Berkeley Public Health

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The Liver Forum - PSC 10 Webinar

Current State of PSC Diagnosis and Monitoring

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Faculty Disclosure

I herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments, and anything else which could potentially be viewed as a conflict of interest:

Advisor

Abbvie, Albireo, Agomab, Alfasigma, Boehringer Ingelheim, BiomX, Chemomab, Dexoligo Therapeutics, Falk, Genfit, Gilead, GSK, Hightide, Intercept, Ipsen, Janssen, Mirum, MSD, Novartis, Phenex, Pliant, ProQR Therapeutics, Rectify, Regulus, Siemens, Shire

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Speakers bureau

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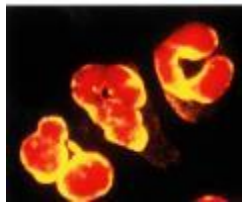
AbbVie, Falk, Gilead, Intercept, Ipsen, Jannsen

Property rights

Co-inventor (service inventions) for patents on medical use of *nor*UDCA (filed by the Medical Universities of Graz and Vienna)

Clinical & diagnostic features of PSC

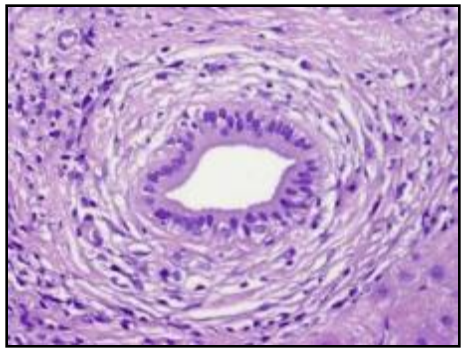


Atypical pANCA

Björnsson et al. *Gastro* 2008

~5-10%
Small Duct PSC

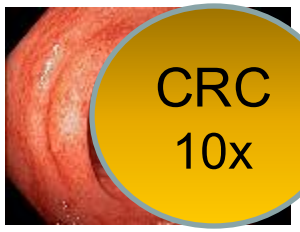
23%/8 y



Obliterative fibrosis of bile ducts

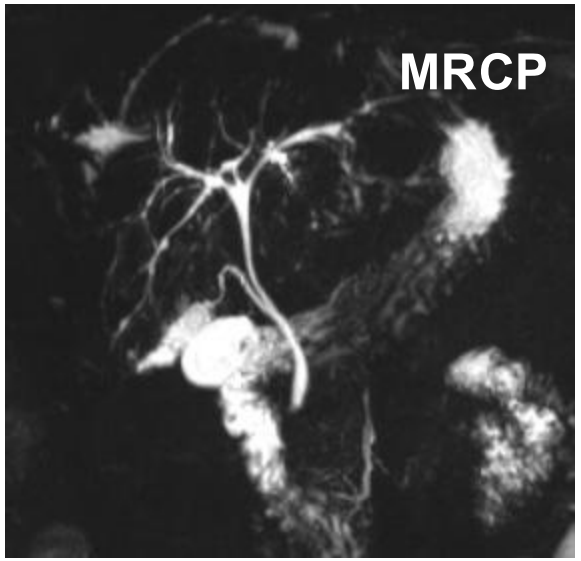
PSC-IBD
- Oligo-symptom.
- Rectal sparing
- Right sided
- Backwash Ileitis
- CRC (5x>UC)

Loftus et al., Gut 2005



IBD in PSC (~70%)

Large Duct PSC



Reviews: Lazaridis & LaRusso, *N Engl J Med* 2016
Karlsen et al., *J Hepatol* 2017; Dyson et al., *Lancet* 2018; Seth et al., *Lancet* 2026

Structured algorithm for work-up of chronic cholestasis

Cholestasis lasting for >6 months
Elevated ALP +/- GGT +/- Bilirubin

↓

Ultrasound, physical exam, history
Dilated intrahepatic and/or extrahepatic ducts?
Signs for chronic liver disease?

↓ Bile ducts without dilation

Autoantibodies
AMA-M2, ANA (Sp100, Gp210)

↓ Negative

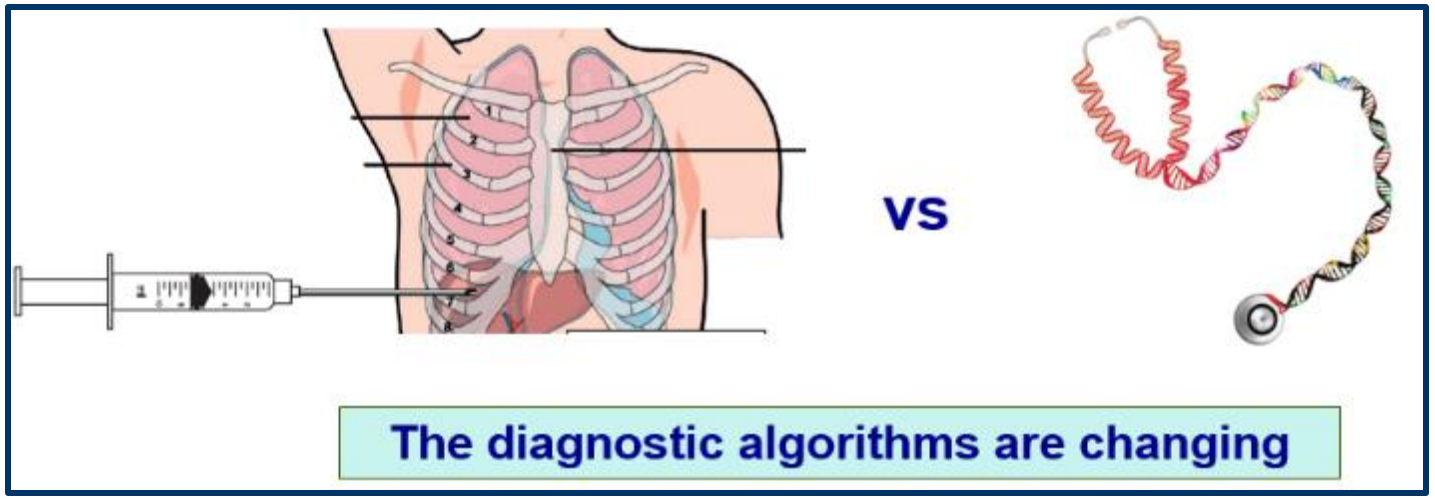
MRCP

↓ Negative

Liver biopsy

↓ Negative / nonspecific

Genetic Analysis
(Whole Exome Sequencing, Whole Genome Seq.)



PSC, SSC, IgG4

Small duct PSC, seronegative PBC, VBDS, cholangiopathy?

Hereditary cholestasis or cholangiopathy
(ABCB4, ABCB11, ATP8B1, KIF12, ZFYVE19, DCDC2)

