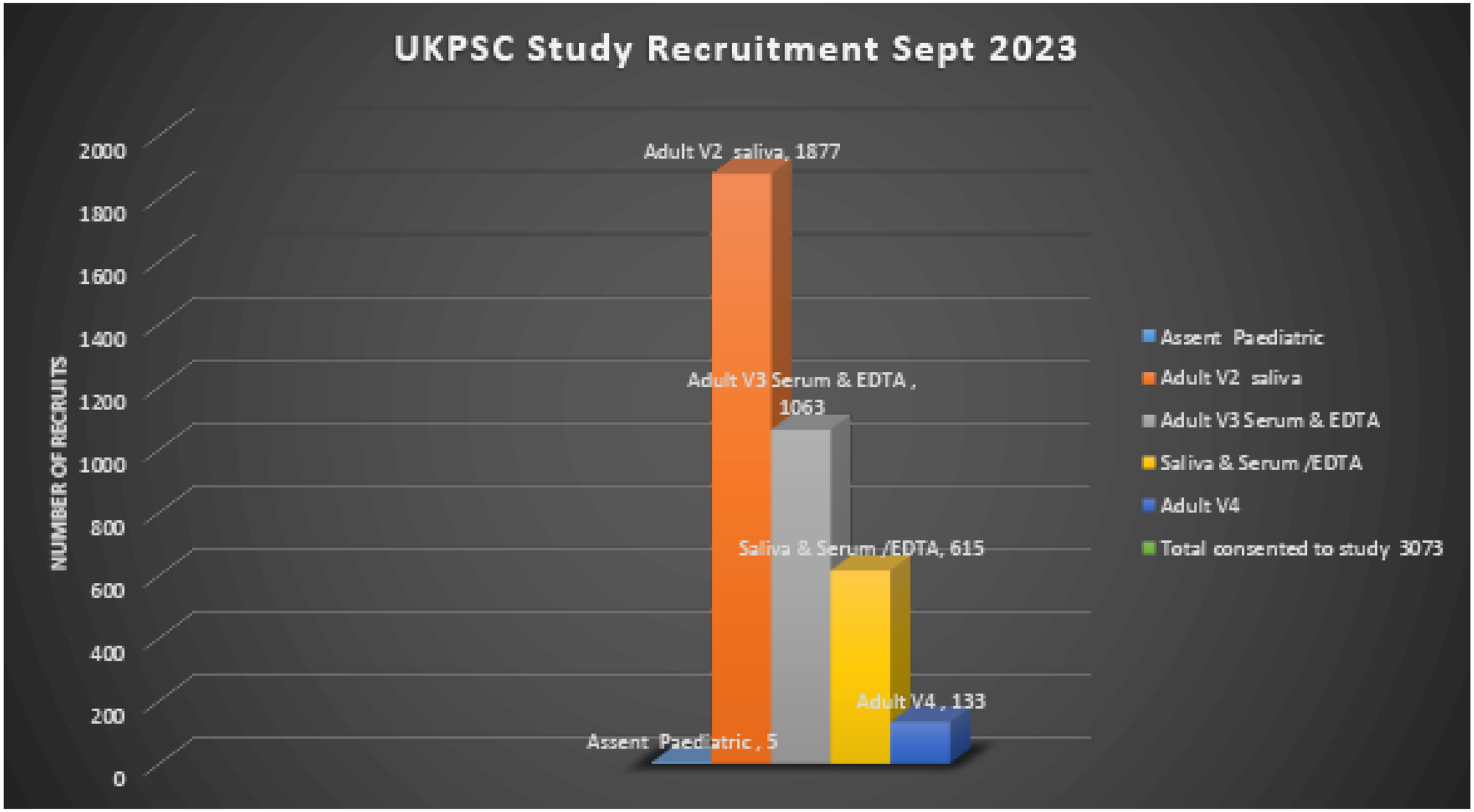
UK-PSC Status Update

Current status of the UK PSC registry (1)

- **Prospective, consent-driven recruitment (postal)**
  - 3,639 invitees
  - 2,400 registrants thus far (predominantly adults);* clinical data with annual event updates
  - 1,135 who have donated blood samples (serum / DNA), 14,154 aliquots
  - Single time point blood sample collections
  - Version 5 consent permits serial blood sample collection (not actioned, not funded)
  - Currently pursuing data linkage with national administrative healthcare datasets

