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Title	Burden of migraine in patients with preventive treatment failure attending European headache specialist centers: Real-world evidence from the BECOME study
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3 Appendix 1

4 **PRO tools**

5 **EuroQoL 5 dimensions (EQ-5D) questionnaire**

6 The EQ-5D questionnaire comprises of two parts. In the first part, the EQ-5D utility index, patients rated
7 their general health status functioning in five dimensions (mobility, self-care, usual activities,
8 pain/discomfort, and anxiety/depression). The response to each dimension was captured using five levels
9 (no problems, slight problems, moderate problems, severe problems, and extreme problems) to derive
10 the weighted EQ-5D utility index score, with a possible range from 0 (worst) to 1 (perfect health status). In
11 the second part, the EQ-5D visual analogue scale (VAS), patients rated their current HRQoL on a scale
12 ranging from 0 (worst imaginable health status) to 100 (best imaginable health status).

13 **MSQ questionnaire**

14 In the 14-item MSQ questionnaire, the response to each domain was captured at six levels (none of the
15 time, a little bit of the time, some of the time, a good bit of the time, most of the time, and all of the time)
16 and rescaled to a 0 to 100 scale, with higher scores indicating a better HRQoL.

17 **HIT-6 score**

18 The HIT-6 questionnaire reflects participants' self-assessment of the magnitude of the effect of headache
19 on their daily life. The total HIT-6 score (range: 36–78) is a sum of the responses to each item on a five-
20 point scale and is categorized into little or no impact (score ≤ 49), some impact (50–55), substantial impact
21 (56–59), and severe impact (≥ 60), with higher scores indicating a greater impact of headache on daily life.

22 **MIDAS questionnaire**

23 The mMIDAS questionnaire captures missed days of work, missed household chores, missed non-work
24 activity, and $\geq 50\%$ reduced productivity in professional or personal work. The mMIDAS scores (on a scale
25 from 0 to 40) indicate minimal (grade I, 0–5), mild (grade II, 6–10), moderate (grade III, 11–20), or severe
26 (grade IV, 21+) disability experienced by a patient due to migraine. In the BECOME study, a mMIDAS
27 questionnaire with a 1-month recall period was used. Therefore, the total mMIDAS score was multiplied

28 by three to generate a score analogous to the universal 3-month MIDAS score. The proportion of patients
29 with MIDAS disability grades I, II, III, and IV was also analyzed.

30 **WPAI questionnaire for headache**

31 Patients reported WPAI-headache scores on a scale of 0 to 100, with higher scores indicating greater
32 impairment of activity due to migraine. The working population (full time, part time, or self-employed)
33 completed the absenteeism, presenteeism, and overall work productivity loss metrics while all participants
34 completed the activity impairment metric.

35 **HADS questionnaire**

36 The HADS is a self-reported 14-item scale consisting of anxiety and depression subscales of seven items
37 each. With a four-point Likert scale (0–3) scoring to each item, each subscale has a possible score range
38 of 0 to 21, indicating normal (0 to 7), suggested presence (8 to 10), or probable presence (≥ 11) of the
39 mood.

40

41 **Appendix 2**

42 **Description of participating centers**

43 Of the 163 headache specialist centers participating in the study, data from 156 centers were available for Part 1 and
 44 Part 2 endpoint analyses. The size and capacity of the included centers varied widely, reflecting the real-world
 45 differences among healthcare systems. On average, each center had five (range: 1–50) physicians managing
 46 patients with migraine to treat an average of 1140 patients every year (range: 50–12,000). Some centers received as
 47 many as 18,000 referrals per year, whereas others reported none (mean [95% CI] patients referred per year: 1079.9
 48 [0–18,000]). Among the participating sites, 75.6% (118/156) had a dedicated headache clinic and 23.7% (37/156) had
 49 an ED dedicated to headache. Physicians specializing in headache disorders were available to treat patients at
 50 83.3% (130/156) of the participating sites, and 52.6% (82/156) of sites had general neurologists and/or specialist
 51 neurologists (42.9% [67/156]) to treat patients with migraine. Most centers reported following the European
 52 Federation of Neurological Societies/American Academy of Neurology guidelines (119/156, 76.3%) as well as
 53 local/national guidelines (115/156, 73.7%) for migraine/headache management.

Number of sites	Headache specialist centers, N=163
Spain	28 (17.2%)
Germany	24 (14.7%)
France	20 (12.3%)
Greece	15 (9.2%)
Italy	12 (7.4%)
Switzerland	10 (6.1%)
Czech Republic	8 (4.9%)
Portugal	6 (3.7%)
United Kingdom	6 (3.7%)
Belgium	5 (3.1%)
Slovakia	5 (3.1%)
Sweden	5 (3.1%)
Denmark	4 (2.5%)
Ireland	4 (2.5%)
Bulgaria	3 (1.8%)
Croatia	3 (1.8%)
Israel	3 (1.8%)
Slovenia	2 (1.2%)

Supplementary Tables

Table S1. Questionnaire administered to headache specialist centers during Part 1 of the study

Parameters	Outcomes	Items
1. Number of physicians that manage patients with migraines at the center		
2. Dedicated headache clinic at the center?	Yes/No	
3. Inpatient specific service?	Yes/No	
4. Emergency department dedicated to headache?	Yes/No	
5. Leading center in other areas of neurology?	Yes/No	If Yes, Dementia Epilepsy Head trauma/stroke Movement disorder Neurointensive care Sleep disorder Pain Multiple sclerosis Neuromuscular diseases Other
6. Who would treat a migraine patient?		General neurologist Specialist neurologist Headache specialist Another specialist (not neurologist) Multidisciplinary team Other
7. How many nurses are dedicated to migraine and/or headache?		
8. Focus areas for specialist nurses		Review of patients Administration of therapies Monitoring of treatment

		<p>response</p> <p>Prescription of treatments</p> <p>Patient education program training</p> <p>Other</p>
9. Clinical guidelines considered or implemented at the center for the management of headache and migraine?		<p>EFNS/AAN clinical guidelines</p> <p>National guidelines</p> <p>Center-specific guidelines</p> <p>None</p>
10. Any networks/links with other centers for the treatment and management of patients with migraine?		<p>GPs</p> <p>Other center</p> <p>General neurologists</p>
11. Number of people living in the catchment area of the center?		
12. Approximate number of migraine patients treated at the center each year		
13. Number of patients referred to the center each year		
14. Percentage of referrals received by the center	<p>Followed up by this center only</p> <p>Received return to the community/GP or referral neurologist</p> <p>Referred to another headache/migraine center</p>	
15. Percentage of the referrals received from	<p>GPs</p> <p>Other center</p> <p>General neurologists</p>	
16. Main reasons for referral to the center	<p>Acute treatment initiation</p> <p>Acute treatment failure</p> <p>Preventive treatment initiation</p> <p>Preventive treatment failure</p> <p>Patient request</p> <p>Need for differential diagnosis</p> <p>Physician referred to has</p>	

	expertise in migraine Ability to prescribe a treatment that referring physician cannot Other reason	
17. When a new treatment is initiated, how often are the patients with migraine seen?	Every X months On demand	
18. Average number of months it takes to get an appointment for a new patient		
19. Average number of months to follow-up patients		
20. Center regularly providing education or training in migraine to	GPs Neurologists Specialists Patients	
EFNS/AAN, European Federation of Neurological Societies/American Academy of Neurology; GPs, general practitioners		

Table S2. PRO scores among the subgroups of the Part 2 population

Assessment tool	Subgroups*									
	LFEM-1	LFEM-≥4	HFEM-1	HFEM-≥4	LFCM-	LFCM-≥4	HFCM-	HFCM-≥4	CM-1	CM≥4
	PPTF N=436	PPTF N=75	PPTF N=258	PPTF N=89	1PPTF N=120	PPTF N=73	1PPTF N=219	PPTF N=134	PPTF N=339	PPTF N=207
EQ-5D-5L										
Utility index score	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)
VAS score	75.1 (17.6)	67.9 (18.2)	74.1 (17.7)	70.8 (18.4)	66.4 (20.0)	55.9 (19.6)	59.0 (21.0)	56.3 (21.9)	61.6 (20.9)	56.1 (21.1)
Mobility, n (%)										
No problem	369 (84.6)	64 (85.3)	222 (86.0)	74 (83.1)	89 (74.2)	54 (74.0)	161 (73.5)	97 (72.4)	250 (73.7)	151 (72.9)
Slight problem	45 (10.3)	7 (9.3)	22 (8.5)	12 (13.5)	15 (12.5)	9 (12.3)	35 (16.0)	24 (17.9)	50 (14.7)	33 (15.9)
Moderate problem	17 (3.9)	4 (5.3)	9 (3.5)	3 (3.4)	12 (10.0)	8 (11.0)	17 (7.8)	8 (6.0)	29 (8.6)	16 (7.7)
Severe problem	4 (0.9)	NR	4 (1.6)	NR	4 (3.3)	2 (2.7)	5 (2.3)	4 (3.0)	9 (2.7)	6 (2.9)
Unable to walk	1 (0.2)	NR	NR	NR	NR	NR	1 (0.5)	1 (0.7)	1 (0.3)	1 (0.5)
Self-care, n (%)										
No problems washing or	405 (92.9)	67 (89.3)	243 (94.2)	83 (93.3)	109 (90.8)	65 (89.0)	195	115 (85.8)	304 (89.7)	180 (87.0)