ABCB4 deficiency as mimic of small duct PSC

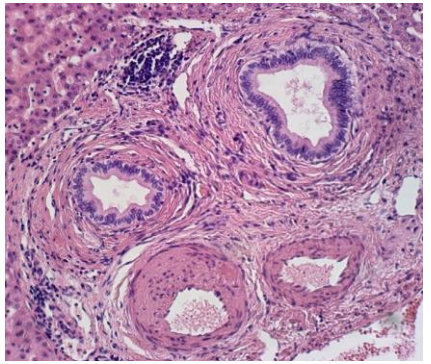


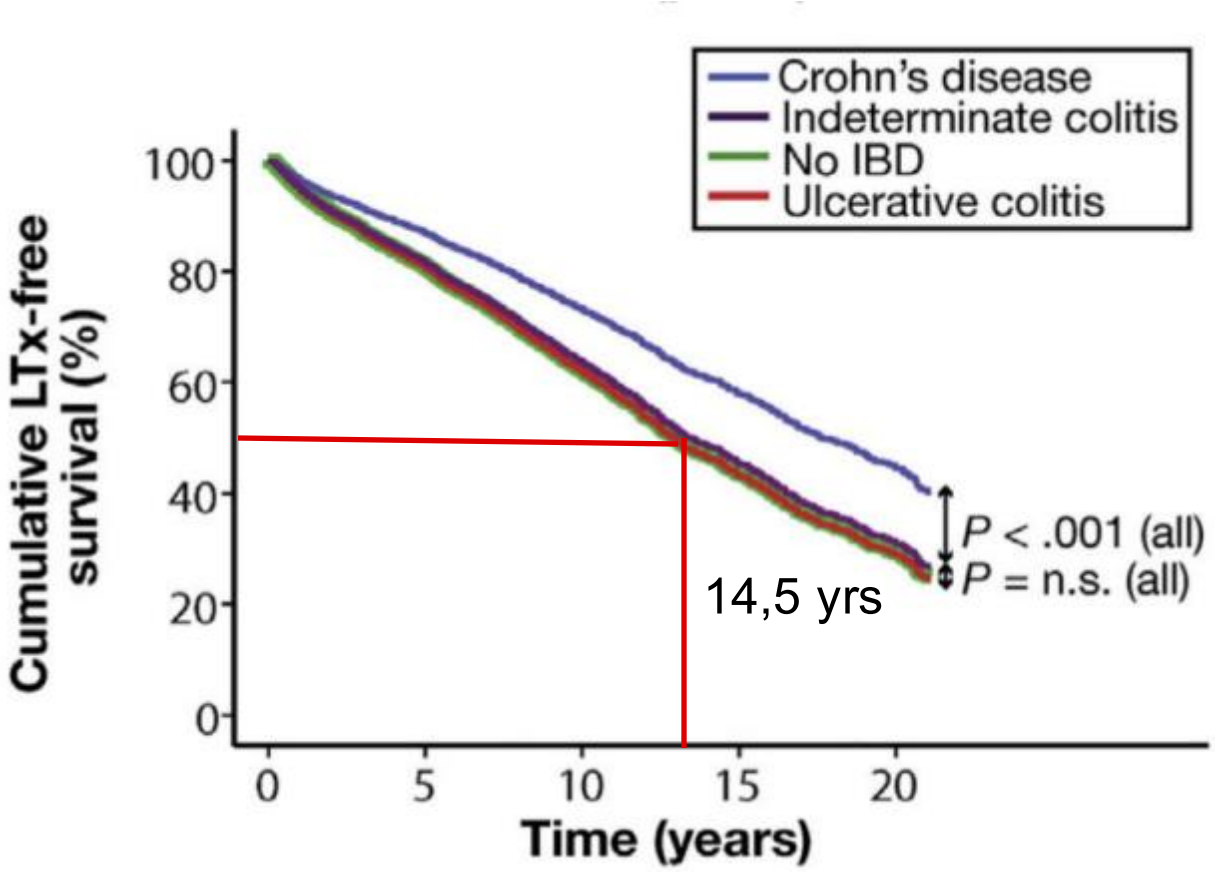
Fig. De Vries et al., *Liver Int* 2020

~30% additional diagnostic insights

EASL CPG SC, *J Hepatol* 2022
(modification after slide courtesy Verena Keitel)

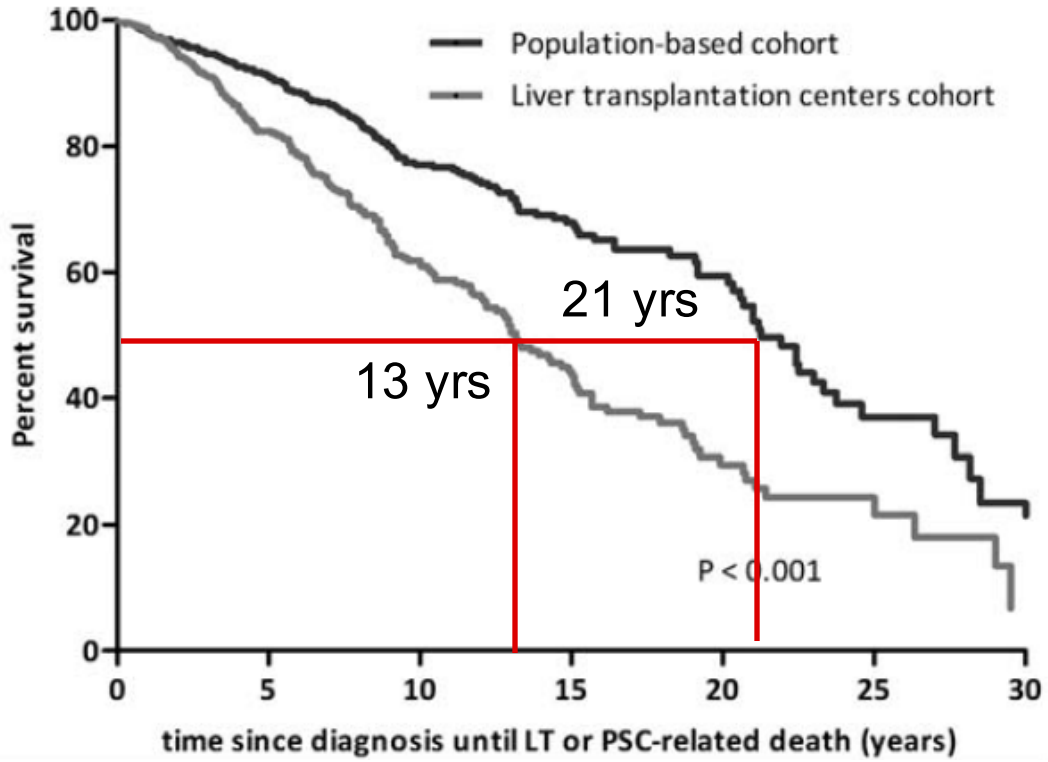
Real life data on prognosis in PSC

IPSSG (n=7121)



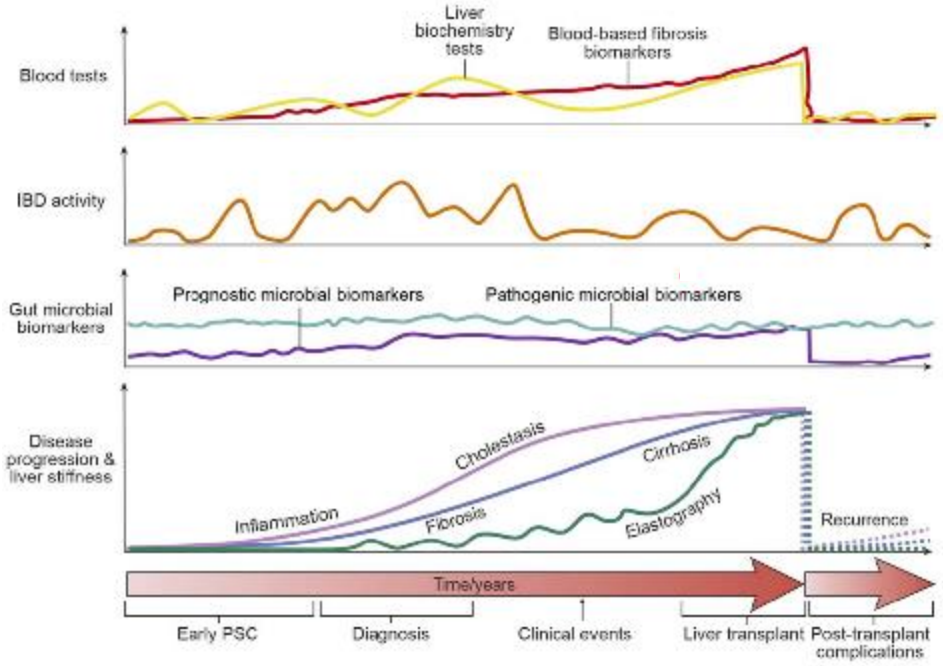
Weismüller et al., *Gastroenterology* 2017

Netherlands (n=1012)

