

# Alcoholic beverages as trigger factor and the effect on alcohol consumption behavior in patients with migraine

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**Background and purpose:** Alcoholic beverages are frequently reported migraine triggers. We aimed to assess self-reported alcohol consumption as a migraine attack trigger and to investigate the effect on alcohol consumption behavior in a large migraine cohort.

**Methods:** We conducted a cross-sectional, web-based, questionnaire study among 2197 patients with migraine from the well-defined Leiden University MIGRAINE Neuro-Analysis (LUMINA) study population. We assessed alcoholic beverage consumption and self-reported trigger potential, reasons behind alcohol abstinence and time between alcohol consumption and migraine attack onset.

**Results:** Alcoholic beverages were reported as a trigger by 35.6% of participants with migraine. In addition, over 25% of patients with migraine who had stopped consuming or never consumed alcoholic beverages did so because of presumed trigger effects. Wine, especially red wine (77.8% of participants), was recognized as the most common trigger among the alcoholic beverages. However, red wine consistently led to an attack in only 8.8% of participants. Time of onset was rapid (<3 h) in one-third of patients and almost 90% had an onset <10 h independent of beverage type.

**Conclusions:** Alcoholic beverages, especially red wine, are recognized as a migraine trigger factor by patients with migraine and have a substantial effect on alcohol consumption behavior. Rapid onset of provoked migraine attacks in contrast to what is known about hangover headache might point to a different mechanism. The low consistency of provocation suggests that alcoholic beverages acting as a singular trigger is insufficient and may depend on a fluctuating trigger threshold.

## Introduction

Migraine is an episodic brain disorder, characterized by recurrent, disabling attacks of severe typically unilateral pulsating headache accompanied by nausea, vomiting and/or photophobia and phonophobia for up to 3 days, affecting approximately 15% of the general

population [1–4]. The severity, frequency, unpredictability of attacks and high prevalence of migraine cause a great burden to patients and society [2,5].

Susceptibility for migraine is thought to be determined by a combination of non-modifiable genetic factors and modifiable internal (hormonal fluctuations and comorbid diseases) and external (sleep pattern, alcohol, fatigue and food consumption) risk modulation factors [6–11]. Patients strive to get a sense of personal control over their attacks [10,12]. Identifying and modifying or avoiding external risk modulation factors, also called trigger factors, could potentially prevent attacks [12]. Alcoholic beverages,

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a trigger factor that may be avoided, are frequently reported in the top 10 trigger factors [6,10,12,13]. However, mainly small and retrospective studies have been performed focusing on a (limited) collection of different beverages [14–16]. From those studies, red wine in particular was suggested as a trigger factor, with rapid onset of headache after consumption [14,16,17]. It has been hypothesized that susceptibility to alcohol might affect behavior, leading to less alcohol consumption or abstinence by patients with migraine [18–22], but the reasons for patients with migraine to abstain from alcohol consumption have not been explored in detail.

The aim of the present study was to investigate which alcoholic beverages are frequently reported as a migraine trigger, estimate trigger consistency and the time to attack onset in a large, well-defined cohort of patients with migraine, and explore the effect on alcohol consumption behavior.

## Methods

### Subjects

The present study was conducted as part of the Leiden University MIGRAINE Neuro-Analysis (LUMINA) project [23]. Participants in the LUMINA project were Dutch adults aged 18–80 years with migraine with or without aura who fulfilled the International Classification of Headache Disorders (previously ICHD-2, now ICHD-3) criteria [24]. Patients with migraine with aura could also experience attacks without aura. Patients with migraine were recruited via public announcement, advertising in the lay press and on our research website, and were considered eligible after a two-step inclusion process. An elaborate description of LUMINA participants and procedures is given in Data S1. We consider the cohort to be a well-defined web-based cohort. The study was approved by the medical ethics committee of Leiden University Medical Center. All subjects provided written informed consent prior to the study.

### Study design

The study was observational with cross-sectional data collection using a web-based questionnaire provided via email invitation. Recruitment for the LUMINA project is still ongoing. Participants in this alcohol-trigger questionnaire study were all patients with migraine included in LUMINA between February 2008 and January 2013. Subjects were reminded by email three times to participate in this alcohol-trigger questionnaire study in January 2013; subjects not

participating after these reminders were defined as non-responders.