- **Ongoing projects:**
  - Temporal changes in disease epidemiology (Linkage with NHS Digital)
  - Health economics, cost-of-illness analysis to facilitate health technology assessments
  - National trial pre-screening

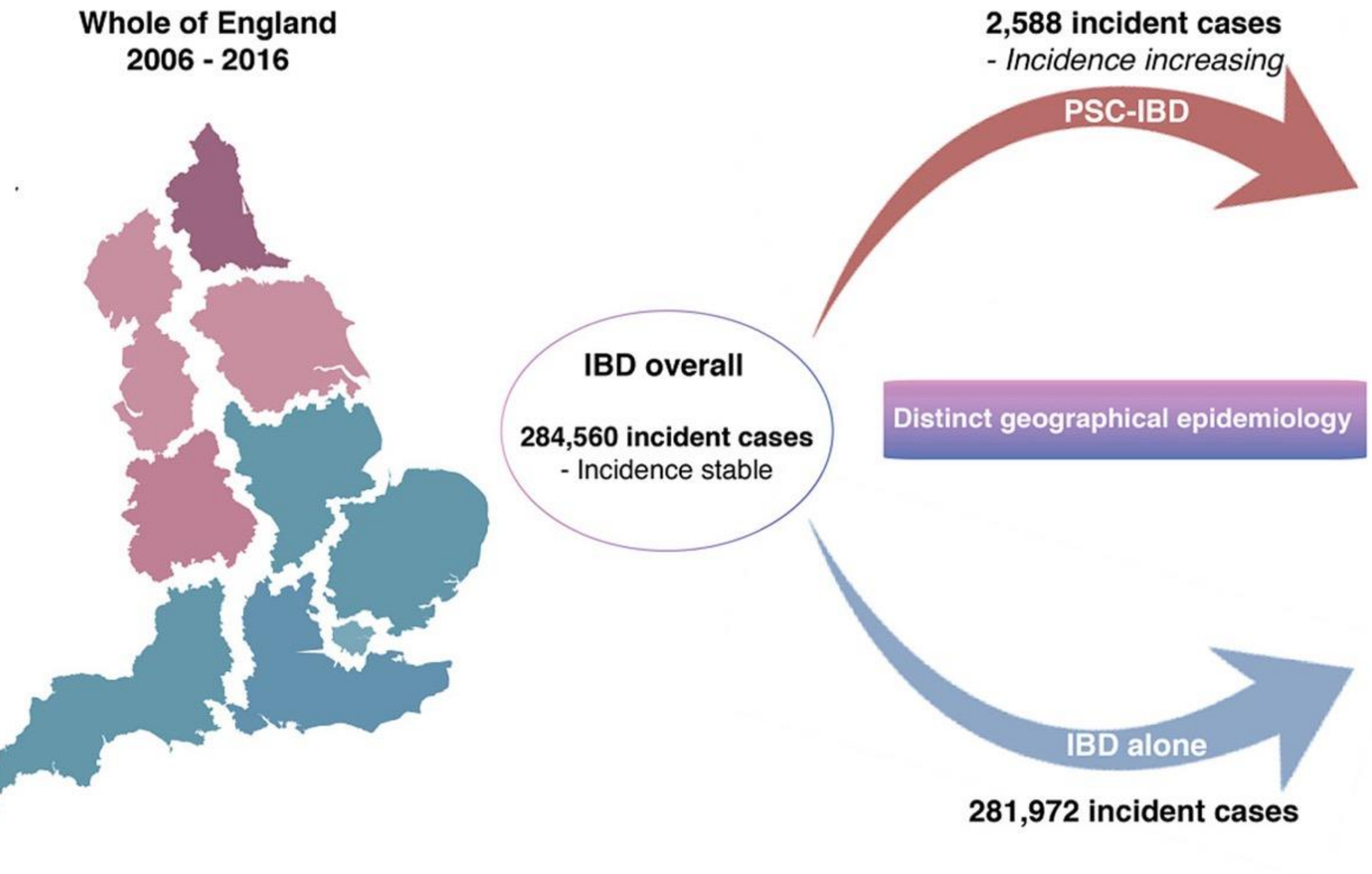
*Not all who have consented have participated



Monthly Recruitment 2023 – New amendment 9

200 packs to be sent. Pending new OID agreements from Sites.

