

Symptom experience of patients with primary biliary cholangitis (PBC)

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Background and Aims

- Primary biliary cholangitis (PBC) is a chronic cholestatic liver disease with significant impact on quality of life
- In PBC, symptom burden may remain high despite biochemical control, and fatigue is often under-recognized in routine care
- Laboratory markers do not capture the full day-to-day impact of disease.
- Patient perspectives are essential to understand which symptoms most impair quality of life, and which treatment approaches would represent meaningful improvement.
- This study aimed to capture symptom burden in PBC, and gain patient perspective on the need for new therapeutic options

Method

- An international cohort of 250 adults with primary biliary cholangitis (PBC) from the UK, US, Australia, Canada, and other countries completed an online survey via the PBC Foundation app over a 3-month period
- Survey captured patient reported symptoms, their frequency and severity on a day-to-day basis and on their worst days
 - If patients experienced fatigue, they were asked to differentiate between central and peripheral fatigue with definitions for the same provided for patient reference (i.e. central fatigue characterized by a lack of self-motivation/intention and peripheral fatigue by a lack of ability)
- Survey included structured scales such as the PBC-40, and open-ended questions exploring the impact of PBC on daily living
- In addition to measuring symptom burden and quality of life, the survey explored symptoms that most patients would prioritize treating and clinically meaningful improvement for a new treatment



