

REAL-WORLD OUTCOMES AMONG EPISODIC MIGRAINE PATIENTS WITH MIGRAINE PREVENTIVE MEDICATIONS IN CHINA: RESULTS FROM THE CHINESE ADELPHI DISEASE SPECIFIC PROGRAMME™

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BACKGROUND

- Migraine is a primary headache disorder, which is the second highest cause of years lived with disability with an estimated global prevalence of 14.4%^[1].
- A population-based survey estimated that the 1-year prevalence of migraine in China was 9.3%^[2].
- Migraine adversely impact patients' physical and emotional functioning, leading to reduced productivity, restricted daily and social activities, increased economic burden, and an overall decline in health-related quality of life (HRQoL)^[3-4].
- Pharmaceutical management options for migraine include acute treatment to relieve pain during an attack or to limit an attack, and preventive medication^[5].
- The purposes of migraine preventive medication include: 1) reducing the frequency, severity and disability associated with migraine attacks; 2) improving responsiveness to treatment of acute attacks; 3) reducing overuse of acute medications; and 4) preventing episodic migraine from deteriorating to chronic migraine^[6-7].
- The European Eurolight study and American Migraine Prevalence and Prevention (AMPP) study estimated 34% to 39% of patients with migraine were eligible for preventive migraine treatment^[8-9]. However, both studies suggested undertreatment and inadequate disease management.
- An epidemiological survey demonstrated significant deficiencies in the treatment of migraine patients in China, mainly manifested in insufficient preventive treatment, low visiting rate and overuse of analgesics^[10]. A retrospective analysis of the China Health Insurance Research Association (CHIRA) reported only 15% of migraine patients received preventive medication, of which calcium channel antagonists, β 1-receptor antagonists and antiepileptics were prescribed to 88.3%, 8.4% and 2.7% of patients, respectively^[11].

OBJECTIVE

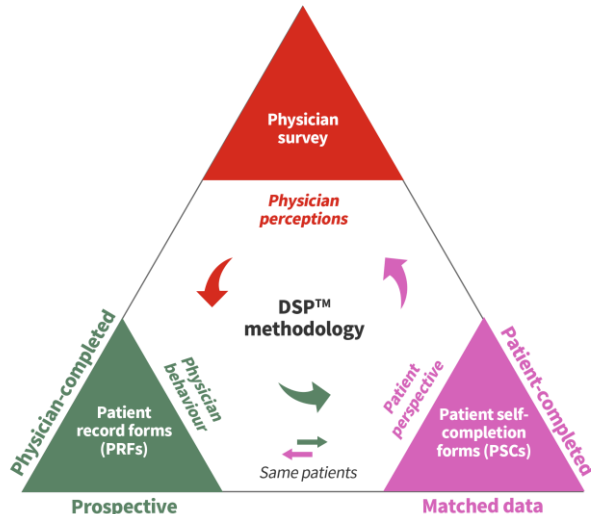
- To estimate the disease burden and unmet needs among Chinese migraine patients, both in those who were preventive-naïve and those receiving preventative treatment.

