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ORIGINAL ARTICLE

Burden of migraine in patients attending Belgian headache specialists: real-world evidence from the BECOME study

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Abstract

Introduction Migraine is a primary headache disorder, which imposes a major burden on the sufferers. The BECOME study (Burden of migrainE in specialist headache Centers treating patients with prOphylactic treatMent failurE) attempted to characterize and assess the prevalence, burden and healthcare resource utilization of migraine patients presenting in specialized headache centers in Europe and Israel. In this paper, we will describe the patient characteristics of the Belgian headache centers.

Methods The BECOME study was a prospective, non-interventional, cross-sectional study consisting of two parts. In the first part of the study, data were collected from subjects with a diagnosis of migraine. Subsequently, patients with ≥ 4 monthly migraine days (MMD) and ≥ 1 prior preventive treatment failure (PPTF) filled out validated questionnaires to assess the burden of disease.

Results In part 1 of the Belgian study population ($N = 806$), 45% of patients reported ≥ 8 MMD and 25% had failed ≥ 4 preventive treatments. In part 2 ($N = 90$), more than 90% of patients reported having severe impact of headache on daily life and having severe migraine-related disability. The impact was the highest for patients with ≥ 15 MMD, however, even within the patient population with < 8 MMD, the burden was significant. Almost 40% of the study population suffered from anxiety.

Conclusions These findings in the Belgian sample of the BECOME study demonstrate the substantial burden and unmet need for the management of difficult-to-treat migraine.

Keywords Burden · Migraine · Patient-reported outcomes · Treatment failure

Introduction

Migraine is a primary headache disorder, which is a public health concern and imposes a recognized burden on the sufferers. The burden of migraine is wide-ranging and encompasses many domains. It leads to substantial personal suffering, impaired quality of life, financial cost and may also predispose the individual to other illnesses [1–4]. Studies showed limitation on career potential within 33% of the migraine patients. Furthermore, more than 20% of patients have a concern for losing their job. The burden of migraine also affects the family. Migraine patients indicated that migraine negatively affects their partner relationship (49%) and parenting (39%). Up to 13% of adolescent children reported that parental migraine affected their academic performance. Because of migraines, 3% of patients suggested not to have children, delayed having children, or had fewer children [5].

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Migraine is currently the top cause of Years Lived with Disabilities (YLD) among individuals in the age group 15–49 years worldwide [6].

Multiple previous studies and surveys described various manifestations of the burden of migraine, such as the Global Burden of Disease (GBD) study [4], the My Migraine Voice study [7], the American Migraine Prevalence and Prevention (AMPP) study [8], the Eurolight project [9], the International Burden of Migraine Study (IBMS) [10] and the Chronic Migraine Epidemiology and Outcomes (CaMEO) study [11]. However, the current understanding of migraine burden among individuals experiencing 4 or more monthly migraine days (MMDs) and prior preventive treatment failure (PPTF) is limited [7].

Recently, the BECOME study attempted to characterize and assess the prevalence, burden and healthcare resource utilization (HRU) of migraine patients presenting in 163 specialized headache centers in 18 countries from Europe and Israel [12]. In this paper, we will describe the patient characteristics of the participating Belgian headache centers.

Methods

Study design and participants

The BECOME (Burden of migrainE in specialist headache Centers treating patients with prOphylactic treatMent failurE) study was a prospective, non-interventional, cross-sectional study performed in headache specialist centers across Europe and Israel.

Data were collected in two parts between 27 November 2017 and 5 October 2018 (Fig. 1). The participating centres did not have any formal requirement in order to become a patient (apart from a referral letter), however, the treating neurologist working at that centre had a particular clinical and/or scientific interest in headache disorders.

In the first part of the study, data were collected from patients visiting headache specialist care sites during 3 consecutive months. Women and men between 18 and 65 years with a diagnosis of migraine (per the International Classification of Headache Disorders-3b criteria) were prospectively included.

Immediately after Part 1 or within a window of 14 days, patients with ≥ 4 MMD in the previous 3 months and ≥ 1 PPTF in the foregoing 5 years were invited to participate in the second part of the study. PPTF was defined as efficacy failure, tolerability failure or "not eligible for" due to contraindications. They were asked to fill out validated questionnaires to assess the burden of disease using both general health and disease-specific tools. Demographic data such as age (Part 1) and sex and working status (Part 2) were collected. Additionally, the HRU among these patients was investigated [12].

Endpoints and other variables

Endpoints in part 1 included the proportion of patients visiting Belgian headache centres within a 3-month period stratified according to MMD, PPTF, new versus follow-up visit, disease duration and medication-overuse (headache).

