

Supplementary Material

Bile Acid Profiles in Primary Sclerosing Cholangitis and their Ability to Predict Hepatic

Decompensation

Omar Y. Mousa, Brian D. Juran, Bryan M. McCauley, Mette N. Vesterhus, Trine Folseraas, Coleman T. Turgeon, Ahmad H. Ali, Erik M. Schlicht, Elizabeth J. Atkinson, Chang Hu, Denise Harnois, Elizabeth J. Carey, Andrea A. Gossard, Devin Oglesbee, John E. Eaton, Nicholas F. LaRusso, Gregory J. Gores, Tom H. Karlsen, Konstantinos N. Lazaridis

Table of Contents

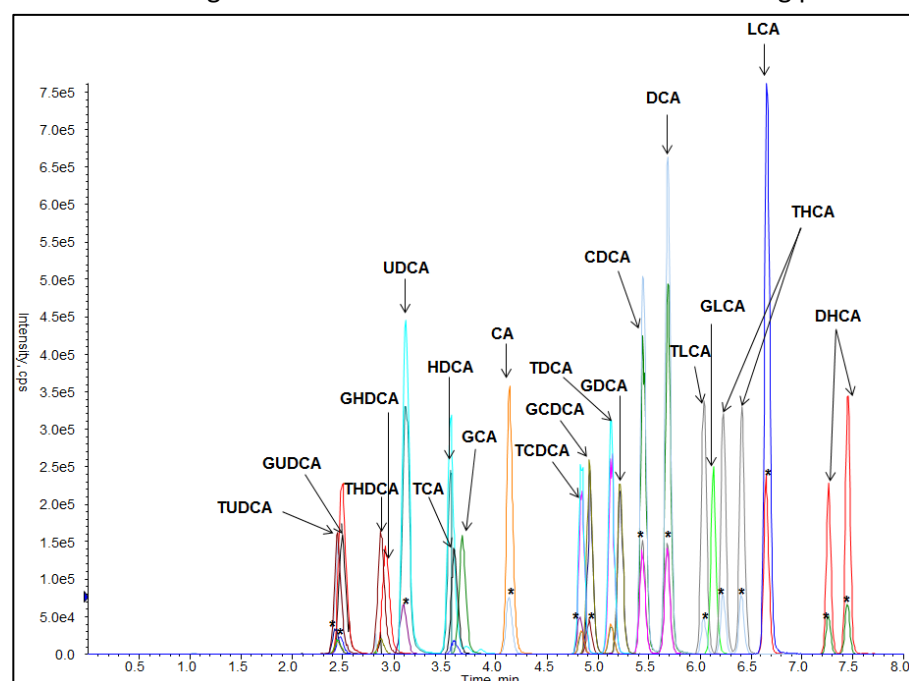
| Pages | Item | Title |
|-------|------------------------|---|
| 3-5 | Supplemental Methods | Bile acid profile method and validation |
| 6-9 | Supplementary Table 1 | Bile acids in PSC patients and controls |
| 10-14 | Supplementary Table 2 | Bile acids in NN PSC patients and controls. |
| 15-19 | Supplementary Table 3 | Bile acids in NN and NY PSC patients. |
| 20-24 | Supplementary Table 4 | Bile acids in HN and HY PSC patients. |
| 25-28 | Supplementary Table 5 | Bile acids in NN and HN PSC patients. |
| 29-32 | Supplementary Table 6 | Bile acids in NY and HY PSC patients. |
| 33-36 | Supplementary Table 7 | Bile acids in Control and No IBD PSC patients. |
| 37-40 | Supplementary Table 8 | Bile acids in No IBD and UC PSC patients. |
| 41-44 | Supplementary Table 9 | Bile acids in No IBD and CD PSC patients. |
| 45-48 | Supplementary Table 10 | Bile acids in No IBD and Ind. IBD PSC patients. |
| 49-52 | Supplementary Table 11 | Bile acids in cirrhotic and non-cirrhotic PSC patients |
| 53-56 | Supplementary Table 12 | Bile acids in autoimmune hepatitis (AIH) overlap and non-overlap large duct PSC patients. |
| 57-60 | Supplementary Table 13 | Bile acids in small duct (SD) and large duct (LD) PSC patients. |
| 61-62 | Supplementary Table 14 | Univariate time to event analyses. |
| 63-64 | Supplementary Table 15 | Univariate event rate by quartiles analyses. |
| 65 | Supplementary Table 16 | Variables and relative influence on GBM Model. |

| | | |
|-------|------------------------|---|
| 66-69 | Supplementary Table 17 | Bile acids in PSC patients: Der. and Val. cohorts. |
| 70 | Supplementary Figure 1 | Bile acids by age in PSC and controls. |
| 71 | Supplementary Figure 2 | Bile acids by sex in PSC and controls. |
| 72 | Supplementary Figure 3 | Bile acids in controls and PSC patients by bile acid group. |
| 73 | Supplementary Figure 4 | Bile acids in cirrhotic and non-cirrhotic PSC patients |
| 74 | Supplementary Figure 5 | BA correlation plots in PSC and controls. |
| 75 | Supplementary Figure 6 | Alternate GBM models using BA profiles |