METHODS

STUDY DESIGN

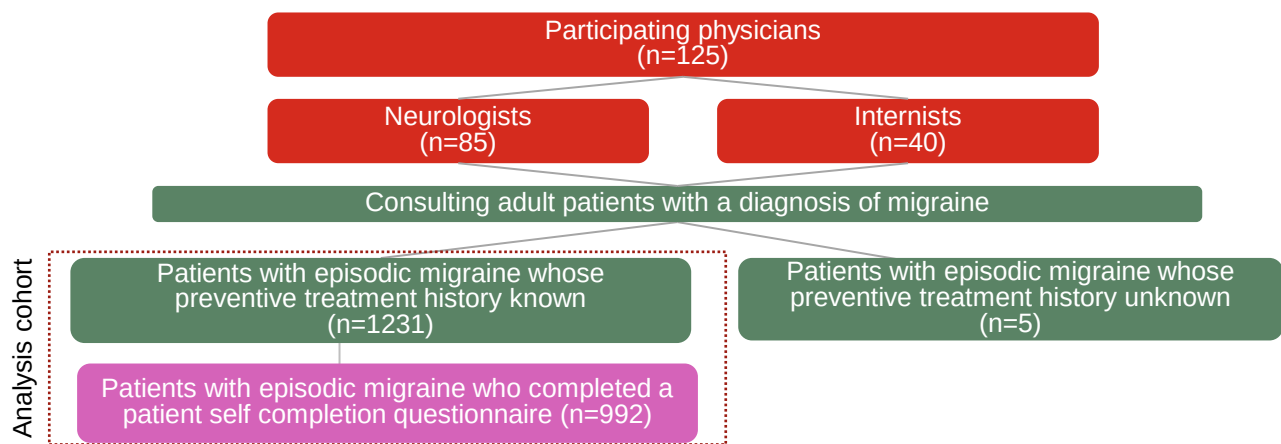
- Data were collected from the Adelphi Migraine Disease Specific Programme™, a point-in-time real-world survey involving physicians and their consulting patients conducted in China between January and June 2014.
- The survey's methodology (Figure 1) has been previously published and validated^[12-13].

Figure 1: Adelphi Migraine Disease Specific Programme – Methodology



- Physicians and patients provided written informed consent to participate in the survey.
- Physicians were either eligible neurologists or internists, who consulted with at least 10 or 5 patients with migraine, in a typical week, respectively. The physicians were required to complete a detailed patient record form for the next 9 consecutively consulting patients (aged 18+) with a diagnosis of migraine. These patients were then invited to independently complete a patient self completion questionnaire. Patients who experienced episodic migraine (14 or fewer headache days, on average, per month over the past 6 months) whose preventive treatment history is known were included in the analysis (Figure 2).

Figure 2: Adelphi Migraine Disease Specific Programme – Analysis Cohort



- Patient record forms captured details on patient demographics, clinical characteristics, treatment patterns (including acute and preventive medication) and unmet needs with current treatment.
 - Patient self completion questionnaires captured information on levels of headache-related disability via the Migraine Disability Assessment Scale (MIDAS)^[14] and work/activity impairment via the Work Productivity and Activity Impairment (WPAI) questionnaire^[15].
 - Patients provided information regarding their level of response to acute treatment, answering 'in approximately how many migraine attacks would you say your prescription acute medicine stops the migraine pain entirely within 2 hours of taking the medication?' (options: 0 to 5 of 5 attacks). Insufficient responder was defined as the patient whose migraine pain was reported to be entirely stopped within 2 hours by acute medication (AM) in ≤ 3 of 5 attacks. Responder was defined as the patient who reported their pain to be entirely stopped within 2 hours by AM in ≥ 3 of 5 attacks.
- ## PATIENT-REPORTED OUTCOMES
- MIDAS:
 - Measures headache-related disability over a 3-month period.
 - Consists of 5 items that reflect the number of days patients reported missing work or experiencing reduced productivity at work or home and social events because of headache. Possible scores range from 0 to 270, with lower scores indicating lower headache-related disability.
 - The sum of responses to the 5 items gives a total MIDAS score that can be mapped to the following disability categories: 0-5 = I: little or no disability, 6-10 = II: mild disability, 11-20 = III: moderate disability, 21-40 = IV-A: severe disability and ≥ 41 = IV-B: very severe disability.
 - WPAI:
 - Measures work and activity impairment related to health problems over the last 7 days.
 - 4 scores are calculated: absenteeism (work time missed), presenteeism (reduced effectiveness while at work), overall work impairment and activity impairment.
 - All domains are measured on a scale of 0-100%, with higher scores indicating greater impairment and less productivity.

STATISTICAL ANALYSIS

- Descriptive summary statistics were generated using Stata 16.1 (StataCorp, College Station, TX, USA).
- Continuous variables were compared using student t-test and categorical variables were compared using Pearson's chi-squared test. Fisher's exact test was applied for 2x2 tables.
- Missing data were not imputed; therefore, the base of patients for analysis varies between variables and is reported separately for each analysis.

