# Better cholangiocarcinoma surveillance in PSC?

**Dermot Gleeson**

**BASL SIG meeting 6th October 2023**

# PSC outcomes (over 10-20 years)

- Liver transplant 17-30%
- Death: 10-20%
- Causes: Liver failure 16-37%

  Non liver-related 10-50%

  Cancer 40-60% - Colorectal 2-25%

  - Hepatocellular 1-2%

  - Gallbladder 1-2%

  - Cholangiocarcinoma 25-58%

*Bergquist 2002 Tischendorf AJG 2007 Classen J Hepatol 2009, Fevery Scan J Gastro 2100, Boonstra Hepatol 2013, Weismuller Gastro 2017, Trivedi Gastro 2020)*

# Evidence supporting surveillance in PSC

- **Colon cancer (IBD) – 12 monthly colonoscopy**

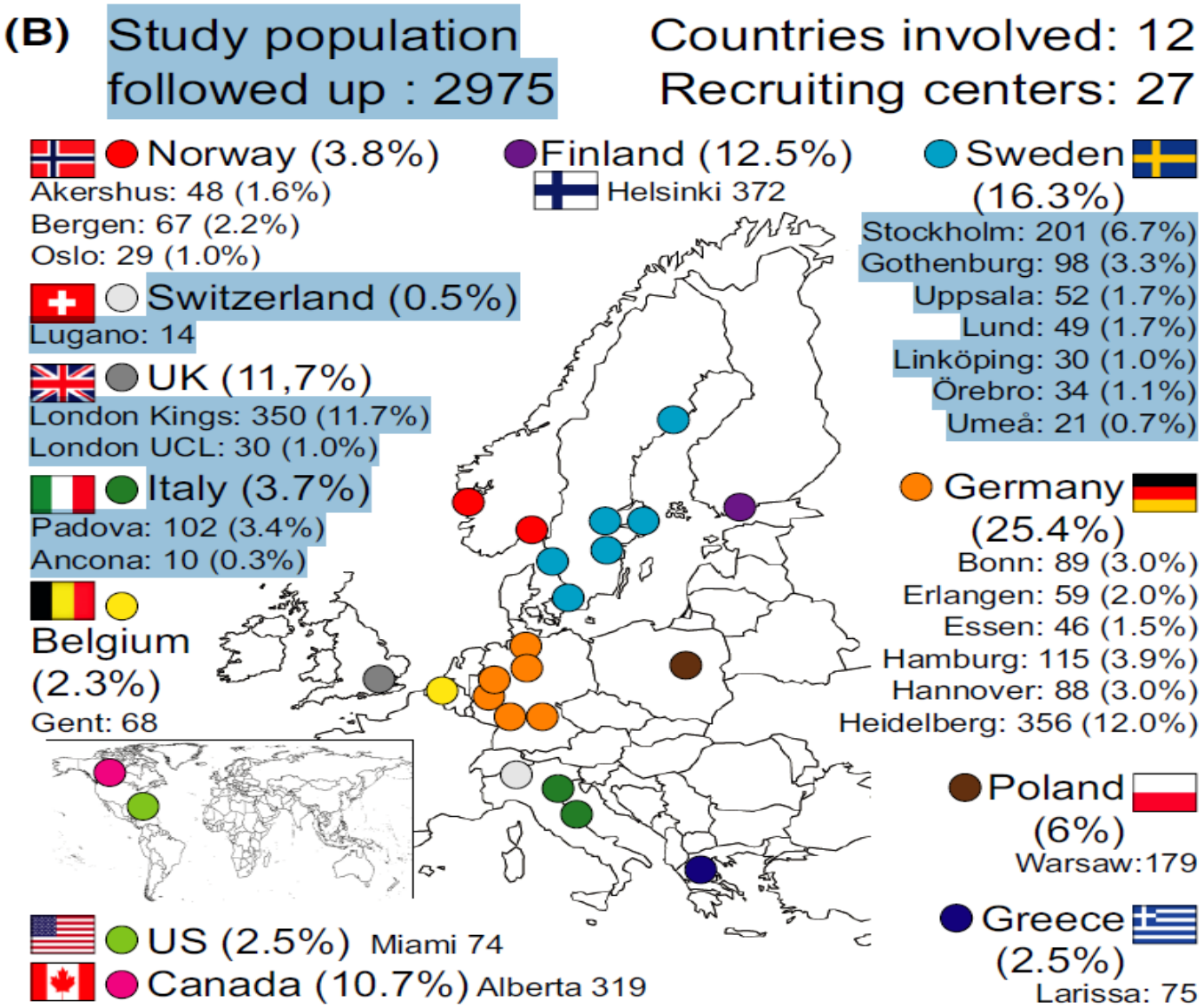
- **HCC (cirrhosis): 6- monthly ultrasound**