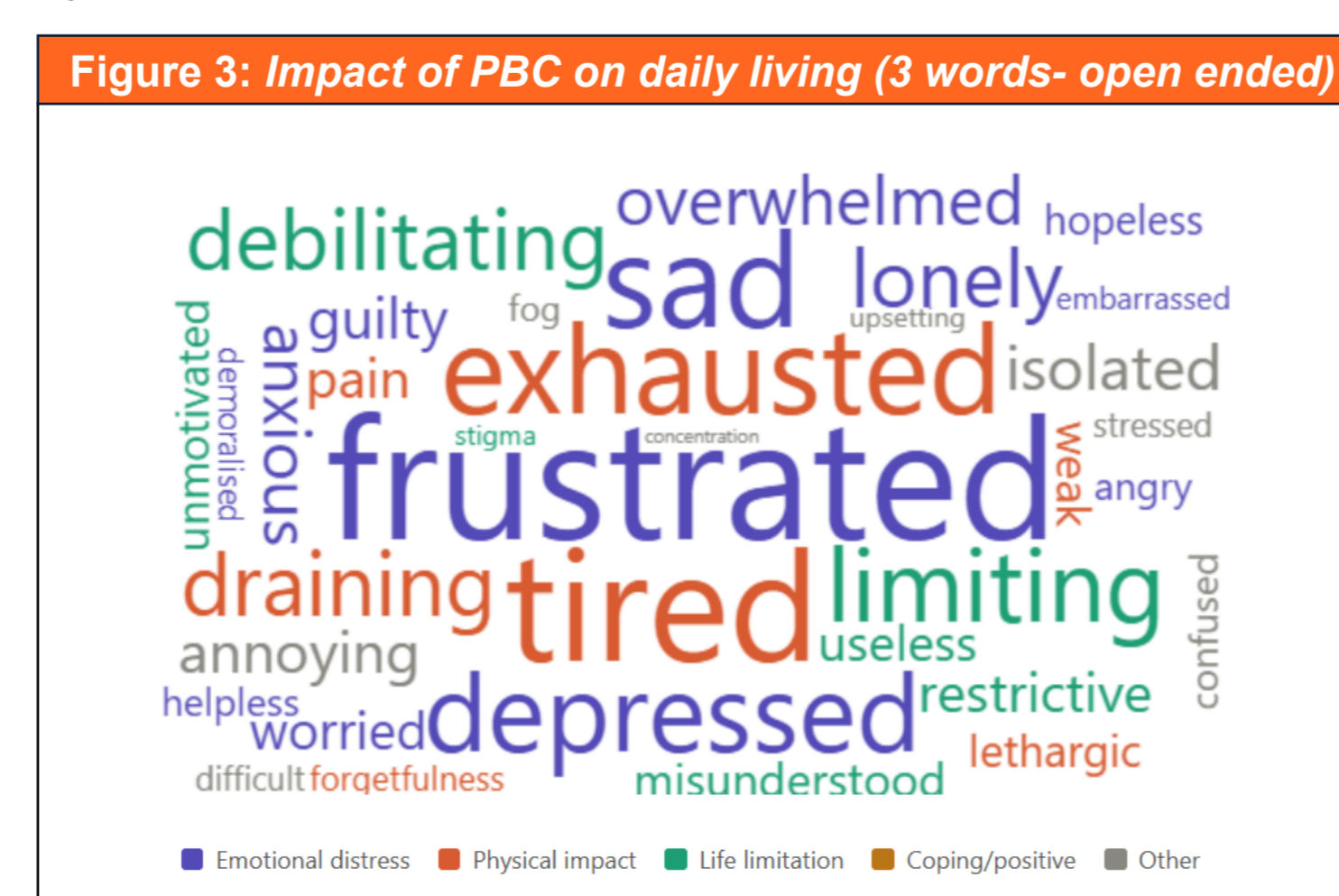