Supplemental Methods: Bile acid profile method and validation

BA Profiling Method

Samples were prepared by precipitating matrix proteins with an acetonitrile/water (50/50) mixture containing deuterated internal standards at appropriate concentrations. Protein precipitate was removed by filtering through an AcroPrep 0.45 μm GHP filter plate. The filtrate was diluted into water/methanol (80/20) solvent for injection into the LC-MS/MS system (ABSciex API 3200 LC-MS/MS with TurbolonSpray source, LEAP HTC Pal Autosampler, and a Shimadzu LC-20 AB Binary Pump) with an inline Poroshell 120 EC-C18, 2.1x50 mm, 2.7 micron column. Reverse-phase liquid chromatography was initiated with 42% mobile phase A (10 mM Ammonium Acetate in 95%Water/5% Methanol) and 58% mobile phase B (10 mM Ammonium Acetate in 99 % Methanol/ 1% Water) at 0.3 ml/min rate with a binary flow over 13 min. The MS/MS instrument collected 37 scheduled MRMs in negative ion mode with a 60 sec target window and a 0.8 sec scan time. Declustering potential (DP) ranged from -75 volts



to -115 volts, collision energy potential (CEP) ranged from -20 to -30 volts, collision energy (CE) from -20 to -125 volts, and collision cell exit potential (CXP) ranged from -5 to -45 volts across the method. An example chromatogram is shown in **Methods Figure 1**. Analyte concentrations were derived from calculations in Analyst 1.6.2 and peak area ratios with internal labeled standards.

Methods Figure 1. A chromatogram with each measured BA analyte. Cholic Acid (CA), Chenodeoxycholic Acid (CDCA), Deoxycholic Acid (DCA), Ursodeoxycholic Acid (UDCA), Hyodeoxycholic Acid (HDCA), Lithocholic Acid (LCA), Glycocholic Acid (GCA), Glycochenodeoxycholic Acid (GCDCA), Glycodeoxycholic Acid (GDCA), Glycoursodeoxycholic Acid (GUDCA), Glycohyodeoxycholic Acid (GHDCa), Glycolithocholic Acid (GLCA), Taurocholic Acid (TCA), Taurochenodeoxycholic Acid (TCDCA), Taurodeoxycholic Acid (TDCA), Tauroursodeoxycholic Acid (TUDCA), Taurohyodeoxycholic Acid (THDCA), Taurolithocholic Acid (TLCA), Dihydroxycholestanic Acid (DHCA), Trihydroxycholestanic Acid (THCA). The asterisks (*) indicate isotopically labeled internal standards for each analyte with the same retention time. This includes d4-Cholic Acid (CA-d4), d4-Chenodeoxycholic Acid (CDCA-d4), d4-Deoxycholic Acid (DCA-d4), d5-Ursodeoxycholic Acid (UDCA-d5), d4-Lithocholic Acid (LCA-d4), d4-Glycochenodeoxycholic Acid (GCDCA-d4), d5-Glycoursodeoxycholic Acid (GUDCA-d5), d5-Taurochenodeoxycholic Acid (TCDCA-d5),

d5-Tauroursodeoxycholic Acid (TUDCA-d5), d3-Dihydroxycholestanic Acid (DHCA-d3), and d3-Trihydroxycholestanic Acid (THCA-d3).

Plasma and Serum Specimen Equivalency

Equivalency between serum and plasma BA analytical performance was shown previously. **Reference:** Max Scherer, Carsten Gnewuch, Gerd Schmitz, Gerhard Liebisch. Rapid quantification of bile acids and their conjugates in serum by liquid chromatography-tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci. 2009 Nov 15;877(3):3920-3925. PMID: 19819765.

Bile Acid Profile Imprecision

Intra-assay imprecision of BA assay was performed with quality control specimens in matrix at low BA concentrations (QC 1) and high concentrations (QC 2) over 20 replicates in a single batch. Inter-assay imprecision was evaluated by preparing and analyzing a low (QC1) and high (QC2) control across 20 separate runs. The calculated coefficient of variation and mean concentrations for each analyte detected by these methods is shown in **Methods Table 1**.