**Gallbladder cancer: 12- monthly ultrasound**

# CCA SURVEILLANCE IN PSC: GUIDELINES to 2019

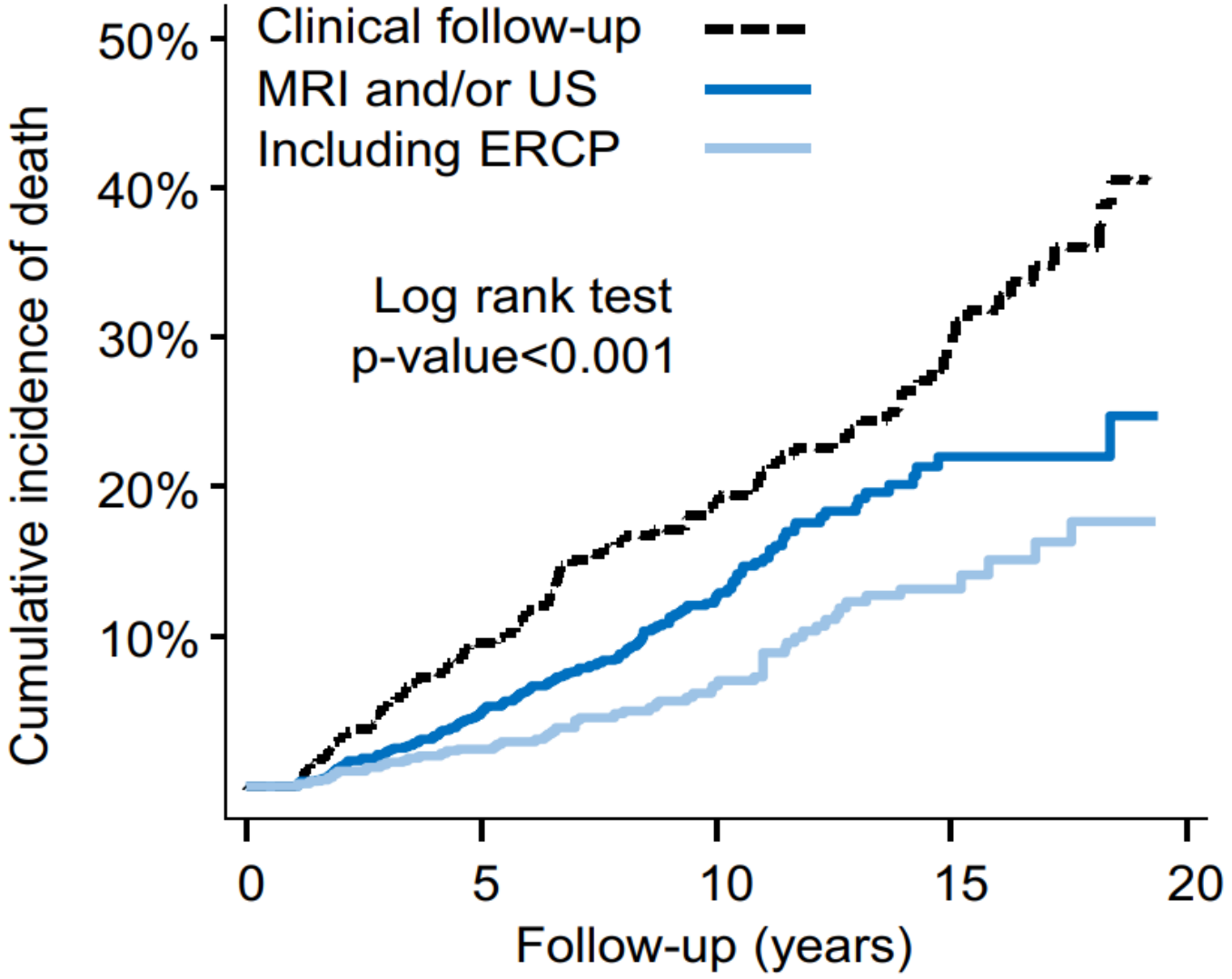
- **EASL, AASLD, ACG, BSG….**
- "Consider" or "suggest" annual…
- "No modality can be recommended"
- "In absence of evidence….."
- "conditional, low-quality evidence"
- "though no evidence…."
- "not shown to be effective..not routinely recommended