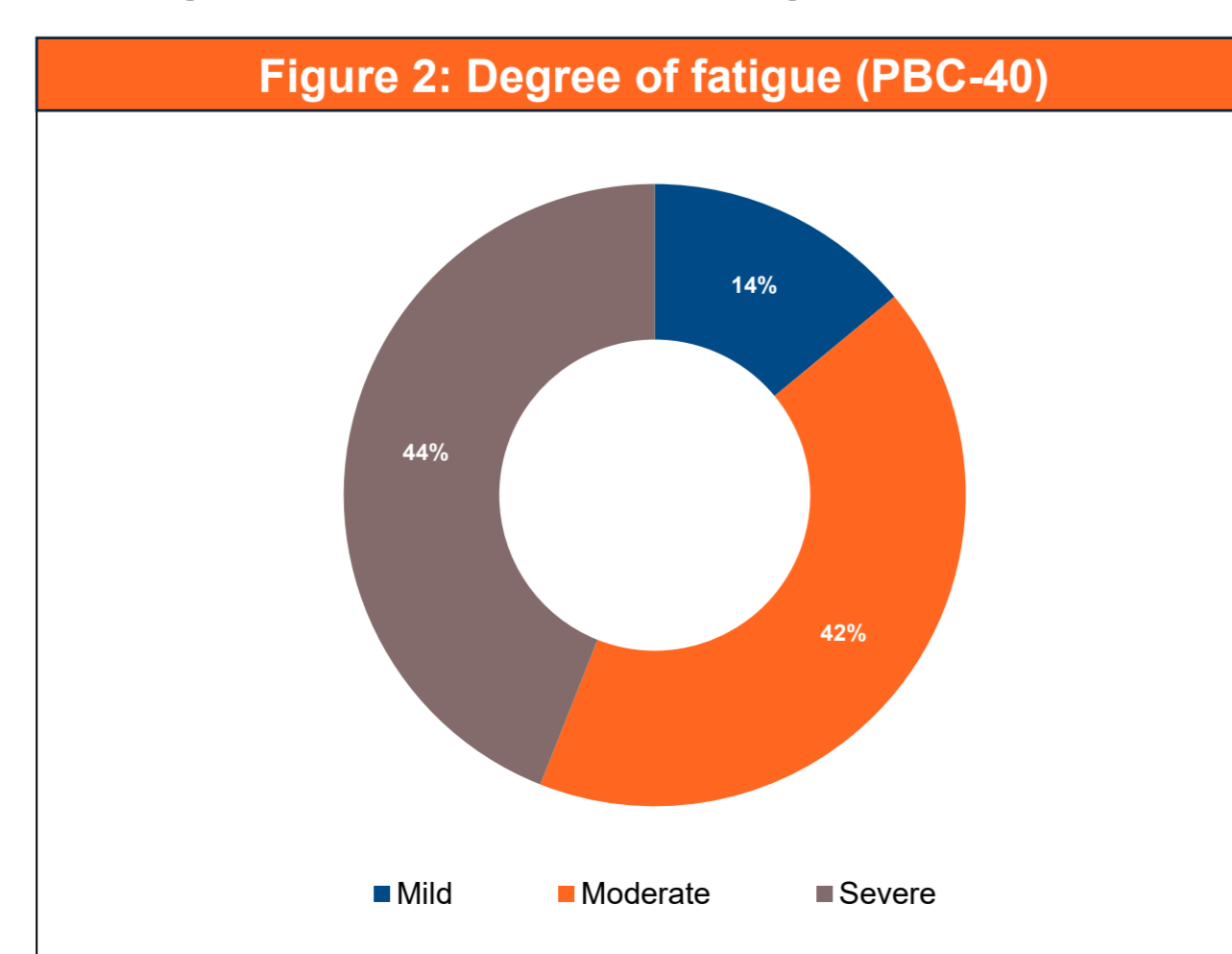