### Measurements

Within LUMINA, alcohol consumption and migraine attack provocation by alcoholic drinks were assessed using an electronic questionnaire. The first question assessed whether subjects had consumed alcohol in the previous 3 months. Those who responded that they had not consumed alcohol in the previous 3 months or ever were asked for the reasons. Participants who had ever consumed were asked about the number of days and amounts of alcohol consumption in the past month (alcoholic beverages in general and specifically red wine and vodka), whether alcoholic beverages provoked migraine attacks (overall for all attacks; with or without aura) and, if so, which alcoholic beverages did provoke migraine attacks (red wine, white wine, champagne, beer, whisky, vodka, rum or other type of alcoholic beverage). Specifically for red wine and vodka, we assessed how often attacks were provoked on a 0–5 scale (as a measure of trigger consistency) [0 (never, 0%), 1 (rarely, 1%–24%), 2 (sometimes, 25%–49%), 3 (often, 50%–74%), 4 (mostly, 75%–99%) and 5 (always, 100%)], after how many glasses (in standard units) and after how much time (in hours). Red wine and vodka consumption were assessed in more detail because these were frequently mentioned in the literature and vodka contains almost no substances other than ethanol and water [17,25–28].

### Data analysis and statistics

Descriptive characteristics were reported as mean  $\pm$  SD or percentage. Differences in means were compared between groups using an independent-samples *t*-test for normally distributed continuous data, Mann–Whitney *U*-test for non-normally distributed continuous data and chi-squared test for categorical data. All analyses were performed using SPSS 23.0 (SPSS Inc., IBM, New York, NY, USA).  $P < 0.05$  were considered to indicate statistical significance.

## Results

### Study flow

The study flow is outlined in Fig. 1. In total, 3785 patients with migraine enrolled in the LUMINA project were sent an invitation to fill out the questionnaire. After three reminders, 2424 patients with migraine (64.0%) had responded. Non-response

analysis (Table S1) showed that responders were older ( $46.2 \pm 12.0$  vs.  $43.4 \pm 12.2$  years,  $P < 0.001$ ), with a longer disease duration ( $27.3 \pm 13.4$  vs.  $24.5 \pm 12.8$  years,  $P < 0.001$ ), higher body mass index (BMI) ( $24.6 \pm 4.2$  vs.  $24.2 \pm 3.9$ ,  $P = 0.02$ ) and higher annual attack frequency ( $P = 0.04$ ) and number of migraine days ( $P = 0.02$ ). Gender and migraine subtype did not differ between responders and non-responders. The data from 2197 patients with migraine were eligible for analysis.

### Alcohol consumption and reported trigger

Overall, 783 (35.6%) patients reported alcohol as a migraine trigger. Of the 1547 participants with migraine who were consuming alcohol, 658 (42.5%) reported alcohol as a trigger, 694 (44.9%) did not and the remaining 195 (12.6%) did not know. Patients reporting alcohol as a migraine trigger had a lower BMI, were more frequently patients with migraine without aura, had a higher annual migraine attack frequency and number of migraine days, drank slightly more per occasion and consumed more vodka and considerably less red wine (Table 1). Apart from a longer disease duration (migraine with aura), no differences were found between patients with migraine with and without aura reporting alcohol as a trigger for their attacks (Table S2).

When alcohol-consuming patients were asked whether a particular alcoholic beverage could provoke a migraine attack, red wine was mentioned most frequently (512/658, 77.8%) and vodka least frequently (56/658, 8.5%) (Fig. 2). Patients also replied 'don't know' either because they were not sure or did not drink the particular beverage. To illustrate, for both red wine (89/105, 84.8%) and vodka (538/544, 98.9%), participants who replied 'don't know' did not consume these beverages. Patients estimated that

