Fatigue in Primary Sclerosing Cholangitis

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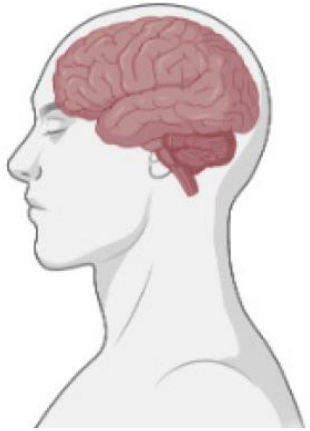
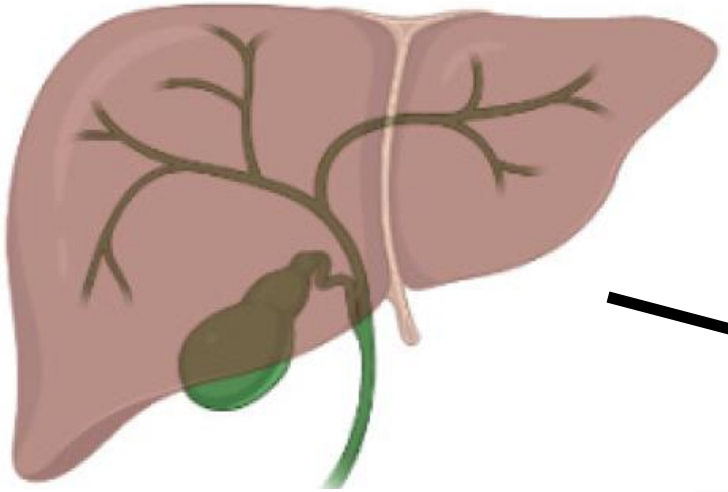
PSC Support

Fatigue

CENTRAL





PERIPHERAL

Memory Disturbances
Sleep Disturbance
Reduced Sleep Quality
Increased Daytime Somnolence

Reduced Functional Capacity
Increased Anaerobic Metabolism
Increased Lactic Acid
Increased Recovery Times

Adapted Images: Lynch EN et al, 2022 World Journal of Hepatology

Fatigue- what does it mean to you?

Question: Do you get asked about fatigue?

Yes

No

Question: What advice are you given?

Something

Nothing

Fatigue in cholestatic liver disease

>70% prevalence
Mechanisms poorly understood

If assessed the advice is inconsistent or vague

High burden with ↓ QoL

‘There is no treatment’

Fatigue is not routinely assessed within PSC

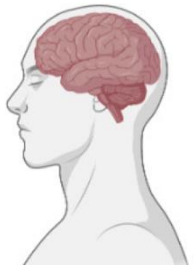
Some suggestion of lifestyle/coping mechanism advice

Abbas et al. *JHep Reports,* 2024; Chapman et al. Gut, 2019; Hirschfield et al. *BMJGut*, 2018; Mitchell et al. *Journal of Hepatology,* 2022

What do we believe to be contributors to fatigue?

PSC Support

Autonomic Dysfunction



Physical Pain

Psychological Distress

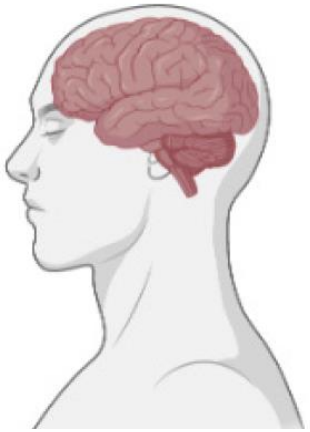
Sleep Disturbances

Underlying Inflammatory Disease

Contributing mechanisms

Autonomic Dysfunction

Parasympathetic autonomic nervous system (PANS)



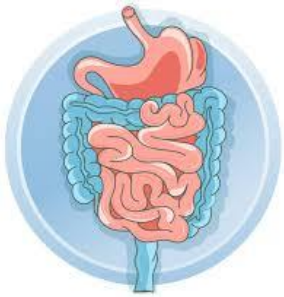
Sympathetic autonomic nervous system (SANS)

