Acute medication overuse in people with migraine from the 2022 European National Health & Wellness Survey

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INTRODUCTION

- Acute medication overuse (AMO) is a cycle of high frequency analgesic use to acutely treat headache that may result in medication overuse headache (MOH)[1]
- AMO is assessed in two ways (over 1 month period):
  - **Criterion 1:** Use of triptans, combination analgesics, ergotamines, or opioids for ≥ 10 cumulative days in month
  - **Criterion 2:** Use of nonopioid analgesics, acetaminophen, or NSAIDs for ≥ 15 cumulative days in month
- There is limited understanding of the frequency of analgesic use for both prescription and over-the-counter (OTC) medications that contribute to AMO in people with migraine (PwM).
- The objective of this study was to estimate the prevalence of AMO among PwM and assess the characteristics of the AMO population in Europe.

METHODS

- **Study Design:** Retrospective analysis of cross-sectional survey
- **Data Source:** 2022 5-country (UK, France, Germany, Spain, Italy) European National Health and Wellness Survey (NHWS, Cerner Enviza) is an annual, self-reported patient survey, using quota-sampling to ensure demographics are representative of the population.
- **Study Sample**:
  - Adult respondents who self-reported having physician-diagnosed migraine
  - Current use of ≥ 1 acute prescription or OTC medication
- Analgesic use information was derived from 1) the migraine disease module only and 2) all pain-related disease modules completed by PwM — these included migraine, pain, arthritis, IBS, and lupus.
- **Measures**: Patient-reported outcome measures included the SF-12, EQ5D 5L, work productivity & activity impairment (WPAI), PHQ-9, and healthcare utilization.
- **Statistical Analysis:** Presence of AMO (meeting criterion 1 or 2) was determined based on number of days with analgesic use in the past month.
  - AMO was separately assessed with medications used only for migraine and adding those for other indications (pain, arthritis, IBS, and lupus).
- PwM with AMO and without AMO were compared using survey weights to represent the adult population in Europe.

RESULTS

Prevalence of Acute Medication Overuse (AMO)

- Among over 16.7 million PwM represented by the survey, 21.2% reported AMO of migraine-specific medications. The prevalence of AMO among all analgesic use was 36.9% **(Table 1)**.
- With migraine-specific analgesics, over half (51.4%) met the first AMO criterion with a cumulative mean of 21.0 (14.1) days and 61.5% met the second criterion with 28.3 (15.9) cumulative days **(Table 1)**.

Table 1. Prevalence of acute medication overuse among treated patients with migraine

	Migraine-specific (N = 16,774)	All analgesic (N = 18,391)
Acute medication overuse (AMO), n (%)	3,554 (21.2%)	6,783 (36.9%)
AMO criterion 1, n (%)	1,828 (51.4%)	3,431 (50.6%)
Cumulative days of use*, mean (SD)	21.0 (14.1)	37.0 (38.2)
AMO criterion 2, n (%)	2,185 (61.5%)	4,969 (73.3%)
Cumulative days of use*, mean (SD)	28.3 (15.9)	44.1 (42.3)

*Days of medication use was reported separately for each medication and disease state. Since days of use could overlap, the sum of medication use may be greater than 30 days.

Demographics and clinical characteristics

Patient demographics and employment status were similar across PwM with AMO vs those without **(Table 2)**.

People with vs. without AMO tended to have **(Table 2)**:

- Higher mean MMD (7.8 vs 3.6) and higher mean MHD (12.3 vs 5.8) respectively.
- Higher mean MIDAS score (37.1 vs 16.2), with a much higher proportion of patients with Grade IV (49.4% vs 25.2%).

37.0% of PwM with AMO had ≥15 monthly headache days (MHD) compared with 9.9% of those without AMO **(Figure 1)**.