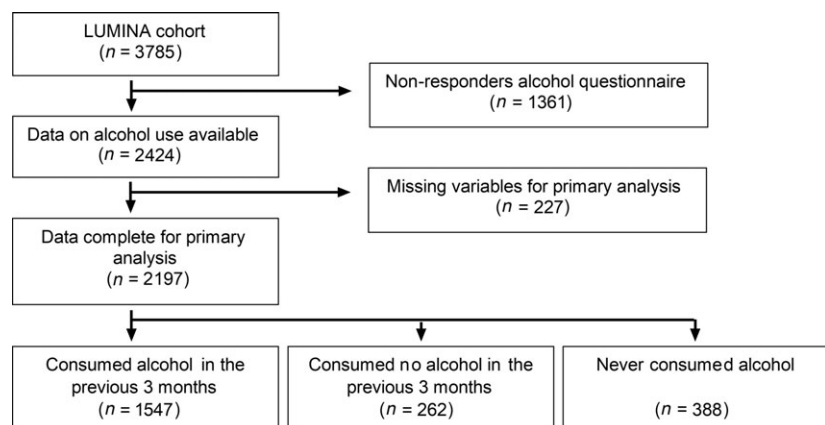
$2.18 \pm 1.3$  (red wine) or  $2.16 \pm 1.9$  (vodka) standard glasses had to be consumed to initiate an attack. However, only 8.8% of patients reported that a migraine attack was provoked consistently (every time) after red wine consumption and 10.7% after vodka consumption. Only 46.5% and 53.6% of patients reported that an attack provocation occurred on >50% of occasions after red wine or vodka consumption. The percentage of patients reporting a migraine attack after red wine and vodka consumption is plotted in Fig. 3. Time of onset was rapid (<3 h) in one-third of patients and almost 90% had an onset <10 h independent of beverage type.

### Effect on alcohol consumption

Overall, 1547 (70.4%) patients with migraine consumed alcoholic beverages during the previous 3 months, whereas 262 (11.9%) patients had stopped consuming alcohol and 388 (17.7%) patients had never consumed alcohol. Patients not consuming alcohol were older, more often women, with a higher BMI and migraine severity (Table S3). Of the 650 patients with migraine not consuming alcohol, 168 (25.8%) had stopped consuming alcohol because it provoked migraine attacks (105/650, 16.2%) or were told by others that this might provoke attacks (9/650, 1.4%) or had never consumed alcohol (54/650, 8.3%) because they were told by others alcohol might provoke attacks. The complete list of reasons why patients had stopped consuming or had never consumed alcoholic beverages can be found in Table 2.

## Discussion

In this large migraine cohort, we investigated migraine trigger frequencies of different alcoholic beverages, trigger consistency, time to attack onset and the effect



**Figure 1** Study flowchart. LUMINA, Leiden University MIgraine Neuro-Analysis project.

**Table 1** Leiden University MIgraine Neuro-Analysis (LUMINA) cohort characteristics of 2197 patients with migraine separated between alcohol consumption and recognition of alcoholic beverages as a migraine trigger