# Impact on follow-up strategies in patients with primary sclerosing cholangitis



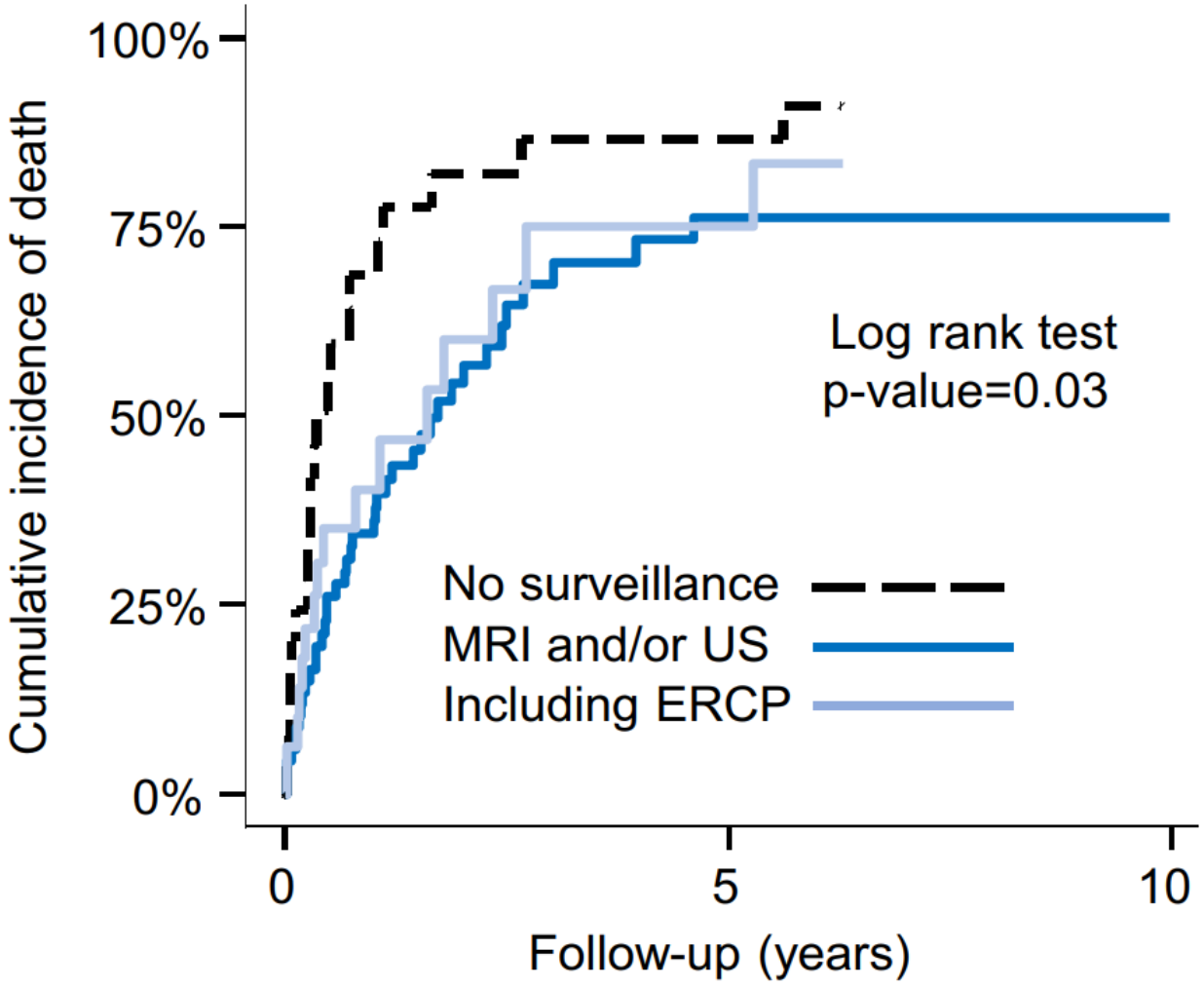

*Beraguist Liver Int. 2022*

# Surveillance (esp with ERCP) associated with better overall survival




*Bergquist Liver Int. 2022*

# Surveillance (+/- ERCP) associated with better survival post CCA diagnosis



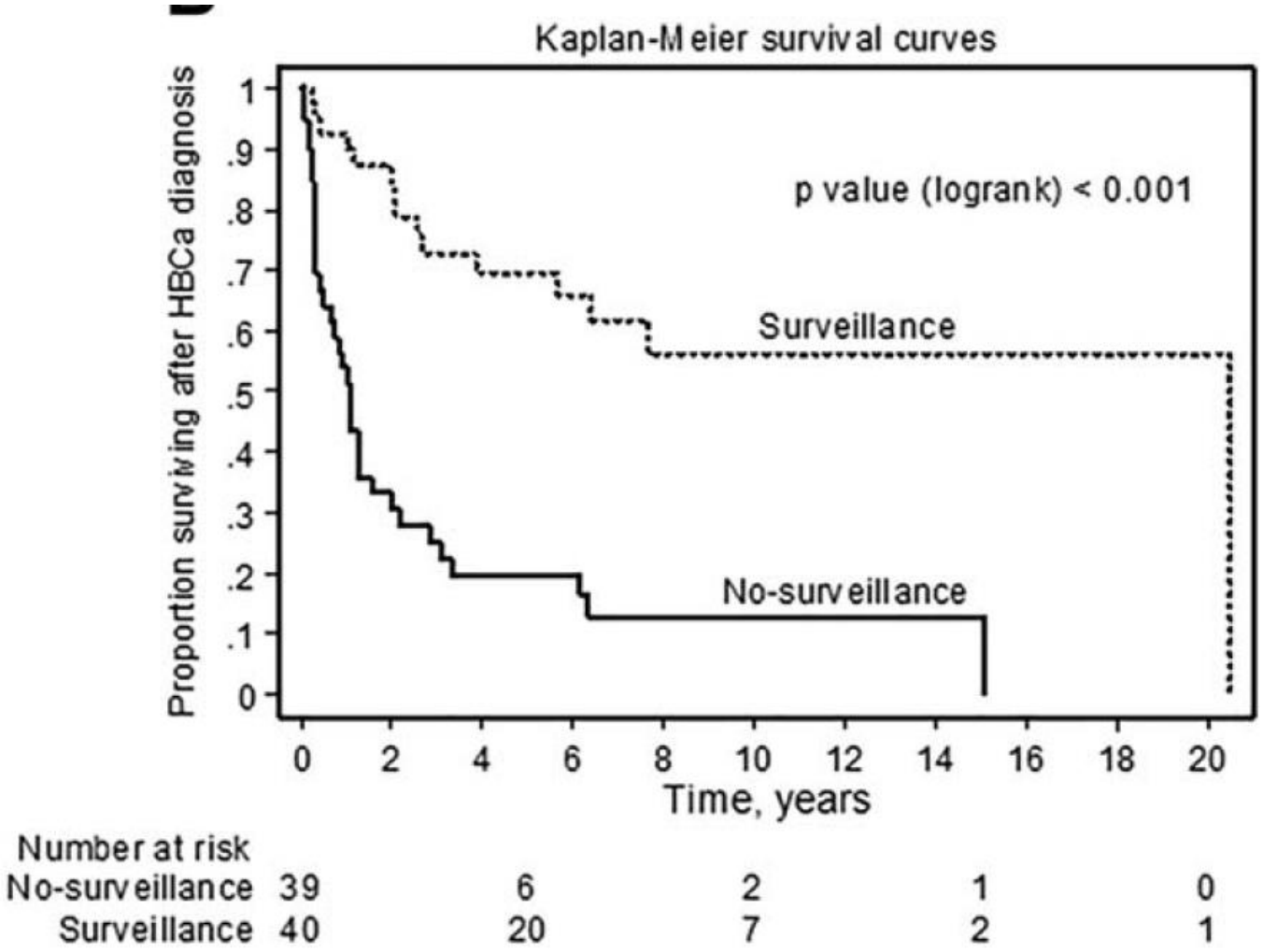

*Bergquist Liver Int. 2022*

# HEPATOBILIARY CANCER SURVEILLANCE IN PSC: MAYO CLINIC STUDY (n=830)

- Annual US, and/or MRI/MRCP, Ca-199; **uptake 50%**
- - 54 CCA (18 intrahepatic);
  - 17 HCC
  - 5 Gallbladder
- Screened patients: - Less spread (17% vs 54%)
  - More transplanted (65% vs 23%)

*Hasan Ali Hepatology 2018*

# CANCERS DIAGNOSED BY SURVEILLANCE: SUSTAINED INCREASE IN SURVIVAL




*Hasan Ali Hepatology 2018*

# But which is the better imaging mode?

- Blind comparison of cMRI/MRCP and ultrasound
- PSC with perihilar CCA only
- Selected group: - 90% listed for transplant