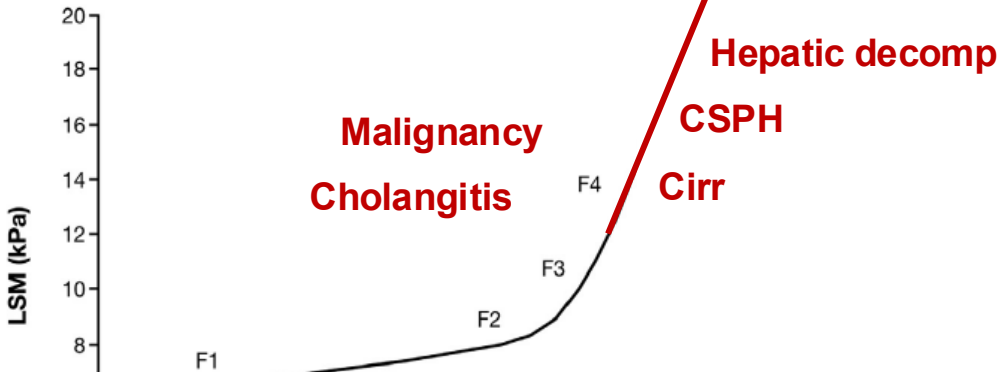


Boonstra et al., *Hepatology* 2013

Disease course and progression in PSC



Karlsen et al., *Hepatology* 2024



PSC diagnosis and risk stratification

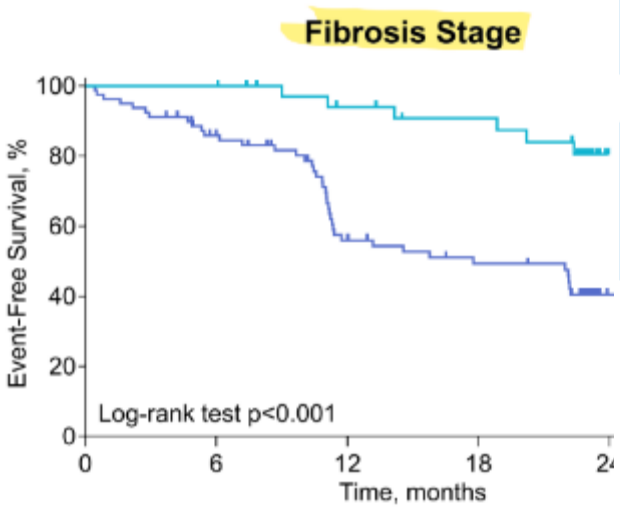
Low risk
Low ALP, normal TB, early-stage fibrosis

- Monitor labs every 6–12 months
- Check LSM every 2–3 years

High risk
ALP > 1.5 × ULN, TB > ULN, LSM > 9.9 kPa

- Monitor labs every 3–6 months
- Check LSM every 1 year
- Consider UDCA versus clinical trial participation

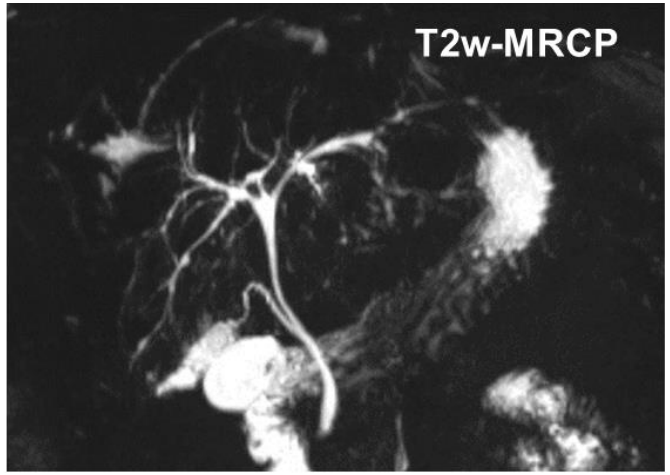
- Assess response to therapy in 6–12 months based on ALP and symptoms
- Decide on maintenance versus treatment discontinuation

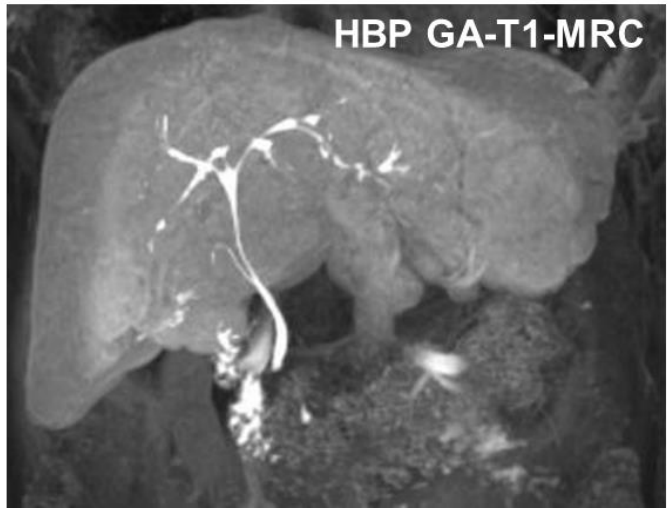


Manns et al.,
Nat Rev Dis Primer 2025

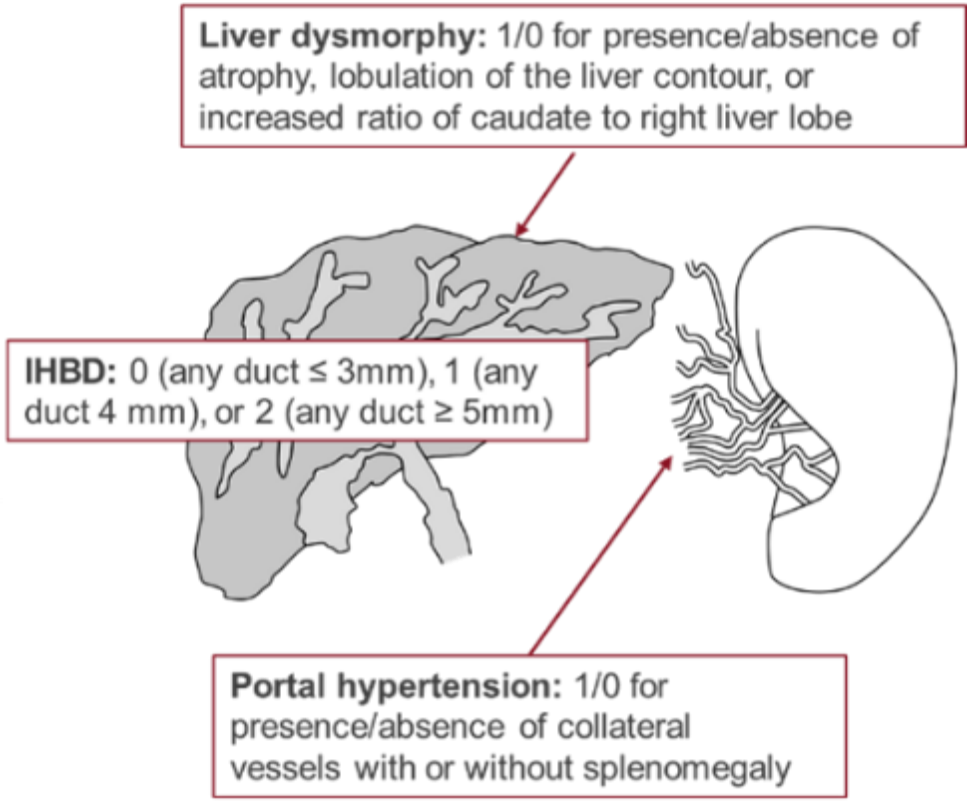
High quality MR imaging* is key to diagnosis