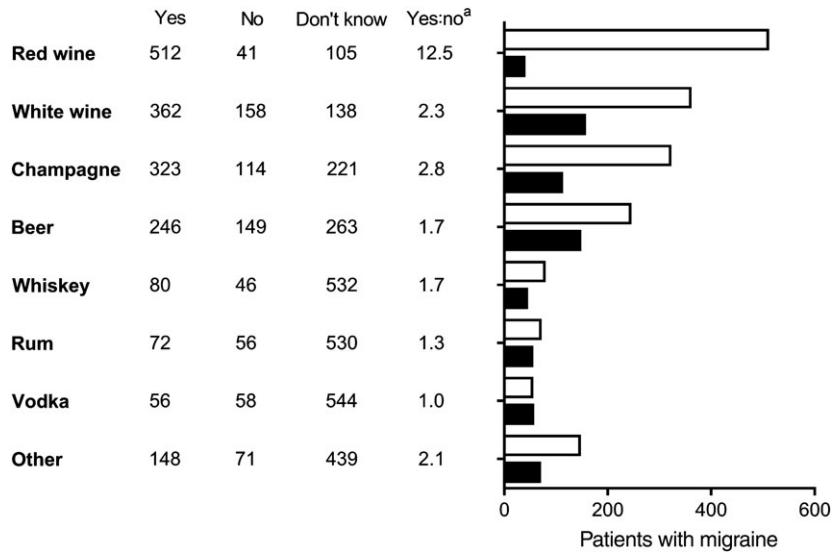
	Total population <i>n</i> = 2197	Never consumed alcohol <i>n</i> = 388	Consumed no alcohol in the previous 3 months <i>n</i> = 262	Consumed alcohol in the previous 3 months		<i>P</i> -value	
				Alcohol trigger ( <i>n</i> = 658)	No alcohol trigger ( <i>n</i> = 694)		
Gender (female)	1887 (85.9)	360 (92.8)	228 (87.0)	1299 (84.0)	549 (83.4)	585 (84.3)	0.67
Age (years) <sup>a</sup>	46.1 ± 12.0	48.0 ± 11.5	45.7 ± 11.9	45.7 ± 12.1	46.3 ± 12.0	45.3 ± 12.4	0.13
BMI (kg/m <sup>2</sup> ) <sup>b</sup>	24.6 ± 4.3	25.3 ± 4.9	24.8 ± 4.8	24.4 ± 4.0	24.1 ± 3.8	24.7 ± 4.3	<b>0.01</b>
Age at onset of migraine (years) <sup>a</sup>	18.9 ± 10.4	19.6 ± 10.8	18.1 ± 9.7	18.9 ± 10.3	19.0 ± 10.5	18.8 ± 10.1	0.61
Migraine without aura	1346 (61.3)	238 (61.3)	157 (59.9)	951 (61.5)	456 (69.3)	376 (54.2)	<b>&lt;0.001</b>
Migraine duration (years) <sup>a</sup>	27.2 ± 13.4	28.4 ± 13.4	27.6 ± 13.1	26.8 ± 13.4	27.3 ± 13.2	26.6 ± 13.8	0.33
Migraine attack frequency (per year) <sup>c</sup>							<b>&lt;0.001</b>
1–2	78 (3.6)	13 (3.4)	7 (2.7)	58 (3.7)	9 (1.4)	41 (5.9)	
3–6	282 (12.8)	44 (11.3)	30 (11.5)	208 (13.4)	51 (7.8)	131 (18.9)	
7–12	628 (28.6)	93 (24.0)	69 (26.3)	466 (30.1)	188 (28.6)	211 (30.4)	
13–54	966 (44.0)	182 (46.9)	119 (45.4)	665 (43.0)	330 (50.2)	255 (36.7)	
>54	243 (11.1)	56 (14.4)	37 (14.1)	150 (9.7)	80 (12.2)	56 (8.1)	
Migraine days (per year) <sup>c</sup>							<b>&lt;0.001</b>
1–2	105 (4.8)	21 (5.4)	12 (4.6)	72 (4.7)	17 (2.6)	44 (6.3)	
3–6	192 (8.7)	23 (5.9)	18 (6.9)	151 (9.8)	40 (6.1)	92 (13.3)	
7–12	359 (16.3)	55 (14.2)	36 (13.7)	268 (17.3)	91 (13.8)	141 (20.3)	
13–54	1021 (46.5)	168 (43.3)	107 (40.8)	746 (48.2)	352 (53.5)	298 (42.9)	
>54	520 (23.7)	121 (31.2)	89 (34.0)	310 (20.0)	158 (24.0)	119 (17.1)	
Alcohol consumption (days/month) <sup>b,d</sup>	7.3 ± 7.7	NA	4.5 ± 6.8	7.8 ± 7.8	7.5 ± 7.3	8.5 ± 8.4	0.14
Beverages on day of alcohol use ( <i>n</i> ) <sup>b,d</sup>	2.0 ± 2.1	NA	1.9 ± 2.2	2.1 ± 2.1	2.2 ± 2.2	2.0 ± 1.8	<b>0.02</b>
Red wine consumption (days/month) <sup>b,d</sup>	3.2 ± 6.0	NA	1.4 ± 3.4	3.5 ± 6.3	2.8 ± 5.3	4.4 ± 7.3	<b>0.001</b>
Vodka consumption (days/month) <sup>b,d</sup>	0.1 ± 0.8	NA	0.3 ± 1.7	0.1 ± 0.5	0.1 ± 0.5	0.1 ± 0.6	<b>0.04</b>

BMI, body mass index; NA, not applicable. Values represent absolute numbers with corresponding means ± SD or percentages. *P*-values are determined using independent-samples *t*-tests (<sup>a</sup>normally distributed) or Mann–Whitney *U*-tests (<sup>b</sup>non-normally distributed) for continuous data or chi-squared tests in case of categorical data. *P*-values depicted in bold (*P* < 0.05) indicate significant differences. <sup>c</sup>Migraine attack frequency and number of migraine days per year were self-reported estimates. Few (*n* = 15) patients reported more than one attack on a single day, probably because migraine recurrences were counted as new attacks. <sup>d</sup>Data from *n* = 1809 patients, people actively drinking (*n* = 1547) were asked about alcohol use during the last month, whereas people not currently consuming alcohol (*n* = 262) were asked how much was consumed in the past.

