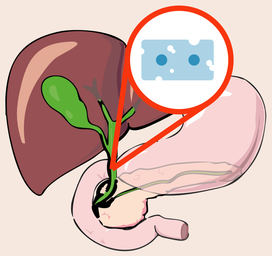
The Burden of Primary Sclerosing Cholangitis (PSC)

What is PSC?

PSC is a cholestatic liver disease that is characterized by chronic and progressive inflammation and fibrosis of the bile ducts.[1] The prevalence of PSC is variable, ranging from 0.22 to 31.7 in 100,000 people in Europe and 0 to 13.6 per 100,000 people in North America[2]



1 Cholestasis/autoimmune response[1]

Both **hereditary** and **environmental factors** may trigger the pathogenesis of PSC

2 Chronic inflammation[1]

Inflammation of the bile ducts can lead to a **build-up of bile** and other toxins (cholestasis)

3 Fibrosis[1]

4 Cirrhosis[1]

Chronic cholestasis can lead to **fibrosis** (scarring of the liver), **cirrhosis** (late-stage scarring of the liver), and eventually **liver failure**

PSC can gradually worsen over time and, without treatment, may eventually lead to end-stage liver disease (requiring liver transplantation).[1] Median transplant-free survival can vary, with a study reporting a range of 9.7 (US) to 20.6 years (Netherlands)[3]

PSC can be divided into three main subtypes[1,4–7]

1. **Large duct (classical) PSC:** Affects the entire biliary tree and has a prevalence of 90%[1]
2. **Small duct PSC:** Affects smaller intrahepatic bile ducts only[1,4,5]
   - Less common than large-duct PSC (<5% of PSC cases)
   - Milder disease, slower progression, and lower risk of malignancies than large duct PSC
   - Approximately one-fifth of cases will progress to large duct PSC
3. **PSC associated with AIH:** Affects small and large bile ducts[1,6,7]
   - Autoimmune responses go beyond affecting the bile ducts, and can damage hepatocytes
   - Diagnostic criteria vary, with between 1.4% and 17% of PSC cases being thought to be associated with AIH

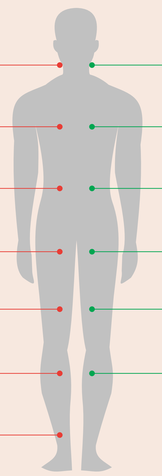
Not all patients are symptomatic at diagnosis: Up to 40% are asymptomatic[8]

Up to 80% of people with PSC develop inflammatory bowel disease (IBD) at some point in their lifetime[9]

Differential diagnosis

PSC manifestations may overlap with those of several hepatic conditions (e.g. autoimmune hepatitis, IgG4-related sclerosing cholangitis, drug induced liver injury, obstructive biliary disorders) which complicates the diagnostic journey.[10]
In particular, it is important to distinguish key features of PSC and primary biliary cholangitis (PBC)[9–12]

PSC[1,9,11]	PBC[11,12]
PSC affects all ages	PBC onset is usually in middle age
60% of people with PSC are men; 40% are women	10% of people with PBC are men; 90% are women
PSC affects bile ducts inside and outside the liver	PBC affects bile ducts inside the liver
Up to 80% of people with PSC have IBD	1% of people with PBC have IBD
Elevated but fluctuating serum ALP levels	Elevated serum ALP levels
Negative AMA test	>90% of patients show detectable AMA
Elevated risk of bile duct and colon cancer	



REFERRAL[9,10]

Hepatologist/gastroenterologist or dermatologist (due to itching)
History *(medical and family history)*
Physical examination
Routine blood tests

DIAGNOSIS[9]

Elevated ALP + GGT and/or bilirubin

↓ Detailed history, physical examination

↓ Ultrasound → Dilated ducts, stones, tumor

↓ Normal

↓ AMA + ANA (sp100, gp210) → PBC

↓ Negative

↓ MRCP → **PSC,** SSC

Symptoms and burden

There are a range of signs and symptoms associated with PSC[13]

- Pruritus
- Fatigue
- Non-hepatic manifestations
- Restless legs
- Fever
- Jaundice
- Ascites
- Cognitive impairment
- Abdominal pain
- Portal hypertension

Pruritus is one of the most commonly reported symptoms in PSC. The cause of itch in PSC is not clear, and several mechanisms have been proposed, including increased levels of bile salts in the blood[14,15]

Pruritus is chronic and negatively affects QoL. Those with a history of recurring cholangitis, advanced fibrosis, and cirrhosis are in the greatest need of anti-pruritic treatment[15]

AIH, autoimmune hepatitis; **ALP,** alkaline phosphatase; **ANA,** anti-nuclear antibody; **AMA,** antimitochondrial antibody; **GGT,** gamma-glutamyl transferase; **IBD,** inflammatory bowel disease; **MRCP,** magnetic resonance cholangiopancreatography; **PBC,** primary biliary cholangitis; **PSC,** primary sclerosing cholangitis; **QoL,** quality of life; **SSC,** secondary sclerosing cholangitis; **US,** United States.

1. Lazaridis KN, LaRusso NF. *N Engl J Med*. 2016;375:1161–1170; **2.** Mehta TI, et al. *Liver International*. 2021;41:2418–2426; **3.** Trivedi PJ, et al. *Clin Gastroenterol Hepatol*. 2022;20:1687–1700; **4.** Culver EL, Chapman RW. *Aliment Pharmacol Ther*. 2011;33:1273–91; **5.** Hirschfield GM, et al. *Lancet*. 2013;382:1587–99; **6.** Bowlus CL. *Clin Liver Dis* (Hoboken). 2014;3:34–37; **7.** Terziroli Beretta-Piccoli B, et al. *Cell Mol Hepatol*. 2022;19:158–176; **8.** Kuo A, et al. *Clin Gastroenterol Hepatol*. 2019;17:1372–1378; **9.** Chazouilleres O, et al. *J Hepatol*. 2022;77:761–806; **10.** Chapman MH, et al. *Gut* 2019;66:1–23; **11.** PSC Partners. PSC & PBC. Available at: https://pscpartners.org/about/what-is-psc/psc-pbc.html. Last accessed August 2025; **12.** Hirschfield GM, et al. *J Hepatol*. 2017;67:145–172; **13.** PSC Partners. Basic PSC Facts. Available at: https://pscpartners.org/about/what-is-psc/basic-facts.html. Last accessed August 2025; **14.** Langedijk JAGM, et al. *Front Med*. 2021;8:639674; **15.** Hussain N, et al. *Gut* 2023;72:A34–A35.

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