RESULTS

- Patients' demographic and clinical characteristics in preventive-naïve and preventive-treated groups are shown in table 1

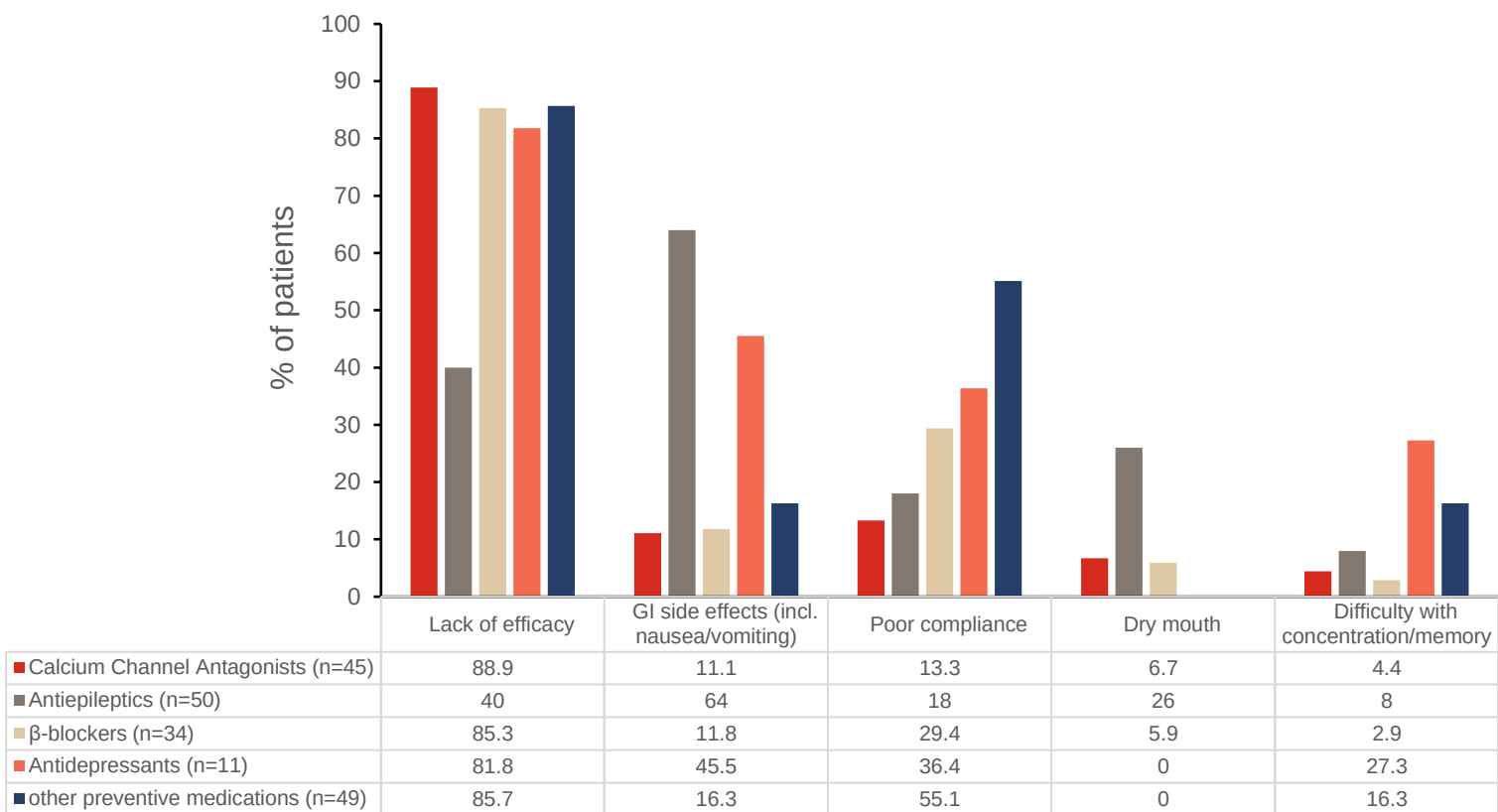
Table 1: Patient demographic/clinical characteristics