Contributing mechanisms

Autonomic Dysfunction

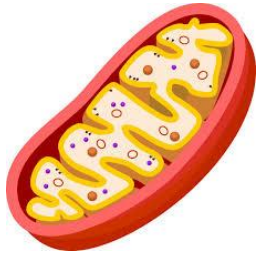
Parasympathetic autonomic nervous system (PANS)

Lowers heart rate



Stimulates digestion

Lowers blood pressure



Conserves energy

Contributing mechanisms

Autonomic Dysfunction

Sympathetic autonomic nervous system (SANS)

Increases heart rate

Increases blood pressure

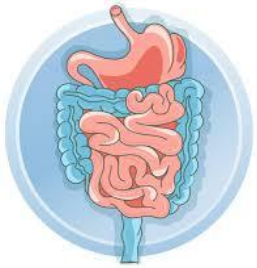
Emergency responses

Contributing mechanisms

Mild

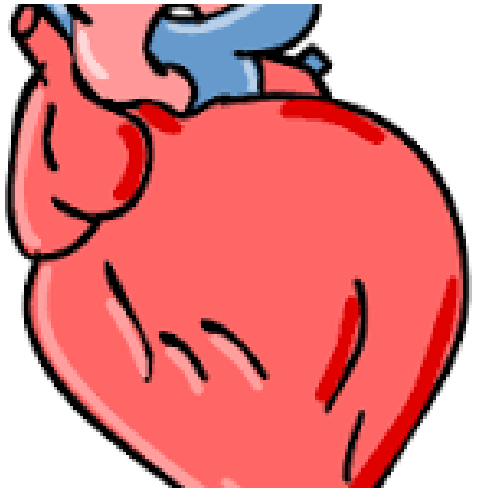
Severe

Digestive difficulties



Urinary problems

Altered heart rate



Dizziness/fainting

Vision problems

Contributing mechanisms

Psychological Distress

SLEEP DISTURBANCES
- Insomnia
- Poor sleep patterns
- Reduced restful sleep

IMMUNE SYSYEM FUNCTION
- Prolonged stress can suppress immunity
- Infection contributes to feeling of fatigue

MOOD AND EMOTIONAL IMPACT
- Increased steroid hormones (cortisol)
- Increased cognitive load
- Impaired ability to ‘switch off’

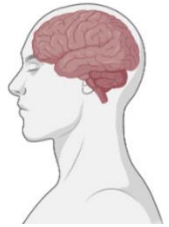
PHYSICAL SYMPTOMS
- Headaches
- Disturbances in gut health
- Muscle tension/pain

OVERALL
- Impairs decision making, contribution in daily tasks and concentration
- Alters perception of fatigue which leads to debilitating cycle

Contributing mechanisms

Sleep Disturbances

- Impact on circadian rhythm from hormone dysregulation
- Altered thermoregulation
- Prolonged state of inflammation
- Altered physical activity levels



CENTRAL DISTURBANCES

- Interferes with brain function
- Impairs memory consolidation
- Impairs cognition
- Impairs concentration

PERIPHERAL DISTURBANCES

- Impaired muscle recovery/repair
- Disruption of hormone regulation
- Impact on immunity

Contributing mechanisms

Physical Pain

MUSCLE TENSION AND OVER COMPENSATION

- Pain contributes to overuse
- Cycle of overuse triggering fatigue resulting in more pain
- Inability to recruit motor circuits

REDUCED PHYSICAL ACTIVITY

- Pain limits participation in functional activity
- Less inclined to exercise resulting in increased fatigability of muscle

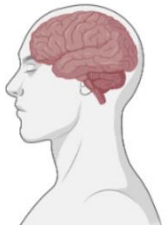
INFLAMMATION

- Pain often triggers an inflammatory response
- Increased energy production to respond to inflammatory response