| | **Overall** | | **Asymptomatic** | |
|---|---|---|---|---|
| | Sensitivity | Specificity | Sensitivity | Specificity. |
| MRI/MRCP | 89 | 86 | 71 | 89 |
| Ultrasound | 52 | 90 | 29 | 89 |

*Eaton Hepatology 2021*

- Tumours seen on MRI only, vs those seen on both MRI and US,  are:

    - Smaller

    - Have better survival, in asymptomatic patients

*Eaton Hepatology 2021*,

# Swedish study:

- Only 7 CCAs detected by imaging (4 at surgery)
- Of 7: 2 resected (survival 10-19 months)

  1 transplanted (survival 54 months)

Why so few???

*Villard J Hepatol 2023*

# Annual % incidence of CCA in PSC

| | Sweden (512) | | |
|---|---|---|---|
| Overall | 0.46<br>0.29 (imaging) | | |
| Yr 1 | 2.9 | | |
| Post yr 1 | 0.42<br>0.25(imaging) | | |
| | | | |
| | | | |

*Bergquist J Hepatol 2002, Burak Am J Gastro 2004, Weismuller Feverey Liver Int 2011 Gastro 2017, , Gleeson Frontline Gastro 2022, Vllard J Hepatol 2023*

# Annual % incidence of CCA in PSC

| | Sweden (512) | Weissmuller (7121) | Sheffield (146) |
