

Disease Manifestations of Patients with Recurrent Acute Hepatic Porphyria (AHP) and Daily Life Impacts in EXPLORE International, Prospective, Natural History Study

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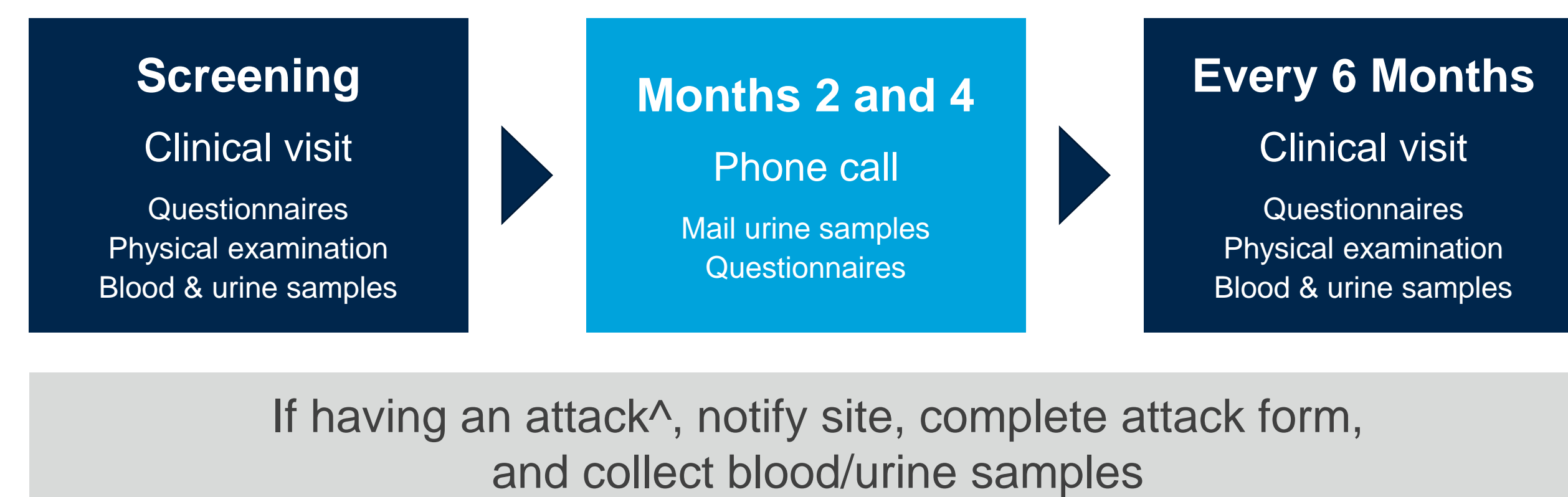
Introduction

- Acute hepatic porphyria (AHP) is a family of rare, genetic diseases characterized by defects in genes encoding heme biosynthetic pathway enzymes.¹ AHP comprises four subtypes: acute intermittent porphyria (AIP), variegate porphyria (VP), and hereditary coproporphyria (HCP), and δ-aminolevulinic acid deficiency porphyria (ADP)^{2,3}
- Patients with AHP can experience potentially life-threatening neurovisceral attacks (predominantly severe abdominal pain), debilitating chronic symptoms and serious long-term complications⁴
- This study aimed to characterize the disease manifestations and daily life impacts of AHP in patients with recurrent attacks (<10% of all patients) in Europe and the United States using data from the EXPLORE study

Methods

- EXPLORE (NCT02240784) is a prospective, international, observational study of the natural history and clinical management of symptomatic patients with AHP (Figure 1)

Figure 1: EXPLORE Study Design



[^]Attacks defined as acute porphyria symptoms requiring increase in treatment (hemin, pain medications, or carbohydrates) or hospitalization

- The study included male and female patients (≥18 years old) experiencing recurrent attacks (≥3/year) or receiving treatment (hemin or gonadotropin-releasing hormone) to prevent attacks
- At baseline, patients reported the number of attacks, attack symptoms, chronic symptoms between attacks, and completed questionnaires
 - Disease impact on social interaction and ability to leave the home was assessed using a healthcare utilization questionnaire
- During the 12-month study, patients also completed a porphyria attack symptom inventory questionnaire when they experienced attacks
 - Symptoms always or usually associated with a porphyria attack were recorded using check boxes for listed symptoms within the following categories: pain; mood/sleep; digestive/bladder; nervous system; other. An option to provide an open answer was included in each category

