

Summary of study results

Fatigue in chronic liver disease: risk factors and treatment options

ISRCTN14379650 • Observational prospective mixed-methods cohort study • Reporting draft, 8 October 2026

Study overview and participant flow

SOMA.LIV investigated fatigue severity, persistence and associated biopsychosocial factors in adults with primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC). Recruitment was conducted at the Yael Center, University Medical Center Hamburg-Eppendorf, between March 2022 and February 2024. The final enrolled cohort comprised 468 participants (239 PBC; 229 PSC), below the original target of 480. Follow-up assessments were scheduled at 6 and 12 months. At 6 months, fatigue data were available for 213 PBC and 208 PSC participants; at 12 months, for 218 PBC and 211 PSC participants. The reported loss to follow-up over 12 months was 9.2% in PBC and 8.0% in PSC. These figures should be checked against the final participant-flow dataset before registry submission.

Primary outcome: fatigue severity and course

The registered primary outcomes were fatigue severity measured by the PBC-40 fatigue domain and the Fatigue Visual Analogue Scale (VAS), assessed at baseline, 6 and 12 months. At baseline, 29% of participants with PBC and 19% with PSC scored above 33 on the PBC-40 fatigue domain. Median baseline PBC-40 fatigue scores were 25 (PBC) and 21 (PSC; $p=0.007$); the between-diagnosis difference was no longer statistically significant after accounting for sex distribution. Fatigue status was relatively persistent: among participants fatigued at baseline, 82% (PBC) and 79% (PSC) remained fatigued at 6 months, and 74% in both groups at 12 months. Among those without baseline fatigue, 92% (both groups) remained below the threshold at 6 months, and 93% (PBC) and 94% (PSC) at 12 months. Complete VAS results and continuous PBC-40 scores by time point are not contained in the supplied summary and should be added before treating this as complete outcome reporting.

Predictors of fatigue

In multivariable analyses pooling PBC and PSC, fear-avoidance (TSK-GV) was associated with higher fatigue at 6 months ($\beta=0.18$, 95% CI 0.04–0.32, $p=0.01$) and 12 months ($\beta=0.20$, 95% CI 0.05–0.34, $p=0.01$). Illness anxiety was associated with 6-month fatigue ($\beta=0.59$, 95% CI 0.09–1.08, $p=0.02$), and childhood adversity with 12-month fatigue ($\beta=0.41$, 95% CI 0.05–0.77, $p=0.03$). The supplied analysis also reports negative coefficients for baseline fatigue in models at both time points; the model specification and interpretation should be verified before public reporting. Biological predictors were analysed by diagnosis. No significant biological predictors emerged in PBC. In PSC, detectable IL-6 was associated with fatigue at 6 months ($\beta=1.90$, 95% CI 0.09–3.72); antidepressant use ($\beta=6.41$, 95% CI 0.90–11.93) and inflammatory bowel disease ($\beta=2.03$, 95% CI 0.01–4.05) were associated with fatigue at 12 months. Cholestasis markers and liver disease stage showed no consistent associations.

Secondary outcomes

Participants with clinically relevant fatigue reported greater depressive and anxiety symptom burden, less favourable social circumstances and higher selected liver enzymes at baseline. The registration additionally specifies PHQ-15 somatic symptom severity, symptom intensity NRS, pruritus NRS, interference NRS, Pain Disability Index, SF-12 and PBC-40 disability-related quality of life at baseline, 6 and 12 months. The supplied DFG summary does not provide complete numeric results for these registered secondary measures. These are

therefore not reported here as if available; outcome tables should be appended or the reporting status explicitly noted.

Complementary microbiome, qualitative and experimental findings

In 151 stool samples (97 PBC; 54 PSC), 17 microbial taxa were associated with fatigue severity after adjustment and false-discovery-rate correction ($FDR < 0.05$). Several short-chain fatty acid-producing taxa were inversely associated with fatigue; *Flavonifractor plautii* showed a positive association. Qualitative interview publications described fatigue-related uncertainty, coping challenges, and impacts on identity and social participation. In an experimental stair-climbing study ($n=49$ PBC), anticipated fatigue predicted post-task fatigue ($\beta=0.75$, $p<0.001$); fatigue expectations and fear of movement predicted slower recovery. In a cognitive experiment ($n=46$ PBC), fatigue-reducing instructions reduced the urge to stop before and during the task. These complementary findings are exploratory and should not be confused with the registered cohort primary outcomes.

Overall interpretation

Fatigue was common and often persistent in both PBC and PSC. Psychological and behavioural factors, particularly fear-avoidance, were associated with fatigue over time, whereas routinely assessed liver disease markers were not consistently predictive. Findings from microbiome and experimental substudies suggest additional hypotheses for future investigation. Because the study is observational, associations should not be interpreted as causal effects.

Published study results

- Toussaint et al. (2026), *J Psychosom Res* — biopsychosocial approach to fatigue in PSC; doi:10.1016/j.jpsychores.2026.112931
- Buck et al. (2025), *Scientific Reports* — symptom expectations and mental fatigue; doi:10.1038/s41598-025-16191-2
- Hartl et al. (2024), *J Hepatol* — fatigue in PSC; doi:10.1016/j.jhep.2024.07.014
- Hasenbank et al. (2024), *Psychother Psychosom Med Psychol* — qualitative PBC study; doi:10.1055/a-2434-6837
- Loesken et al. (2023), *BMC Gastroenterol* — qualitative PSC study; doi:10.1186/s12876-023-02645-2