|---|---|---|---|
| Overall | 0.46<br>0.29 (imaging) | 1.25 | 1.58 |
| Yr 1 | 2.9 | 4.4 | 2.56 |
| Post yr 1 | 0.42<br>0.25(imaging) | 0.75 | 1.68 |
| | | | |
| | | | |

*Bergquist J Hepatol 2002, Burak Am J Gastro 2004, Weismuller Gastro 2017 Feverey Liver Int 2011, Vllard J Hepatol 2023*

# Incidence determines false MRI positives

(Assuming sensitivity 71%  and specificity 89% for CCA diagnosis in asymptomatic patients)

| Cohort | Annual CCA% | PPV | Number false positives |
|---|---|---|---|
| PSC yr 1 | 4.4 | 0.23 | 3 |
| | | | |
| | | | |

*Eaton Hepatology 2021,  Gleeson Frontline Gastro  2022, Vllard J Hepatol 2023*

# Incidence determines false MRI positives

(Assuming sensitivity 71%  and specificity 89% for CCA diagnosis in asymptomatic patients)

| Cohort | Annual CCA% | PPV | Number false positives |
|---|---|---|---|
| PSC yr 1 | 4.4 | 0.23 | 3 |
| PSC post yr 1 | 0.75 | 0.046 | 21 |
| Swedish study | 0.29 (imaging) | 0.018 | 53 |