Results*

Patient Demographics and Disposition

- Overall, 112 patients from 21 centers (56% from 14 EU centers and 44% from 7 US centers) were enrolled. Baseline demographics and characteristics were comparable between the regional groups (Table 1)

Table 1: Patient Demographics and Baseline Characteristics

Characteristic	EU (n=63)	US (n=49)
Mean age, years	41 (13)	37 (12)
Female, n (%)	55 (87)	45 (92)
Race, n (%)		
White/Caucasian	52 (83)	43 (88)
Asian	0	3 (6)
Black/African American	0	3 (6)
Not answered	11 (18)	0
Height, cm	166 (9)	165 (9)
BMI, kg/m ²	24 (5)	26 (6)
AHP subtype, n (%)		
Acute intermittent porphyria	61 (97)	43 (88)
Variegate porphyria	2 (3)	3 (6)
Hereditary coproporphyria	0	3 (6)

Data are mean (SD) unless otherwise stated
AHP, acute hepatic porphyria; BMI, body mass index; SD, standard deviation

Attack Frequency and Chronic Symptoms Reported at Time of Enrollment

- The mean (standard deviation [SD]) of all attacks reported in the last 12 months was 9.0 (10.6) for EU patients and 9.7 (9.2) for US patients (Table 2)
- The rate of attacks requiring hospitalization was similar between the EU and the US (Table 2)

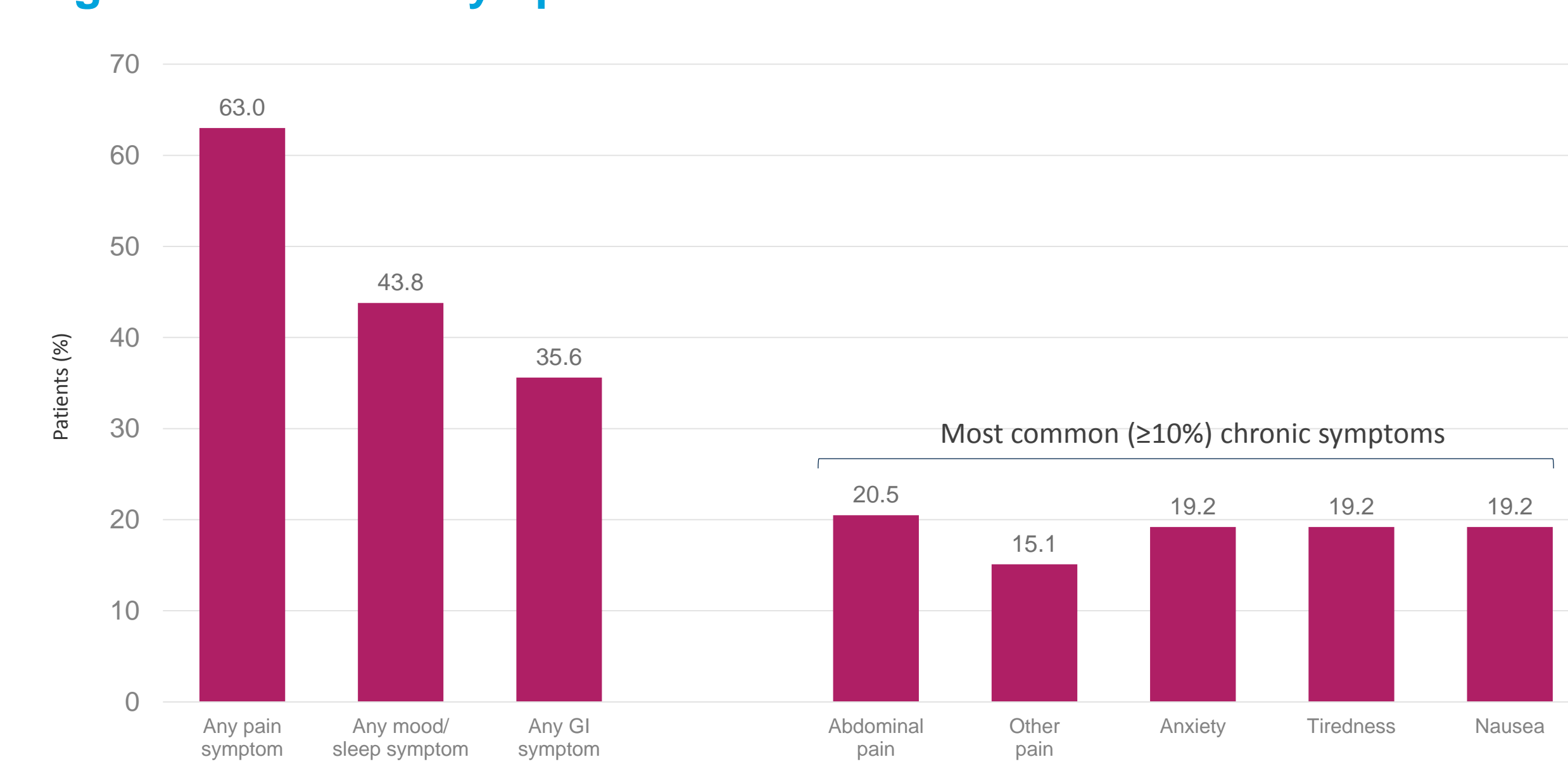
Table 2: Attack Rate in the Last 12 months before EXPLORE