Table 2. Demographic characteristics of patients with migraine-specific analgesic use, with and without AMO

Characteristics	With AMO* (N = 3,544)	Without AMO (N = 13,220)
Age (years), mean (SD)	45.9 (14.4)	44.7 (15.2)
Sex, n (%)		
Male	1,081 (30.4%)	3,977 (30.1%)
Female	2,474 (69.6%)	9,243 (69.9%)
Employed, n (%)		
Yes	2,109 (59.3%)	8,346 (63.1%)
No	1,214 (34.1%)	4,382 (33.2%)
Disabled (Long-term/short-term)	232 (6.5%)	492 (3.7%)
Monthly migraine days (MMD), mean (SD)	7.8 (7.7)	3.6 (4.8)
Monthly headache days (MHD), mean (SD)	12.3 (8.5)	5.8 (6.0)
MIDAS score, mean (SD)	37.1 (46.0)	16.2 (24.9)
MIDAS score groups, n (%)		
Grade I (Little/No Disability)	912 (25.7%)	5,293 (40.0%)
Grade II (Mild Disability)	342 (9.6%)	2,083 (15.8%)
Grade III (Moderate Disability)	544 (15.3%)	2,518 (19.1%)
Grade IV (Severe Disability)	1,756 (49.4%)	3,326 (25.2%)

*AMO = Acute Medication overuse; AMO calculated based on migraine-specific analgesic use only

Medication Use

- PwM with AMO versus without AMO reported higher use of prescribed triptans (38.4% vs. 29.9%), NSAIDs (66.4% vs. 51.4%), and opioids (33.6% vs. 12.5%) **(Table 3)**.
- PwM with AMO reported increased OTC use including 5.2 (3.1) days of triptan use, 10.4 (7.7) days of NSAIDs, 12.3 (8.5) days of acetaminophen, and 10.7 (7.8) days of combination analgesics **(Figure 2)**.
- PwM with AMO reported increased prescription use including 11.0 (7.9) days of triptan use, 15.2 (9.0) days of NSAIDs, 14.4 (10.7) days of opioids, and 12.0 (9.6) days on ergots **(Figure 2)**.

Figure 1. Distribution of monthly headache days (MHD) among patients treated with migraine-specific analgesics

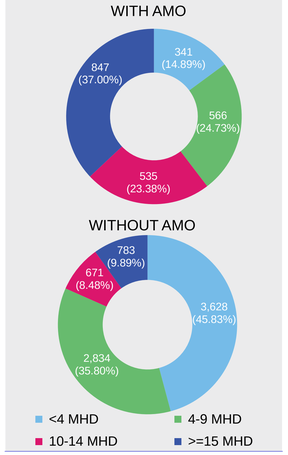
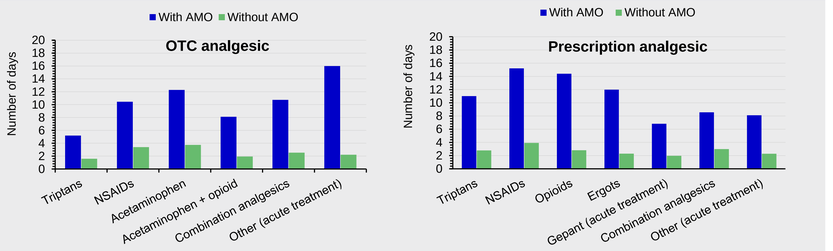


Table 3. Migraine-specific medication use, with and without AMO

Characteristics, n (%)	With AMO* (N = 3,554)	Without AMO (N = 13,220)
Medication type		
Rx only	1,712 (48.2%)	5,704 (43.2%)
Rx and OTC	407 (11.4%)	4,085 (30.9%)
OTC only	1,436 (40.4%)	3,432 (26.0%)
Current prescription analgesics		
Triptans	1,208 (38.4%)	2,732 (29.9%)
NSAIDs	2,089 (66.4%)	4,697 (51.4%)
Opioids	1,058 (33.6%)	1,144 (12.5%)
Ergots	110 (3.5%)	181 (2.0%)
Gepant (acute treatment)	21 (0.7%)	12 (0.1%)
Combination analgesics	48 (1.5%)	102 (1.1%)
Other (acute treatment)	39 (1.3%)	86 (1.0%)
Current OTC analgesics		
Triptans	73 (4.0%)	264 (3.5%)
NSAIDs (Sole ingredient)	773 (41.9%)	2,903 (38.6%)
Acetaminophen (Sole ingredient)	622 (33.8%)	1,776 (23.6%)
Acetaminophen and opioid	117 (6.4%)	310 (4.1%)
Combination analgesics	171 (9.3%)	474 (6.3%)
Other (acute treatment)	55 (3.0%)	42 (0.6%)

*AMO = Medication overuse; AMO calculated based on migraine-specific analgesic use only

Figure 2. Number of days of migraine-specific OTC and prescription analgesic use in past month