*Eaton Hepatology 2021,  Gleeson Frontline Gastro  2022, Vllard J Hepatol 2023*

# RISK FACTORS FOR CCA IN PSC

| | | |
|---|---|---|
| **Age** at diagnosis | | Yes- higher risk if older |
| **PSC** | Duration | Higher in first year |
| | Small/large duct | Small duct 7-10 fold lower risk |
| | Severity - alk phos, bilirubin | Possibly |
| | - cholangiograpy | Yes |
| | - Ca199 | Yes |
| **IBD** | Type | Yes (UC > Crohn's /indeterminate) |
| | Duration | Yes |
| | Colectomy | No independent association |
| | Azathioprine (for IBD) | No association |

*Bergquist 2002 Tischendorf AJG 2007 Al Mamari J Hepatol 2014, Gilamhusein Am J G 2016 Classen J Hepatol 2009, Fevery Scan J Gastro 2100, Boonstra Hepatol 2013, Weismuller Gastro 2017, Barner-Rasmussen, Scand J Gastro 2020, Trivedi Gastro 2020 Zenouzi CGH 2016, Villard J Hepatol 2023 Hu BMC Gastro 2023*

# PSC ? A (relatively) high-risk subgroup for CCA?

- Ulcerative colitis
- ”Severe” stricturing disease
- Raised Ca-199
- First few years….

- **LOW Risk: small duct PSC**

*Gleeson Gut 2022 (Abst); updated*

# WHAT THE LATEST GUIDELINES SAY

| | Imaging | Ca-19.9 |
|---|---|---|
| AGA 2019 (CGH) | Should include imaging by US, CT or MRI every 6-12 months | As for imaging |
| EASL 2022 (J Hepatol) | Surveillance with ultrasound and/or MRI/MRCP for cholangiocarcinoma and gallbladder malignancy is suggested at least yearly in patients with large-duct disease, regardless of disease stage | Not suggested for surveillance; insufficient accuracy |
| AASLD 2023 (Hepatol) | CCA and gallbladder carcinoma surveillance should be performed annually and include abdominal imaging, **preferably** by MRI/MRCP……. | ….with or without serum CA 19-9 |

# Sheffield: imaging prior to CCA Δ (13 of 146 pts)

- **One:** PSC and CCA Δ together
- **Three:** no prior surveillance over 24-30 months
- **Four:** ultrasound 5-9 months before: not seen
- **Five:** MRCP 2-5 months before

  Plus ERCP+cytology (n=3); spyglass in 1

  Serum Ca.19.9 already raised in three (362-1275)

  Two: CCA suspected on imaging review

*Gleeson Gut 2022 (Abst); updated*

# So, what to do?

- **Abandon CCA surveillance in PSC as futile?**

- **Await new surveillance tools?**

  **(eg biliary methylation markers)** *Vedeld Hepatology 2023*

- **Try to improve current strategy**

# A way forward?

1. **Update BSG Guidelines;** recommend annual imaging (MRI if “high-risk”) PLUS 6 monthly Ca19.9