SLEEP DISTURBANCES

- Increased sleep latency
- Reduced quality sleep
- Reduced sleep quantity

Contributing mechanisms



CENTRAL DISTURBANCES

- Central nervous system disruption (sending messages from the brain to the muscle)

DNA

- Abnormal modifications
- Breakage of DNA strands
- Cellular dysfunction

OXIDATIVE STRESS

↓

Imbalance between antioxidants and reactive oxygen species (ROS)

↓

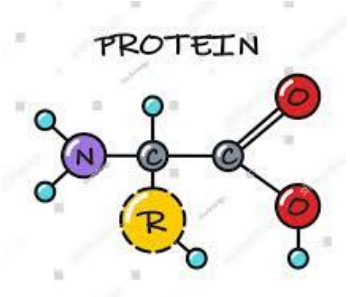
Activate the immune system

↓

Increased inflammation

GUT

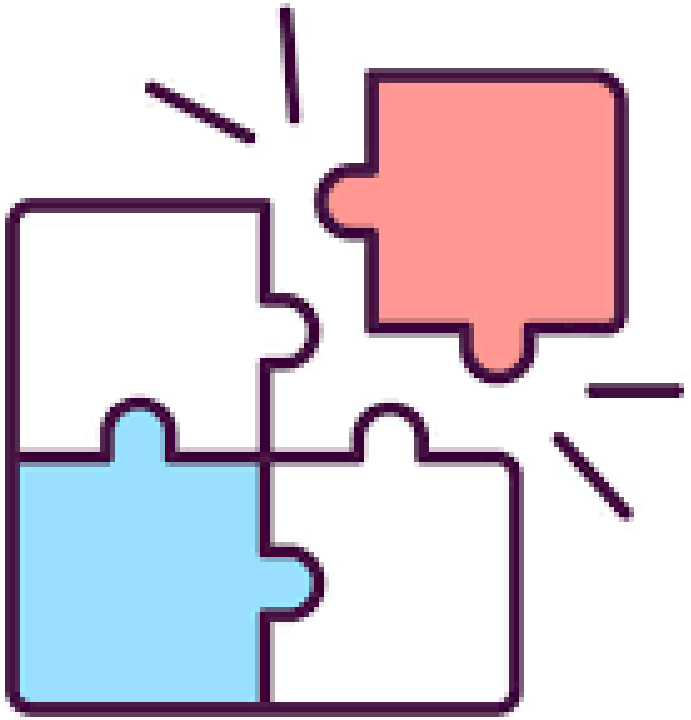
- Disturbs gut microbiome
- Damages intestinal barrier
- Reduction of ‘good bacteria’



PROTEIN

- Damages, dysfunction and degradation
- Disrupts cellular function

How does this all fit together?



Where do physiotherapists sit within the healthcare system?