dressing myself							(89.0)			
Slight problems washing or dressing myself	22 (5.0)	6 (8.0)	11 (4.3)	5 (5.6)	8 (6.7)	5 (6.8)	13 (5.9)	11 (8.2)	21 (6.2)	16 (7.7)
Moderate problems washing or dressing myself	8 (1.8)	2 (2.7)	3 (1.2)	1 (1.1)	2 (1.7)	2 (2.7)	6 (2.7)	7 (5.2)	8 (2.4)	9 (4.3)
Severe problems washing or dressing myself	1 (0.2)	NR	NR	NR	1 (0.8)	1 (1.4)	4 (1.8)	1 (0.7)	5 (1.5)	2 (1.0)
Unable to washing or dressing myself	NR	NR	NR	NR	NR	NR	1 (0.5)	NR	1 (0.3)	NR
Usual activities, n (%)										
No problem	280 (64.2)	45 (60.0)	166 (64.3)	44 (49.4)	63 (52.5)	21 (28.8)	84 (38.4)	39 (29.1)	147 (43.4)	60 (29.0)
Slight problem	76 (17.4)	10 (13.3)	56 (21.7)	24 (27.0)	30 (25.0)	17 (23.3)	52 (23.7)	35 (26.1)	82 (24.2)	52 (25.1)
Moderate problem	61 (14.0)	15 (20.0)	29 (11.2)	16 (18.0)	15 (12.5)	27 (37.0)	49 (22.4)	34 (25.4)	64 (18.9)	61 (29.5)
Severe problem	16 (3.7)	5 (6.7)	5 (1.9)	4 (4.5)	9 (7.5)	8 (11.0)	31 (14.2)	19 (14.2)	40 (11.8)	27 (13.0)
Unable to do	3 (0.7)	NR	1 (0.4)	1 (1.1)	3 (2.5)	NR	3 (1.4)	7 (5.2)	6 (1.8)	7 (3.4)
At least moderate problem	80 (18.3)	20 (26.7)	35 (13.6)	21 (23.6)	27 (22.5)	35 (47.9)	83 (37.9)	60 (44.8)	110 (32.4)	95 (45.9)
Discomfort, n (%)										

No pain or discomfort	151 (34.6)	20 (26.7)	78 (30.2)	20 (22.5)	20 (16.7)	5 (6.8)	22 (10.0)	15 (11.2)	42 (12.4)	20 (9.7)
Slight pain or discomfort	128 (29.4)	20 (26.7)	80 (31.0)	28 (31.5)	38 (31.7)	18 (24.7)	47 (21.5)	20 (14.9)	85 (25.1)	38 (18.4)
Moderate pain or discomfort	99 (22.7)	20 (26.7)	65 (25.2)	27 (30.3)	29 (24.2)	25 (34.2)	71 (32.4)	47 (35.1)	100 (29.5)	72 (34.8)
Severe pain or discomfort	49 (11.2)	13 (17.3)	28 (10.9)	11 (12.4)	26 (21.7)	24 (32.9)	63 (28.8)	41 (30.6)	89 (26.3)	65 (31.4)
Extreme pain or discomfort	9 (2.1)	2 (2.7)	4 (1.6)	3 (3.4)	7 (5.8)	1 (1.4)	16 (7.3)	11 (8.2)	23 (6.8)	12 (5.8)
At least moderate pain of discomfort	157 (36.0)	35 (46.7)	97 (37.6)	41 (46.1)	62 (51.7)	50 (68.5)	150 (68.5)	99 (73.9)	212 (62.5)	149 (72.0)
Anxiety and depression, n (%)										
Not anxious or depressed	231 (53.0)	36 (48.0)	125 (48.4)	47 (52.8)	42 (35.0)	20 (27.4)	75 (34.2)	57 (42.5)	117 (34.5)	77 (37.2)
Slightly anxious or depressed	122 (28.0)	22 (29.3)	76 (29.5)	25 (28.1)	43 (35.8)	26 (35.6)	57 (26.0)	36 (26.9)	100 (29.5)	62 (30.0)
Moderately anxious or depressed	58 (13.3)	16 (21.3)	39 (15.1)	11 (12.4)	25 (20.8)	20 (27.4)	55 (25.1)	26 (19.4)	80 (23.6)	46 (22.2)
Severely anxious or depressed	16 (3.7)	1 (1.3)	11 (4.3)	5 (5.6)	6 (5.0)	6 (8.2)	24 (11.0)	10 (7.5)	30 (8.8)	16 (7.7)
Extremely anxious or depressed	9 (2.1)	NR	5 (1.9)	1 (1.1)	4 (3.3)	1 (1.4)	8 (3.7)	5 (3.7)	12 (3.5)	6 (2.9)

At least moderately anxious or depressed	83 (19.0)	17 (22.7)	55 (21.3)	17 (19.1)	35 (29.2)	27 (37.0)	87 (39.7)	41 (30.6)	122 (36.0)	68 (33.0)
HIT-6 total score	63.3 (6.1)	64.3 (5.0)	64.5 (5.2)	66.1 (5.5)	65.6 (5.4)	66.4 (3.9)	67.0 (5.0)	67.5 (5.3)	66.5 (5.2)	67.1 (4.9)
Little or no impact, n (%)	8 (1.8)	NR	4 (1.6)	2 (2.2)	1 (0.8)	NR	NR	1 (0.7)	1 (0.3)	1 (0.5)
Some impact, n (%)	38 (8.7)	5 (6.7)	10 (3.9)	NR	5 (4.2)	NR	6 (2.7)	3 (2.2)	11 (3.2)	3 (1.4)
Substantial impact, n (%)	52 (11.9)	7 (9.3)	13 (5.0)	4 (4.5)	6 (5.0)	2 (2.7)	10 (4.6)	2 (1.5)	16 (4.7)	4 (1.9)
Severe impact, n (%)	337 (77.3)	63 (84.0)	230 (89.1)	83 (93.3)	108 (90.0)	71 (97.3)	203 (92.7)	128 (95.5)	311 (91.7)	199 (96.1)
mMIDAS total score	15.4 (13.8)	20.7 (16.9)	20.1 (14.9)	23.4 (16.1)	30.7 (20.2)	34.3 (18.3)	35.9 (22.3)	38.3 (20.4)	34.1 (21.7)	36.9 (19.7)
Disability grade 1, n (%)	45 (10.3)	4 (5.3)	19 (7.4)	4 (4.5)	5 (4.2)	2 (2.7)	13 (5.9)	6 (4.5)	18 (5.3)	8 (3.9)
Disability grade 2, n (%)	30 (6.9)	4 (5.3)	10 (3.9)	NR	3 (2.5)	NR	3 (1.4)	1 (0.7)	6 (1.8)	1 (0.5)
Disability grade 3, n (%)	54 (12.4)	7 (9.3)	22 (8.5)	3 (3.4)	5 (4.2)	1 (1.4)	7 (3.2)	2 (1.5)	12 (3.5)	3 (1.4)
Disability grade 4, n (%)	301 (69.0)	60 (80.0)	203 (78.7)	79 (88.8)	105 (87.5)	69 (94.5)	193 (88.1)	124 (92.5)	298 (87.9)	193 (93.2)
MSQ-RFR score	52.6 (21.4)	47.4 (19.0)	47.1 (19.4)	42.2 (17.6)	41.4 (18.6)	35.6 (17.0)	37.4 (20.2)	31.6 (20.1)	38.8 (19.7)	33.0 (19.1)
MSQ-RFP score	66.2 (23.9)	62.1 (22.5)	63.2 (21.4)	58.4 (20.7)	58.2	50.3 (24.1)	53.0	48.0 (23.9)	54.8	48.8 (23.9)