	Overall (N=1231)	Preventive-naïve (N=680)	Preventive-treated (past or current) (N=551)	P value
Mean age, years (SD)	44.3 (13.2)	44.3 (13.5)	44.3 (12.8)	0.9769 ^a
Sex, n (%) ^a				
Female	704 (57.2)	347 (51.0)	357 (64.8)	<0.0001 ^b
Male	527(42.8)	333 (49.0)	194 (35.2)	
Employment status, n (%)				
Employed-Full time	747 (60.8)	416 (61.3)	331 (60.3)	0.0884 ^c
Employed-Part time	19 (1.6)	11 (1.6)	8 (1.5)	
Student	37 (3.0)	26 (3.8)	11 (2.0)	
Unemployed	26 (2.1)	9 (1.3)	17 (3.1)	
Others (retired/homemaker/others)	399 (32.5)	217 (32.0)	182 (33.2)	
Concomitant conditions ^{**} , n (%)				
Anxiety [*]	87 (7.1)	16 (2.4)	71 (13.0)	<0.0001 ^b
Sleep disorders [*]	103 (8.4)	35 (5.2)	68 (12.4)	
Hypertension [*]	209 (17.1)	62 (9.1)	147 (26.8)	<0.0001 ^b
Ischaemic heart disease	11 (0.9)	7 (1.0)	4 (0.7)	
Post myocardial infarction	10 (0.8)	8 (1.2)	2 (0.4)	0.1996 ^d
Diabetes	121 (9.9)	67 (9.9)	54 (9.9)	1 ^a
Hyperlipidaemia	93 (7.6)	54 (8.0)	39 (7.1)	0.5897 ^e
Menstrual disorders	64 (5.2)	31 (4.6)	33 (6.0)	0.3016 ^e
Congestive heart failure	7 (0.6)	6 (0.9)	1 (0.2)	0.1387 ^e
No comorbidities [*]	564 (46.0)	352 (51.9)	212 (38.7)	<0.0001 ^b
Mean monthly migraine headache days [*] (SD)	3.2 (1.7)	2.8 (1.7)	3.7 (1.6)	<0.0001 ^a
Mean Total monthly headache days [*] (SD)	3.6 (1.9)	3.1 (1.8)	4.2 (1.8)	<0.0001 ^a

SD, standard deviation; *Significant difference found between preventive-treated and preventive-naïve patients; **Most frequently experienced concomitant conditions ($\geq 5\%$ in overall population) and key cardiovascular conditions are shown; ^a Student t-test; ^b Fisher' exact test; ^c Pearson's chi-square test.

- 85 neurologists and 40 internists completed 1231 patient record forms for patients with episodic migraine; 992 of these patients completed the patient self completion questionnaire. The preventive-treated subpopulation had a higher proportion of female patients in comparison to preventive-naïve subgroup (64.8% vs 51.0%), showing a statistically significant difference in gender distribution ($p<0.0001$). Most patients were at working age (44.3 ± 13.5 vs 44.3 ± 12.8) and statistically significant differences were not found in patient age ($p=0.98$) and employment status ($p=0.09$) between preventive-naïve and preventive-treated subgroup. The most frequently experienced comorbidities ($\geq 5\%$) were included and analyzed as shown in table 1. The percentage of patients without comorbidities was statistically significantly less in preventive-treated subgroup than preventive-naïve patients (38.7% vs 51.9%, $p<0.0001$). Both mean total migraine headache days and total headache days per month were statistically significant greater in preventive-treated subgroup than preventive-naïve patients (both $p<0.0001$).
- The preventive-treated subgroup had a significantly lower insufficient response rate to current acute treatment than preventive-naïve subgroup (37.3% vs 47.4%, " $p=0.0049$) ("Fisher' exact test).
- Among preventive treated group, the most frequently-used medication was calcium channel antagonists (58.6%), followed by β -blockers (21.6%), antiepileptics (19.4%), and antidepressants (9.3%). 16.2% patients used preventive medication other than the above class.
- Lack of efficacy was the main reason for switching away from a regimen that contained calcium channel antagonists, β blockers or antidepressants in 88.9%, 85.3% and 81.8% of patients, respectively. The other common reasons of switching away from previous medications include gastrointestinal (GI) side effects, poor compliance, dry mouth and difficulty with concentration/memory (Figure 3).