Physiotherapy in PSC

PSC Support

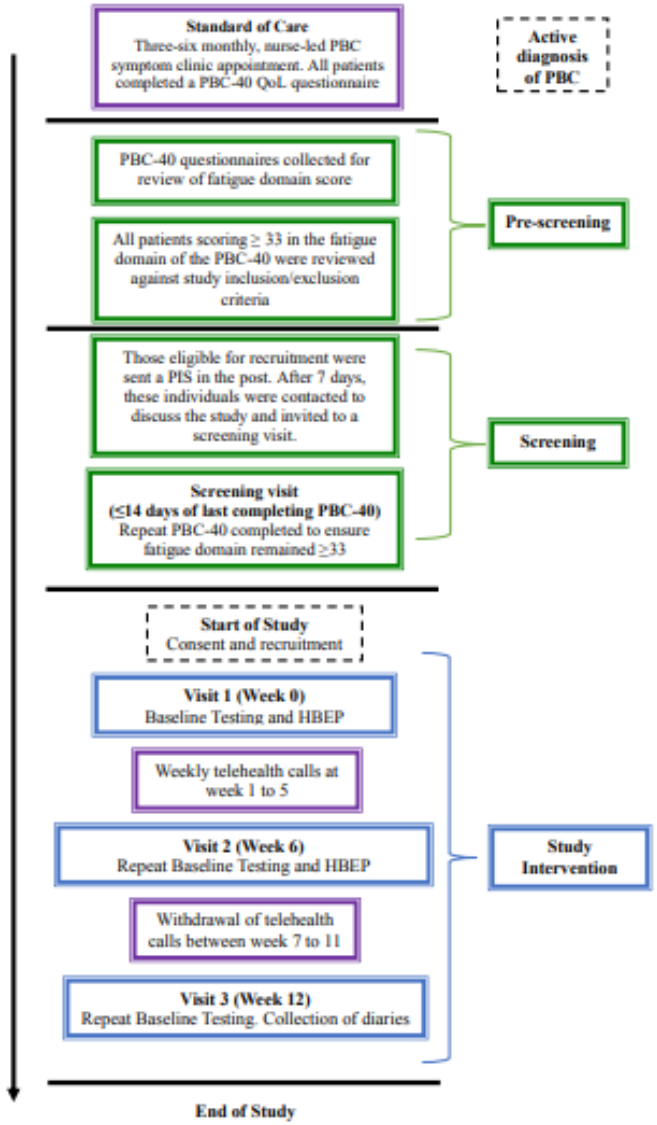
Hepatology

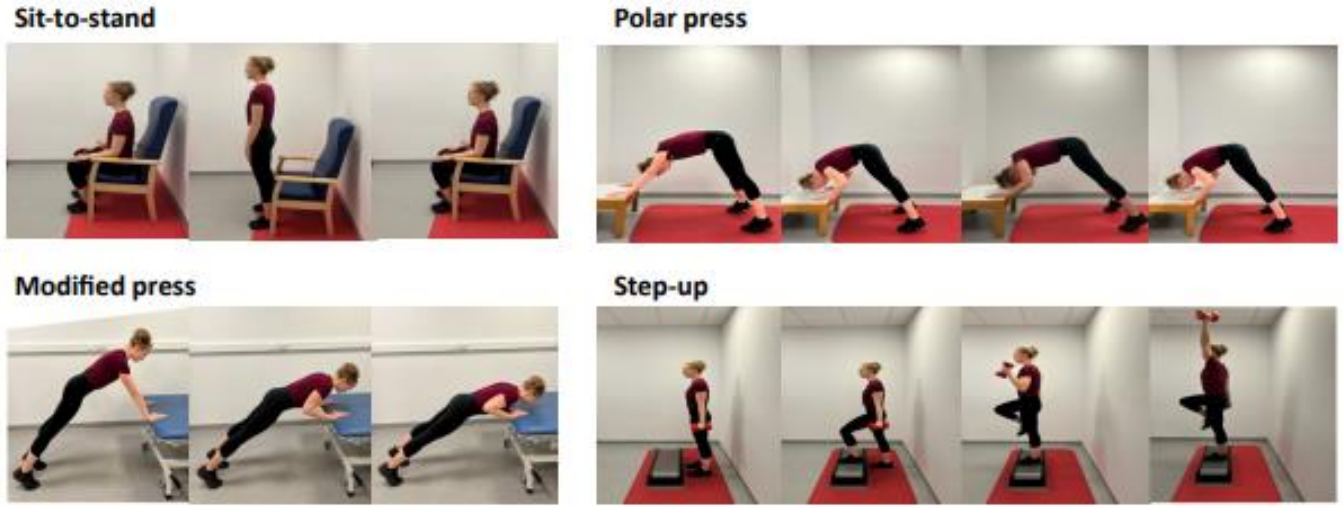
BMJ Open Gastroenterology

Home-based exercise in patients with refractory fatigue associated with primary biliary cholangitis: a protocol for the EXerCise Intervention in cholesTatic LivEr Disease (EXCITED) feasibility trial

Alice Freer,[1,2] Felicity Williams,[1,3] Simon Durman,[4] Jennifer Hayden,[2] Palak J Trivedi ,[1,2,5] Matthew J Armstrong[2]

Supplementary Figure 1: Participant identification, recruitment strategy and trial design.
Schematic presentation of the participant timeline from pre-screening, screening, consent, and delivery and completion of trial intervention.