					(20.2)		(23.5)		(22.5)	
MSQ-EF score	60.8 (27.1)	51.9 (28.0)	55.3 (26.5)	50.4 (23.3)	50.6 (25.1)	40.5 (26.2)	41.5 (26.6)	37.2 (28.3)	44.7 (26.4)	38.3 (27.6)
WPAI percent work time missed	10.6 (21.7)	14.3 (25.1)	12.2 (20.9)	16.5 (26.8)	21.9 (31.6)	22.7 (28.9)	21.8 (33.5)	21.8 (31.2)	21.8 (32.7)	22.1 (30.2)
WPAI percent impairment while working	39.6 (28.5)	47.1 (29.4)	48.9 (25.4)	53.4 (25.2)	55.6 (25.8)	55.1 (20.0)	55.3 (24.3)	55.8 (21.3)	55.4 (24.8)	55.5 (20.7)
WPAI percent overall work impairment	42.6 (29.3)	51.6 (30.9)	52.7 (26.8)	57.9 (26.2)	60.5 (27.1)	62.0 (21.8)	59.4 (24.9)	61.0 (21.6)	59.8 (25.7)	61.4 (21.6)
WPAI percent activity impairment	47.3 (29.1)	52.3 (26.7)	52.3 (25.4)	59.2 (25.7)	61.1 (26.7)	64.7 (19.2)	63.7 (23.8)	67.5 (24.3)	62.8 (24.8)	66.5 (22.6)
HADS overall score	12.7 (7.5)	13.3 (7.9)	13.6 (7.8)	13.0 (8.0)	16.2 (8.1)	16.8 (7.6)	17.1 (8.2)	15.7 (8.7)	16.8 (8.2)	16.1 (8.3)
Normal (0-15), n (%)	280 (64.2)	47 (62.7)	154 (59.7)	62 (69.7)	57 (47.5)	32 (43.8)	98 (44.7)	74 (55.2)	155 (45.7)	106 (51.2)
Borderline abnormal (16+), n (%)	152 (34.9)	28 (37.3)	99 (38.4)	27 (30.3)	62 (51.7)	41 (56.2)	119 (54.3)	60 (44.8)	181 (53.4)	101 (48.8)
Abnormal (22+), n (%)	55 (12.6)	13 (17.3)	46 (17.8)	15 (16.9)	33 (27.5)	20 (27.4)	66 (30.1)	33 (24.6)	99 (29.2)	53 (25.6)
HADS anxiety score	7.2 (4.2)	7.3 (4.3)	7.8 (4.6)	6.9 (4.5)	8.7 (4.4)	8.9 (4.5)	8.9 (4.7)	8.2 (4.9)	8.8 (4.6)	8.4 (4.8)
Normal (0-7), n (%)	240 (55.0)	35 (46.7)	125 (48.4)	54 (60.7)	51 (42.5)	31 (42.5)	88 (40.2)	69 (51.5)	139 (41.0)	100 (48.3)

Borderline abnormal and abnormal (8+), n (%)	194 (44.5)	40 (53.3)	129 (50.0)	35 (39.3)	68 (56.7)	42 (57.5)	130 (59.4)	65 (48.5)	198 (58.4)	107 (51.7)
Abnormal (11+), n (%)	91 (20.9)	14 (18.7)	73 (28.3)	20 (22.5)	42 (35.0)	26 (35.6)	79 (36.1)	43 (32.1)	121 (35.7)	69 (33.3)
HADS depression score	5.6 (4.0)	6.0 (4.4)	5.8 (4.2)	6.1 (4.1)	7.4 (4.4)	7.9 (3.9)	8.1 (4.5)	7.5 (4.6)	7.9 (4.5)	7.6 (4.3)
Normal (0-7), n (%)	308 (70.6)	50 (66.7)	174 (67.4)	62 (69.7)	60 (50.0)	34 (46.6)	103 (47.0)	74 (55.2)	163 (48.1)	108 (52.2)
Borderline abnormal and abnormal (8+), n (%)	124 (28.4)	25 (33.3)	80 (31.0)	27 (30.3)	60 (50.0)	39 (53.4)	114 (52.1)	60 (44.8)	174 (51.3)	99 (47.8)
Abnormal (11+), n (%)	53 (12.2)	10 (13.3)	36 (14.0)	14 (15.7)	29 (24.2)	18 (24.7)	68 (31.1)	29 (21.6)	97 (28.6)	47 (22.7)
<p>Data presented are mean (SD) unless specified; Percentages do not add to 100% as there are missing data. *LFEM: 4–7 MMD; HFEM: 8–14 MMD; LFCM, ≥15 MHD, of which 8–14 are MMD; HFCM, ≥15 MHD, of which ≥15 are MMD; CM, ≥15 MHD, of which ≥8 are MMD. CM, chronic migraine; EF, emotional function; EM, episodic migraine; EQ-5D-5L, EuroQoL 5 dimensions, 5 levels; HADS, Hospital Anxiety and Depression scale; HF, high frequency; HIT-6, Headache Impact Test; LF, low frequency; MIDAS, Migraine Disability Assessment; MMD, monthly migraine days; MSQ, Migraine-Specific Quality of life; PPTF, prior preventive treatment failures; PRO, patient-reported outcome; RFP, role function-preventive; RFR, role function-restrictive; VAS, visual analogue scale; WPAI, Work Productivity and Activity Impairment</p>										

Table S3. Summary of the number of follow-up patients (according to PPTF and MMD status) who visited centers with and without dedicated headache clinics

	Center with a dedicated headache clinic (N=1506)	Center without a dedicated headache clinic (N=343)
Follow-up patients	1506/1970 (76.4)	343/432 (79.4)
PPTF		
1 PPTF	530 (35.2)	181 (52.8)
2 PPTF	441 (29.3)	98 (28.6)
3 PPTF	239 (15.9)	31 (9.0)
≥4 PPTF	296 (19.7)	33 (9.6)
MMD		
4–7 MMD	464 (30.8)	155 (45.2)
8–14 MMD	393 (26.1)	81 (23.6)
≥15 MMD	649 (43.1)	107 (31.2)
All data are n (%). MMD, monthly migraine days; N, number of patients in the centers; n, number of patients in a subgroup; PPTF, prior preventive treatment failure		

Table S4. Other alternative office-based practitioners who managed inpatients in the previous 3 months

Other hospital-based practitioners	Part 2 (N=2419), n (%)	Consultations, mean (SD)
Psychologist	65 (2.7)	3.4 (3.7)
Acupuncturist	23 (1.0)	3.7 (4.4)
Homeopath	7 (0.3)	5.6 (8.4)
Physiotherapist	80 (3.3)	5.6 (5.5)
Reflexologist	2 (0.1)	2.0 (1.4)
Chiropractor	13 (0.5)	2.8 (3.4)
Osteopath	10 (0.4)	1.6 (1.3)
Dietary adviser	14 (0.6)	1.4 (0.9)
Stress management adviser	8 (0.3)	3.3 (3.1)
Occupational therapist	2 (0.1)	1.0 (0.0)
Non-medical practitioner	11 (0.5)	5.7 (6.9)
Other alternative practitioners	28 (1.2)	2.5 (3.0)
N, total number of patients in Part 2; n, number of patients managed by other hospital-based practitioners; SD, standard deviation		

Table S5. Healthcare resource utilization by participating country in the Part 2 population (N=2419)

	Patients (N)	ED visits, n (%)	Mean (SD) visits	MRI scans, n (%)	Mean (SD) visits	CT scans, n (%)	Mean (SD) visits
Germany	316	48 (15.2)	2.6 (4.6)	54 (17.1)	1.1 (0.3)	17 (5.4)	1.1 (0.3)
Spain	208	82 (39.4)	4.5 (8.3)	37 (17.8)	1.1 (0.3)	36 (17.3)	1.0 (0.2)
Italy	192	31 (16.1)	3.8 (12.3)	44 (22.9)	1.1 (0.3)	24 (12.5)	1.0 (0.2)
Denmark	187	27 (14.4)	1.6 (1.1)	41 (21.9)	1.0 (0.2)	12 (6.4)	1.2 (0.4)
France	169	29 (17.2)	1.8 (1.8)	38 (22.5)	1.2 (0.4)	22 (13.0)	1.0 (0.2)
Greece	159	50 (31.4)	4.1 (5.5)	44 (27.7)	1.2 (0.7)	18 (11.3)	1.1 (0.3)
Switzerland	155	41 (26.5)	3.4 (4.6)	49 (31.6)	1.2 (0.7)	17 (11.0)	1.3 (1.2)
Czech Republic	148	40 (27.0)	2.1 (1.4)	28 (18.9)	1.1 (0.3)	11 (7.4)	1.3 (0.7)
Sweden	139	10 (7.2)	1.5 (1.3)	12 (8.6)	1.0 (0)	16 (11.5)	1.2 (0.8)
Portugal	138	49 (35.5)	3.1 (2.6)	17 (12.3)	1.0 (0)	36 (26.1)	1.3 (0.8)
United Kingdom	128	26 (20.3)	1.9 (2.7)	26 (20.3)	1.1 (0.3)	18 (14.1)	1.1 (0.5)
Croatia	95	30 (31.6)	2.6 (3.6)	32 (33.7)	1.0 (0.2)	13 (13.7)	1.0 (0)
Belgium	90	12 (13.3)	1.5 (1.0)	18 (20.0)	1.0 (0)	8 (8.9)	1.0 (0)
Israel	82	9 (11.0)	2.6 (3.1)	11 (13.4)	1.1 (0.3)	11 (13.4)	1.0 (0)
Slovakia	78	9 (11.5)	1.9 (1.1)	13 (16.7)	1.0 (0)	6 (7.7)	1.2 (0.4)
Ireland	59	6 (10.2)	2.3 (1.5)	15 (25.4)	1.4 (0.9)	8 (13.6)	1.0 (0)
Bulgaria	47	2 (4.3)	1.0 (0)	2 (4.3)	1.5 (0.7)	5 (10.6)	1.0 (0)
Slovenia	29	13 (44.8)	3.0 (2.1)	12 (41.4)	1.1 (0.3)	3 (10.3)	1.3 (0.6)