In part 2, Patient Related Outcome (PRO) questionnaires were administered to assess the disease burden and quality of life for pre-specified subgroups based on the frequency of MMD and medication overuse. HRU was assessed by a questionnaire completed by the treating physician during consultation, the following data were collected: emergency department visits, investigations by MRI or CT scan, admissions for headache and number of outpatient general practitioner visits in the past year or 3 months.

The questionnaires

In the BECOME study, the following PRO questionnaires were used (either in Dutch or French, translated according

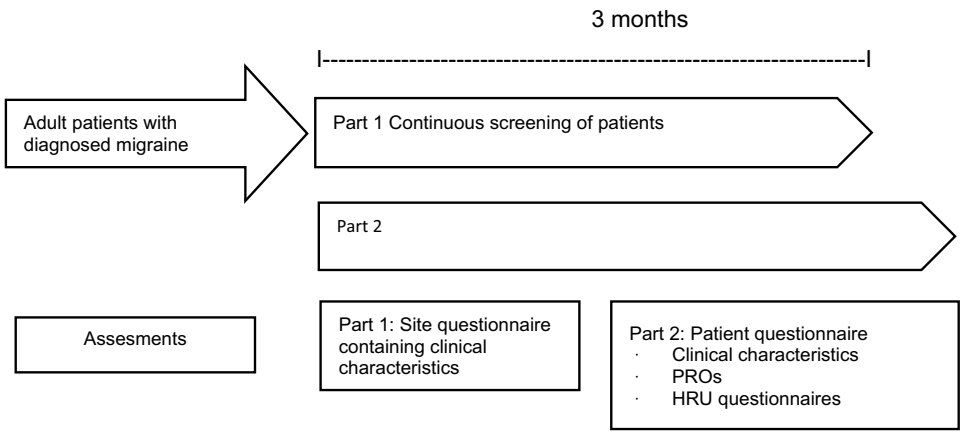

Fig. 1 Design of the BECOME study

to standard procedures using the latest validated version in English): (1) EuroQoL 5 dimensions 5 level (EQ-5D-5L) Utility Index Score and Visual Analogue Score (VAS), (2) Migraine-Specific Quality of life (MSQ), (3) Work Productivity and Activity Impairment for headache (WPAI-headache), (4) Headache Impact Test-6 (HIT-6), (5) modified Migraine Disability Assessment questionnaire (mMIDAS) and, (6) Hospital Anxiety and Depression Scale (HADS) (for the Dutch and French versions of all scales, see the supplementary document).

The EQ-5D-5L questionnaire comprises two components. In the first component, the EQ-5D-5L utility index, patients rate their general health status functioning in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). The response to each dimension is captured using five levels (no problems, slight problems, moderate problems, severe problems, and extreme problems) to derive the weighted EQ-5D-5L utility index score, with a possible range from 0 (worst) to 1 (perfect health status). In the EQ-5D-5L VAS, patients rate their current health-related quality of life on a scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health status) [13].

The 14-item MSQ questionnaire examines 3 dimensions of functional status specific to migraine: the Role Function-Restrictive (RFR) dimension, measuring the degree to which performance of normal activities is limited by migraines; the Role Function-Preventive (RFP) dimension, measuring the degree to which performance of normal activities is interrupted by migraines; and the Emotional Function (EF) dimension, measuring the emotional effects of migraine. The response to each domain is captured at six levels (none of the 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) and rescaled to a 0 to 100 scale, with 100 reflecting the best imaginable health state [14, 15].

Patients reported WPAI-headache scores on a scale of 0 to 100, with higher scores indicating greater impairment of activity due to migraine. The working population (full-time, part-time, or self-employed) completed the absenteeism, presenteeism, and overall work productivity loss metrics while all participants completed the activity impairment metric [16, 17].

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

The mMIDAS questionnaire captures missed days of work, missed household chores, missed non-work activity, and $\geq 50\%$ reduced productivity in professional or personal work. The mMIDAS scores (on a scale from 0 to 40) indicate minimal (grade I, 0–5), mild (grade II, 6–10), moderate (grade III, 11–20), or severe (grade IV, 21 +) disability experienced by a patient due to migraine. In the BECOME study, a mMIDAS questionnaire with a 1-month recall period was used. Therefore, the total mMIDAS score was multiplied by three to generate a score analogous to the universal 3-month MIDAS score [20, 21].