Characteristic	EU (n=63)	US (n=49)
	Mean (SD)	Mean (SD)
Number of attacks	9.0 (10.6)	9.7 (9.2)
Number of attacks requiring hospitalization	3.2 (3.9)	3.5 (4.1)
Number of attacks requiring treatment at outpatient clinic or infusion center	3.9 (8.2)	3.7 (7.0)
Number of attacks requiring treatment at home	3.3 (8.6)	3.0 (5.7)

SD, standard deviation

- Most patients (73/112=65.2%) experienced chronic symptoms between attacks; these occurred more frequently among US patients than EU patients (71.4% and 60.3%, respectively) and more often manifested daily (80.0% and 63.2%, respectively)
- Among patients experiencing chronic symptoms, 63.0% had any pain symptom, 43.8% had any mood/sleep symptom, and 35.6% had any gastrointestinal (GI) symptom (Figure 2)
- The most common symptoms were pain and those involving the central nervous system (Figure 2)

Figure 2: Chronic Symptoms Between Attacks at Time of Enrollment

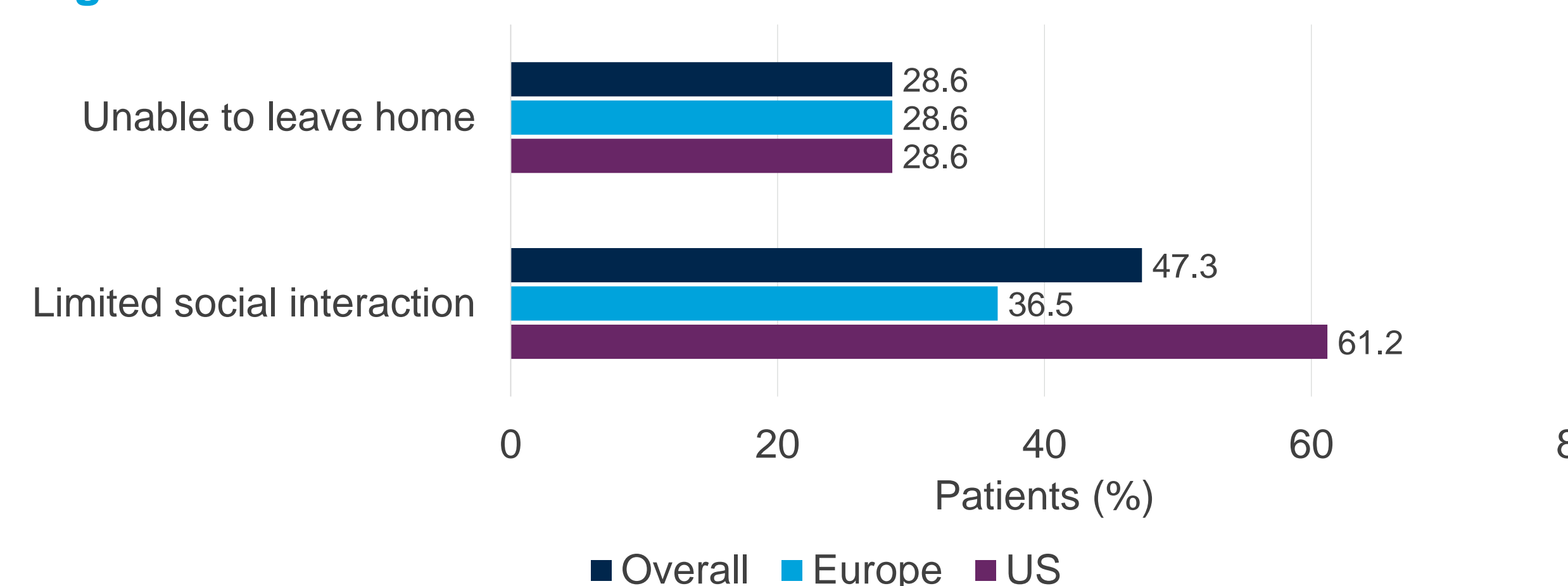


Percentages are based on n=73 patients who experienced chronic symptoms
Chronic symptoms are those occurring during asymptomatic periods