PSC-IBD in England Epidemiology Project



Post-doc.; Hannah Crothers

Gastroenterology

Phenotypic variation: 2,588pts. with PSC-IBD

41,055 deaths

173 liver transplants (LT)

31,587 colonic resections

5,608 colorectal cancers (CRC)

164 cholangiocarcinomas

103 gallbladder cancers

47 liver cancers

800 pancreatic cancers

6,608 cholecystectomies

Age	**Young presenting age (<40y)** >7-fold increased mortality rate vs. IBD alone >5-fold increased CRC rate vs. IBD alone >75% of clinical events PSC-related **Older presenting age (>60y)** <1.5-fold increased mortality rate vs. IBD alone <1.5-fold increased CRC rate vs. IBD alone <40% of clinical events PSC-related
Race	**Afro-Carribean race** ~2-fold increase in LT/PSC-related death
Sex	**Female sex** 25% lower risk of LT/PSC-related death
HPB cancer	**Annual imaging surveillance** 2-fold reduction in cancer-related death

Predicting the current and future prevalence of PSC-IBD: a nationwide population-based study

BACKGROUND & AIMS

- PSC is a leading indication for transplantation and a major risk factor for colorectal cancer in patients with IBD
- However, the scale of unmet need is not well defined, and it is not known how the epidemiology of PSC is changing as that of IBD evolves
- **AIM**: To quantify the current and future prevalence of PSC-IBD in England

METHOD

- Nationwide population-based health administrative data were analyzed to quantify the prevalence of PSC-IBD in 18–60-year-olds across the whole of England (start: 1st Jan 2015) [a]
- Incidence and mortality models were fitted and combined with population projections from the Office for National Statistics to forecast prevalence[b] with 95% PIs from 2020–2027

RESULTS

- The point prevalence of PSC with prior IBD increased from 5.0 to 7.6 per 100,000 population from 2015 to 2020. AAPC 8.8% **(Figure 1)**
- An additional 12% were diagnosed with IBD in the 5 years following PSC presentation
- The prevalence of IBD alone increased from 384.3 to 538.7 per 100,000 population from 2015 to 2020. AAPC 7.0% **(Figure 2)**
- Predictions on held-out data fit well