The HADS is a self-reported 14-item scale consisting of anxiety and depression subscales of seven items each. With a four-point Likert scale (0–3) scoring each item, each subscale has a possible score range of 0 to 21, indicating normal (0 to 7), suggested (8 to 10), or probable presence (≥ 11) of either anxiety or depression [22].

For the migraine scales, only the HIT-6 has been validated in Dutch and French [23]. As for the other non-migraine scales, the EQ-5D-5L and HADS have been validated in Dutch and French [24–26].

Subgroup analysis

To investigate whether the MMD load and medication-overuse headache modulated the burden of migraine, a subgroup analysis was performed.

Statistical analysis

Descriptive statistics were used to present the demographics and characteristics of the study population. Categorical variables were presented as absolute numbers and relative frequencies, and continuous variables as simple statistics.

Ethics approval

The study was approved by an independent ethics committee and conducted in accordance with the ethical principles laid down in the Declaration of Helsinki. All participants provided informed consent before study initiation.

The central EC for Belgium was the UZ Brussel EC (B.U.N. 143,201,733,560).

Results

A total of 20,837 patients were screened in part 1 in Europe and Israel. From these, 806 patients were recruited from 5 Belgian headache centers (Koen Paemeleire, Annelies Van Dycke, Nina De Klippel, Jean Schoenen and Jan Versijpt).

Study population in part 1

Of the 806 patients with migraine examined during the 3 months in part 1 of the study, 45% reported ≥ 8 MMD. Overall, 37% never tried a prophylactic therapy and 25% had failed ≥ 4 preventive treatments. Medication-overuse headache was reported in 15% of patients. Most patients examined in part 1 visited the centre for a follow-up visit, representing 69% of the Belgian study population (Table 1).

Study population in part 2

Part 2 included 90 patients with ≥ 4 MMD in the previous 3 months and ≥ 1 PPTF in the foregoing 5 years. Among these patients, 70% had ≥ 8 MMD. Overall, 24% of patients had failed ≥ 4 prophylactic treatments. Tolerability was about as often the reason for treatment failure compared to ineffectiveness.

In up to 26% of the patients there was a suspicion of medication-overuse headache. More than 90% of patients had experienced migraine for more than 5 years (Table 1).

In the past year, 12 patients (13%) visited the emergency department for headache or migraine, while 13 patients (14%) were admitted as inpatients for headache complaints. Overall, 8 patients (9%) underwent a CT scan, while 18 patients (20%) received an MRI scan in the previous 12 months because of headache. On average, patients consulted their general practitioner for headache 1.5 times in the past 3 months.

Burden of disease

Patients reported a mean (SD) HIT-6 score of 66.0 (4.3) and a mean (SD) mMIDAS score of 26.5 (17.6), indicating a severe impact of headache on daily life and substantial migraine-related disability, respectively (Table 2). In the part 2 population, 94% of the patients reported a severe impact of headache on daily life (HIT-6 score ≥ 60) and 91% had a severe migraine-related disability (MIDAS ≥ 21). Abnormal Hospital Anxiety subscale scores of ≥ 11 were observed in 39% of the Part 2 population.

When the HIT-6 responses were analyzed according to the MMD subgroups, the total score remained in the range of 'severe impact' for all subgroups. The mMIDAS score within the 4–7 MMD group and 8–14 MMD group was comparable. However, we see a substantial increase in disability within the subgroup of ≥ 15MMD patients.

The presenteeism (21.5 to 33.1), overall work productivity loss (55.1 to 63.7) and the activity impairment (55.9 to 69.8) increased with the number of migraine days (Table 3).

In patients with medication-overuse headache, there was a higher burden compared to patients without medication-overuse headache, however, both groups had a severe impact (HIT-6) and substantial disability (mMIDAS) (Table 4).

Discussion

In part 2, 70% of the migraine patients had ≥ 8 MMD. Among those patients, 24% reported ≥ 4 PPTF, with tolerability and ineffectiveness being as often the reason for treatment failure. Furthermore, within 26% of the patients there was a suspicion of medication-overuse headache. These findings highlight both the high burden of disease and the difficulties in managing migraine.

Migraine patients in the Belgian population under study reported a substantial migraine-related disability (mMIDAS 26.5), while the migraine-related disability as assessed in a French population study was only mild (MIDAS 6.5) [27]. This is probably related to the inclusion criteria of the current BECOME study targeting patients with ≥ 4 MMD and ≥ 1 PPTF.