Figure 3. Most common reasons for switching from previous preventive medication



- The preventive-treated subgroup reported a statistically significant higher MIDAS than preventive-naïve subgroup (8.2 ± 9.6 vs 4.4 ± 5.5 , $p<0.0001$), indicating a greater headache-related disability in patients who were treated with preventive medications. Consistently, 52.9% of preventive-treated patients reported statistically significantly more mild-to-severe disability in comparison to 26.8% of preventive-naïve subpopulation ($p<0.0001$) (Table 2)

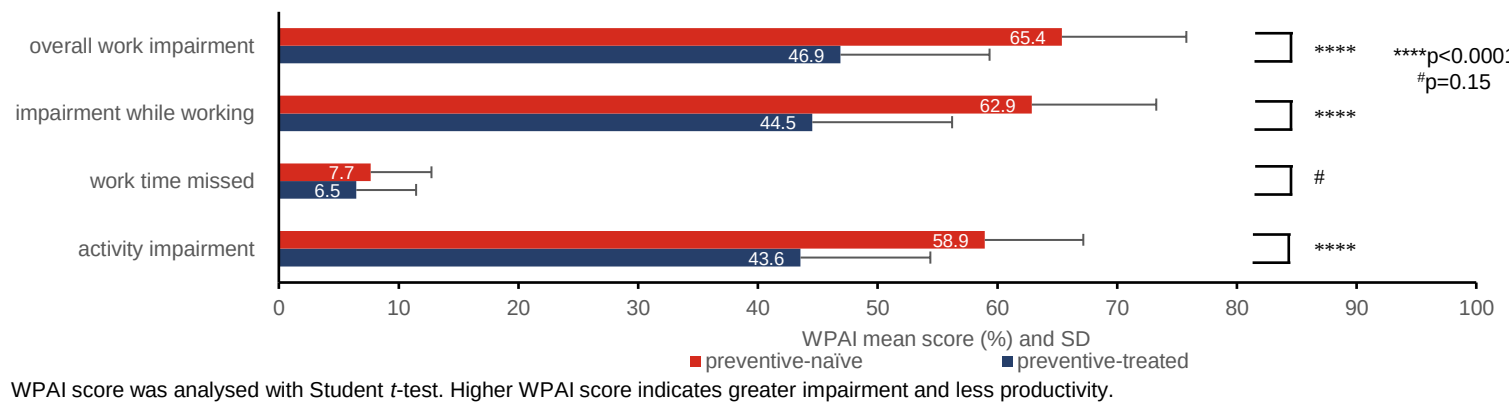
Table 2. Comparison of MIDAS score and MIDAS score in categorized between preventive-treated and preventive-naïve subgroups

	Overall (N=984)	Preventive-naïve (N=593)	Preventive-treated (N=391)	P value
MIDAS score, mean (SD)	5.9 (7.6)	4.4 (5.5)	8.2 (9.6)	<0.0001*
MIDAS score categorized, n (%)				
Grade I: Little/No disability	618 (62.8)	434 (73.2)	184 (47.1)	<0.0001**
Grade II: Mild Disability	194 (19.7)	83 (14.0)	111 (28.4)	
Grade III: Moderate Disability	130 (13.2)	64 (10.8)	66 (16.9)	
Grade IV-A/B: Severe/Very Severe Disability	42 (4.3)	12 (2.0)	30 (7.7)	

SD, standard deviation; *Student t-test; **Pearson's chi-square test.

- Considerable impairment in work productivity for employed patients and regular, non-working activity for all patients were observed in both preventive-treated and preventive-naïve subgroups (Figure 4).

Figure 4. Comparison of WPAI score between preventive-treated and preventive-naïve subgroups



WPAI score was analysed with Student t-test. Higher WPAI score indicates greater impairment and less productivity.