Methods Table 1. BA profile Intra-assay and Inter-assay Imprecision

| Analyte | Intra-assay imprecision (N = 20 Specimens) | | Inter-assay imprecision (N = 20 Runs) | |
|---------|--|--------------------------|---------------------------------------|--------------------------|
| | QC1 | QC2 | QC1 | QC2 |
| | CV (mean conc., μ M) | CV (mean conc., μ M) | CV (mean conc., μ M) | CV (mean conc., μ M) |
| LCA | 4.8% (0.80) | 4.2% (7.69) | 9.6% (0.81) | 4.5% (7.51) |
| CDCA | 5.8% (1.18) | 4.2% (7.90) | 21.0% (1.20) | 6.4% (7.53) |
| DCA | 5.1% (1.60) | 5.4% (8.43) | 11.8% (1.59) | 8.2% (8.15) |
| UDCA | 5.0% (0.79) | 3.6% (7.07) | 9.0% (0.79) | 8.4% (7.05) |
| HDCA | 18.5% (0.26) | 10.1% (2.50) | 23.0% (0.29) | 25.8% (2.64) |
| CA | 4.9% (1.07) | 3.7% (7.41) | 7.4% (1.08) | 4.5% (7.37) |
| GLCA | 11.1% (0.31) | 11.8% (3.15) | 22.8% (0.38) | 22.6% (3.79) |
| GCDCA | 5.5% (3.16) | 4.5% (9.72) | 10.3% (3.22) | 8.6% (9.56) |
| GDCA | 11.7% (0.88) | 9.4% (5.61) | 15.6% (0.91) | 17.0% (5.76) |
| GUDCA | 7.0% (0.99) | 4.6% (7.44) | 9.1% (1.00) | 6.9% (7.11) |
| GHDCA | 11.8% (0.31) | 11.5% (2.76) | 29.2% (0.30) | 32.7% (2.54) |
| GCA | 6.2% (1.85) | 10.5% (9.32) | 10.6% (1.78) | 14.2% (8.92) |
| TLCA | 18.6% (0.34) | 16.8% (3.80) | 41.1% (0.45) | 52.1% (5.31) |
| TCDCA | 4.2% (1.21) | 4.3% (7.64) | 7.6% (1.20) | 6.6% (7.39) |
| TDCA | 10.2% (0.41) | 9.4% (4.68) | 29.1% (0.45) | 28.0% (4.73) |
| TUDCA | 4.8% (0.72) | 4.2% (6.86) | 4.2% (0.72) | 5.3% (6.65) |
| THDCA | 11.0% (0.56) | 8.4% (6.26) | 18.2% (0.49) | 27.0% (5.51) |
| TCA | 6.2% (0.92) | 11.2% (7.68) | 14.7% (0.89) | 23.5% (7.40) |
| DHCA | 6.9% (0.82) | 4.5% (7.66) | 22.2% (0.90) | 9.3% (7.11) |
| THCA | 9.0% (1.42) | 4.6% (8.24) | 12.0% (1.47) | 4.8% (8.23) |

BA Profile Limit of Detection, Biological Limit of Detection and Linearity

The limit of detection (LOD) was determined by the analysis of 12 reagent blanks. The biological limit of detection (BLD) was determined by the analysis (N = 6) of a single serum specimen spiked with BA analyte concentrations near the LOD and measured in triplicate on two separate runs. Linearity was assessed by the analysis of 12-point analyte calibration curves (0.00, 0.05, 0.10, 0.20, 0.50, 1.0, 2.0, 5.0,

10.0, 20.0, 50.0, 100.0 μM), 5 times, inter-assay. An 11-point calibration curve with each analytical batch was necessary for BA quantitation as a few conjugated bile acids demonstrated correlation coefficients of 0.96-0.98. The LOD and BLD values and linearity results are shown in **Methods Table 2**.

Methods Table 2. Analytical Sensitivity and Linearity

| Analyte | LOD (μM) | BLD (μM) | Curve 1 | Curve 2 | Curve 3 | Curve 4 | Curve 5 |
|---------|--------------------------|--------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| | | | Correlation Coefficient | Correlation Coefficient | Correlation Coefficient | Correlation Coefficient | Correlation Coefficient |
| LCA | 0.00 | 0.01 | 0.99714 | 0.99910 | 0.99944 | 0.99790 | 0.99819 |
| CDCA | 0.00 | 0.02 | 0.99861 | 0.99961 | 0.99939 | 0.99925 | 0.99866 |
| DCA | 0.00 | 0.02 | 0.99776 | 0.99819 | 0.99788 | 0.99748 | 0.99828 |
| UDCA | 0.01 | 0.02 | 0.99974 | 0.99977 | 0.99918 | 0.99958 | 0.99954 |
| HDCA | 0.00 | 0.01 | 0.98951 | 0.99365 | 0.99310 | 0.99533 | 0.99575 |
| CA | 0.00 | 0.00 | 0.99793 | 0.99895 | 0.99870 | 0.99770 | 0.99783 |
| GLCA | 0.00 | 0.02 | 0.99115 | 0.99709 | 0.99449 | 0.99407 | 0.99757 |
| GCDCA | 0.00 | 0.01 | 0.99968 | 0.99974 | 0.99948 | 0.99924 | 0.99972 |
| GDCA | 0.00 | 0.02 | 0.98578 | 0.99065 | 0.98901 | 0.98844 | 0.99669 |
| GUDCA | 0.02 | 0.03 | 0.99950 | 0.99927 | 0.99765 | 0.99896 | 0.99715 |
| GHDCA | 0.00 | 0.00 | 0.98449 | 0.98087 | 0.98442 | 0.98278 | 0.99136 |
| GCA | 0.00 | 0.02 | 0.99602 | 0.99848 | 0.99804 | 0.99748 | 0.99924 |
| TLCA | 0.01 | 0.01 | 0.98667 | 0.99129 | 0.98845 | 0.98842 | 0.98399 |
| TCDCA | 0.00 | 0.03 | 0.99796 | 0.99775 | 0.99790 | 0.99726 | 0.99822 |
| TDCA | 0.00 | 0.03 | 0.98190 | 0.99064 | 0.96426 | 0.96745 | 0.98078 |
| TUDCA | 0.01 | 0.03 | 0.99955 | 0.99908 | 0.99938 | 0.99847 | 0.99962 |
| THDCA | 0.01 | 0.02 | 0.99761 | 0.99440 | 0.99238 | 0.99298 | 0.99269 |
| TCA | 0.00 | 0.03 | 0.99771 | 0.99760 | 0.99499 | 0.99735 | 0.99879 |
| DHCA | 0.00 | 0.01 | 0.97576 | 0.98129 | 0.97869 | 0.97720 | 0.97848 |
| THCA | 0.00 | 0.23 | 0.97297 | 0.98018 | 0.98044 | 0.97546 | 0.97733 |