Weekly regression vs. progression in exercise prescription

BASED ON:

- CONFIDENCE
- DAYS FATIGUED
- PERCEIVED EFFORT

Supported by telehealth calls in the first 6 weeks

Competence

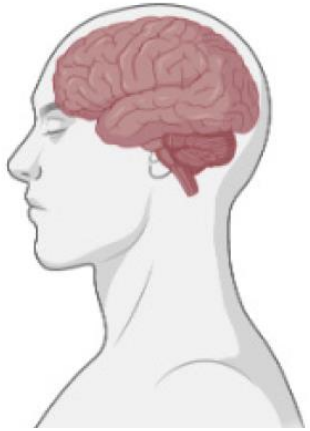
Confidence

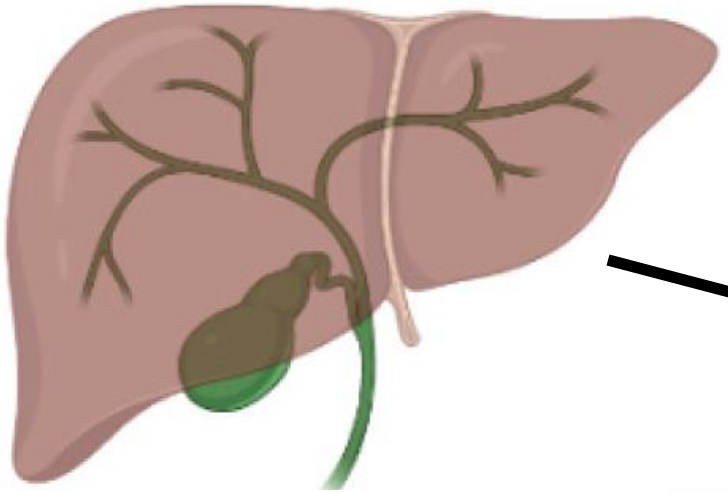
- Lifestyle
- Social dynamics/support
- Sleep
- Stigmatism
- Health literacy
- Accessibility
- Comorbidities/symptom burden/hospital admissions

The future for fatigue in PSC

PSC Support

CENTRAL





PERIPHERAL

Treatments that work!

Mechanisms

Physiotherapy in PSC

Exercise referral

Health and wellbeing

Holistic care

Energy expenditure

Fatigue

Sleep

Considerations

PSC Support

Internal Battery

Does your fatigue define you?

Check in on your mental wellbeing

Sit-to-stand

Polar press

Modified press

Step-up

Considerations

The "TrACE" approach

Management element	Associated feature
Treat the treatable	Pruritus (especially nocturnal)
	Autoimmune disease
	Hypothyroidism
	Arthritis
	Celiac disease
	Autoimmune anaemias
	Type 2 DM
	Anaemia
	Autoimmune
	Ulcer-related
	Variceal bleeding related
Ameliorate the Amelioratable	Sleep disturbance (especially daytime somnolence)
	Vasomotor autonomic dysfunction
	Depression
Cope	"Ownership of the problem"
	Coping Strategies
	Pacing during the day
	Avoiding shift work
	Maintaining social structures
	Exercise & diet
Empathise	Be understanding and supportive
	Don't pity feel sorry for people

Swain and Jones, 2019 *Liver International*

Considerations

- Personalised approach critical
- Responsive and adaptive holistic programme
- Behaviour intervention is crucial for long-term change
- Rapport with clinician invaluable throughout the patient journey

Summary

- Fatigue is complex and presents differently in each individual

- Mechanisms are not well understood but the future is bright!


Exercise referral


Health and wellbeing


Holistic care


Energy expenditure


Fatigue


Sleep

PSC Support