Ethics Committee of the Ghent University Hospital, Belgium. Participants were recruited from the Headache Clinic of the Department of Neurology at the Ghent University Hospital: 490

consecutive patients with an episodic migraine diagnosis, or with a diagnosis of MOH with a history of migraine, were invited by their treating physician at the Headache Clinic. They received a letter containing information about the study, an informed consent letter and the questionnaires. When patients consented to participate, they signed the informed consent letter, filled out the questionnaires at home and sent both back to the Headache clinic by regular mail.

Migraine diagnosis was consistent with the criteria of the International Headache Society (IHS) [24]. The diagnosis of MOH was based upon the revised ICHD-II criteria, proposed by the IHS [25]. According to these criteria, MOH is diagnosed in patients who report headache on ≥ 15 days/month for >3 months and who use ergotamine, triptans, or combination analgesics on ≥ 10 days/month, or simple analgesics or any combination of ergotamine, triptans, analgesics and opioids on ≥ 15 days/month. One hundred and eighty eight patients returned the questionnaires (38%). Compared to a complete patient database that has been held in the Headache Clinic of the Department of Neurology since October 2004 and in which the overall ratio of migraine over MOH was 2.8 (73% migraine patients, 27% MOH), we found no differential response rate between patients with migraine and MOH patients in the present study (76% migraine patients, 24% MOH). No data are available on those patients who failed to complete the questionnaires. Subsequently, headache classification was double-checked by one of the authors (KP). Based on a verification of headache diagnosis, thirteen patients were excluded, resulting in a final sample of 175 patients.

The sample of migraine patients comprised of 133 patients (84.2% female), aged between 17 and 68 (mean age = 38.86 years, SD = 12.04). Further, 63.4% had a higher education (longer than the age of 18 years). More

than half of the patients (67.7%) was in paid employment, whilst only 4.8% received state supported income replacement because of their pain.

The MOH sample consisted of 42 patients (83.3% female), aged between 23 and 75 years (mean age = 45.57 years, SD = 11.45). Approximately half of the patients (45.2%) had a higher education (longer than the age of 18 years). Further, 65.8% was working and 7.9% was recipient of disablement insurance benefits. Of the total MOH sample, 7 patients fulfilled the ICHD- II criteria [25] of analgesic-overuse headache, 4 patients those of triptan-overuse headache and 2 patients those of opioid-overuse headache. The other 29 MOH patients could not be subclassified as they used at least 2 classes of medications.

2.2. Measures

2.2.1. Medication intake

Information was collected about medication intake during the past three months. Patients were asked to indicate on how many days during the past three months they had been using pain medication. Patients were also asked to report about the names of the pain medication they used, the exact dose and daily and monthly frequency of intake of each individual medication. The medication information was used to calculate the different classes of medications and the number of active constituents being taken for pain. Active constituents were classified as ergotamine, triptans, simple analgesics (NSAID's, acetylsalicylic acid, paracetamol), opioids, barbiturates or caffeine.

2.2.2. Pain frequency, pain intensity and disability

The Migraine Disability Assessment Questionnaire (MIDAS) [49] measures headache-related disability, frequency of headaches and the intensity of

headache pain. Headache-related disability during the past three months is measured by means of five disability questions. Patients record the number of missed days due to headache on three questions concerning school or paid work (“On how many days in the last 3 months did you miss work or school because of your headaches?”), household work (“On how many days in the last 3 months did you not do household work because of your headaches?”) and family, social or leisure activities (“On how many days in the last 3 months did you miss family, social, or leisure activities because of your headaches?”). Two further questions assess the number of additional days with significant limitations to activity (defined as at least 50% reduced productivity) in the domains of employment (“How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches?”) and household work (“How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches?”). Disability is assessed as the sum of lost days due to headache recorded for all of the above questions. Two additional questions assessed the frequency of headaches (“On how many days in the last 3 months did you have any headache (if a headache lasted more than one day, count each day)?”) and the intensity of the headache pain (“On a scale from 0 to 10, on average how painful were these headaches?”). The latter question is scored on a 11-point scale, ranging from 0, no pain at all, to 10, pain is as bad as it can be. The MIDAS has demonstrated good reliability and validity [49]. Cronbach’s alpha for the summed disability measure in this study was $\alpha = .85$.