CT, computed tomography; ED, emergency department; MRI, magnetic resonance imaging; N, total number of patients analyzed from the participating country; n, number of patients utilizing the healthcare resource; SD, standard deviation

Table S6. Co-morbidities among the subgroups of the Part 2 population

Co-morbidities	Subgroups*									
	LFEM-1	LFEM-≥4	HFEM-1	HFEM-≥4	LFCM-	LFCM-≥4	HFCM-	HFCM-≥4	CM-1	CM≥4
	PPTF	PPTF	PPTF	PPTF	1PPTF	PPTF	1PPTF	PPTF	PPTF	PPTF
	N=436	N=75	N=258	N=89	N=120	N=73	N=219	N=134	N=339	N=207
Presence of co-morbidities	237 (54.4)	45 (60.0)	139 (53.9)	59 (66.3)	75 (62.5)	52 (71.2)	133 (60.7)	97 (72.4)	208 (61.4)	149 (72.0)
Comorbidities per patient, mean (SD)	1.1 (1.5)	1.3 (1.6)	1.0 (1.4)	1.2 (1.3)	1.3 (1.4)	1.6 (1.5)	1.5 (1.7)	2.0 (2.3)	1.4 (1.6)	1.8 (2.1)
Psychiatric disorders	70 (16.1)	14 (18.7)	48 (18.6)	16 (18.0)	26 (21.7)	23 (31.5)	61 (27.9)	44 (32.8)	87 (25.7)	67 (32.4)
Musculoskeletal and connective tissue disorders	54 (12.4)	14 (18.7)	24 (9.3)	10 (11.2)	17 (14.2)	11 (15.1)	28 (12.8)	22 (16.4)	45 (13.3)	33 (15.9)
Endocrine disorders	49 (11.2)	7 (9.3)	28 (10.9)	11 (12.4)	11 (9.2)	7 (9.6)	20 (9.1)	18 (13.4)	31 (9.1)	25 (12.1)
Gastrointestinal disorders	37 (8.5)	4 (5.3)	22 (8.5)	6 (6.7)	13 (10.8)	12 (16.4)	28 (12.8)	19 (14.2)	41 (12.1)	31 (15.0)
Vascular disorders	38 (8.7)	8 (10.7)	20 (7.8)	11 (12.4)	15 (12.5)	10 (13.7)	19 (8.7)	23 (17.2)	34 (10.0)	33 (15.9)
Data presented are n (%) unless specified. *LFEM: 4–7 MMD; HFEM: 8–14 MMD; LFCM, ≥15 MHD, of which 8–14 are MMD; HFCM, ≥15 MHD, of which ≥15 are MMD; CM, ≥15 MHD, of which ≥8 are MMD. CM, chronic migraine; EM, episodic migraine; HF, high frequency; LF, low frequency; MMD< monthly migraine days; PPTF, prior preventive treatment failures; SD, standard deviation										

Table S7. Summary of responses to the site questionnaire from all participating centers

Parameters	Centers in Part 1 (N=156)
Number of physicians managing migraine per site, mean (SD)	5.1 (5.6)
Centers with a dedicated headache clinic	118 (75.6)
Centers with an inpatient-specific service	62 (39.7)
Centers with a dedicated headache emergency department	37 (23.7)
Centers that are leading centers in other areas of neurology	121 (77.6)
Multiple sclerosis	78 (50.0)
Movement disorder	70 (44.9)
Dementia	65 (41.7)
Type of physicians managing patients with migraine	
General neurologist	82 (52.6)
Specialist neurologist	67 (42.9)
Headache specialist	130 (83.3)
Another specialist (not neurologist)	19 (12.2)
Multidisciplinary team	38 (24.4)
Number of nurses dedicated to migraine and/or headache per center, mean (SD)	1.2 (1.8)
Focus areas for specialist nurses	
Administration of therapies	59 (37.8)
Patient education	49 (31.4)
Monitoring of treatment response	44 (28.2)
Review of patients	42 (26.9)
Prescription of treatments	14 (9.0)
Clinical guidelines followed by the centers for migraine and headache management	
EFNS/AAN clinical guidelines	119 (76.3)
National guidelines	115 (73.7)
Center-specific guidelines	34 (21.8)
Networks/links with other centers for managing patients	
GPs	73 (46.8)
General neurologists	69 (44.2)
Other center	69 (44.2)
People living in the catchment area of the center, median (Q1, Q3)	500,000 (240,000 to 1,000,000)

Approximate number of patients treated at site per year, mean (SD)	1136.1 (1355.9)
Patients referred at site per year, mean (95% CI)	1079.9 (0 to 18,000)
Referrals received, mean (SD)	
Followed up by the same center	61.3 (27.4)
Received return to the community/GP or referral neurologist	33.5 (26.0)
Referred to another center	3.0 (5.1)
Proportion of referrals received, mean (SD)	
Referrals from GPs	61.5 (27.3)
Referrals from general neurologists	26.4 (24.1)
Referrals from other centers	9.7 (11.3)
Reasons for referral	
Preventive treatment failure	147 (94.2)
Patient request	134 (85.9)
Referred to physician who has expertise in migraine	123 (78.8)
Need for differential diagnosis	120 (76.9)
Preventive treatment initiation	118 (75.6)
Acute treatment failure	109 (69.9)
Ability to prescribe a treatment that referring physician cannot	83 (53.2)
Acute treatment initiation	74 (47.4)
Other reason	15 (9.6)
Frequency of patient follow-up after initiation of new therapy, mean (min, max), months	3.1 (1 to 12)
Waiting time for an appointment for new patients, mean (min, max), months	3.3 (0 to 18)
Patient follow-up duration, mean (SD), months	27.3 (50.4)
Regular education or training provided to	
GPs	115 (73.7)
Neurologists	114 (73.1)
Patients	65 (41.7)
Specialists	64 (41.0)
All values are n (%), unless indicated. For parameters with multiple responses, the sum of responses may not be 156, as the percentages were calculated for the total number of sites. CI, confidence interval; EFNS/AAN, European Federation of Neurological Societies/American Academy of Neurology; GPs, general practitioners; n, number of participating sites or patients; N, total number of sites; Q, quarter; SD, standard deviation	

Table S8. Number of patients who have failed any prophylactic treatment (Part 2)

	Overall	Tolerability failure	Efficacy failure	Other failure (not suitable)
Topiramate	1093 (45.2%)	555 (22.9%)	546 (22.6%)	9 (0.4%)
Amitriptyline	721 (29.8%)	308 (12.7%)	414 (17.1%)	4 (0.2%)
Propranolol	572 (23.6%)	233 (9.6%)	341 (14.1%)	9 (0.4%)
Flunarizine	332 (13.7%)	128 (5.3%)	204 (8.4%)	1 (0.0%)
Metoprolol	325 (13.4%)	140 (5.8%)	182 (7.5%)	8 (0.3%)
Valproic acid	285 (11.8%)	114 (4.7%)	171 (7.1%)	7 (0.3%)
Botulinum toxin type A	170 (7.0%)	15 (0.6%)	154 (6.4%)	1 (0.0%)
Candesartan	136 (5.6%)	52 (2.1%)	84 (3.5%)	-
Venlafaxine	111 (4.6%)	47 (1.9%)	63 (2.6%)	1 (0.0%)
Pregabalin	88 (3.6%)	32 (1.3%)	56 (2.3%)	1 (0.0%)
Pizotifen	82 (3.4%)	36 (1.5%)	45 (1.9%)	1 (0.0%)
Gabapentin	79 (3.3%)	39 (1.6%)	39 (1.6%)	1 (0.0%)
Magnesium	71 (2.9%)	13 (0.5%)	58 (2.4%)	-
Oxetorone	58 (2.4%)	22 (0.9%)	38 (1.6%)	-
Duloxetine	56 (2.3%)	22 (0.9%)	35 (1.4%)	-
Lamotrigine	55 (2.3%)	28 (1.2%)	27 (1.1%)	-
Riboflavin	50 (2.1%)	3 (0.1%)	46 (1.9%)	1 (0.0%)
Zonisamide	42 (1.7%)	15 (0.6%)	27 (1.1%)	-
Cinnarizine	40 (1.7%)	5 (0.2%)	35 (1.4%)	-
Bisoprolol	38 (1.6%)	17 (0.7%)	21 (0.9%)	-
Lisinopril	34 (1.4%)	16 (0.7%)	18 (0.7%)	-
Mirtazapine	28 (1.2%)	16 (0.7%)	12 (0.5%)	-
Naproxen	28 (1.2%)	10 (0.4%)	19 (0.8%)	-
Verapamil	24 (1.0%)	13 (0.5%)	11 (0.5%)	-
Escitalopram	23 (1.0%)	5 (0.2%)	18 (0.7%)	-
Nortriptyline	23 (1.0%)	8 (0.3%)	14 (0.6%)	1 (0.0%)