When analyzing whether the MMD load modulated the burden of disease, a higher MMD frequency was associated with more limitations and restrictions on daily activities, according to the mMIDAS scores, compared to patients with fewer MMD. As described in a cross-sectional observation from the Medication Overuse Treatment Strategy trial, within the group of patients who have chronic migraine with medication overuse, those with higher headache frequency have even greater disability [28]. However, in the present study, there still was a substantial disability reported in the subgroup with ≤ 8 MMD. These findings were already described by several studies [10, 29]. According to the International Burden of Migraine Study (IBMS), there was a substantial amount of patients with severe disability within the subgroup of patients with less than 8 MMD [10]. This might be partly related to the fact that the burden of migraine extends well beyond the amount of headache days itself, suggesting the

Table 1 Characteristics of the Belgian BECOME study population (Part 1 and 2)

Part 1	Migraine patients ($N=806$)
Migraine days	
<4	231 (28.7%)
4–7	210 (26.1%)
8–14	180 (22.3%)
15+	185 (23.0%)
Prior prophylactic treatment failures	
0	297 (36.9%)
1	155 (19.2%)
2	95 (11.8%)
3	61 (7.6%)
4+	198 (24.6%)
At least one prior prophylactic treatment failure	509 (63.2%)
Novelty status	
New patients	248 (30.8%)
Follow-up patients	558 (69.2%)
Medication overuse	
Any	192 (23.8%)
Medication-overuse headache	121 (15.0%)
Part 2	Migraine patients ($N=90$)
Gender	
Women	79 (87.8%)
Men	11 (12.2%)
Mean age (years)	
Women	40.5
Men	45.6
Working status	
Full-time employed	27 (30.0%)
Part-time employed	24 (26.7%)
Homemaker	2 (2.2%)
Other	15 (16.7%)
Retired	3 (3.3%)
Self-employed/freelance	3 (3.3%)
Sick leave	5 (5.6%)
Full-time student	4 (4.4%)
Part-time student	1 (1.1%)
Unemployed	6 (6.7%)
Migraine days	
<4	0 (0.0%)
4–7	27 (30.0%)
8–14	21 (23.3%)
15+	42 (46.7%)
Prior prophylactic treatment failures	
0	0 (0.0%)
1	34 (37.8%)
2	16 (17.8%)
3	18 (20.0%)
4+	22 (24.4%)

Table 1 (continued)

Part 2	Migraine patients ($N=90$)
Reasons for treatment failure (since ≥ 1 failure was possible, numbers exceed 90)	
Tolerability	105 (45.5%)
Efficacy	123 (53.2%)
Other (e.g. not eligible)	3 (1.3%)
Disease duration (years)	
< 1 year	0 (0.0%)
1 to < 3 years	2 (2.2%)
3 to < 5 years	5 (5.6%)
5 years and above	83 (92.2%)
Suspected overuse headache	
No	67 (74.4%)
Yes	23 (25.6%)

Table 2 Summary of the total PRO scores and number of patients by domain for the part 2 population

Assessment tool	*N*	Mean (SD) score
EQ-5D-5L utility index score	90	0.6 (0.2)
EQ-5D-5L VAS score	90	63 (21)
MSQ. RFR score	90	38.3 (16.5)
MSQ. RFP score	90	55.4 (20.6)
MSQ. EF score	90	39.5 (24.4)
WPAI. Percent work time missed	55	18.4 (31.9)
WPAI. Percent impairment while working	90	29.1 (30.6)
WPAI. Percent overall work impairment	55	60.0 (25.1)
WPAI. Percent activity impairment	90	62.6 (22.8)
HIT-6 score	90	66.0 (4.3)
mMIDAS score	86	26.5 (17.6)
HADS anxiety subscale	90	9.5 (4.9)
HADS depression subscale	90	6.7 (4.2)

interictal phase being attributable to substantial disabilities [7, 30].

There was a significant detrimental effect of migraine on the productivity in the working population, either due to absenteeism from work or reduced productivity for those going to work, according to responses to the WPAI-headache questionnaire. This is also in line with results described in other studies [28, 31, 32]. Although the current study did not investigate the underlying reasons for presenteeism, we can only speculate this might be related to inadequate treatment efficacy and a lack of a migraine-friendly work environment [33]. Comparing the current results to another paroxysmal disorder, we noted on average a numerically lower impairment on the work productivity in idiopathic generalized epilepsy according to an analysis from the Nation Health and Wellness Survey [34].

Almost 40% of the population under study had a HADS anxiety subscale score indicative of anxiety. The association of anxiety and depression with migraine has been previously reported [22, 35]. There was a normal score on the HADS depression subscale in this sample, which was also seen in the EU BECOME population [12]. Comparing these data with results of patients with refractory epilepsy, numerically lower scores for anxiety were found [36].