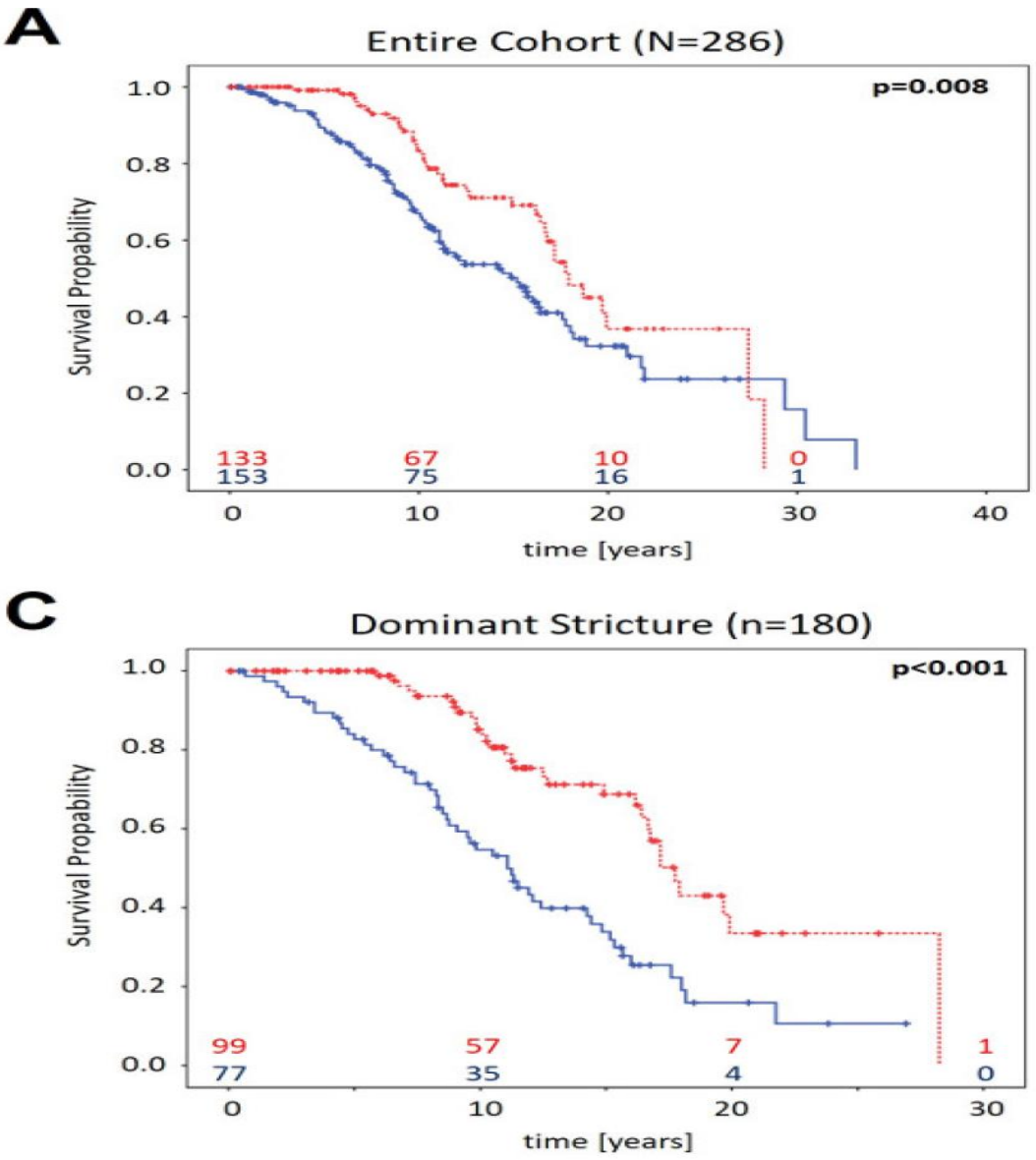
**2.** Find what **patients** understand, want, worry about and will put up with…

**3. Pilot evaluation of more intensive strategies**

Annual gadolinium MRI, 6 monthly tumour markers

Annual ERCP plus cytology (+/- FISH/ cholangioscopy..)

# Benefit of annual ERCP & dilation of dominant strictures




*Ruff Gut 2019*

# A UK-wide audit*: questions

1. Which variables are associated with CCA resectability, and “good” outcome?

**2.** Surveillance prior to CCA diagnosis?

Done or not?

Modality, protocol,

CCA present on prior imaging in retrospect?

Can diagnostic criteria be improved?

**D Gleeson B Rea, M Walmsley, D Joshi, P Trivedi*

# Strategy: electronic case-capture

1. All CCA diagnoses at HPB MDTs (only 3% have PSC)

2. "Link" with "PSC database"