Doxepin	21 (0.9%)	8 (0.3%)	12 (0.5%)	1 (0.0%)
Nadolol	19 (0.8%)	9 (0.4%)	10 (0.4%)	-
Nebivolol	19 (0.8%)	7 (0.3%)	12 (0.5%)	-
Atenolol	18 (0.7%)	4 (0.2%)	14 (0.6%)	-
Clomipramine	18 (0.7%)	7 (0.3%)	11 (0.5%)	-
Opipramol	16 (0.7%)	6 (0.2%)	10 (0.4%)	-
Citalopram	15 (0.6%)	7 (0.3%)	9 (0.4%)	-
Beta blocking agents	14 (0.6%)	9 (0.4%)	4 (0.2%)	1 (0.0%)
Sertraline	14 (0.6%)	3 (0.1%)	11 (0.5%)	-
Fluoxetine	12 (0.5%)	4 (0.2%)	9 (0.4%)	-
Indoramin	11 (0.5%)	5 (0.2%)	6 (0.2%)	-
Medical devices	11 (0.5%)	3 (0.1%)	8 (0.3%)	-
Tizanidine	11 (0.5%)	1 (0.0%)	10 (0.4%)	-
Amlodipine	10 (0.4%)	6 (0.2%)	4 (0.2%)	-
Chlorzoxazone	10 (0.4%)	1 (0.0%)	9 (0.4%)	-
Indometacin	10 (0.4%)	5 (0.2%)	5 (0.2%)	-
Dihydroergotamine	9 (0.4%)	1 (0.0%)	7 (0.3%)	1 (0.0%)
Paroxetine	9 (0.4%)	3 (0.1%)	6 (0.2%)	-
Limbitrol	8 (0.3%)	3 (0.1%)	5 (0.2%)	-
Acetylsalicylic acid	7 (0.3%)	1 (0.0%)	6 (0.2%)	-
Clonazepam	7 (0.3%)	2 (0.1%)	5 (0.2%)	-
Diclofenac	7 (0.3%)	2 (0.1%)	5 (0.2%)	-
Timolol	7 (0.3%)	2 (0.1%)	5 (0.2%)	-
Melatonin	6 (0.2%)	2 (0.1%)	4 (0.2%)	-
Metamizole	6 (0.2%)	2 (0.1%)	4 (0.2%)	-
Quetiapine	6 (0.2%)	2 (0.1%)	4 (0.2%)	-
Trimipramine	6 (0.2%)	4 (0.2%)	1 (0.0%)	1 (0.0%)
Carbamazepine	5 (0.2%)	2 (0.1%)	2 (0.1%)	1 (0.0%)
Etrafon-d	5 (0.2%)	1 (0.0%)	4 (0.2%)	-

Ginkgo biloba	5 (0.2%)	-	5 (0.2%)	-
W/riboflavin/ubidecarenone	-	-	-	-
Levetiracetam	5 (0.2%)	-	5 (0.2%)	-
Methylprednisolone	5 (0.2%)	-	5 (0.2%)	-
Paracetamol	5 (0.2%)	2 (0.1%)	3 (0.1%)	-
Petasites hybridus	5 (0.2%)	-	5 (0.2%)	-
Clonidine	4 (0.2%)	2 (0.1%)	2 (0.1%)	-
Depo-medrol med lidokain	4 (0.2%)	-	4 (0.2%)	-
Dosulepin	4 (0.2%)	3 (0.1%)	1 (0.0%)	-
Flupirtine	4 (0.2%)	2 (0.1%)	2 (0.1%)	-
Lacosamide	4 (0.2%)	1 (0.0%)	3 (0.1%)	-
Magne-b6 oral	4 (0.2%)	-	4 (0.2%)	-
Ubidecarenone	4 (0.2%)	1 (0.0%)	3 (0.1%)	-
Apydan	3 (0.1%)	2 (0.1%)	1 (0.0%)	-
Bromazepam	3 (0.1%)	-	3 (0.1%)	-
Cyclandelate	3 (0.1%)	2 (0.1%)	1 (0.0%)	-
Ginkgo biloba	3 (0.1%)	-	3 (0.1%)	-
Lithium	3 (0.1%)	1 (0.0%)	2 (0.1%)	-
Memantine	3 (0.1%)	2 (0.1%)	1 (0.0%)	-
Nicardipine	3 (0.1%)	2 (0.1%)	1 (0.0%)	-
Nobritol-f	3 (0.1%)	-	3 (0.1%)	-
Prazepam	3 (0.1%)	1 (0.0%)	2 (0.1%)	-
Telmisartan	3 (0.1%)	1 (0.0%)	2 (0.1%)	-
Trazodone	3 (0.1%)	2 (0.1%)	1 (0.0%)	-
Vortioxetine	3 (0.1%)	-	3 (0.1%)	-
Baclofen	2 (0.1%)	-	2 (0.1%)	-
Betahistine	2 (0.1%)	-	2 (0.1%)	-
Bupivacaine	2 (0.1%)	-	2 (0.1%)	-
Buspirone	2 (0.1%)	1 (0.0%)	1 (0.0%)	-

Desipramine	2 (0.1%)	1 (0.0%)	1 (0.0%)	-
Diazepam	2 (0.1%)	-	2 (0.1%)	-
Dietary supplement	2 (0.1%)	-	2 (0.1%)	-
Guaifenesin	2 (0.1%)	-	2 (0.1%)	-
Levosulpiride	2 (0.1%)	1 (0.0%)	1 (0.0%)	-
Magnesium carbonate	2 (0.1%)	-	2 (0.1%)	-
Magosolv	2 (0.1%)	2 (0.1%)	-	-
Melperone	2 (0.1%)	1 (0.0%)	1 (0.0%)	-
Methysergide	2 (0.1%)	1 (0.0%)	1 (0.0%)	-
Mydocalm	2 (0.1%)		2 (0.1%)	-
Nifedipine	2 (0.1%)	2 (0.1%)	-	-
Olanzapine	2 (0.1%)	1 (0.0%)	1 (0.0%)	-
Oxtripitan	2 (0.1%)	-	2 (0.1%)	-
Paracofdal	2 (0.1%)	-	2 (0.1%)	-
Acebutolol	1 (0.0%)	-	1 (0.0%)	-
Aceclofenac	1 (0.0%)	-	1 (0.0%)	-
Acetazolamide	1 (0.0%)	-	1 (0.0%)	-
Agomelatine	1 (0.0%)		1 (0.0%)	-
Alprazolam	1 (0.0%)	1 (0.0%)	-	-
Amisulpride	1 (0.0%)	-	1 (0.0%)	-
Antidepressants	1 (0.0%)	1 (0.0%)	-	-
Benzodiazepine derivatives	1 (0.0%)	1 (0.0%)	-	-
Bupivacaine;lidocaine;methylp	1 (0.0%)	-	1 (0.0%)	-
Rednisolone	-	-	-	-
Buprenorphine	1 (0.0%)	-	1 (0.0%)	-
Bupropion	1 (0.0%)	-	1 (0.0%)	-
Carvedilol	1 (0.0%)	-	1 (0.0%)	-
Chlordiazepoxide	1 (0.0%)	1 (0.0%)	-	1 (0.0%)
Corticosteroids for systemic	1 (0.0%)	-	1 (0.0%)	-