BA Profile Specimen Dilution Limit

As patient specimens with BA concentrations above the analytical measurement range (AMR) of 100 μM were expected for certain clinical conditions, dilutions limits for each BA analyte were determined by measuring 2 serum specimens spiked to an approximate concentration of 15 μM for each bile acid. The spiked serum specimens were then diluted 2x, 5x, 10x, 20x, 25x, 40x, and 50x with water, and diluted solutions were carried through the analytical procedure. At a 2-fold dilution, the resulting %-difference from expected concentration was near, or less than, 20%. Beyond a 2-fold dilution, various conjugated bile acids resulted in significant overestimation (greater than 25%) of their original concentration. Therefore, it was concluded that only a 2x specimen dilution would yield acceptable BA calculated concentrations, which increased the effective AMR of the assay to 200 μM for most BAs when completing a specimen dilution.

Use of BA Profile Concentration Values in This Study

As our study is broadly based on comparing BA concentrations between relatively large groups we used the actual reported values for BA concentrations even when they were below the previously determined LOD or above the AMR. Low values approximate a concentration of zero, which could affect results of low-abundance bile acids such as the LCAs and HDCAs. Values above the AMR were only found for GUDCA in 4 of the 400 PSC patients and likely do not significantly impact our findings.

Supplementary Table 1. Bile acids in PSC patients and controls.

| | Control | PSC | p-value | Con (n) | PSC (n) |
|----------------------------|---------------------|---------------------|---------|---------|---------|
| Age in years | | | | | |
| Median (IQR) | 56.40 (48.49-65.29) | 48.44 (32.99-59.65) | <0.001 | 302 | 400 |
| Range | 19.28-86.12 | 10.13-80.48 | | | |
| Sex (% Male) | 58.3 | 57.8 | 0.888 | 302 | 400 |
| Total BA | | | | | |
| Median (IQR) | 1.90 (1.02-3.52) | 16.34 (6.04-44.31) | <0.001 | 302 | 400 |
| Range | 0.19-17.79 | 0.54-646.47 | | | |
| CA (total) | | | | | |
| Median (IQR) | 0.22 (0.11-0.49) | 2.09 (0.73-10.01) | <0.001 | 302 | 400 |
| Range | 0.01-6.43 | 0.04-224.36 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.04 (0.02-0.12) | 0.06 (0.03-0.22) | <0.001 | 302 | 400 |
| Range | 0.00-5.23 | 0.00-10.65 | | | |
| GCA | | | | | |
| Median (IQR) | 0.12 (0.05-0.25) | 1.60 (0.44-6.12) | <0.001 | 302 | 400 |
| Range | 0.01-5.84 | 0.01-165.50 | | | |
| TCA | | | | | |
| Median (IQR) | 0.02 (0.01-0.04) | 0.25 (0.06-2.44) | <0.001 | 302 | 400 |
| Range | 0.00-1.50 | 0.00-58.61 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 0.63 (0.33-1.39) | 4.09 (1.61-9.81) | <0.001 | 302 | 400 |
| Range | 0.05-10.77 | 0.10-268.56 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.23) | 0.15 (0.05-0.46) | <0.001 | 302 | 400 |
| Range | 0.00-5.28 | 0.00-14.78 | | | |
| GCDCA | | | | | |
| Median (IQR) | 0.42 (0.21-0.88) | 2.87 (1.10-6.90) | <0.001 | 302 | 400 |
| Range | 0.02-5.38 | 0.02-214.48 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.05 (0.03-0.11) | 0.47 (0.13-2.12) | <0.001 | 302 | 400 |
| Range | 0.00-2.49 | 0.00-52.46 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.65 (0.36-1.21) | 0.66 (0.03-1.76) | 0.328 | 302 | 400 |
| Range | 0.00-8.26) | 0.00-24.36 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.33 (0.19-0.58) | 0.10 (0.01-0.44) | <0.001 | 302 | 400 |
| Range | 0.00-4.49 | 0.00-5.99 | | | |