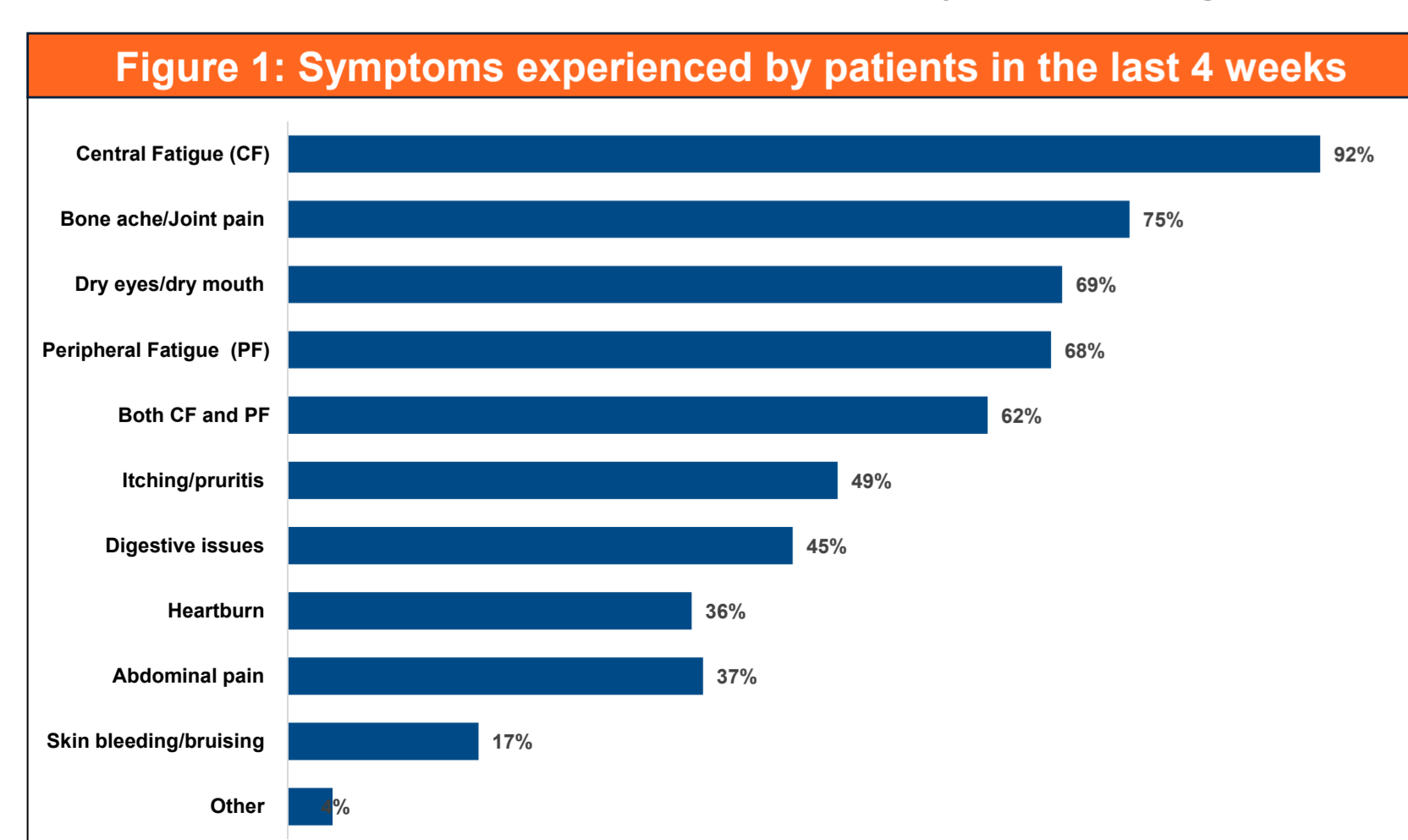
Results