use, combination				
Cortisone	1 (0.0%)	-	1 (0.0%)	-
Cyclobenzaprine	1 (0.0%)	-	1 (0.0%)	-
Cyproheptadine	1 (0.0%)	1 (0.0%)	-	-
Desvenlafaxine	1 (0.0%)	1 (0.0%)	-	-
Dexibuprofen	1 (0.0%)	-	1 (0.0%)	-
Diane	1 (0.0%)	-	1 (0.0%)	-
Drospirenone	1 (0.0%)	-	-	1 (0.0%)
W/ethinylestradiol		-	-	-
Eslicarbazepine	1 (0.0%)	-	1 (0.0%)	-
Homeopathic preparation	1 (0.0%)	-	1 (0.0%)	-
Ibuprofen	1 (0.0%)	-	1 (0.0%)	-
Imipramine	1 (0.0%)	-	1 (0.0%)	-
Ketamine	1 (0.0%)	1 (0.0%)	-	-
Levobupivacaine	1 (0.0%)	-	1 (0.0%)	-
Lidocaine	1 (0.0%)	-	1 (0.0%)	-
Lidocaine	1 (0.0%)	-	1 (0.0%)	-
W/methylprednisolone	-	-	-	-
Losartan	1 (0.0%)	-	1 (0.0%)	-
Magnesium w/nicotinamide	1 (0.0%)	-	1 (0.0%)	-
Maprotiline	1 (0.0%)	1 (0.0%)	-	-
Mefenamic acid	1 (0.0%)	-	1 (0.0%)	-
Metergoline	1 (0.0%)	-	1 (0.0%)	-
Methocarbamol	1 (0.0%)	1 (0.0%)	-	-
Metipranolol	1 (0.0%)	-	1 (0.0%)	-
Mianserin	1 (0.0%)	1 (0.0%)	-	-
Migralgine	1 (0.0%)	-	-	1 (0.0%)
Milnacipran	1 (0.0%)	-	1 (0.0%)	-
Moclobemide	1 (0.0%)	1 (0.0%)	-	-

Morphine	1 (0.0%)	-	1 (0.0%)	-
Norethisterone	1 (0.0%)	-	1 (0.0%)	-
Oxcarbazepine	1 (0.0%)	-	1 (0.0%)	-
Paynocil	1 (0.0%)	-	1 (0.0%)	-
Pineal	1 (0.0%)	-	1 (0.0%)	-
Pipethiadene	1 (0.0%)	1 (0.0%)	-	-
Prednisolone	1 (0.0%)	-	1 (0.0%)	-
Prochlorperazine	1 (0.0%)	-	1 (0.0%)	-
Ramipril	1 (0.0%)	-	1 (0.0%)	-
Rizatriptan	1 (0.0%)	-	1 (0.0%)	-
Salures-k	1 (0.0%)	-	-	1 (0.0%)
Sertaconazole	1 (0.0%)	1 (0.0%)	-	-
Silicon dioxide	1 (0.0%)	-	1 (0.0%)	-
Sotalol	1 (0.0%)	-	1 (0.0%)	-
Tapentadol	1 (0.0%)	-	1 (0.0%)	-
Thioridazine	1 (0.0%)	-	1 (0.0%)	-
Tramadol	1 (0.0%)	-	1 (0.0%)	-
Ultracet	1 (0.0%)	-	1 (0.0%)	-
Vinpocetine	1 (0.0%)	-	1 (0.0%)	-

Notes: The antimigraine preparations erenumab and galcanezumab, as well as - All other non-therapeutic products (ATC3) - were excluded from the analysis of prophylactic treatments as well as from determination of the - Treatment failure frequency (1, 2, 3, 4+) variable.

Table S9. List of Independent Ethics Committees (IEC) or Institutional Review Boards (IRB) by study center

Center No.	Ethics Committee or Institutional Review Board	Department/ Organization	City, Postal Code Country
1000	Jessa Ziekenhuis	Ethische Toetsingscommissie	Hasselt, 3500 Belgium
1001	CHR de la Citadelle	Comite d'Ethique	Liege, 4000 Belgium
1002	AZ Sint Jan Brugge-Ostende av	Commisie voor Ethiek	Brugge, 8000 Belgium
1003	AZ Gent	Commisie voor Medische Ethiek	Gent, 9000 Belgium
1004	UZ Brussel	Commisie voor Medische Ethiek	Brussel, 1090 Belgium
1050	Ethics Committee for Multicenter Trials		Sofia, 1000 Bulgaria
1051	Ethics Committee for Multicenter Trials		Sofia, 1000 Bulgaria
1052	Ethics Committee for Multicenter Trials		Sofia, 1000 Bulgaria
1100	Sredisnje eticko povjerenstvo Central Ethics Committee		Zagreb, 10 000 Croatia
1101	Sredisnje eticko povjerenstvo Central Ethics Committee		Zagreb, 10 000 Croatia
1102	Sredisnje eticko povjerenstvo Central Ethics Committee		Zagreb, 10 000 Croatia
1150	General Faculty Olomouc Ethic Committee		Olomouc, 779 00 Czech Republic
1151	Ethics Committee of the Institute for Clinical and Experimental Medicine and Thomayer Hospital		Praha 4, 140 59 Czech Republic
1152	Ethics Committee of the Institute for Clinical and Experimental Medicine and Thomayer Hospital		Praha 4, 140 59 Czech Republic
1153	Fakultni Nemocnice u sv. Anny v Brne	Eticka Komise	Brno, 656 91 Czech Republic
1154	Ethics Committee NZZ Research Site s.r.o.		Plzen, 326 00 Czech Republic
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1157	Ethics Committee of the Central Military		Praha 6, 169 02 Czech

	Hospital		Republic
1250	CPP Ouest 6	CHU Cavale Blanche	Brest, 29609 France
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1300	Ethikkommission bei der Medizinische Fakultät der LMU Muenchen		Muenchen, 80336 Germany
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1306	Ethikkommission bei der Medizinische		Muenchen, 80336

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1342	Ethikkommission bei der Medizinische Fakultaeet der LMU Muenchen		Muenchen, 80336 Germany

1400	SC/BoD of Ag Anargyroi General Oncology Hospital		Kifissia, 145 64 Greece
1401	SC/BoD of Athens Naval Hospital		Athens, 115 21 Greece
1403	SC/BoD of Euromedica General Clinic of Thessaloniki		Thessaloniki, 546 45 Greece
1405	SC/BoD of General Hospital of Patras "Agios Andreas"		Patras, 263 35 Greece
1406	SC/BoD of 401 Military Hospital of Athens		Athens, 115 27 Greece
1408	SC/BoD of 401 Military Hospital of Athens		Korinthos, 201 31 Greece
1410	SC/BoD of General Hospital of Athens "Evangelismos"		Athens, 106 76 Greece
1411	SC/BoD of Mediterraneo Hospital		Glyfada, 166 75 Greece
1412	SC/BoD of Iatriko Athinon		Marousi, 151 25 Greece
1413	SC/BoD of University General Hospital of Patras "Panagia I Voithia"		Patras, 265 00 Greece
1414	SC/BoD of University Hospital of Thessaloniki AXEPA		Thessaloniki, 546 21 Greece
1416	SC/BoD of General Hospital of Thessaloniki Papanikolaou		Thessaloniki, 570 10 Greece
1417	SC/BoD of Aeginition Hospital of Athens, University of Athens		Athens, 115 28 Greece
1419	SC/BoD of General Hospital of Athens "G. Gennimatas"		Athens, 115 27 Greece
1420	SC/BoD of University General Hospital of Heraklion		Heraklion Crete, 711 10 Greece
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1451	Beaumont Hospital	Ethics (Medical Reasearch) Committee	Dublin 9, Ireland
1452	Bon Secours Health System	Clinical EthicsCommittee	Dublin 9, Ireland
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1501	Soroka Medical Center	Helsinki Committee	Beer-Sheva, Israel
1502	Rambam Heathcare Campus	Helsinki Committee	Haifa, Israel