| | Control | PSC | p-value | Con (n) | PSC (n) |
|----------------------------|------------------|-------------------|---------|---------|---------|
| GDCA | | | | | |
| Median (IQR) | 0.21 (0.10-0.46) | 0.28 (0.02-0.96) | 0.339 | 302 | 400 |
| Range | 0.00-5.94 | 0.00-15.49 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.04 (0.02-0.08) | 0.06 (0.00-0.27) | 0.013 | 302 | 400 |
| Range | 0.00-1.13 | 0.00-8.55 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.03 (0.02-0.05) | 0.04 (0.00-0.15) | 0.037 | 302 | 400 |
| Range | 0.00-0.42 | 0.00-2.85 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.01 (0.00-0.04) | 0.512 | 302 | 400 |
| Range | 0.00-0.21 | 0.00-0.96 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.02 (0.00-0.09) | 0.002 | 302 | 400 |
| Range | 0.00-0.19 | 0.00-2.14 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.02) | <0.001 | 302 | 400 |
| Range | 0.00-0.07 | 0.00-0.56) | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.03 (0.01-0.05) | 0.01 (0.00-0.04) | <0.001 | 302 | 400 |
| Range | 0.00-0.29 | 0.00-0.73 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.01-0.03) | 0.01 (0.00-0.02) | <0.001 | 302 | 400 |
| Range | 0.00-0.11 | 0.00-0.24 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | <0.001 | 302 | 400 |
| Range | 0.00-0.11 | 0.00-0.73 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.007 | 302 | 400 |
| Range | 0.00-0.09 | 0.00-0.07 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 0.13 (0.07-0.27) | 1.95 (0.19-18.27) | <0.001 | 302 | 400 |
| Range | 0.00-2.15 | 0.00-537.71 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.01-0.06) | 0.17 (0.01-2.02) | <0.001 | 302 | 400 |
| Range | 0.00-0.92 | 0.00-52.33 | | | |
| GUDCA | | | | | |
| Median (IQR) | 0.09 (0.05-0.19) | 1.53 (0.12-13.52) | <0.001 | 302 | 400 |
| Range | 0.00-1.78 | 0.00-472.47 | | | |

| | Control | PSC | p-value | Con (n) | PSC (n) |
|-------------------------------|-------------------|-------------------|---------|---------|---------|
| TUDCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.01) | 0.09 (0.01-0.52) | <0.001 | 302 | 400 |
| Range | 0.00-0.25 | 0.00-51.06 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.64 (0.49-0.79) | 0.91 (0.74-0.98) | <0.001 | 302 | 400 |
| Range | 0.11-0.97 | 0.13-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.75 (0.53-0.89) | 0.97 (0.85-0.99) | <0.001 | 302 | 400 |
| Range | 0.21-1.00 | 0.09-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.87 (0.70-0.94) | 0.95 (0.83-0.99) | <0.001 | 302 | 400 |
| Range | 0.19-1.00 | 0.12-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.44 (0.29-0.60) | 0.80 (0.52-0.95) | <0.001 | 299 | 345 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.50 (0.40-0.69) | 0.75 (0.56-0.87) | <0.001 | 274 | 286 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.20 (0.00-0.50) | 1.22 (0.00-0.55) | 0.106 | 261 | 231 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.83 (0.67-0.94) | 0.90 (0.75-0.97) | 0.001 | 301 | 392 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 7.66 (4.89-11.17) | 8.36 (3.57-17.44) | 0.320 | 300 | 399 |
| Range | 0.91-139.00 | 0.37-93.11 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 6.00 (3.50-9.00) | 5.56 (2.72-9.23) | 0.180 | 263 | 393 |
| Range | 0.83-31.00 | 0.27-70.33 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 8.00 (5.33-12.14) | 5.76 (2.80-10.30) | <0.001 | 298 | 399 |
| Range | 1.00-100.00 | 0.36-92.17 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.50 (3.74-8.00) | 4.90 (2.13-8.26) | 0.007 | 272 | 292 |
| Range | 0.50-61.00 | 0.22-45.00 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 2.00 (1.00-4.25) | 3.00 (1.40-6.22) | 0.061 | 79 | 169 |
| Range | 0.50-13.00 | 0.10-36.00 | | | |

| | Control | PSC | p-value | Con (n) | PSC (n) |
|-----------------------------|--------------------|--------------------|---------|---------|---------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.22 (1.00-3.00) | 1.17 (1.00-1.88) | 0.666 | 5 | 12 |
| Range | 1.00-4.00 | 0.71-11.00 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 10.00 (5.00-18.00) | 18.40 (7.25-35.75) | <0.001 | 177 | 330 |
| Range | 1.00-95.00 | 0.14-145.00 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.13 (0.08-0.18) | 0.18 (0.08-0.36) | <0.001 | 302 | 400 |
| Range | 0.02-0.55 | 0.01-0.79 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.35 (0.27-0.45) | 0.26 (0.15-0.46) | <0.001 | 302 | 400 |
| Range | 0.06-0.75 | 0.04-0.93 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.37 (0.24-0.47) | 0.04 (0.01-0.14) | <0.001 | 302 | 400 |
| Range | 0.00-0.78 | 0.00-0.64 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.02 (0.01-0.03) | 0.01 (0.00-0.01) | <0.001 | 302 | 400 |
| Range | 0.00-0.13 | 0.00-0.12 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.00 (0.00-0.01) | <0.001 | 302 | 400 |
| Range | 0.00-0.14 | 0.00-0.05 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.07 (0.04-0.12) | 0.18 (0.02-0.66) | <0.001 | 302 | 400 |
| Range | 0.00-0.39 | 0.00-0.91 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.38 (0.24-0.54) | 0.60 (0.35-1.12) | <0.001 | 302 | 400 |
| Range | 0.06-3.10 | 0.05-5.26 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 0.36 (0.19-0.73) | 2.60 (0.79-26.43) | <0.001 | 299 | 345 |
| Range | 0.04-103.00 | 0.09-3796.67 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 3.00 (1.78-5.07) | 1.57 (0.22-13.81) | 0.001 | 302 | 392 |
| Range | 0.44-35.00 | 0.04-1310.00 | | | |