2.2.3. *Problem Solving and acceptance*

The Pain Solutions Questionnaire (PaSol) [11] measures efforts at changing, solving or accepting pain and the problems associated with pain. The PaSol has 14 items grouped into four interrelated scales: (1) Solving Pain scale (4 items; e.g., “I try everything to get rid of my pain”), (2) Meaningfulness of Life Despite Pain scale (5 items; e.g., “Even when I have severe pain, I still find my life meaningful”), (3) Acceptance of the Insolubility of Pain scale (3 items; e.g., “I can live with the idea that there is no solution for my pain”), and (4) Belief in a Solution scale (2 items; e.g., “I am convinced that there is a treatment for my pain”). Whereas the ‘Solving Pain’ subscale is an indicator of a problem solving or assimilative approach, both the ‘Meaningfulness of life despite pain’ and ‘Acceptance of the insolubility of pain’ subscales represent the accommodative mode of coping. Each item is answered on a 7-point Likert scale, ranging from 0, not at all applicable, to 6, highly applicable. The PaSol has demonstrated good reliability and validity [11]. Cronbach’s alpha’s in this study ranged from .82 to .88.

2.2.4. *Attitudes about pain medication*

The Pain Medication and Attitudes Questionnaire (PMAQ) [37] assesses perceived need and concerns held by patients regarding their use of medication. The PMAQ has 47 items grouped into seven scales: (1) Addiction (5 items; e.g., “I worry about becoming addicted to my pain medication/s”), (2) Need (8 items; e.g., “I rely on my pain medication/s”), (3) Scrutiny (8 items; e.g., “I worry about how other people view my use of pain medication/s”), (4) Side effects (7 items; e.g., “I have concerns about the side effects from my pain medication/s”), (5) Tolerance (6 items; e.g., “I worry that over time I will need more pain medication/s”), (6) Mistrust of doctors (7 items; e.g., “I worry that I have been told different

information about my pain medication/s by different doctors”), and (7) Withdrawal (6 items; e.g. “I worry that I will have some withdrawal symptoms if I stop my medication”). Each item is answered on a 6-point Likert scale, ranging from 0, never true, to 6, always true. The PMAQ has demonstrated good reliability and validity [37]. Cronbach’s alpha’s in this study ranged from .64 (Mistrust of doctors) to .91 (Addiction).

2.3. Data - Analytical strategy

Statistical analyses were performed using SPSS 15.0 for Windows. First, descriptive statistics were calculated to investigate differences in pain frequency, pain intensity, disability and intake of medication between the two patient groups. Correlational analyses were carried out in order to examine the relations of problem solving and acceptance with attitudes about pain medication. Second, the value of demographic variables, pain intensity, problem solving, acceptance and attitudes about pain medication in explaining Medication-Overuse Headache were assessed by means of separate univariate logistic regression analyses. Finally, we investigated the unique value of problem solving and attitudes about pain medication in explaining Medication-Overuse Headache using a multivariate logistic regression analysis, while accounting for the effects of demographic variables and pain intensity.

3. Results

3.1. Descriptive and Correlational Statistics

A series of t-tests for independent samples was used to assess differences in pain frequency, pain intensity, headache-related disability, and amount of

active constituents taken between the two patient groups. Whenever the assumption of normality was violated, the Mann-Whitney U statistic instead of the Student t-statistic was used. MOH patients reported more frequent headaches ($u = 832.5, p < .001, d = -1.54$) and more intense pain ($t(166) = 1.79, p < .05, d = 0.33$) compared to migraine patients. No significant differences in headache-related disability were found ($u = 1549, ns, d = -0.32$). Furthermore, analyses revealed significant differences in the number of active constituents taken ($t(55.271) = -4.29, p < .001, d = -0.89$), with MOH patients taking a greater number of active constituents ($M = 3.36, SD = 1.67$) compared to migraine patients ($M = 2.17, SD = 1.21$). Furthermore, we analysed whether there was a significant difference in the proportion of patients who had a higher education between the migraine and the MOH sample (63.4% versus 45.2%). The chi-square test just failed significance ($\chi^2 (1) = 3.87, p = .05$).

Chi-square tests and Fisher's exact test were used to assess differences in the distribution of medication type intake between both patient groups (see Table 1). The intake of opioids ($\chi^2 (1) = 18.52, p < .001$) and preparations containing caffeine ($\chi^2 (1) = 7.27, p < .01$) was found to be higher in MOH patients compared to migraine patients. Fisher's exact test comparing ergotamine intake between patient groups reached significance ($p = .06$). No significant differences were found concerning the intake of triptans ($\chi^2 (1) = 0.01, ns$) and analgesics ($\chi^2 (1) = 0.02, ns$). Within the entire sample, there were no patients taking barbiturates.