Impact of Disease on Daily Life at Time of Enrollment

- At baseline, all patients who responded to the questions reported that they had limited social interactions (n=23 EU and n=30 US respondents) or were unable to leave home (n=18 EU and n=14 US respondents) due to disease-related issues in the last 12 months
- Overall, 36.5% of EU patients (23/63) and 61.2% of US patients (30/49) included in the study had limited social interactions and 28.6% of both EU (18/63) and US patients (14/49) were home-bound in the last 12 months (Figure 3)

Figure 3: Disease-Related Social Limitations

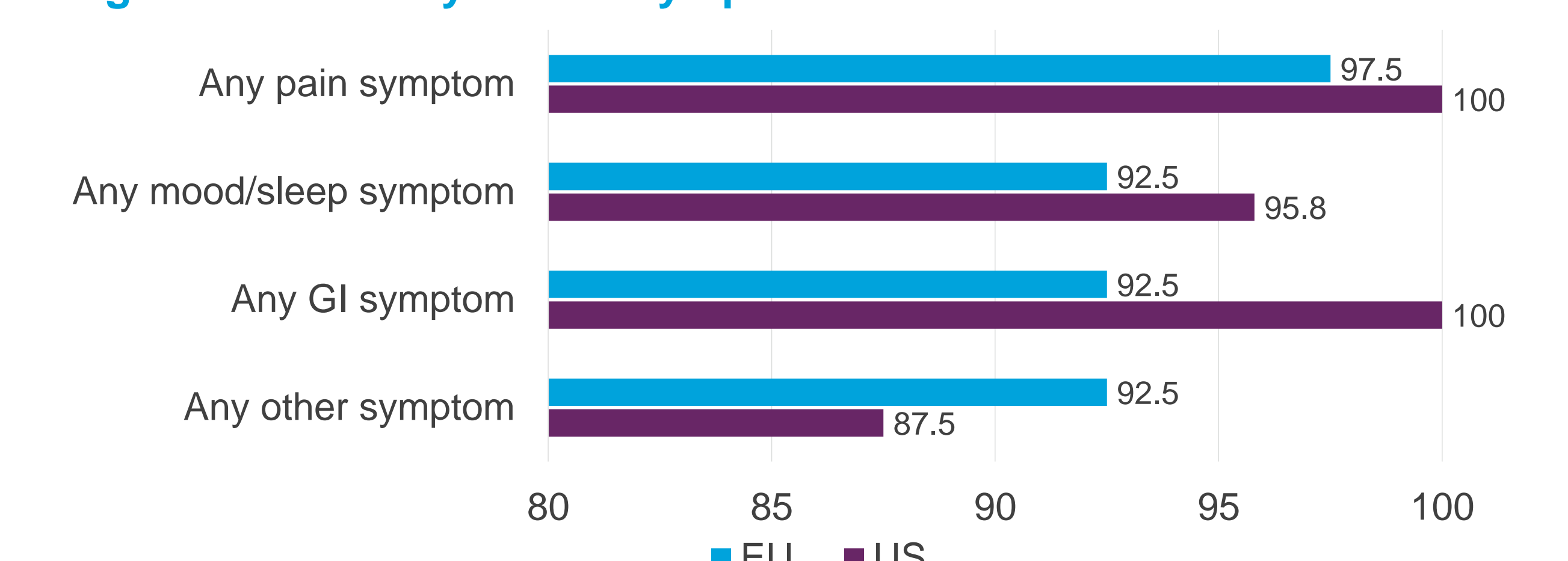


Percentages are calculated as a proportion of total EU patients (n=63) and US patients (n=49) included in the study
EU, Europe; US, United States