PSC





ANALI Score**

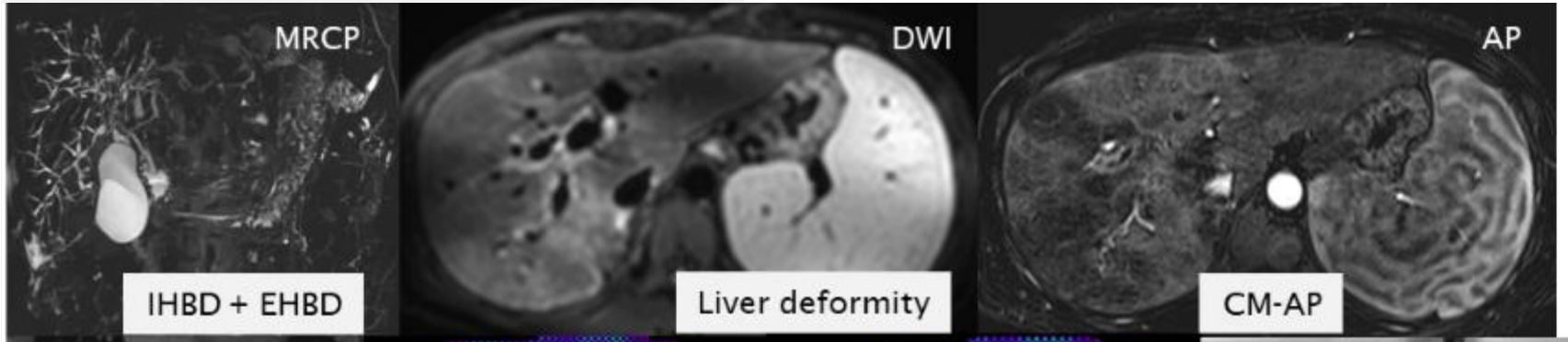


- Total score range: 0–5
- Patients with ANALI score > 2 have been shown to have a higher risk of PSC-related clinical events

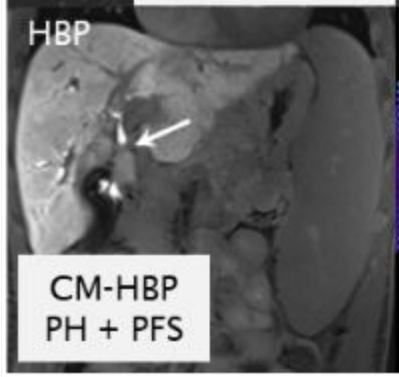
*Team of Prof. Ahmed Ba-Ssalamah (GI/Liver Radiology, Dept. of Biomedical Imaging & Image Guided Therapy)
**Ruiz et al., *Hepatology* 2014; diagram from Poetter-Lang et al., *Eur Radiol* 2024

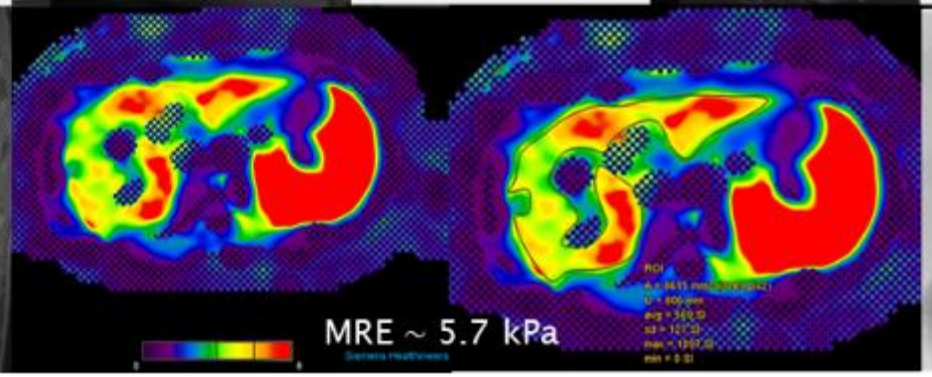
Overview – MR-based prognostic tools

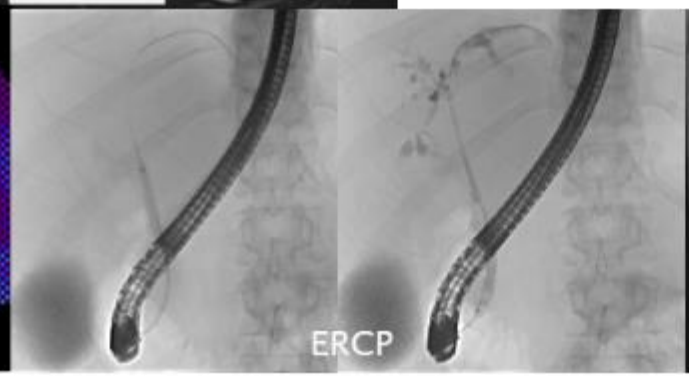
Prognostic Tool	Strengths	Limitations
Anali Scores	Integrates **cholangiographic and morphologic feature for risk stratification**, **strong negative predictive value**, supports non-contrast follow-up for low-risk patients	Relies on detailed radiologic assessment, subject to interreader variability

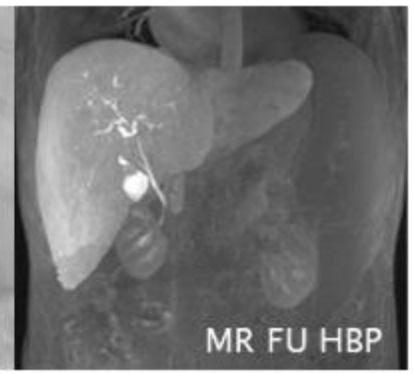


DiStrict	7 (severe)
$ANALI_{NoGd}$	4 (high risk)
$ANALI_{Gd}$	2 (high risk)
NFS/PFS	PFS
MRE	> 4. 32 kPa (high risk)









MRE = MR elastography
PFS = potential functional stricture

Slide courtesy Sarah Poetter-Lang, MUW Radiology

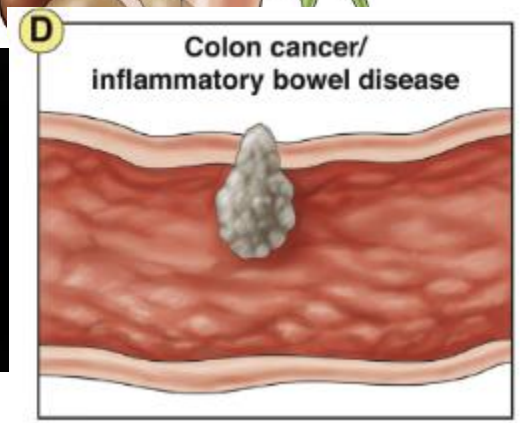
Cancer surveillance in PSC

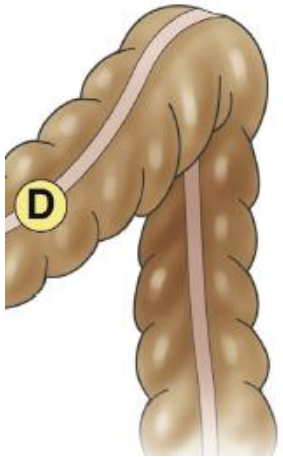
44% of deaths in PSC are due to cancer

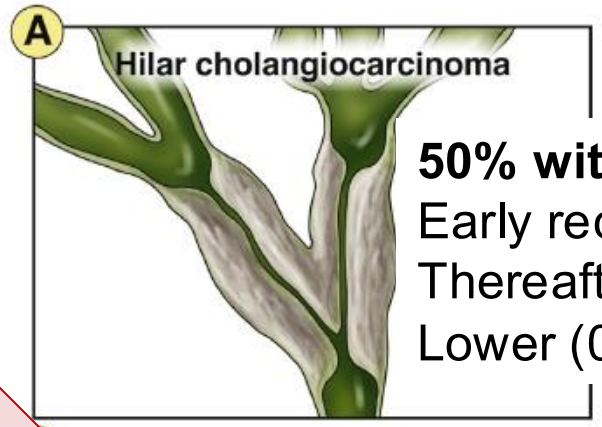
Bergquist et al., *J Hepatol* 2002; 36: 321–27

Surveillance (EASL & AASLD CPG):
MRI/MRCP and/or **US** (incl GB) every 12 mo
- US every 6 mo for cirr. (HCC)

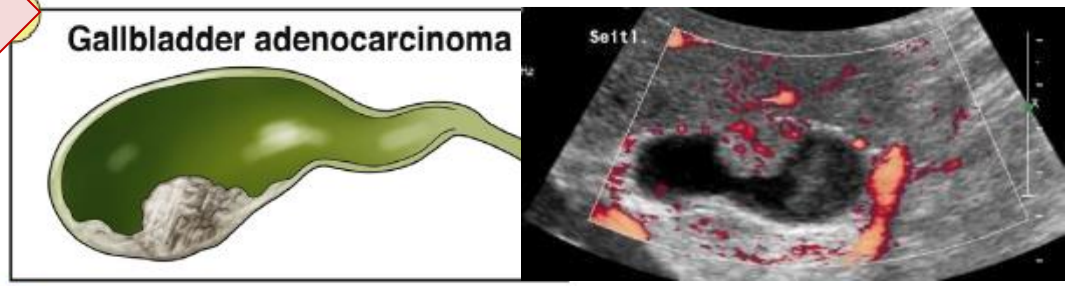
Colonoscopy every 12 (-24) mo
- recall after 5 yrs for those without IBD