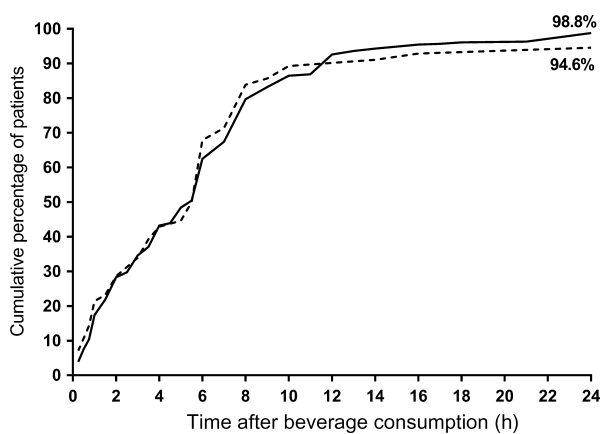
that this has on alcohol consumption behavior. Alcoholic beverages are reported by 35.6% of patients as a trigger for attacks. Red wine is indicated as the most common trigger among the alcoholic beverages, although it consistently leads to an attack in only 8.8% of participants. Time to onset is rapid (<3 h) in one-third of patients, with almost 90% having an onset <10 h independent of beverage type. Finally, our study shows the effect that this trigger has on patients with over 25% of patients with migraine not

consuming alcohol because of the (presumed) triggering effect.

Migraine has been associated with reduced alcohol consumption. However, the reasons behind this association have not been explored in detail [14,15,18]. We find that the behavioral effect of alcohol triggers is considerable as this is a major reason for patients to stop consuming alcohol and patients who report alcohol as a trigger consume less red wine. A total of 16% of patients who stopped consuming alcohol did



**Figure 2** Beverages reported to trigger a migraine attack. The category 'champagne' also includes other sparkling wines and category 'other' includes other types of alcoholic beverages apart from those listed. <sup>a</sup>Yes:no ratio of each individual beverage. □, yes; ■, no.



**Figure 3** Reported time of onset of migraine after red wine or vodka consumption. The x-axis was truncated at 24 h. Nine participants who reported time of migraine onset after either red wine (two after 48 h and four after 72 h) or vodka (three after 72 h) consumption are not displayed. Solid line, red wine ( $n = 512$ ); dashed line, vodka ( $n = 56$ ).

so because it triggered their attacks, which is a much higher percentage than reported in a previous study [18]. However, in that study young people (minimum inclusion age of 14 years) who abstained from alcohol were also included, making the studies not comparable [18]. In our present study, the belief that alcohol acts as a migraine trigger is illustrated by 10% of patients refraining from alcohol because they were told by others that it would trigger attacks without experiencing this themselves.

In a small percentage of patients reporting to be sensitive to red wine or vodka, attacks are triggered

consistently. This triggering inconsistency is also seen in most of the prospective studies [17,25,27–29]. We hypothesize that low consistency does not contradict the potential triggering effect of alcoholic beverages because the triggering potential depends on the susceptibility status of the patient to have an attack. Internal fluctuations in neuronal excitability creating a fluctuating trigger threshold [4,30] likely influence susceptibility status, as does the co-occurrence of other external triggers [25,31]. This is illustrated by patients with more severe migraine who more often report alcohol as a trigger factor, making the association between triggers and attack provocation a complex one [25,31].

In order to identify if ethanol in general or certain specific beverages were responsible for this effect, we presented patients with a list composed of seven different beverages. Wine, especially red wine, was recognized as the most frequent migraine-provoking beverage. These results are consistent with previous findings, with wine being regarded as a migraine trigger factor for decades [16,17,32]. In Europe, results differ between countries, with red wine being reported most often in the UK and white wine most often in France and Italy [14,15,32]. This inconsistency has been speculated to be caused by differences in the popularity and availability of particular beverages across countries [14]. Vodka was identified as the least frequent migraine-provoking beverage but this might be because wine is consumed on a more regular basis compared with vodka. This is certainly true for our cohort. Other studies also report a low triggering potential for vodka or other spirits

**Table 2** Alcohol consumption in the study population and reasons for abstaining from alcohol consumption

	Migraine with aura	Migraine without aura	Total
Total population	851 (38.7)	1346 (61.3)	2197
Subjects who consumed alcohol	596 (38.5)	951 (61.5)	1547
Reasons why subjects never consumed alcohol	150 (38.7)	238 (61.3)	388
For preventative reasons because subjects heard from others that alcohol consumption in general or the consumption of certain alcoholic beverages could provoke migraine attacks	20 (37.0)	34 (63.0)	54
Because alcohol is harmful	27 (41.5)	38 (58.5)	65
Because of any other reason(s)	103 (38.3)	166 (61.7)	269
Reasons why subjects did not consume alcohol in the last 3 months	105 (40.1)	157 (59.9)	262
Because alcohol consumption in general or the consumption of certain alcoholic beverages could provoke a migraine attack in these subjects	42 (40.0)	63 (60.0)	105
For preventative reasons because subjects heard from others that alcohol consumption in general or the consumption of certain alcoholic beverages could provoke migraine attacks (they themselves have never consciously experienced this)	4 (44.4)	5 (55.6)	9
Because alcohol is harmful	11 (35.5)	20 (64.5)	31
Because of any other reason(s)	48 (41.0)	69 (59.0)	117

Values represent absolute numbers with corresponding percentages.