< Table 1 about here >

Correlational analyses were carried out in order to examine the relations of problem solving and acceptance with attitudes about pain medication.

Interestingly, solving pain was positively related to perceived need for medication

($r=.30, p < .001$), to concerns about tolerance ($r=.26, p < .01$) and withdrawal ($r=.15, p < .05$). Acceptance of the insolubility of pain showed moderate negative associations with concerns about scrutiny ($r=-.26, p < .01$), tolerance ($r=-.17, p < .05$) and withdrawal ($r=-.16, p < .05$). Meaningfulness of life despite pain was negatively related both to perceived need for medication ($r=-.27, p < .001$) and to concerns about addiction ($r=-.24, p < .01$), scrutiny ($r=-.35, p < .001$), tolerance ($r=-.26, p < .01$), mistrust of doctors ($r=-.30, p < .001$) and withdrawal ($r=-.34, p < .001$). Lastly, belief in a solution was negatively related to concerns about scrutiny ($r=-.25, p < .01$), tolerance ($r=-.16, p < .05$) and mistrust of doctors ($r=-.31, p < .001$).

3.2. Value of demographic variables, pain intensity, problem solving, acceptance and attitudes about pain medication in explaining Medication-Overuse Headache

First, a series of separate univariate logistic regression analyses were performed to investigate the value of age, gender (0 = male; 1 = female), pain intensity, problem solving, acceptance and attitudes about pain medication in explaining Medication-Overuse Headache (0 = migraine; 1 = MOH). Table 2 summarizes the results of these analyses. As expected, MOH was significantly associated with a higher age. No association was found between pain intensity and MOH diagnosis. Furthermore, the values of OR indicated that an increase of one unit on solving pain increased the odds of being diagnosed with MOH (relative to being diagnosed with migraine) with a factor of 1.14 [18]. Also, an increase of one unit on meaningfulness of life despite pain decreased the odds of being diagnosed with MOH with a factor of 0.95. Finally, need for medication and

all concerns about pain medication had significant value in explaining MOH, with OR's ranging from 1.10 to 1.24.

Second, a multivariate logistic regression analysis was executed to investigate the unique value of problem solving and attitudes about pain medication in explaining Medication-Overuse Headache, while accounting for the effects of demographic variables and pain intensity. Variance-inflation factors suggested that there was no problem of collinearity. As shown in Table 2, need for medication had a significant value in explaining MOH diagnosis: an increase of one unit on need for medication increased the odds of being diagnosed with MOH with a factor of 1.24. Furthermore, scrutiny also made a significant contribution in explaining MOH. Results showed that an increase of one unit in experiencing unfavourable scrutiny by others because of medication intake increased the odds of being diagnosed with MOH with a factor of 1.12. Interestingly, solving pain had unique value in accounting for MOH diagnosis. The OR showed that an increase of one unit on solving pain increased the odds of being diagnosed with MOH with a factor of 1.23.

< Table 2 about here >

4. Discussion

The present study aimed at clarifying the role of problem solving (assimilative coping mode) and beliefs about pain medication in relationship to MOH. The results can be readily summarized. First, an assimilative coping mode aimed at solving pain was related to a higher perceived need for medication and higher levels of concerns about tolerance to medication and withdrawal symptoms. Second, attempts to solve pain, need for medication and concerns

about pain medication were positively related to MOH. Third, after controlling for demographic variables and pain intensity, attempts to solve pain, need for medication and concerns about unfavorable scrutiny by others were found to have unique value in explaining MOH.