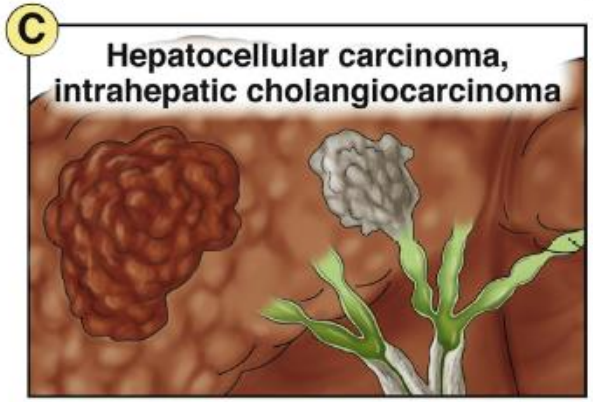




50% within first 4-12 mo
Early recall after diagnosis?
Thereafter 1,5%/year
Lower (0.5%) in recent studies



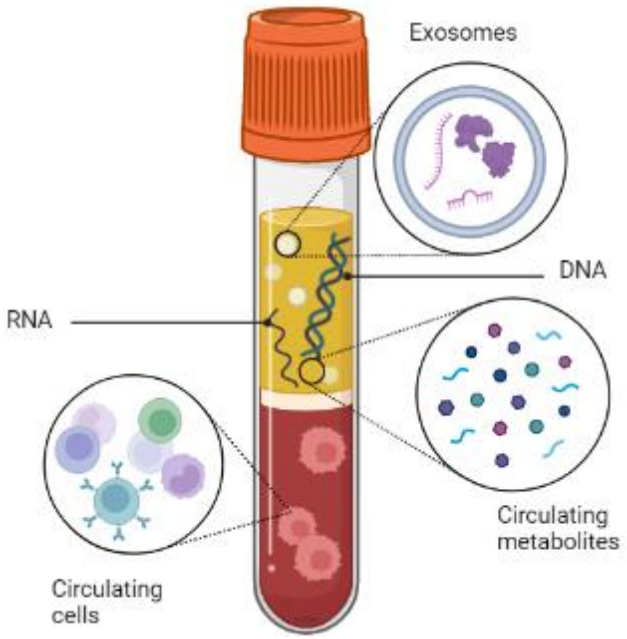
GB polyp 8mm → CHE

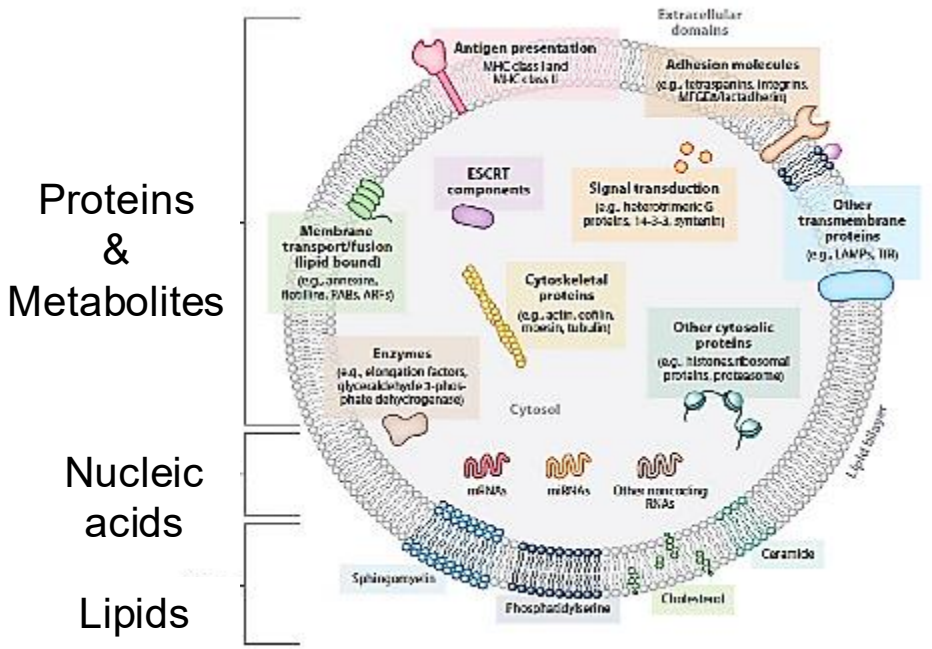


Modified after: Ilyas et al., *Clin Gastroenterol Hepatol* 2015

Next-generation liquid biopsy biomarkers for CCA

Liquid biopsy for risk prediction, early diagnosis and prognosis of CCA





Isolation and analysis of **cell-derived material**

(e.g., DNA, RNA, EV, metabolites, CTC, …)

from **blood** or other **body fluids**

Molecular composition of extracellular vesicles (EVs)

Lapitz A …Banales JM. *Frontiers Immunology* 2018
Colombo M, et al. *Annu Rev Cell Dev Biol.* 2014

Slide courtesy Jesus Banales

Surveillance of primary sclerosing cholangitis – a comparison of scheduled or on-demand ERCP with annual MRI surveillance: a multicenter study

Barner-Rasmussen Nina et al. Surveillance of primary … Endoscopy 2025; 57: 431–440

GRAPHICAL ABSTRACT

Surveillance strategies for primary sclerosing cholangitis: a multicenter prospective study

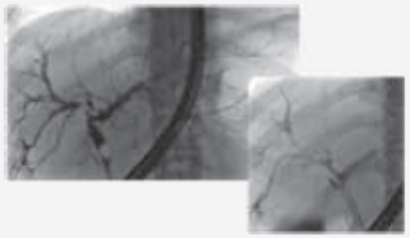
Surveillance strategies

1 Scheduled ERCP
- ERCP timing based on individual risk factors and need for dilation
- Brush cytology, LFTs and CA19-9 at time of ERCP

2 MRI/MRCP surveillance
- Annual MRI/MRCP
- LFTs and CA19-9 yearly

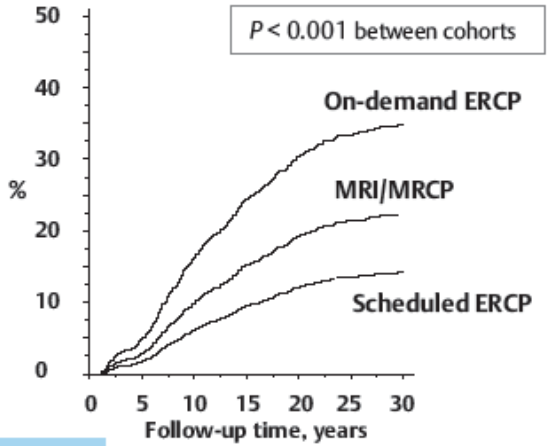
3 On-demand ERCP
- Annual LFTs and CA19-9
- ERCP performed according to the ESGE/EASL guidelines

Composite end point:
hepatobiliary malignancy, transplantation, or liver-related death



ERCP, endoscopic retrograde cholangiopancreatography; LFTs, liver function tests; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging

Cumulative incidence of patients reaching the composite end point



Scheduled ERCP improves overall prognosis vs. current guidelines or MRI/MRCP surveillance

Endoscopy

Bârner-Rsamussen et al., *Endoscopy* 2025

Value of proactive scheduled ERC in PSC?