Quality of Life, Productivity, and Healthcare Utilization

- PwM with AMO reported lower quality of life: SF-12 mental and physical health composite T mean (SD) scores: 33.1 (10.9) & 36.3 (10.8) respectively for those with AMO, vs 36.4 (10.6) and 40.4 (10.2) for those without AMO **(Table 4)**.
- Health status, as assessed by EQ5D summary and VAS scores, was also lower for those with AMO vs those without **(Table 4)**.
- PwM with AMO also had higher degrees of activity impairment regardless of employment status, suffered great productivity loss if employed, and were more likely to be severely depressed (11.8% vs 6.6% without AMO) **(Table 4)**.
- Patients with AMO were also more likely to receive treatment at the emergency department (35.0 vs. 24.1%), hospital setting (20.6 vs. 13.7%), and neurologist (21.9 vs. 11.7%) in the past 6 months **(Table 4)**.

Table 4. Health outcomes of patients with migraine-specific analgesic use, with and without AMO

Characteristics	With AMO* (N = 3,554)	Without AMO (N = 13,220)
SF-12, mean (SD)		
Mental health composite T score	33.1 (10.9)	36.4 (10.6)
Physical health composite T score	36.3 (10.8)	40.4 (10.2)
EQ5D-5L summary score, mean (SD)	0.6 (0.3)	0.7 (0.3)
EQ5D-5L VAS Score (0-100), mean (SD)	52.8 (27.7)	60.7 (26.3)
Work Productivity & Activity Impairment (WPAI), mean (SD)		
Work productivity loss among employed	47.6 (29.6)	40.5 (31.1)
Activity impairment among employed	47.2 (27.5)	38.6 (28.0)
Activity impairment among unemployed	54.0 (27.2)	44.9 (27.2)
Activity impairment among disabled	77.4 (17.2)	68.9 (20.6)
PHQ-9 Depression Scale, n (%)		
None - Minimal depression	772 (21.7%)	4,026 (30.5%)
Mild depression	917 (25.8%)	3,947 (29.9%)
Moderate depression	808 (22.8%)	2,789 (21.1%)
Moderately severe depression	637 (17.9%)	1,585 (12.0%)
Severe depression	420 (11.8%)	874 (6.6%)
Healthcare Resource Utilization, n (%)		
Visited ER in past six months	1,243 (35.0%)	3,187 (24.1%)
Been hospitalized in past six months	731 (20.6%)	1,816 (13.7%)
Visited Neurologist	777 (21.9%)	1,551 (11.7%)

*AMO = Medication overuse; AMO calculated based on migraine-specific analgesic use only

CONCLUSIONS

There is a high prevalence of AMO among PwM utilizing acute treatments for their migraine in Europe.

- NSAIDs are the most used prescribed treatment as well as the most used OTC, being used more frequently by patients with AMO.
- Compared to individuals without AMO, those with AMO experienced worse quality of life, higher migraine disability scores, decreased productivity, and increased use of healthcare resources.
- Treatments not associated with developing MOH are needed for this patient population.

Limitations

PwM with higher headache and migraine attack frequencies are more likely to use acute medications and be at risk of developing AMO. Through subgroup analyses, we confirmed a direct relationship between MHDs and AMO prevalence, however, we were unable to determine whether the outcomes of those with AMO were due to the underlying disease severity or burden of AMO.

REFERENCES

1: Schwedt TJ, et al. *Neurol Clin Pract.* 2021 Jun;11(3):216-226

CONFLICTS OF INTEREST

GC has received honoraria for participation in clinical trials and contribution to advisory boards or presentations from TEVA, Biohaven, Eli Lilly, Abbvie, and Pfizer. He serves as an Associate Editor for Cephalalgia, BMC Neurology – Pain section, Frontiers in Neurology – Neurotechnology section, Frontiers in Human Neuroscience – Brain Imaging and Stimulation section, and on the Advisory Board of The Journal of Headache and Pain. AG reports financial support for ad boards, consulting and speaker honoraria from: Grünenthal, Mundipharma, Abbvie/Allergan, Lilly, Teva, Amgen, Novartis, Hormosan, Stada, Lundbeck, Pfizer, Hexal, Esanumperfood, Medscape, streamed up, Ärztekammer Nordrhein, Ärztekammer Westfalen Lippe, DGS, Regionalbeauftragte der DMKG. ML, AJ, JC, KHB, JY, LA, and JB, are employed by and own stock or holds stock option in Pfizer.

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