Supplementary Table 2. Bile acids in NN PSC patients and controls.

| | Control | NN PSC | p-value | Con (n) | NN PSC (n) |
|----------------------------|---------------------|---------------------|---------|---------|------------|
| Age in years | | | | | |
| Median (IQR) | 56.40 (48.49-65.29) | 51.14 (32.76-61.38) | <0.001 | 302 | 137 |
| Range | 19.28-86.12 | 11.82-78.53 | | | |
| Sex (% Male) | 58.3 | 59.1 | 0.868 | 302 | 137 |
| Total BA | | | | | |
| Median (IQR) | 1.90 (1.02-3.52) | 4.98 (2.45-8.50) | <0.001 | 302 | 137 |
| Range | 0.19-17.79 | 0.59-16.35 | | | |
| CA (total) | | | | | |
| Median (IQR) | 0.22 (0.11-0.49) | 1.00 (0.46-2.12) | <0.001 | 302 | 137 |
| Range | 0.01-6.43 | 0.04-10.09 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.04 (0.02-0.12) | 0.07 (0.03-0.23) | <0.001 | 302 | 137 |
| Range | 0.00-5.23 | 0.00-2.99 | | | |
| GCA | | | | | |
| Median (IQR) | 0.12 (0.05-0.25) | 0.52 (0.27-1.44) | <0.001 | 302 | 137 |
| Range | 0.01-5.84 | 0.02-6.74 | | | |
| TCA | | | | | |
| Median (IQR) | 0.02 (0.01-0.04) | 0.09 (0.04-0.34) | <0.001 | 302 | 137 |
| Range | 0.00-1.50 | 0.00-3.67 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 0.63 (0.33-1.39) | 2.14 (1.22-4.11) | <0.001 | 302 | 137 |
| Range | 0.05-10.77 | 0.16-10.18 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.23) | 0.14 (0.05-0.46) | <0.001 | 302 | 137 |
| Range | 0.00-5.28 | 0.00-5.23 | | | |
| GCDCA | | | | | |
| Median (IQR) | 0.42 (0.21-0.88) | 1.47 (0.69-2.44) | <0.001 | 302 | 137 |
| Range | 0.02-5.38 | 0.10-8.29 | | | |
| TCDC | | | | | |
| Median (IQR) | 0.05 (0.03-0.11) | 0.20 (0.08-0.61) | <0.001 | 302 | 137 |
| Range | 0.00-2.49 | 0.00-3.25 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.65 (0.36-1.21) | 0.39 (0.00-1.26) | <0.001 | 302 | 137 |
| Range | 0.00-8.26) | 0.00-7.81 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.33 (0.19-0.58) | 0.09 (0.00-0.40) | <0.001 | 302 | 137 |
| Range | 0.00-4.49 | 0.00-5.99 | | | |

| | Control | NN PSC | p-value | Con (n) | NN PSC (n) |
|----------------------------|------------------|------------------|---------|---------|------------|
| GDCA | | | | | |
| Median (IQR) | 0.21 (0.10-0.46) | 0.13 (0.00-0.56) | 0.004 | 302 | 137 |
| Range | 0.00-5.94 | 0.00-2.41 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.04 (0.02-0.08) | 0.03 (0.00-0.12) | 0.067 | 302 | 137 |
| Range | 0.00-1.13 | 0.00-1.35 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.03 (0.02-0.05) | 0.02 (0.00-0.06) | <0.001 | 302 | 137 |
| Range | 0.00-0.42 | 0.00-1.18 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.00 (0.00-0.02) | <0.001 | 302 | 137 |
| Range | 0.00-0.21 | 0.00-0.41 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.01 (0.00-0.04) | 0.022 | 302 | 137 |
| Range | 0.00-0.19 | 0.00-0.71 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.367 | 302 | 137 |
| Range | 0.00-0.07 | 0.00-0.06 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.03 (0.01-0.05) | 0.01 (0.00-0.04) | <0.001 | 302 | 137 |
| Range | 0.00-0.29 | 0.00-0.41 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.01-0.03) | 0.01 (0.00-0.02) | <0.001 | 302 | 137 |
| Range | 0.00-0.11 | 0.00-0.24 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | 0.002 | 302 | 137 |
| Range | 0.00-0.11 | 0.00-0.17 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.158 | 302 | 137 |
| Range | 0.00-0.09 | 0.00-0.02 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 0.13 (0.07-0.27) | 0.13 (0.03-0.33) | 0.280 | 302 | 137 |
| Range | 0.00-2.15 | 0.00-1.98 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.01-0.06) | 0.01 (0.00-0.06) | 0.106 | 302 | 137 |
| Range | 0.00-0.92 | 0.00-0.83 | | | |
| GUDCA | | | | | |
| Median (IQR) | 0.09 (0.05-0.19) | 0.09 (0.03-0.22) | 0.234 | 302 | 137 |
| Range | 0.00-1.78 | 0.00-1.71 | | | |