On-Study Symptoms During Attacks

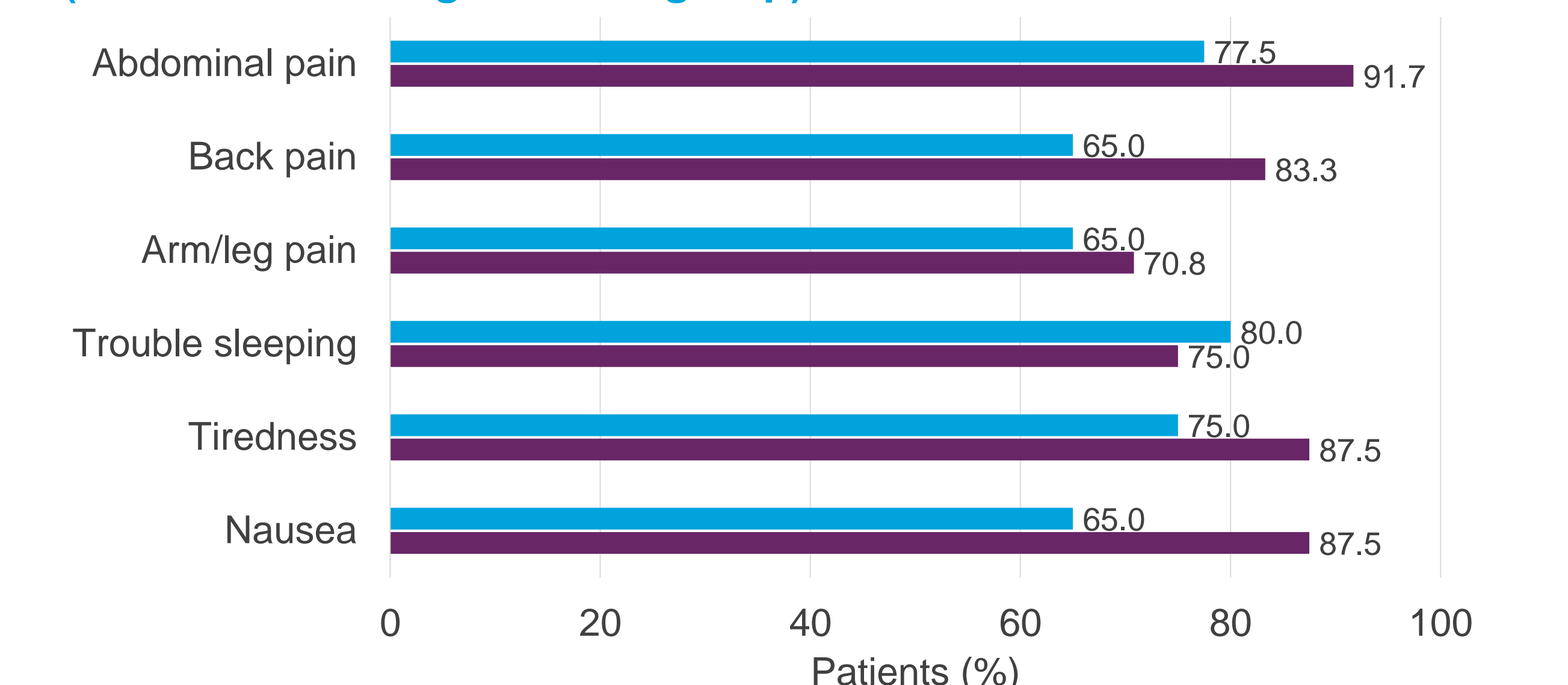
- During attacks in this 12-month study, most patients who responded to the questions reported having pain symptoms, mood/sleep symptoms, GI symptoms, and other symptoms (Figure 4)
- During attacks, EU and US patients commonly experienced pain symptoms (particularly in the abdomen, back, and arm/leg), nausea, tiredness, and trouble sleeping (Figure 5)
 - Other pain symptoms experienced were muscle pain (EU: 47.5%; US: 66.7%), headache (EU: 45.0%; US: 62.5%), skin pain (EU: 22.5%; US: 29.2%), and other pain (EU: 25.0%; US: 33.3%)
 - Aside from trouble sleeping, the incidences of these symptoms were higher among US patients than EU patients (Figure 5)

Figure 4: On-Study Attack Symptoms



Patients are counted once per symptom
Percentages are calculated based on n=40 EU respondents and n=24 US respondents
EU, Europe; US, United States

Figure 5: Commonly Reported Symptoms During Attacks (≥65% in Each Regional Subgroup)



Patients are counted once per symptom
Percentages are calculated based on n=40 EU respondents and n=24 US respondents

Conclusions

- Overall, patients with AHP in the EU and US showed similar symptoms during attacks and experienced comparable chronic symptoms
 - Common symptoms during attacks included pain (particularly in the abdomen, back, or arm/leg), nausea, tiredness, and trouble sleeping
- Many patients with AHP experienced negative impacts on daily life, specifically related to the disease, including limited social interactions and being home-bound
- This study demonstrates that most patients with recurrent attacks of AHP in the EU and the US have chronic symptoms in addition to the significant burden associated with acute attacks

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