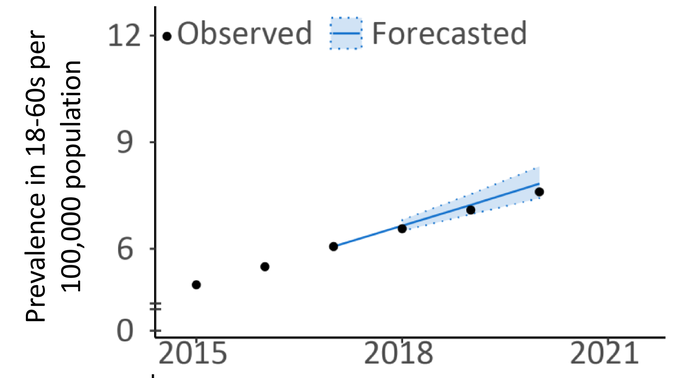


Fig 1: Observed vs forecasted prevalence of PSC-IBD 2015-2020

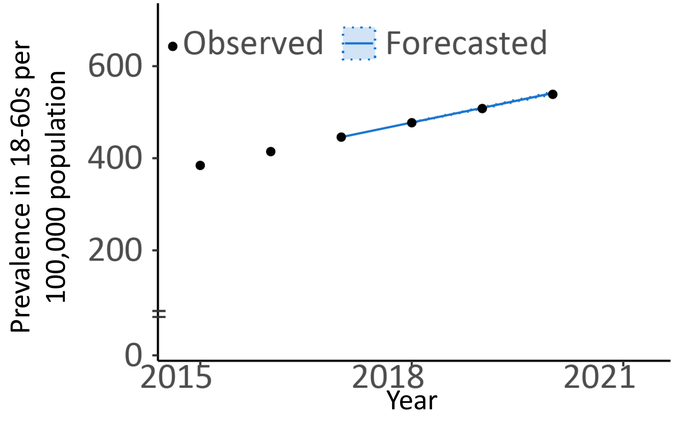


Fig 2: Observed vs forecasted prevalence of IBD alone 2015-2020

[a]Methods adapted from those used for Cystic Fibrosis in Keogh, R.H. et al Sci Rep 10, 10660 (2020).
[b]Prevalence estimates were censored at the point of death or transplantation.
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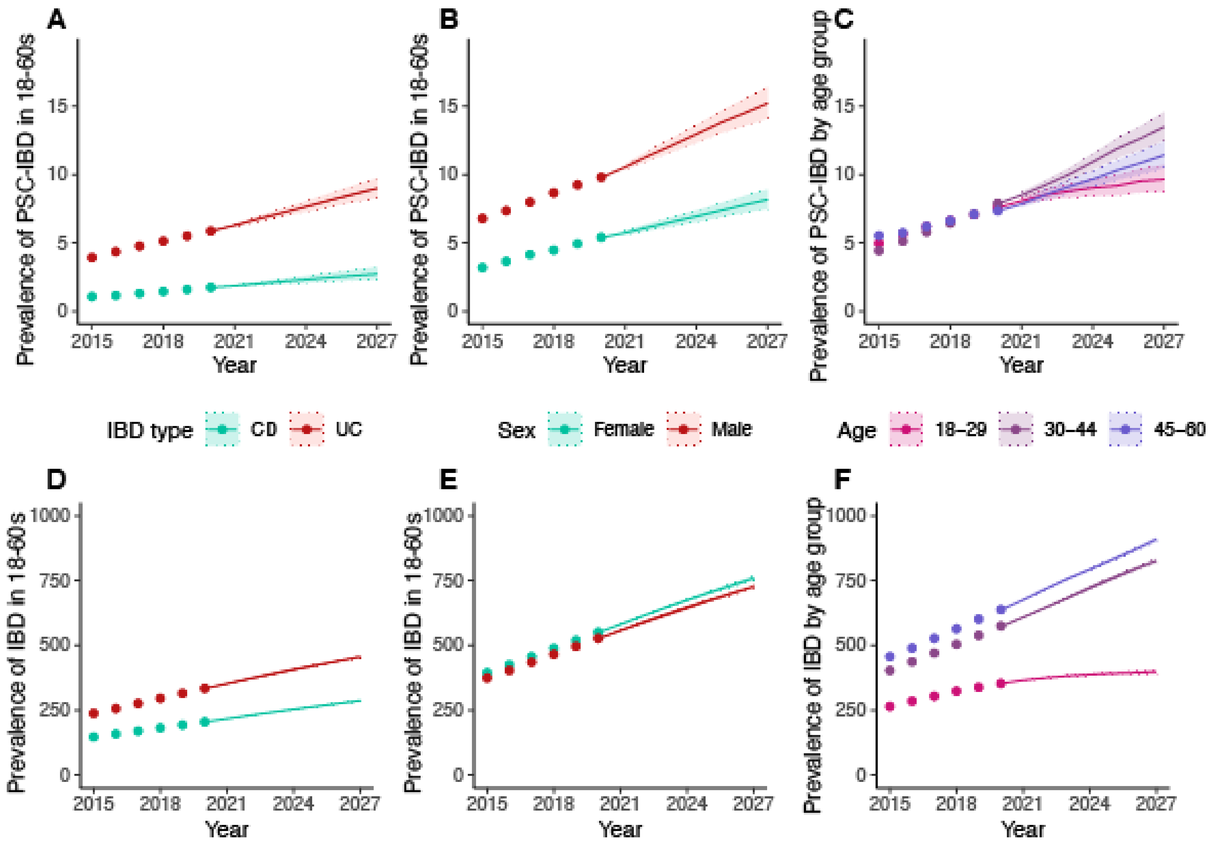
Predicting the current and future prevalence of PSC-IBD: a nationwide population-based study

RESULTS (cont.)

Figure 3: Current and Future Prevalence of PSC-IBD and IBD Alone Across England



Observed (dots) and forecasted (solid lines) adjusted prevalence with 95% PIs (shading and dotted lines, respectively)

- PSC-IBD patient subgroups with the largest growth were (**Figure 3A–C**):
  - **Men** over women (AAPC: 11.1% vs. 7.6%)
  - **PSC-CD** over PSC-UC (AAPC: 10.3% vs. 8.4%)
  - Patients aged **30-44 years** (AAPC: 18–29 years, 8.8%; 30–44 years, 12.3%; 45–60 years, 5.9%)
- For IBD alone, the AAPC for men and women, CD and UC, and across age groups were all similar, falling between 5.9% and 7.3% (**Figure 1D–F**)
- The prevalence of PSC-IBD in 2027 is forecasted to increase to 11.7 per 100,000 (95% PI: 10.8–12.7), yielding an estimated 3683 people living with the condition
  - This increases to 4125 when including patients diagnosed with IBD after PSC