Of particular interest to this study was the finding that a problem solving mode aiming at pain control was uniquely related to MOH. Correlational analyses further showed that attempts at solving pain were related to a higher perceived need for medication and higher levels of concerns about tolerance and withdrawal. This is in line with earlier findings in which patients with MOH were found to have a negative attitude towards analgesics but believed that they could not cope without [22]. Our findings point out that patients who frame the problem of pain as one that has to be solved, may be at a higher risk of developing MOH. The role of solving pain, as an indicator of assimilative coping, is in line with the Dual Process Model of coping as outlined by Brandstädter and Renner [6]. A problem approach that is characterized by persistent attempts to solve the pain may increase the need for medication, despite clear negative consequences. An important issue pertains to the reasons for this behavioural pattern. There are at least two possible reasons. First, the pain relieving effect of the medication in the short term may be more salient than its long-term negative consequences. As such, it may provide a sense of control over pain that is not easily relinquished. Second, it may be that the ongoing activities and goals that are interrupted by pain are of central importance in a patient's life. A patient may then prefer to search for a solution instead of giving up highly valued goals [52]. Paradoxically, a focus on solving pain may inadvertently heighten attention to pain and may add to the problem. This mechanism may partially explain why some MOH patients

persevere in using medication, and relapse in medication overuse after successful withdrawal. In accordance with this line of reasoning is the finding that patients reporting their life as meaningful despite the pain, were less likely being diagnosed with MOH. These patients may have been successful in adapting their goals in a way that pain interferes less with goal attainment [52].

Although univariate regression analyses showed that all medication concerns were positively related to MOH, only concerns about unfavorable scrutiny by others had unique value in explaining MOH. This is in line with the findings of McCracken and colleagues [37], who found that overuse was predominantly predicted by perceiving medication as needed and secondarily related to concern about negative scrutiny in chronic pain patients. It is possible that patients overusing their medication become ashamed and embarrassed because they cannot maintain an optimal level of dosing.

Our results argue for an action-oriented and goal-dependent theory that allows us to gain insight into how patients deal with the interference of life activities by persistent headache. This view may complement other explanations of MOH. For example, some studies focus upon an addiction or dependence component in a subgroup of MOH patients. Indeed, some drugs taken by patients contain substances with psychotropic effects, i.e. barbiturates, opioids, and caffeine [17,35,41,42]. Although some patients may be classified as addicted to their medication, this may not apply to all patients. First, there is still some doubt whether drugs like triptans and simple analgesics may result in pharmacological dependence [14]. Second, some studies did not find any difference in self-reported dependence-related behavior between patients with MOH on the one hand and patients with episodic migraine and healthy individuals on the other

hand [45]. Third, the uncritical use of the DSM-IV or ICD-10 criteria for substance-related disorders in patients with MOH, may result in an inflation of cases. MOH patients with long-term drug use may easily fulfill some of the defining features of addiction, such as tolerance, withdrawal symptoms, use of medication in a larger amount or for a longer period than intended, unsuccessful efforts to cut down or control the use despite harmful consequences and a high priority given to drug use [2,56]. However, often overlooked is that for a diagnosis of addiction, drug use needs to be associated with a progressive increase of time in obtaining or taking the drug or an increased recovery from the effects of the drug. Moreover, addiction is often characterized by a progressive neglect of alternative pleasures or interests because of drug use and may result in a reduction of social, occupational or recreational activities. This is often not the case in MOH patients. Instead, our results may point out that MOH patients overuse their medication in order to retain functioning. Further studies are needed to validly assess the relative contribution of dependence in MOH. A recent PET study, for example, showed hypo-function in the orbitofrontal cortex, a brain region known for its role in substance dependence, after 3 weeks drug withdrawal, but more so in patients overusing combination analgesics [21]. Besides neuroimaging data, recent neurobiological and pharmacogenetic studies appear to support the existence of dependence in some patients with MOH (for an overview, see Radat et al. [43]). This all might reflect an underlying susceptibility predisposing specific subgroups of MOH patients to substance dependence.

The results of this study may have a number of implications. When pain blocks valued goals, patients may be highly motivated to solve or control their pain, and may engage in medication use, despite clear negative consequences

and risks. As a consequence, withdrawal of medication, commonly accepted as the first and primordial step in treating MOH [5,39], may only be partially effective in those patients. At least, education of patients about the problem seems to be an important treatment component [10,14,51]. Additionally, some patients may benefit from techniques within traditional programs of cognitive behavioral therapy aimed at increasing problem solving skills and changing the functional approach to pain in order to cope more effectively with disability, discomfort and distress [3, 20]. Such techniques may be compatible with the therapeutic approach of 'acceptance' in behavior therapy [23,38]. Within the pain literature, acceptance refers to "... *a willingness to experience continuing pain without needing to reduce, avoid or otherwise change it*" [38]. Similar to acceptance, we found that a coping mode directed at relinquishing pain control was associated with less need for medication, less concerns about intake and an overall lesser chance of being diagnosed with MOH. Still, these results are preliminary and further studies examining the effects of 'acceptance' of pain in chronic headache samples are awaiting. Lastly, effective preventive medication in order to treat the underlying migraine condition and reduce the number of headache attacks and/or the early assessment of behavioral and psychological co-factors are recommended [14,29,33,39].