- The preventive-treated subgroup had a statistically significantly lower overall work impairment (including work time missed and impairment while working), presenteeism and non-working activity impairment in comparison to preventive-naïve subgroup ($46.9\%\pm 24.9\%$ vs $65.4\%\pm 20.8\%$, $44.5\%\pm 23.4\%$ vs $62.9\%\pm 20.8\%$, $43.6\%\pm 21.7\%$ vs $58.9\%\pm 16.5\%$, respectively, all $p<0.0001$).
- Absenteeism was fairly low in both subgroups and no statistically significant difference of absenteeism was found between the preventive-treated and preventive-naïve subgroups ($p=0.15$, Figure 4 lower middle), suggesting that patients may attempt to continue to work despite their migraine.

DISCUSSION

- Preventive medication was prescribed for 44.8% (551/1231) of Chinese patients in Adelphi Migraine Disease Specific Programme, which was comparable to 43.8% (622/1418) and 39.5% (1727/4367) of US and EU patients, respectively, who received preventive treatments in the US/EU Adelphi preventive study^[16].
- Preventive-treated patients had a statistically significantly lower insufficient response rate to current acute treatment than preventive-naïve subpopulations.
- Lack of efficacy was the main reason for switching from previous preventive medications, indicating that more effective drugs are needed.
- Similar to US/EU Adelphi Migraine Disease Specific Programme study results^[16], preventive-treated patients reported a statistically significant higher MIDAS than preventive-naïve subpopulations, indicating higher disability and unmet needs for patients who received preventive medication.
- Inconsistent to US/EU Adelphi Migraine Disease Specific Programme study results^[16], preventive-treated patients showed statistically significantly lower WPAI scores in comparison to preventive-naïve subpopulations in our analysis, indicating productivity and activity of migraine patients could be improved by utilization of preventive medication.

CONCLUSIONS

- Our analysis suggested that although patients receiving preventive treatment had lower work productivity impairment and were more likely to respond to acute treatment, there remains considerable unmet needs in terms of migraine related disability.

LIMITATIONS

- While minimal inclusion criteria governed the selection of participating physicians, participation was influenced by willingness to complete the survey.
- Patients were actively consulting, which limits the generalizability of the results to all patients with migraine.
- All data collected relied on accurate reporting by physicians and patients.

DISCLOSURES

- Data collection was undertaken by Adelphi Real World as part of an independent survey, entitled the Adelphi Migraine Disease Specific Programme (DSP™). Eli Lilly and Company, Indianapolis, IN, USA was one of several companies subscribed to the dataset from which this analysis is derived and did not influence study design or data collection.
- Lei Zhang, Junpeng Zhuang and Jinnan Li are employees of Eli Lilly China, Shanghai, China. Sarah Cotton is an employee of Adelphi Real World, Bollington, UK.
- Data availability: all data that support the findings of this study are the intellectual property of Adelphi Real World and so are not publicly available. Data are however available upon reasonable request and with permission of Adelphi Real World (contact sarah.cotton@adelphigrp.com)

REFERENCES

- GBD 2016 Headache Collaborators. Lancet Neurology. 2018; 17: 954–76.
- Shengyuan Yu, et al. Headache. 2012; 52 (4): 582–91.
- Baigi K, et al. Handb Clin Neurol.2015;131:447–463.
- Steiner TJ, et al. J Headache Pain. 2015;16:58.
- Chinese Medical Association Group. Chin J Pain Med 2016; 22: 721–727.
- Buse DC, et al. Cephalalgia. 2018;38(10):1622–1631.
- Shengyuan Yu, et al. Chinese Journal of New Drugs. 2014;23(14):1631–1636.
- Lipton RB, et al. Neurology. 2007;68:343–349.
- Katsarava Z, et al. J Headache Pain. 2018;19:10.
- Liu R, et al. J Headache Pain. 2013 Jun 3;14(1):47.
- Yu S, et al. J Headache Pain. 2020;21(1):53.
- Anderson P, et al. Current Medical Research and Opinion. 2008; 24 (11): 3063–72.
- Bathineaux SM, et al. British Medical Journal Open. 2016; 6: e010352.
- Stewart WF, et al. Neurology. 2001; 56 (6 Supplement 1): S20–28.
- Reilly MC, et al. Pharmacoeconomics. 1993; 4 (5): 353–365.
- Ford J, et al. Clinicoecon Outcomes Res. 2021;13:647–660.

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