CONCLUSION

- The growth rate in PSC-IBD is not explained by that of IBD alone
- This study provides nationwide estimates reflecting the current and future landscape of PSC-IBD, which may inform service development, HTAs and rare liver disease care strategies

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Burden, Impact and Variability of Pruritus in Primary Sclerosing Cholangitis (PSC): A Prospective Observational Study

Hussain N[1], Hirschfield B[1], Ferguson J[1], Abbas N[1], Gungabissoon U[2], Bhandal K[1], Burke E[1], Hull D[1], Rogers P[1], Casillas L[3], Mukherjee S[3], Ribeiro A[4], Walmsley M[5], Harford P[5], McLaughlin M[3], Trivedi P[1]

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EASL CONGRESS Vienna, Austria 21–24 June 2023

Background

- Overarching goal: to quantify the burden of pruritus in PSC and identify factors associated with its intensity and variability over time.

Method

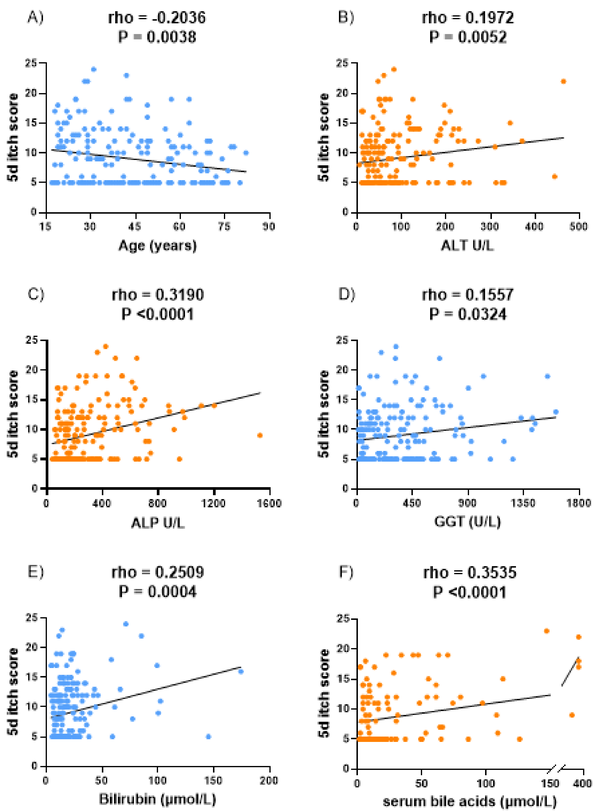
- Patients with PSC (aged >16, non transplanted) underwent disease-specific quality of life assessment at twelve-weekly intervals over the course of one year.
- The following QoL tools were completed: the 5D itch score, NRS itch score, CLDQ and EQ5D-5L.
- The study was registered as a prospective observational clinical trial: ISRCTN 15518794

Results

Table 1: Baseline characteristics (n=200)

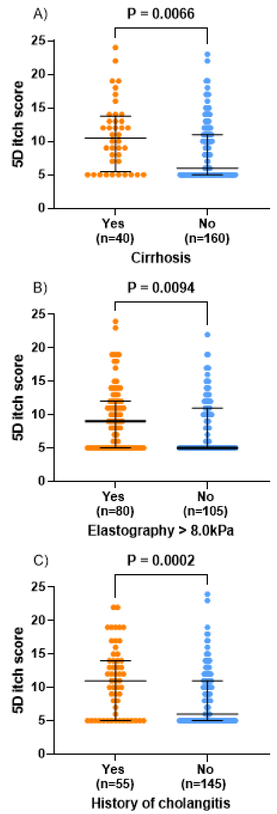
	n/median	%/IQR
Age at study entry	39	28.0-57.0
Male	115	57.5
Disease Extent:		
Small duct	19	9.50
Isolated intrahepatic disease	104	52.0
Intra and extrahepatic disease	77	38.5
MELD	7	6.0-8.0
Elastography	7.4	5.1-11.2
Cirrhosis:	40	20.0
Inflammatory Bowel Disease:	170	85.0
Serum ALT (U/L)	58	31-115
Serum ALP (U/L)	214	127-377
Serum Bilirubin (µmol/L)	15	9-24
Total serum bile acids (µmol/L)	12.5	6.0-34.8
NRS Average Itch Scale		
No itch	100	50.0
Any degree of itch	100	50.0
Mild (NRS 1-3)	59	29.5
Moderate (NRS 4-6)	24	12.0
Severe (NRS 7-10)	17	8.50
5D itch score	8.0	5.0-12.0
Antipruritic treatment		
Monotherapy	30	15.0
Dual therapy	3	1.50