1550	Comitato Etico dell'IRCCS San Raffaele Pisana di Roma		Roma, 00166 Italy
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1552	Comitato Etico Interaziendale A.O.U. Città della Salute e della Scienza di Torino		Torino, 10126 Italy
1553	Universita Campus Bio-Medico di Roma	Comitato Etico	Roma, 00128 Italy
1554	Comitato Etico dell'Istituto Neurologico Mediterraneo Neuromed		Pozzilli, 86077 Italy
1555	Comitato Etico Regionale per la Sperimentazione Clinica della Regione Toscana		Firenze, 50134 Italy
1556	Il Comitato Etico dell'Ospedale San Raffaele - Milano		Milano, 20132 Italy
1557	Comitato Etico Università degli Studi della Campania "L. Vanvitelli"	Istituto di Ricovero e Cura a Carattere Scientifico	Napoli, 80138 Italy
1558	Comitato Etico dell'Università "Sapienza"	AORN "Ospedali dei Colli"	Roma, 00189 Italy
1559	Comitato Etico di Brescia	ASST Spedali Civili	Brescia, 25123 Italy
1563	Comitato Etico A.O. "Santa Croce e Carle" di Cuneo		Cuneo, 12100 Italy
1564	Comitato Etico Regione Lombardia	Sezione Fondazione IRCCS Istituto Neurologico "Carlo Besta"	Milano, 20133 Italy
1650	Comissao de Etica para a Saude	Hospital da Luz	Lisboa, 1500-650, Portugal
1652	Comissao de Etica do CHLN e do CAML		Lisboa, 1769-001, Portugal
1653	Comissão de Ética	Campus Neurologico Senior	Torres Vedras, 2560-280, Portugal
1654	Comissao de Etica para a Saude	Hospila Garcia de Orta, E.P.E	Almada, 2805-267, Portugal
1655	Comissao de Etica da ULSM Matosinhos, E.P.E.		Senhora da Hora, 464-513, Portugal
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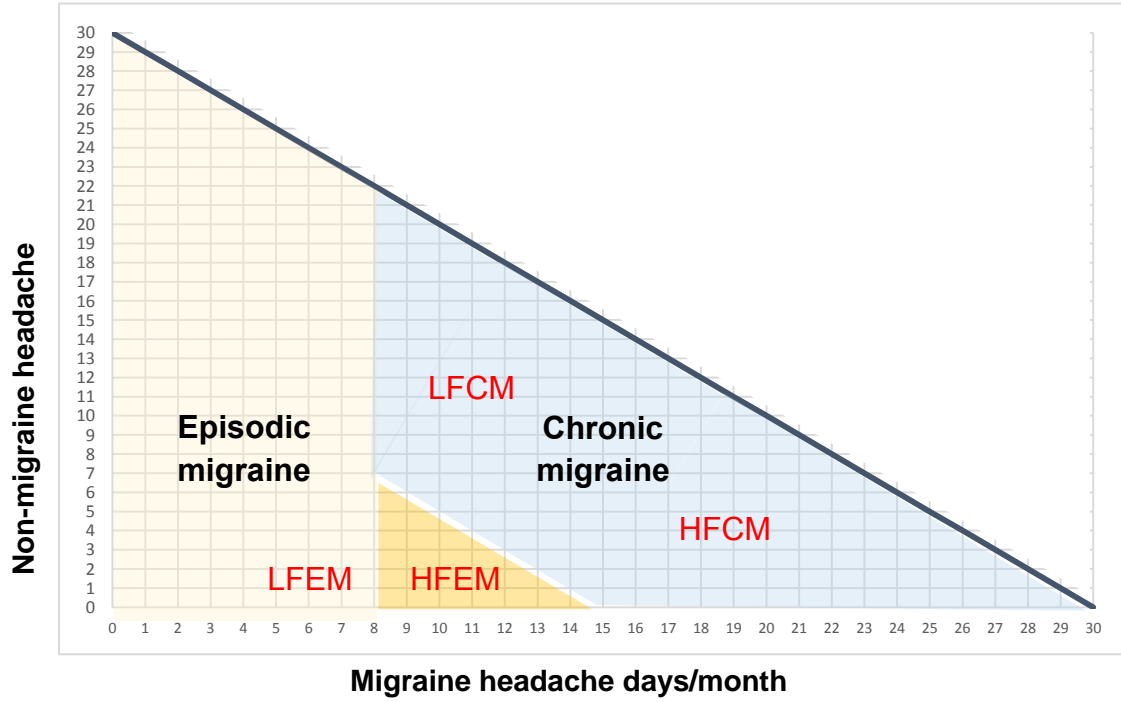
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1750	Eticka komisia Univerzitna nemocnica Bratislava	Multicentricka eticka komisia	Bratislava, 833 05, Slovakia
1751	Eticka komisia Presovsky samospravny kraj	Lokalna eticka komisia	Presov, 080 01, Slovakia
1752	Eticka komisia Univerzitna nemocnica Bratislava	Lokalna eticka komisia	Bratislava, 826 06, Slovakia
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1754	Eticka komisia pri Nemocnici sv. Michala	Lokalna eticka komisia	Bratislava, 811 08, Slovakia
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1802	CEIm de les Illes Balears	Consejería de Salud	Palma, 07010, Spain
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1805	CEIm Hospital General Universitario de Alicante	Centro de Diagnósticos	Alicante, 03010, Spain
1806	CEIm de Euskadi	Dirección de Farmacia	Vitoria, 01010, Spain
1807	CEIm Hospital Universitari de Bellvitge		Hospitalet, 08907, Spain
1808	CEIm Área de Salud de Burgos y Soria	Hospital Universitariode Burgos	Burgos, 09006, Spain
1809	CEI Hospital Universitario de Fuenlabrada		Madrid, 28942, Spain
1810	CEIm de Euskadi		Vitoria, 01010, Spain
1811	CEIm Hospital General Universitario Gregorio Marañón		Madrid, 28007, Spain
1812	CEIm Hospital Universitario y Politécnico La Fe	Hospital U. i P. La Fe,	Valencia, 46026, Spain
1813	CEIm Hospital Universitario La Paz		Madrid, 28046, Spain
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1818	CEIm Fundació de Gestió Sanitaria Hospital de la Santa Creu i Sant Pau	Servei de Farmacologia Clínica	Barcelona, 08025, Spain
1819	CEIm de les Illes Balears	Consejería de Salud	Palma, 07010, Spain
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1821	CEIm de Cantabria	IDIVAL Instituto de Investigación Marqués de Valdecilla	Santander, 39011, Spain
1822	CEIm Hospital General Universitario de Valencia	Consortio Hospital General Universitario de Valencia	Valencia, 46014, Spain
1823	CEIm del Área de Salud de Valladolid Este	Hospital Clínico Universitario de Valladolid	Valladolid, 47003, Spain
1824	CEIm del Hospital Universitari Vall d'Hebron		Barcelona, 08035, Spain
1825	CEIm Hospital Universitari de Bellvitge		Hospitalet, 08907, Spain
1826	CEIm Hospital Clínico San Carlos		Madrid, 28040, Spain
1827	CEIm Autonómico de Galicia	Secretaria Xeral. Conselleria de Sanidade	Santiago de Compostela, 15781, Spain
1828	CEIm Hospital Universitario Puerta de Hierro Majadahonda		Madrid, 28222, Spain
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1830	CEIm del Principado de Asturias		Oviedo, 33011, Spain
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1851	EPN - Regionala etikproevningsnaemnden i Stockholm	Karolinska Institutet i Solna	Solna, 171 65, Sweden
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1900	Kantonale Ethikkommission Zuerich		Zuerich, ZH, 8090, Switzerland
1901	Kantonale Ethikkommission Zuerich		Zuerich, ZH, 8090,

			Switzerland
1902	Kantonale Ethikkommission Zuerich		Zuerich, ZH, 8090, Switzerland
1903	Kantonale Ethikkommission Zuerich		Zuerich, ZH, 8090, Switzerland
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1908	Kantonale Ethikkommission Zuerich		Zuerich, ZH, 8090, Switzerland
1909	Kantonale Ethikkommission Zuerich		Zuerich, ZH, 8090, Switzerland
1950	North East York Research Ethics Committee		Jarrow, NE32 3DT, UnitedKingdom
1951	North East York Research Ethics Committee		Jarrow, NE32 3DT, UnitedKingdom
1952	North East York Research Ethics Committee		Jarrow, NE32 3DT, UnitedKingdom
1953	North East York Research Ethics Committee		Jarrow, NE32 3DT, UnitedKingdom
1955	North East York Research Ethics Committee		Jarrow, NE32 3DT, UnitedKingdom
1956	North East York Research Ethics Committee		Jarrow, NE32 3DT, UnitedKingdom

Supplementary Figures

Figure S1: Visualization of burden of migraine across the migraine spectrum (EM and CM)



CM, chronic migraine; EM, episodic migraine; HFEM, high frequency EM; LFCM, low frequency CM; HFCM, high frequency CM; LFEM, low frequency EM

Figure S2. Percentages of headache specialist centers screened (Part 1; N=163) and proportion of patients included in Part 2 of the study (N=2419) by participating country