Patient Demographics:

- Respondents were predominantly female (95%) with majority aged 51-70 years (70%)
- 41% were employed full-time/part-time by choice, 17% were employed part-time or retired due to illness, 11% were unable to work due to illness, 28% retired by choice and 3% are unemployed
- 98% of patients were on UDCA with 47% being responders, 8% non-responders, and 45% unsure/not told if they were responders
- Only 12% of patients had been informed that they had cirrhosis

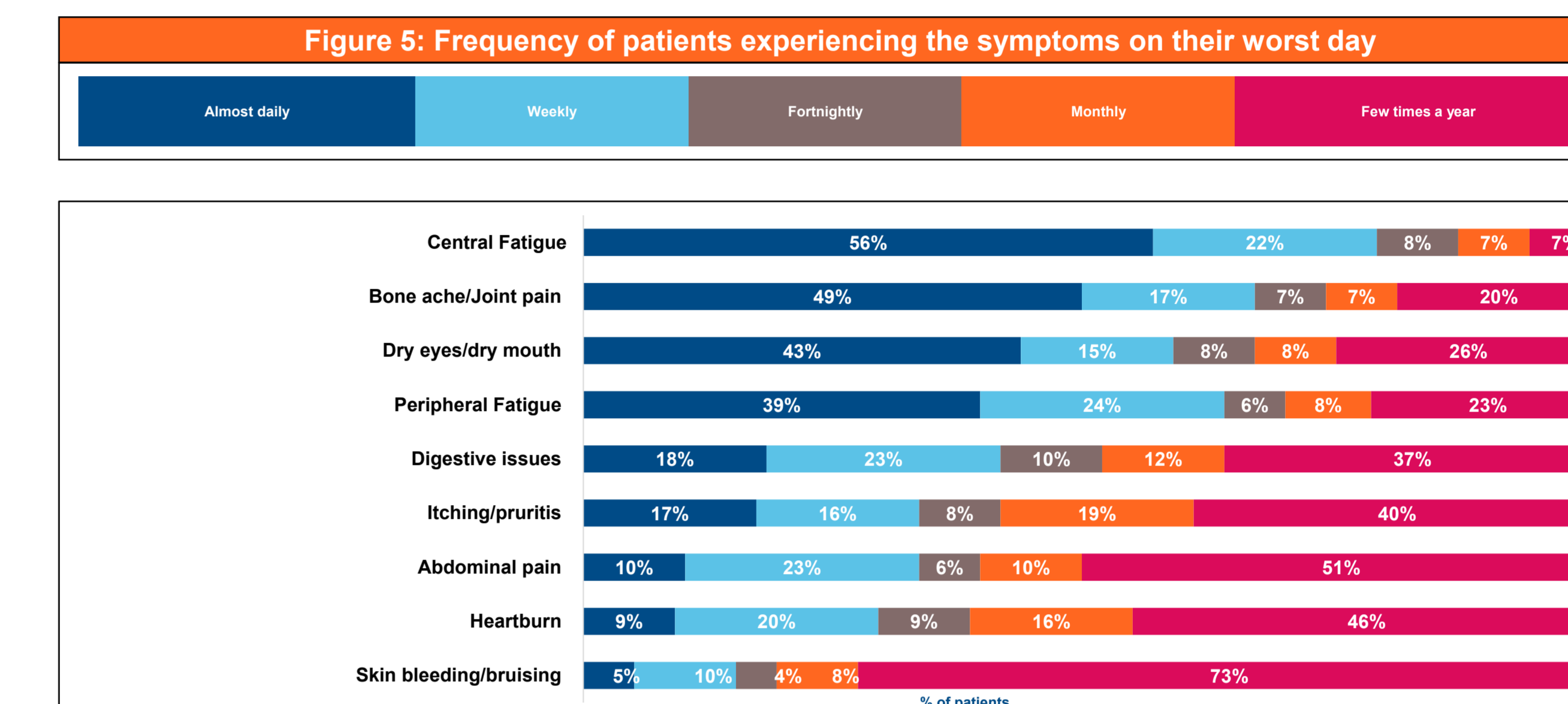
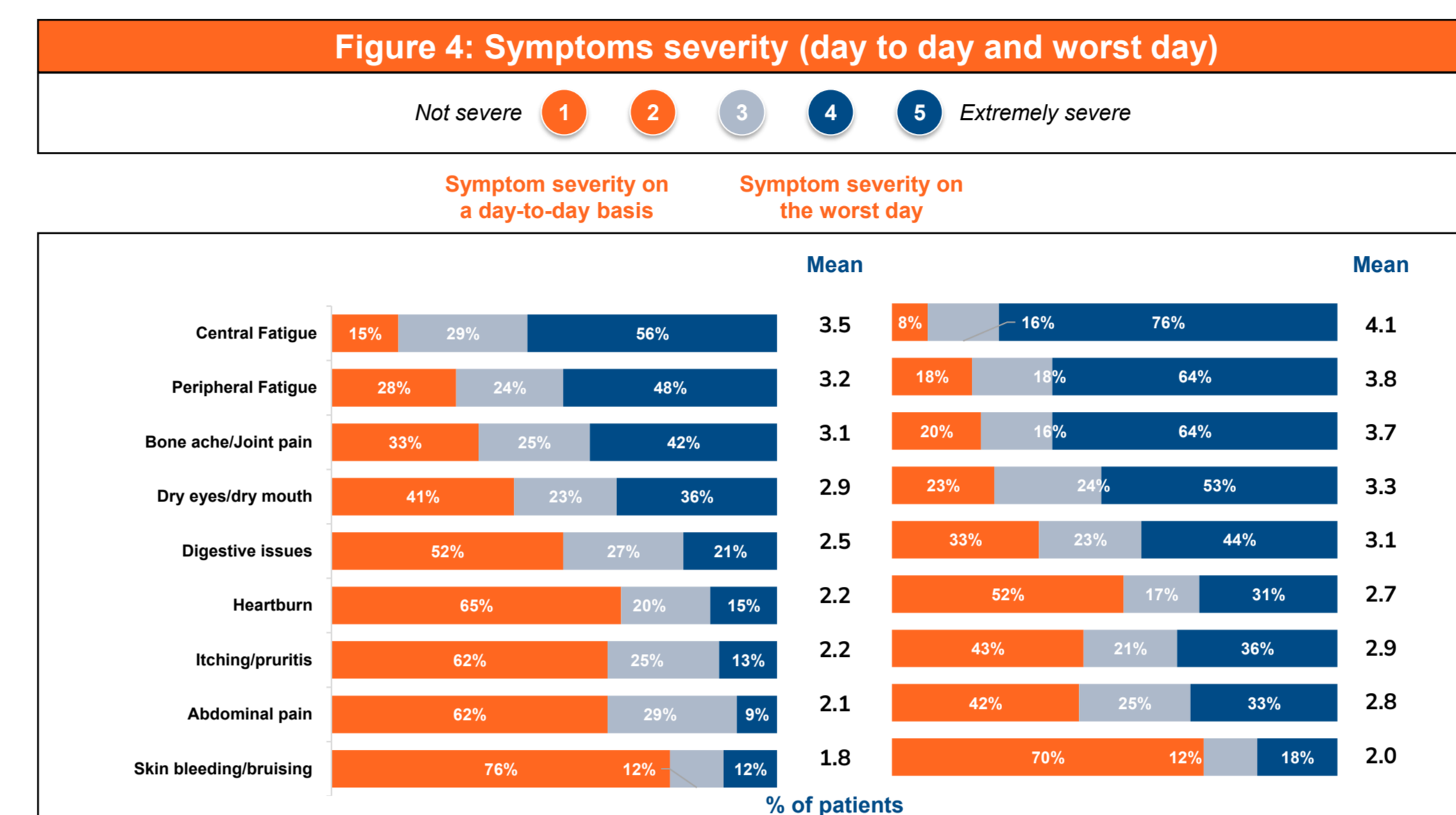
Symptom burden and impact of PBC on daily living:

- Majority of patients reported experiencing central fatigue (92%) followed by bone ache/joint pain (75%), dry eyes/dry mouth (69%), peripheral fatigue (68%) and itching/pruritis (49%) in the last 4 weeks
 - 62% of patients reported experiencing both central and peripheral fatigue
- 86% of patients reported moderate to severe fatigue on the PBC-40 questionnaire (42% moderate- score of 29 to 39; and 44% severe- score of ≥ 40)
- When asked to report impact of PBC on daily living in three words (open-ended), patients cited experiencing exhaustion, frustration, tiredness, and isolation collectively resulting in a debilitating and overwhelming burden on quality of life



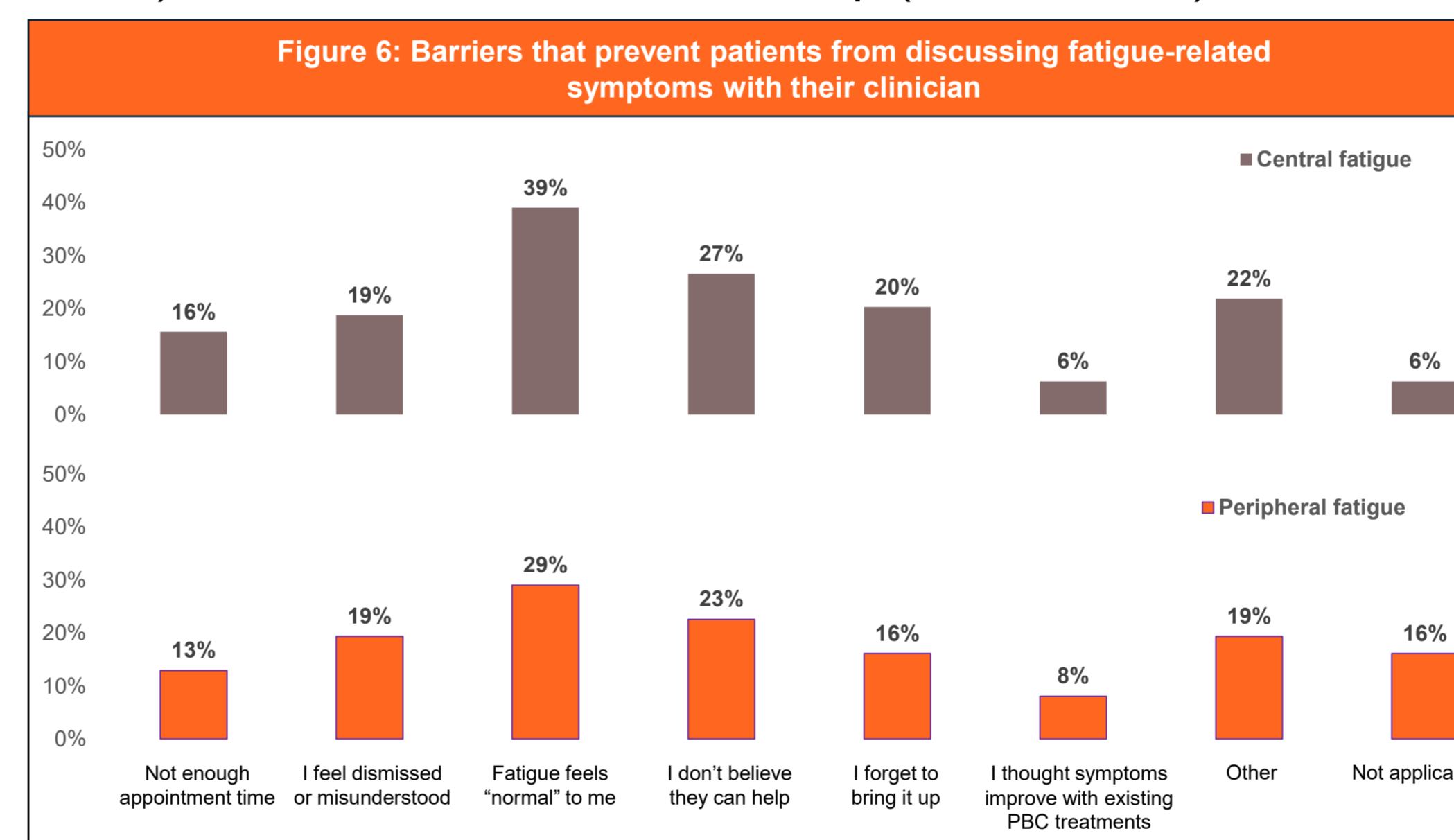
Symptom burden and impact of PBC on daily living:

- Central fatigue was patients' most burdensome / severe symptom (56%), followed by peripheral fatigue (48%) and bone ache (42%)
- More than half (56%) of patients reported experiencing their worst days due to central fatigue almost daily