| | Control | NN PSC | p-value | Con (n) | NN PSC (n) |
|-------------------------------|-------------------|-------------------|---------|---------|------------|
| TUDCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.01) | 0.01 (0.00-0.02) | 0.742 | 302 | 137 |
| Range | 0.00-0.25 | 0.00-0.17 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.64 (0.49-0.79) | 0.86 (0.62-0.94) | <0.001 | 302 | 137 |
| Range | 0.11-0.97 | 0.13-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.75 (0.53-0.89) | 0.89 (0.67-0.97) | <0.001 | 302 | 137 |
| Range | 0.02-1.00 | 0.09-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.87 (0.70-0.94) | 0.93 (0.76-0.98) | 0.003 | 302 | 137 |
| Range | 0.19-1.00 | 0.12-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.44 (0.29-0.60) | 0.66 (0.38-0.83) | <0.001 | 299 | 102 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.50 (0.40-0.69) | 0.70 (0.50-0.86) | <0.001 | 274 | 80 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.20 (0.00-0.50) | 0.26 (0.00-0.50) | 0.582 | 261 | 76 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.83 (0.67-0.94) | 0.88 (0.69-0.97) | 0.239 | 301 | 129 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 7.66 (4.89-11.17) | 6.60 (3.59-10.24) | 0.063 | 300 | 136 |
| Range | 0.91-139.00 | 0.58-93.11 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 6.00 (3.50-9.00) | 6.00 (3.60-9.38) | 0.851 | 263 | 135 |
| Range | 0.83-31.00 | 0.50-70.33 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 8.00 (5.33-12.13) | 6.53 (3.34-11.17) | 0.012 | 298 | 136 |
| Range | 1.00-100.00 | 0.38-92.17 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.50 (3.74-8.00) | 5.09 (2.54-8.00) | 0.133 | 272 | 83 |
| Range | 0.50-61.00 | 0.30-44.50 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 2.00 (1.00-4.25) | 2.58 (1.08-6.75) | 0.363 | 79 | 30 |
| Range | 0.50-13.00 | 0.50-17.00 | | | |

| | Control | NN PSC | p-value | Con (n) | NN PSC (n) |
|--------------------------------|--------------------|--------------------|---------|---------|------------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.22 (1.00-3.00) | 3.50 (3.25-3.75) | 0.232 | 5 | 2 |
| Range | 1.00-4.00 | 3.00-4.00 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 10.00 (5.00-18.00) | 10.50 (5.00-22.00) | 0.833 | 177 | 73 |
| Range | 1.00-95.00 | 0.71-124.00 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.13 (0.08-0.17) | 0.25 (0.17-0.38) | <0.001 | 302 | 137 |
| Range | 0.02-0.55 | 0.04-0.79 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.35 (0.27-0.45) | 0.48 (0.38-0.61) | <0.001 | 302 | 137 |
| Range | 0.06-0.75 | 0.14-0.93 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.37 (0.24-0.47) | 0.11 (0.00-0.26) | <0.001 | 302 | 137 |
| Range | 0.00-0.78 | 0.00-0.64 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.02 (0.01-0.03) | 0.00 (0.00-0.01) | <0.001 | 302 | 137 |
| Range | 0.00-0.13 | 0.00-0.12 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.00 (0.00-0.01) | <0.001 | 302 | 137 |
| Range | 0.00-0.14 | 0.00-0.05 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.07 (0.04-0.12) | 0.03 (0.01-0.07) | <0.001 | 302 | 137 |
| Range | 0.00-0.39 | 0.00-0.29 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.38 (0.24-0.54) | 0.50 (0.31-0.80) | <0.001 | 302 | 137 |
| Range | 0.06-3.10 | 0.07-3.77 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 0.36 (0.19-0.73) | 1.16 (0.45-5.25) | <0.001 | 299 | 102 |
| Range | 0.04-103.00 | 0.09-822.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 3.00 (1.78-5.07) | 9.33 (4.00-23.00) | <0.001 | 302 | 129 |
| Range | 0.44-35.00 | 0.66-422.00 | | | |
| Total BA* | | | | | |
| Median (IQR) | 1.72 (0.94-3.24) | 4.54 (2.37-7.83) | <0.001 | 302 | 137 |
| Range | 0.19-16.79 | 0.59-16.10 | | | |
| Total BA (conj. frac.)* | | | | | |
| Median (IQR) | 0.62 (0.47-0.78) | 0.85 (0.61-0.94) | <0.001 | 302 | 137 |
| Range | 0.10-0.97 | 0.12-1.00 | | | |