The EQ-5D-5L Utility Index score and VAS score in the present study were lower than the mean score in the Belgian population (0.84 and 77.1 respectively), suggesting migraine patients having a less favourable health status than the overall Belgian population [37]. When comparing these data with data found in (medically refractory) epilepsy patients, numerically higher scores were found in two studies on the EQ-5D-5L Utility Index and VAS score, stressing again the substantial disability associated with migraine [38, 39].

In this paper, we tried to assess the burden of migraine in patients with ≥ 1 PPTF visiting Belgian headache specialists. Since data were collected from headache specialists, it is expected that the diagnosis of migraine would be more accurate ensuring a correct assessment of true treatment failure as well as a precise attribution of burden to migraine. On the other hand, these data may not be representative of patients visiting the general physician or neurologist.

There are more limitations to consider. First, since some elements were self-reported, recall bias may affect the data

Table 3 PRO questionnaires by monthly migraine days

Assessment tool	Monthly migraine days		
	4–7	8–14	15+
HIT-6 score			
N	27	21	42
Mean (SD)	65.4 (4.0)	64.9 (4.9)	66.9 (4.2)
mMIDAS score			
N	25	20	39
Mean (SD)	18.7 (12.2)	18.2 (12.1)	35.8 (18.6)
EQ-5D-5L utility index score			
N	27	21	42
Mean (SD)	0.7 (0.3)	0.7 (0.2)	0.6 (0.2)
EQ-5D-5L VAS score			
N	27	21	42
Mean (SD)	65.5 (19.0)	69.6 (15.5)	57.2 (22.7)
MSQ. RFR score			
N	27	21	42
Mean (SD)	42.9 (16.7)	44.1 (16.6)	32.5 (14.8)
MSQ. RFP score			
N	27	21	42
Mean (SD)	62.0 (19.3)	60.2 (19.5)	48.7 (20.2)
MSQ. EF score			
N	27	21	42
Mean (SD)	47.4 (22.7)	47.3 (23.7)	30.5 (23.2)
WPAI. Percent work time missed			
N	17	13	25
Mean (SD)	23.6 (38.3)	20.4 (36.8)	13.9 (24.2)
WPAI. Percent impairment while working			
N	27	21	42
Mean (SD)	21.5 (27.6)	31.0 (29.1)	33.1 (32.8)
WPAI. Percent overall work impairment			
N	17	13	25
Mean (SD)	55.1 (30.4)	59.4 (24.8)	63.7 (21.4)
WPAI. Percent activity impairment			
N	27	21	42
Mean (SD)	55.9 (26.2)	56.7 (24.4)	69.8 (17.3)
HADS anxiety subscale			
N	27	21	42
Mean (SD)	8.8 (4.7)	9.2 (4.9)	10.0 (5.0)
HADS depression subscale			
N	27	21	42
Mean (SD)	6.5 (4.1)	4.8 (3.6)	7.7 (4.3)

reported on PPTF, MMD, and PRO questionnaires. Secondly, data are only based on a small Belgian sample.

Collectively, these findings in the Belgian sample of the BECOME study are aligned with the European findings and demonstrate the high burden of disease and the unmet need for the management of difficult-to-treat migraine.

Table 4 PRO questionnaires by medication-overuse headache

Assessment tool	Suspected medication-overuse headache	
	No	Yes
HIT-6 score		
N	67	23
Mean (SD)	65.6 (4.6)	67.2 (3.3)
mMIDAS score		
N	62	22
Mean (SD)	23.3 (15.7)	35.6 (19.8)

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13760-023-02280-4.

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Data availability Data have not been made available publicly.

Declarations

Conflict of interest Koen Paemeleire has received personal compensation from Allergan/Abbvie, Amgen/Novartis, Eli Lilly, Lundbeck and Teva for consulting, serving on a scientific advisory board, and/or speaking and is a clinical trial investigator for Amgen/Novartis (erenumab), Eli Lilly (galcanezumab), and Autonomic Technologies Inc. (sphenopalatine ganglion stimulation). Josefin Snellman has received personal compensation from Allergan/Abbvie, Amgen/Novartis, Eli Lilly, Lundbeck, Teva, Cefaly Technology, Autonomic Technologies Inc. and Man & Science for consulting, serving on a scientific advisory board, and/or speaking and is an investigator for Eli Lilly, Novartis, Lundbeck and Teva. Shannon Ritter and Josefin Snellman are full employees of Novartis. Jan Versijpt received personal fees and nonfinancial support from Teva, personal fees from Novartis and Lundbeck, and grants and nonfinancial support from Allergan/Abbvie.

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