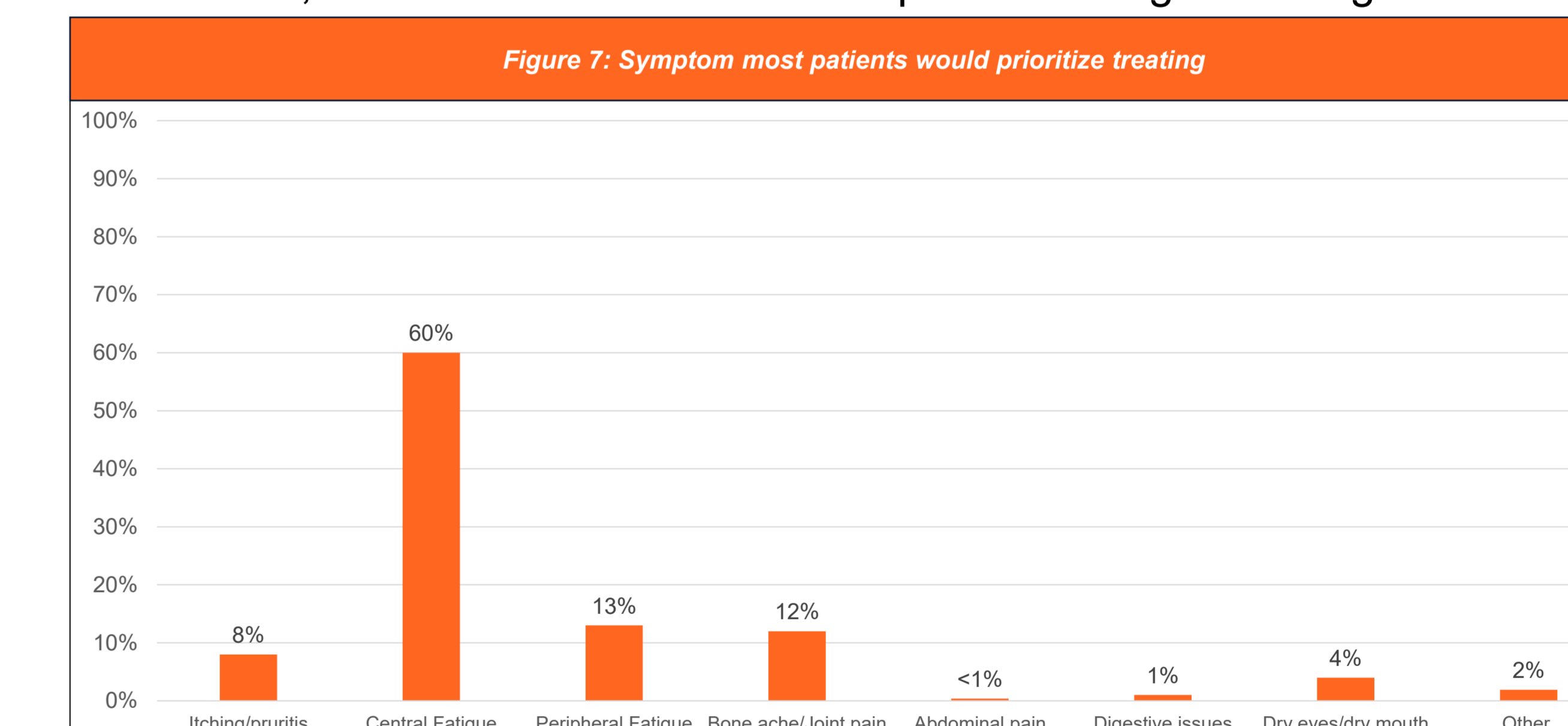
PBC patient interaction with clinician and reported barriers:

- >70% of patients experiencing central fatigue and peripheral fatigue discussed it with their clinicians (*this is higher than general population and could be effect of more proactive patients seeking PBC foundation*)
- Those not discussing fatigue believe it to be "normal" (29% 39%) and that clinicians cannot help (23% to 27%)



Symptom most patients would prioritize treating:

- When asked to choose only one symptom to treat, central fatigue overwhelmingly dominated patient priorities (60%)
 - Even amongst patients with itch, central fatigue is the prioritized symptom
- A clinically meaningful improvement in PBC-related fatigue is sustained energy with reduced brain fog, enabling patients to function, plan daily activities, and maintain restorative sleep without fatigue limiting their lives



Clinically meaningful improvement for a new treatment for fatigue in PBC (verbatim):

- "Recognition that **fatigue can be debilitating**. Develop drugs that don't cause insomnia or disrupt sleep cycle."
- "Something that **reduces brain fog and the complete washed out feeling of fatigue which stops me doing things**"
- "**I can't even imagine a world in which this fatigue was lifted, it would feel like a miracle. I wish I could feel more sharp minded again, quicker witted, and more energy into the afternoon and evening.**"

Conclusions

- Fatigue is commonly reported as one of the most prevalent symptoms of PBC
- This survey highlights the importance of two key constructs within PBC-related fatigue
 - Central fatigue which manifests as cognitive issues like "brain fog," memory and concentration problems and
 - Peripheral fatigue which is characterized by muscle weakness, dysfunction and an inability to sustain exercise
- It also shows the dominance of **central fatigue as the most burdensome symptoms** for which patients seek treatment; **even amongst patients with itch, central fatigue is the prioritized symptom**
- These findings underscore an urgent need for targeted interventions and a patient-focused approach to fatigue management to improve quality of life in PBC