Figure 1: Pruritus intensity is associated with age and liver biochemical values



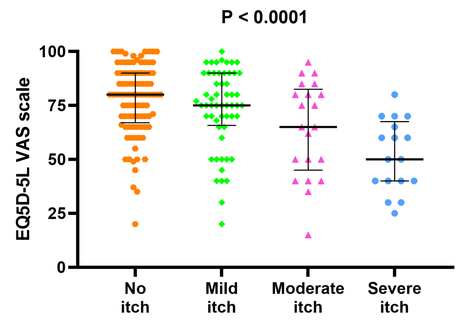
In addition to data presented above, no correlations were found between pruritus intensity and BMI, white cell count, hemoglobin, platelets, albumin, creatinine, CRP or INR. (rho = Spearmans' correlation coefficient)

Figure 2: Factors associated with pruritus severity at baseline



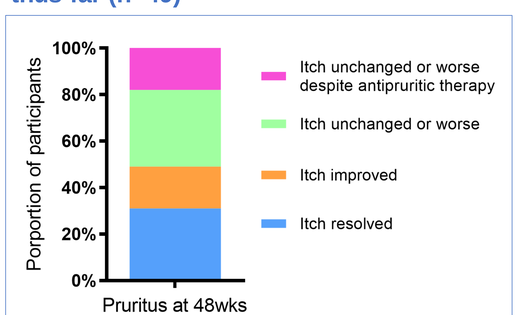
In addition to data presented above, no significant differences in pruritus intensity were seen between sexes, the extent of ductal involvement, presence of IBD or IBD activity

Figure 3: EQ5D VAS score vs pruritus severity at baseline



In addition to data presented above, itch intensity was associated with worse QoL according to CLDQ and EQ5D-5L (P<0.0001, P=0.0026)

Figure 4: NRS pruritus data at 48 weeks thus far (n=49)



Data consists of only those participants who reported itch at baseline, and for whom 48-week NRS data was obtained.

Conclusions

- More than 20% of patients have moderate-severe pruritus and more than 50% have persistence of itch severity over time
- Pruritus in PSC is commonly reported and negatively impacts QoL, despite current available guideline therapies, and persists in the majority of patients over the course of 12 months
- Those with advanced fibrosis, cirrhosis or a history of cholangitis have the greatest need for antipruritic therapy, and should be a principal focus for symptom-directed therapy in PSC

Academic Trials in the UK

PSC-IBD microbial therapeutics' programme

Gut microbial 'depletion'	Gut microbial 'replacement'	Reduced gut 'toxin adsorption'
Vancomycin; n=15 (NCT05376228) Phase 2A; open-label 125 mg QID for 4w, with 4w washout **1º outcome:** IBD remission at 4w **2º outcomes:** IBD remission at 8w; liver biochemistry at 4w, safety (AMR) **Translational outcomes:** colonic microbial, transcriptomic and metabolic profiles	**Faecal microbiota transplantation; n=58** Phase 2A; RCT (blinded) Colonic delivery, once weekly for 8w **1º outcome:** ALP reduction at 48w **2º outcomes:** liver biochemistry, ELF PROs, ProC3/C5, C4M, elastography **Translational outcomes:** colonic microbial, transcriptomic, mucosal immune cell phenotyping, metabolic profiles	**CARBALIVE; n=12** Phase 2A; open-label Seq. dose finding: 8g and 12g OD **1º outcome:** safety; 12w **2º outcomes:** liver biochemistry, ELF PROs, ProC3/C5, C4M **Translational outcomes:** colonic microbial, transcriptomic, metabolic profiles
PSC with active colitis	PSC-IBD without advanced fibrosis	PSC-IBD with mod-advanced fibrosis