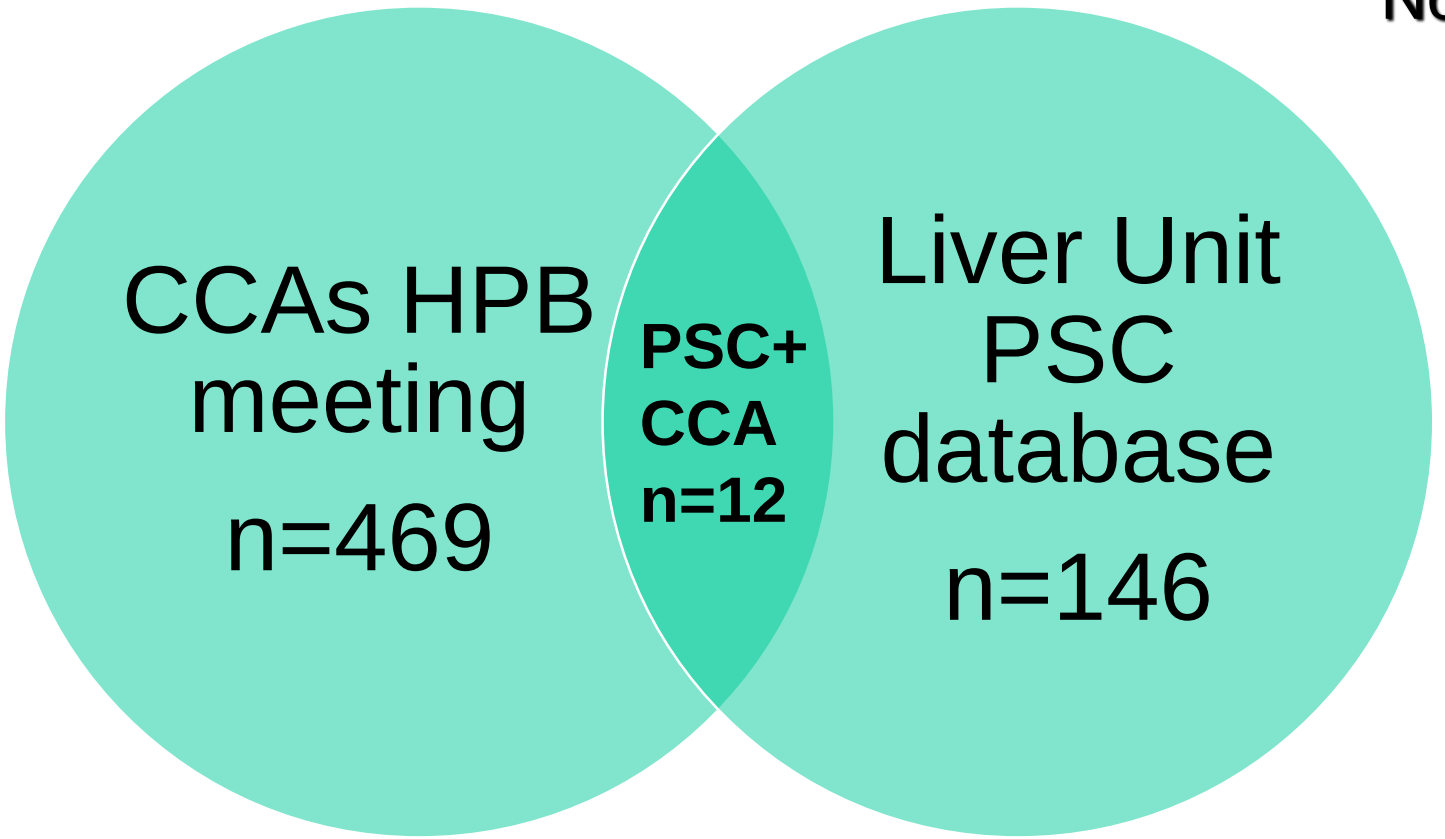
   Coding: not useful (ICD10 K83.0 applied inaccurately)

   Ultrasound request information: "PSC" or:

   "primary" +

   "sclerosing" +

   "cholangitis"




Not PSC

| | | | | |
|---|---|---|---|---|
| Ultrasound request | | | | |
| PSC search | 1 | 8 | 114 | 79 |

# In “most” patients with PSC developing CCA

1. Electronic data collection: Imaging reports

   Laboratory

   Histology

   Endoscopy, Surgery

   Survival (ONS)

2. Anonymisation: transfer to central repository

3. Imaging review - “expert” panel

   - recent reporting standards

*Grigoriadis JHepRep 2022, Venkatesh Eur Radiol 2022*

# Challenges

1. Improve and pilot case-capture strategy
2. Get “most” UK Trusts on board
3. Support from RCP, BSG, BASL, GI Radiology.….
4 Involve HQIP

NCEPOD…..

# Thank you