ORIGINAL ARTICLE

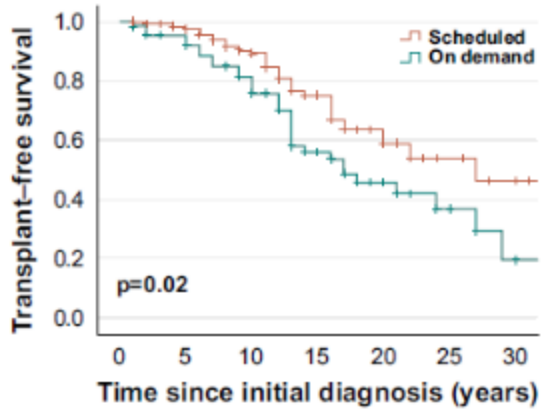
Received: 18 August 2023 | Accepted: 31 March 2024

DOI: 10.1097/HC9.0000000000000494

OPEN

Long-term impact of scheduled regular endoscopic interventions for patients with primary sclerosing cholangitis

Burcin Özdirik[1,2] | Wilfried Veltzke-Schlieker[1] | Jule Marie Nicklaus[1] | Hilmar Berger[1] | Daniel Schmidt[1] | Silke Leonhardt[1] | Volker Penndorf[1] | Andreas Adler[1] | Tobias Müller[1] | Alexander Wree[1] | Frank Tacke[1] | Michael Sigal[1,3]



Endoscopy

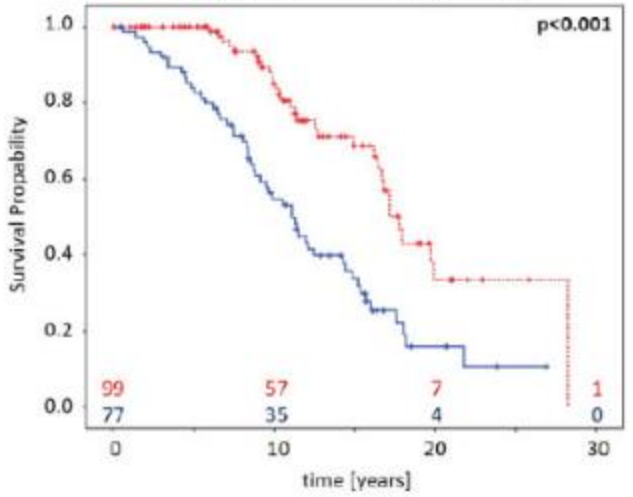
Rupp C, *et al*. *Gut* 2019;**68**:2170–2178. doi:10.1136/gutjnl-2018-316801

OPEN ACCESS

ORIGINAL ARTICLE

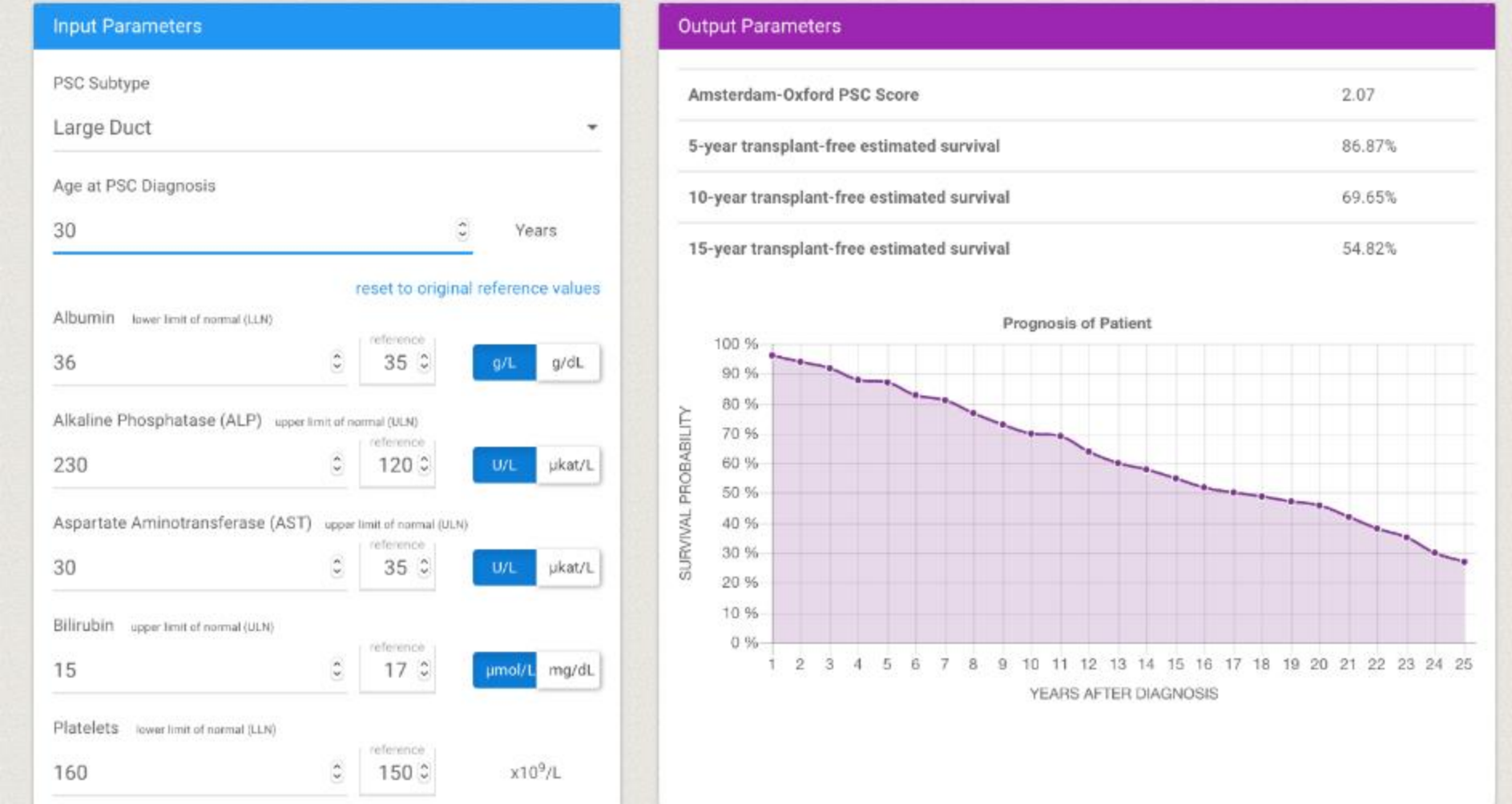
Effect of scheduled endoscopic dilatation of dominant strictures on outcome in patients with primary sclerosing cholangitis

Christian Rupp [1,2] Theresa Hippchen,[1] Thomas Bruckner,[3] Petra Klöters-Plachky,[1] Anja Schaible,[4] Ronald Koschny,[1,2] Adolf Stiehl,[1] Daniel Nils Gotthardt,[1] Peter Sauer[1,2]



Validation of the Amsterdam-Oxford Model for PSC

Amsterdam-Oxford PSC Score Calculator (https://sorted.co/psc-calculator/)

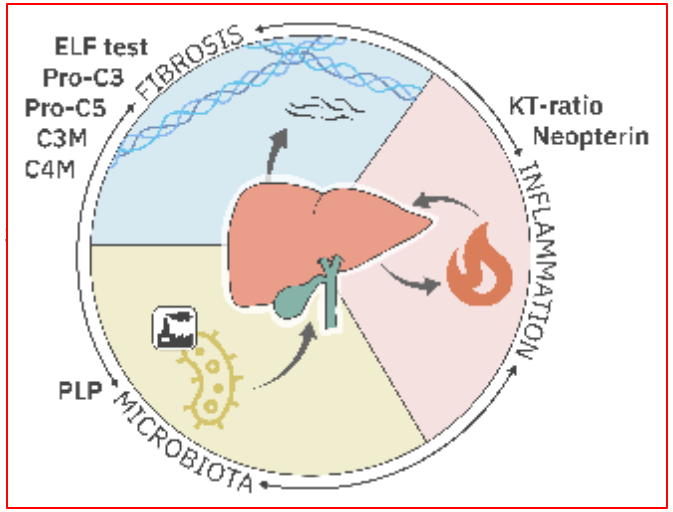


Goet et al., *J Hepatol* 2019; 71: 992-999

Development of a multi-biomarker model to predict transplant-free survival in primary sclerosing cholangitis: A multicentre retrospective study

BACKGROUND & AIM

- Predicting liver transplantation or death in PSC is challenging because of its heterogeneous course and complex pathogenesis, which hinders the design of effective follow-up strategies and clinical trials
- **AIM:** To determine whether a multi-biomarker model, integrating



METHODS

Cross-sectional cohort of people with PSC from Norway, Sweden, and the US
(N=906)

Model validation

	2 years		5 years	
	C-index (IQR)*	Calibration slope	C-index (IQR)*	Calibration slope
Full model	0.834 (0.832–0.836)	0.880	0.822 (0.821–0.822)	0.916
Pragmatic model†	NR	NR	0.817	0.970
ELF-only model	NR	NR	0.79	0.99

Both the full and pragmatic model outperformed the ELF-only model, and provided incremental predictive value beyond the Amsterdam–Oxford PSC model and the PSC Risk Estimate Tool

- Internal validation and subset-fitting assessed overfitting, and generalizability across regions
- Pragmatic subset models were compared with the full model
- All models were benchmarked against the ELF test and established PSC risk scores

Helgadottir H, et al. EASL 2026; OS-006-YI.