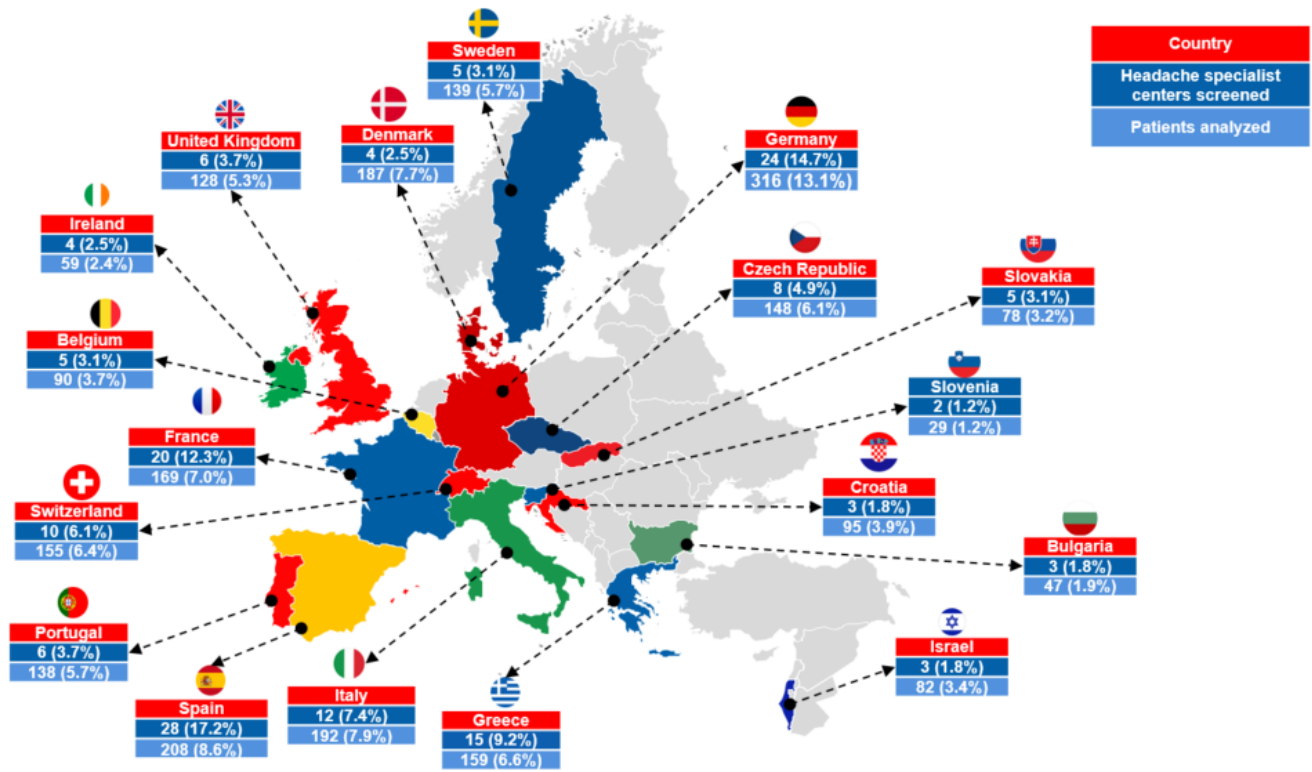
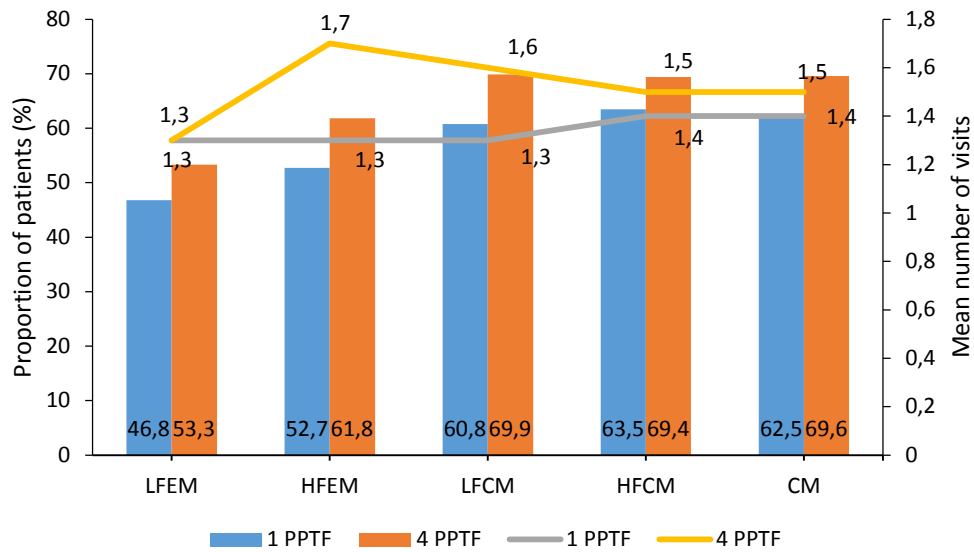


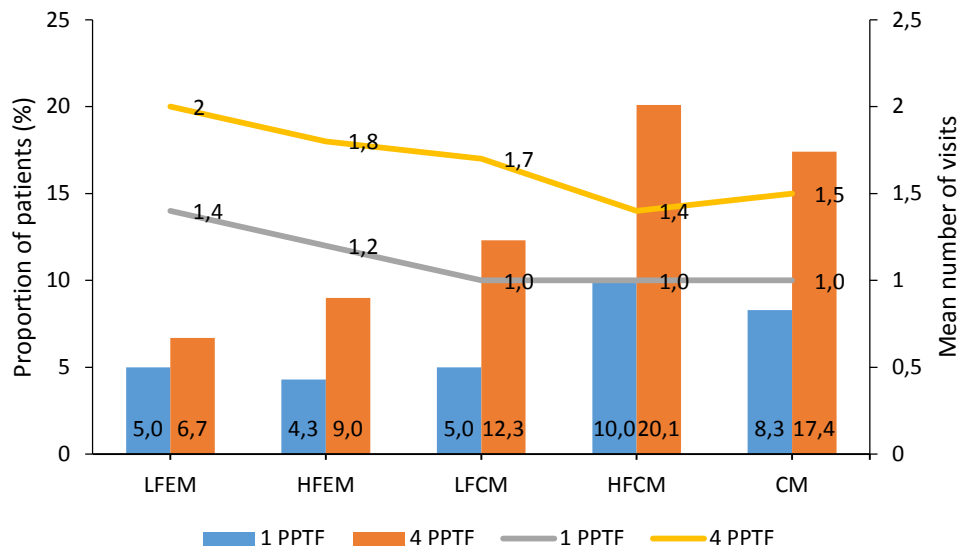
Figure S3: HRU subgroups comparisons

a: Visits to neurologist in the past 3 months



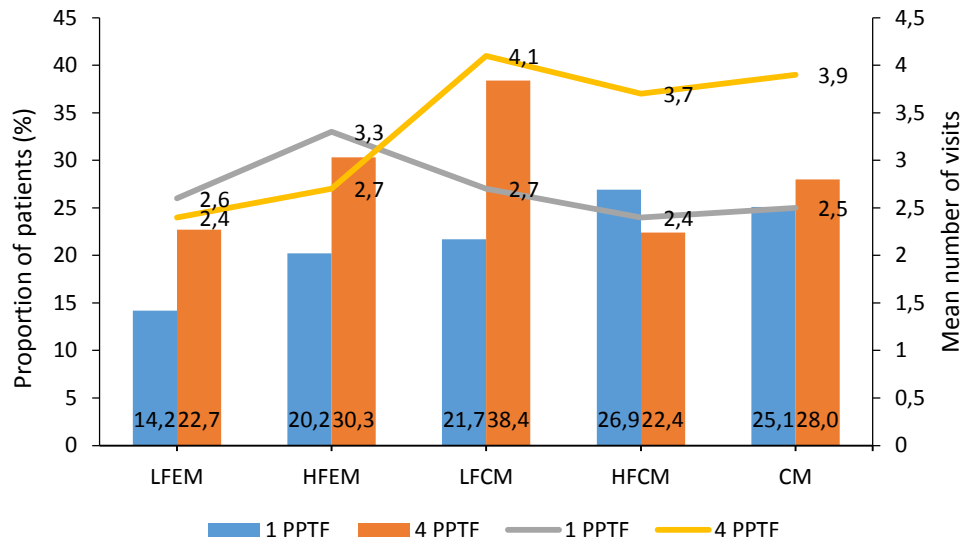
LFEM, low frequency episodic migraine; HFEM, high frequency episodic migraine; CM, chronic migraine; LFCM, low frequency chronic migraine; HFCM, high frequency chronic migraine; HRU, healthcare resource utilization; PPTF, prior prophylactic treatment failure

b: Hospitalizations in the past 12 months



LFEM, low frequency episodic migraine; HFEM, high frequency episodic migraine; CM, chronic migraine; LFCM, low frequency chronic migraine; HFCM, high frequency chronic migraine; PPTF, prior prophylactic treatment failure

c: Emergency department visits in the past 12 months



LFEM, low frequency episodic migraine; HFEM, high frequency episodic migraine; CM, chronic migraine; LFCM, low frequency chronic migraine; HFCM, high frequency chronic migraine; PPTF, prior prophylactic treatment failure