This study has a number of limitations, each of which point to directions for future research. First, all findings are based on cross-sectional and correlational data. No causal interpretations about the order of relationships can be made. Studies with longitudinal designs are needed to provide evidence on the temporal relations between the variables. Second, the overall response rate was relatively low. We believe that the main reason is to be found in the use of a strict

recruitment protocol in which all consecutive patients from a headache clinic were invited. Nevertheless, more studies are needed, and our results need to be confirmed by large-scale studies. Third, the assessment of variables in this study relied on patient self-report. Further research may benefit from the adaptation of experimental paradigms designed to measure (correlates of) problem solving behaviour [53]. A fourth limitation is that the mechanism we propose is probably not the only one contributing to the problem of MOH. Overall, observed effects in this study were relatively small, leaving a substantial amount of variance unexplained. More research is needed on the interplay between the somatic pathophysiology, such as the role of genetic susceptibility and endocrine and neurotransmitter function (for an overview, see Evers et al. [14]), and the psychological mechanisms underlying MOH. Lastly, we performed no subgroup analyses according to the type of overused medication among the patients with MOH. However, the development of the disorder and prognosis after withdrawal seem to be dependent upon which type of medication patients are overusing [31,32]. In general, more research is needed that could unravel the relative contribution of diverse psychological mechanisms, such as substance dependence and a functional coping perspective. It would, for example, be particularly helpful to study the contributing factors to relapse after successful withdrawal in different subgroups of MOH patients and to test these findings in prospective studies.

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Table 1
Percentages of medication type intake in patients with migraine and MOH

	Migraine (N=133)	MOH (N=42)
Ergotamine	3.8%	11.9% ^(*)
Triptans	57.9%	57.1%
Simple analgesics	84.2%	83.3%
Opioids	9.8%	38.1% ^{***}
Barbiturates	0%	0%
Coffeine	9.8%	26.2% ^{**}

$p < .05^*$; $p < .01^{**}$; $p < .001^{***}$

Table 2.

Summary of the univariate and multivariate logistic regression analyses with diagnosis (0=migraine; 1=MOH) as dependent variable and demographic variables, pain intensity, problem solving, acceptance and attitudes about pain medication as independent variables.

Criterion variable	Predictor	Univariate analysis		Multivariate analysis ^a	
		OR	[95%CI]	OR	[95%CI]
Diagnosis	Age	1.05**	[1.02-1.08]	1.03	[0.98-1.09]
	Gender	1.07	[0.42-2.72]	0.54	[0.11-2.72]
	Pain intensity	0.84	[0.69-1.02]	0.82	[0.61-1.12]
	Solving pain	1.14*	[1.02-1.29]	1.23*	[1.01-1.50]
	Meaningfulness	0.95*	[0.91-0.99]	0.96	[0.86-1.07]
	Acceptance	1.00	[0.93-1.07]	1.07	[0.92-1.23]
	Belief	0.95	[0.86-1.05]	1.10	[0.90-1.35]
	Addiction	1.20***	[1.12-1.27]	1.09	[0.96-1.24]
	Need	1.24***	[1.15-1.34]	1.24**	[1.08-1.42]
	Scrutiny	1.14***	[1.08-1.20]	1.12*	[1.01-1.24]
	Side effects	1.10**	[1.04-1.16]	0.93	[0.83-1.05]
	Tolerance	1.12***	[1.05-1.18]	0.90	[0.81-1.01]
	Mistrust of doctors	1.12**	[1.03-1.22]	1.12	[0.97-1.28]
	Withdrawal	1.17***	[1.10-1.24]	1.05	[0.95-1.17]

Notes. ^a $\chi^2(14) = 73.628, p < .001$; .38 (Cox & Snell); .57 (Nagelkerke); 95% CI = 95% Confidence Interval; OR = odds ratio, an OR > 1 reflects a higher probability of MOH and an OR < 1 reflects a lower probability of MOH, compared to episodic migraine

* $p < .05$; ** $p < .01$; *** $p < .001$