Suggested algorithm for follow-up in PSC

Routine surveillance

- Every 12 mo (every 6 mo for ‘signficant risk’*):
  - **Clinical** evaluation (incl. QoL)
  - **Lab** (bilirubin, ALP, AST, plts., PT – AFP when cirrhotic)
- Every 12 mo (also for low risk*)
  - **MRI/MRCP** and/or **US** (incl GB; US every 6 mo for cirr.– HCC)
  - **Colonoscopy** (when unremarkable - recall after 5 yrs)
  - **Elastrography** and/or **ELF** test
- Every 2 - 4 years (all): **DEXA**

* **“Significant risk”** if any present:

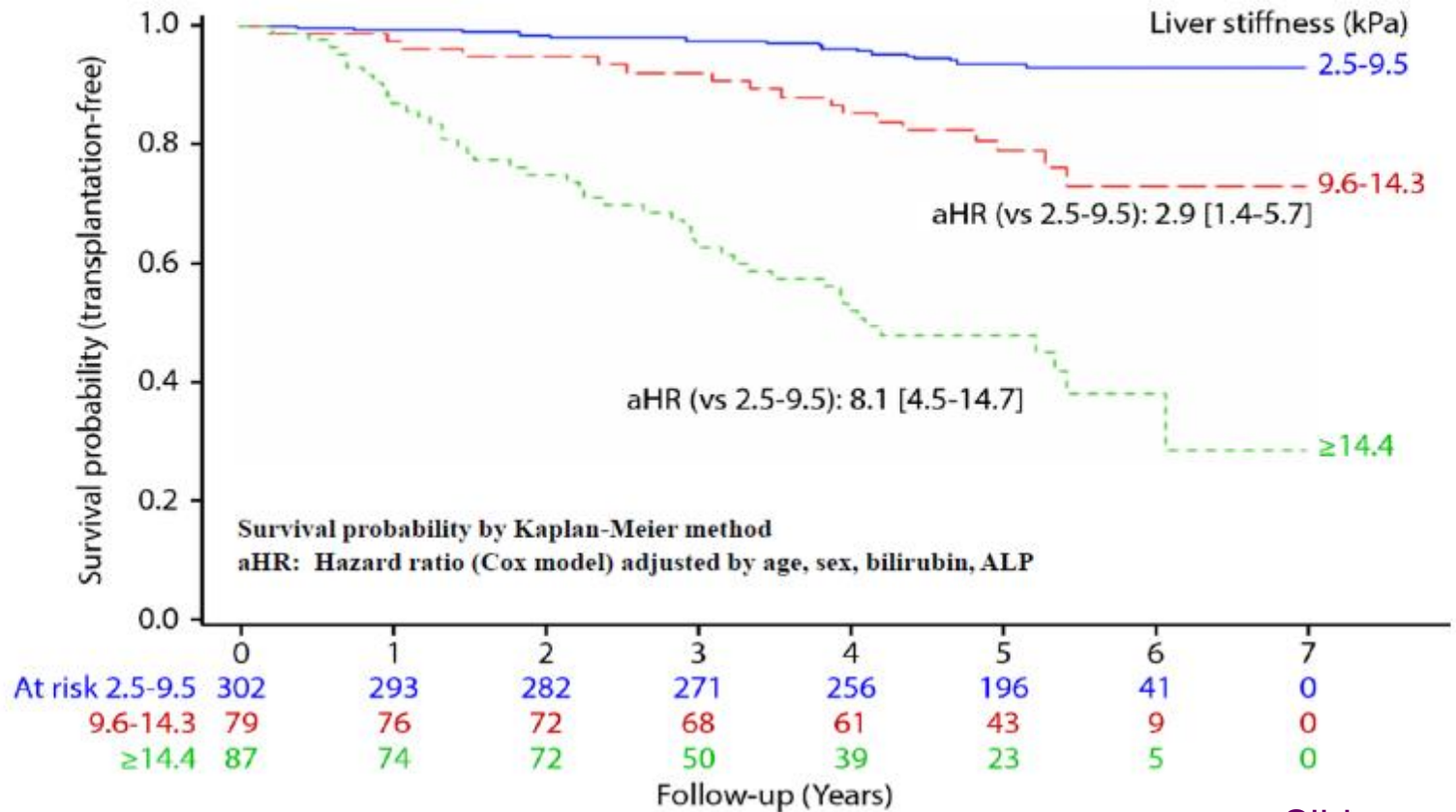
- Symptomatic
- ALP > 1.5 ULN,
- Abnorm. bili, albumin, platelets, or PT
- **LSM > 9.9 kPa (or ELF test > 10.6)**
- Extensive biliary changes (espec. intra-hepatic biliary dilatation)

FICUS study @ EASL 2024

EASL GPG, *J Hepatol* 2022

Prospective validation of the prognostic value of liver stiffness (LS) assessed by Fibroscan in primary sclerosing cholangitis (PSC):final results of the FICUS study.

Prognostic Value of LS according to Pre-established Cut-offs

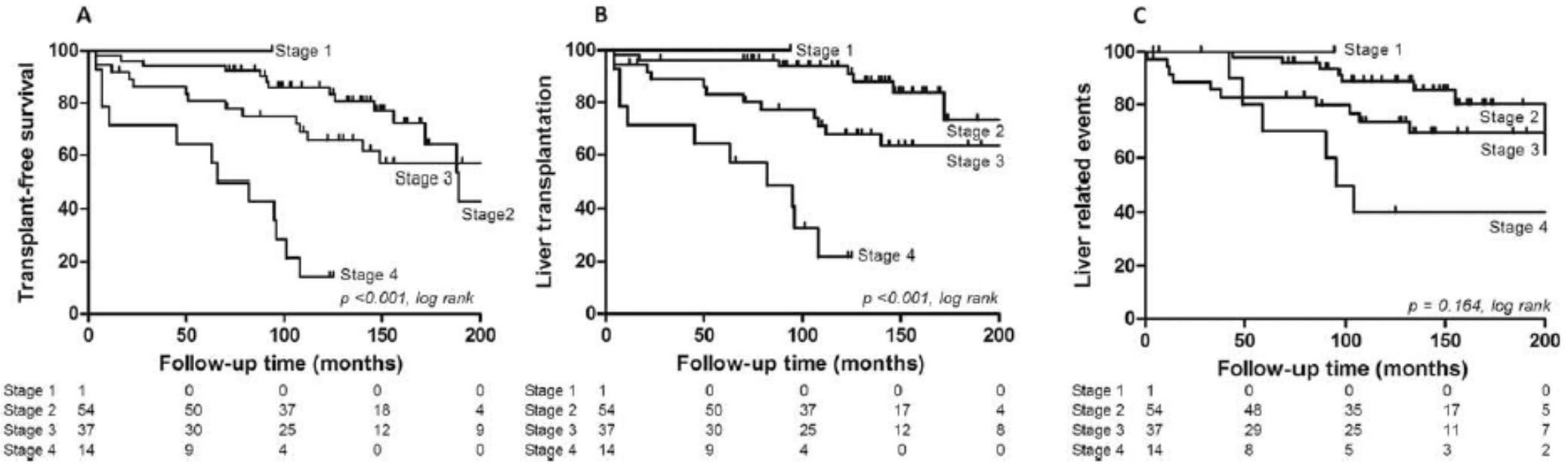


Slide courtesy Olivier Chazouilleres

HEPATOLOGY

HEPATOLOGY, VOL. 65, NO. 3, 2017

Validation of the Prognostic Value of Histologic Scoring Systems in Primary Sclerosing Cholangitis: An International Cohort Study