[17,33,34]. It has been suggested that this might be due to certain biochemical compounds being present in wine and not in other beverages, which would imply that ethanol is not the main culprit [14,27]. Various compounds such as histamine, tyramine, phenylethylamine and flavonoids have been suggested, however, results are inconsistent [14,27] and remain to be studied in more detail.

On average, patients report relatively few standard glasses ( $2.18 \pm 1.3$  glasses for red wine and  $2.16 \pm 1.9$  glasses for vodka) to be consumed to provoke an attack. This may be a reflection of a common number of glasses consumed over dinner or at a party, suggested by the two glasses that the total population drinks on average. A similar amount (two standard glasses) was used in the earliest provocation experiments with alcohol [17]. A relatively large percentage of attacks occurs within 3 h after red wine (34.6%) or vodka (33.9%) consumption, which is in line with previous smaller studies [17,18]. Therefore, it seems unlikely that the pathophysiological pathway is similar to that of hangover headaches (termed delayed alcohol-induced headache in the ICHD-3) [24]. Hangover headache typically occurs when the blood ethanol concentration is declining and is characterized by a typically bilateral pulsating headache aggravated by physical activity without accompanying features [24,35]. Although, in the ICHD-3, headache attacks within 3 h after alcohol consumption are classified as immediate alcohol-induced headaches, the criteria partially overlap with migraine making it complicated to differentiate between a triggered migraine attack and an alcohol-induced headache [24].

Strengths of the current study include the large cohort of well-defined patients with migraine with and without aura, in which detailed information on the triggering capabilities of alcoholic beverages was collected and its effect on patients' alcohol consumption behavior is assessed. Possible limitations of the current study are the retrospective nature and our LUMINA population being predominantly Dutch Caucasian, of relatively young age and recruited via the Internet. We therefore cannot extrapolate our results to other ethnic groups or populations from different socioeconomic backgrounds. Furthermore, responders to our questionnaire had a higher BMI, were older with a longer disease duration, higher attack frequency and number of migraine days per year compared with non-responders. This higher migraine burden probably motivated patients to participate in the current study. Therefore, we cannot exclude some degree of selection bias. Finally, we did not include a control group in the present study, because we decided to focus on various beverages and their relation to migraine attack provocation specifically and not headache in general.

Our results illustrate that alcoholic beverages are frequently recognized as migraine trigger factors and have a substantial effect on alcohol consumption behavior. It can be debated if alcohol is a factual or a presumed trigger. Low consistency of provocation suggests that alcoholic beverages acting as singular migraine trigger is insufficient and may depend on a fluctuating trigger threshold. To further study and unravel this relationship in patients, a three-step model may be applied: (i) a headache-trigger diary to screen for a temporal relation between the suspected

trigger and attack onset; (ii) assign the trigger to different occasions (susceptibility status) in order to check if triggering occurs consistently; and if other triggers are involved (iii) prospectively investigate whether behavioral change of alcohol consumption is of influence on attack occurrence.

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### Disclosure of conflicts of interest

G.G.S. reports support for a conference visit from Pfizer. G.M.T. reports independent support from NWO, ZonMW, the Dutch Heart Foundation, the Dutch Brain Foundation and the European Community. M.D.F. reports grants and consultancy or industry support from Medtronic, and independent support from NWO, ZonMW, NIH, the European Community and the Dutch Heart Foundation. The other authors report no conflicts of interest.

### Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Data S1.** Leiden University MIgraine Neuro-Analysis (LUMINA) background information.

**Table S1.** Non-response analysis.

**Table S2.** Leiden University MIgraine Neuro-Analysis (LUMINA) cohort characteristics of 658 patients with migraine who reported an alcohol trigger separated between patients with migraine with and without aura.

**Table S3.** Leiden University MIgraine Neuro-Analysis (LUMINA) cohort characteristics of 2197 patients with migraine separated between alcohol-consuming and non-alcohol-consuming patients.

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