Stage 1	1	0	0	0	0
Stage 2	54	50	37	18	4
Stage 3	37	30	25	12	9
Stage 4	14	9	4	0	0

Stage 1	1	0	0	0	0
Stage 2	54	50	37	17	4
Stage 3	37	30	25	12	8
Stage 4	14	9	4	0	0

Stage 1	1	0	0	0	0
Stage 2	54	48	35	17	5
Stage 3	37	29	25	11	7
Stage 4	14	8	5	3	2

FIG. 2. Kaplan-Meier survival curves of the Nakanuma staging system. (A) Endpoint 1: transplant-free survival. (B) Endpoint 2: liver transplantation. (C) Endpoint 3: liver-related events.

de Vries et al., *Hepatology* 2017
First report: de Vries et al., *J Hepatol* 2015

Principal Therapeutic Strategies for PSC - Overview Candidates for Recent & Ongoing Clinical Trials

Treatment	Biliary strictures and cholestasis	ALP signal
Bile-acid based therapy and PPARs • UDCA (RWE Japan, NL – survival?)	Norucholic acid (NCA / *nor*UDCA)	✓
		✓
		✗
• Anti-TNFα • Vedolizumab • Simtuzumab (i.e. anti-fibrotic) Cenicriviroc, Tofa?	**Earlier diagnosis (before strictures)**	MRI beyond MRCP FAPI-PET MRI?

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LETTER TO THE EDITOR · Articles in Press, April 17, 2026

Primary sclerosing cholangitis: time to rethink imaging criteria for early disease detection

C. Schramm [1,2] · S. Pötter-Lang [3] · E. Halilbasic [4] · A. Ba-Ssalamah [3] · M. Trauner [4] On behalf of the IPSCSG MRI Working Group

Modified after: Vesterhus & Karlsen, *J Gastroenterol* 2020
Also see: Karlsen et al., *Hepatology* 2024

GS-007-YI Novel “3-in-1” blood metabolomic test for the early diagnosis and risk stratification of primary sclerosing cholangitis and cholangiocarcinoma

Results

Primary sclerosing cholangitis and cholangiocarcinoma

13-metabolite model distinguishes PSC vs. healthy controls
Independent of age, sex, cirrhosis, or UC
AUC: 0.98 (discovery & validation cohorts)

PSC-CCA detection

13-metabolite model detects PSC-CCA vs. PSC

AUC: 0.91 (discovery), 0.90 (validation)
Early-stage detection (0–II): AUC = 0.930
Outperforms CA19.9 (AUC = 0.646)
Still performs well in patients with low CA19-9 (AUC = 0.92)

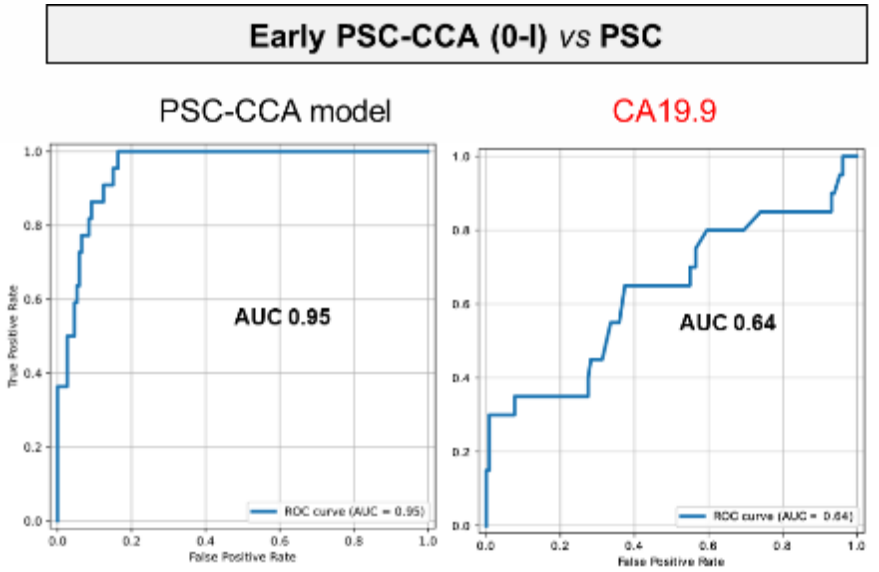
Prediction of CCA

7-metabolite model predicts CCA development in PSC patients

PPV: 83% (discovery), 73% (validation)
Detected up to 8 years before clinical diagnosis

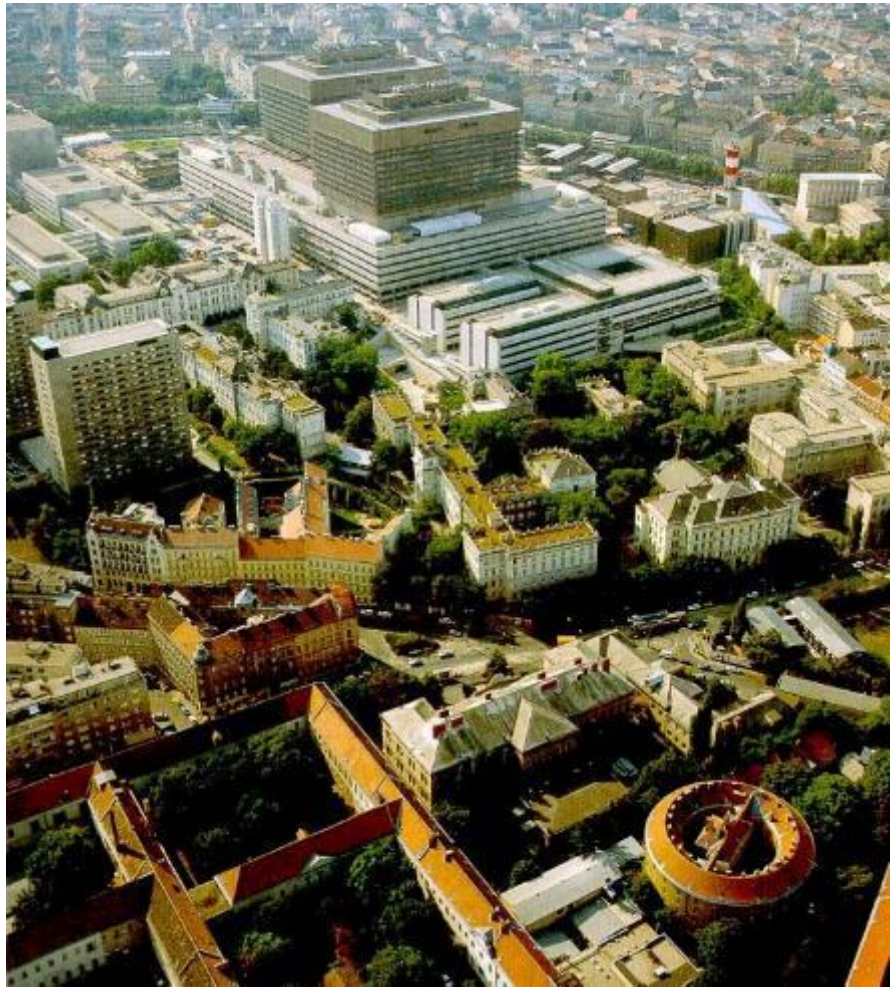
Conclusion

The “3-in-1” metabolomic test is a useful non-invasive tool that enables diagnosis of PSC, early PSC-CCA detection, and prediction of CCA development. Implementation in clinical practice may improve risk stratification and follow-up in patients with PSC, facilitating personalised surveillance, early diagnosis and prioritise therapeutic decisions.



Lapitz et al., … Banales, presented @ EASL 2025

Data courtesy Jesus Banales



Thank you for your attention!

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Gustav Klimt's lost faculty painting *'Medicine'* reconstructed by AI now displayed on the *Anna Spiegel Research Building*

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