| | Control | NN PSC | p-value | Con (n) | NN PSC (n) |
|------------------------------|-------------------|-------------------|---------|---------|------------|
| Total BA (G:T ratio)* | | | | | |
| Median (IQR) | 7.26 (4.62-10.56) | 6.43 (3.48-10.00) | 0.105 | 300 | 136 |
| Range | 0.89-119.00 | 0.58-90.89 | | | |
| CA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.14 (0.09-0.19) | 0.25 (0.18-0.39) | <0.001 | 302 | 137 |
| Range | 0.03-0.56 | 0.04-0.79 | | | |
| CDCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.38 (0.29-0.49) | 0.51 (0.40-0.65) | <0.001 | 302 | 137 |
| Range | 0.06-0.91 | 0.14-0.93 | | | |
| DCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.41 (0.27-0.53) | 0.12 (0.00-0.29) | <0.001 | 302 | 137 |
| Range | 0.00-0.81 | 0.00-0.65 | | | |
| LCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.02 (0.01-0.03) | 0.00 (0.00-0.01) | <0.001 | 302 | 137 |
| Range | 0.00-0.13 | 0.00-0.12 | | | |
| HDCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.01 (0.01-0.03) | 0.00 (0.00-0.01) | <0.001 | 302 | 137 |
| Range | 0.00-0.16 | 0.00-0.06 | | | |

*Values with UDCA and its conjugated forms (GUDCA and TUDCA) removed from the analysis;
 NN PSC: Normal total bile acids, No UDCA treatment

Supplementary Table 3. Bile acids in NN and NY PSC patients.

| | NN PSC | NY PSC | p-value | NN PSC (n) | NY PSC (n) |
|----------------------------|---------------------|---------------------|---------|------------|------------|
| Age in years | | | | | |
| Median (IQR) | 51.14 (32.76-61.38) | 43.92 (33.74-54.55) | 0.058 | 137 | 61 |
| Range | 11.82-78.53 | 10.13-72.71 | | | |
| Sex (% Male) | 59.1 | 50.8 | 0.276 | 137 | 61 |
| Total BA | | | | | |
| Median (IQR) | 4.98 (2.45-8.50) | 9.79 (6.73-14.02) | <0.001 | 137 | 61 |
| Range | 0.59-16.35 | 3.06-17.51 | | | |
| CA (total) | | | | | |
| Median (IQR) | 1.00 (0.46-2.12) | 0.60 (0.31-1.28) | 0.002 | 137 | 61 |
| Range | 0.04-10.09 | 0.04-5.47 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.23) | 0.04 (0.02-0.15) | 0.018 | 137 | 61 |
| Range | 0.00-2.99 | 0.00-0.90 | | | |
| GCA | | | | | |
| Median (IQR) | 0.52 (0.27-1.44) | 0.35 (0.18-0.88) | 0.032 | 137 | 61 |
| Range | 0.02-6.74 | 0.03-4.77 | | | |
| TCA | | | | | |
| Median (IQR) | 0.09 (0.04-0.34) | 0.05 (0.02-0.13) | <0.001 | 137 | 61 |
| Range | 0.00-3.67 | 0.00-0.66 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 2.14 (1.22-4.11) | 1.19 (0.73-1.92) | <0.001 | 137 | 61 |
| Range | 0.16-10.18 | 0.18-4.58 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.14 (0.05-0.46) | 0.17 (0.07-0.44) | 0.688 | 137 | 61 |
| Range | 0.00-5.23 | 0.01-1.73 | | | |
| GCDCA | | | | | |
| Median (IQR) | 1.47 (0.69-2.44) | 0.85 (0.50-1.24) | <0.001 | 137 | 61 |
| Range | 0.10-8.29 | 0.10-3.39 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.20 (0.08-0.61) | 0.07 (0.04-0.18) | <0.001 | 137 | 61 |
| Range | 0.00-3.25 | 0.01-0.79 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.39 (0.00-1.26) | 0.62 (0.09-1.22) | 0.353 | 137 | 61 |
| Range | 0.00-7.81 | 0.00-3.35 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.09 (0.00-0.40) | 0.28 (0.04-0.56) | 0.031 | 137 | 61 |
| Range | 0.00-5.99 | 0.00-1.32 | | | |

| | NN PSC | NY PSC | p-value | NN PSC (n) | NY PSC (n) |
|----------------------------|------------------|------------------|---------|------------|------------|
| GDCA | | | | | |
| Median (IQR) | 0.13 (0.00-0.56) | 0.19 (0.04-0.50) | 0.526 | 137 | 61 |
| Range | 0.00-2.41 | 0.00-2.10 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.03 (0.00-0.12) | 0.02 (0.00-0.08) | 0.514 | 137 | 61 |
| Range | 0.00-1.35 | 0.00-0.50 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.02 (0.00-0.06) | 0.09 (0.00-0.19) | <0.001 | 137 | 61 |
| Range | 0.00-1.18 | 0.00-0.53 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.03 (0.00-0.07) | <0.001 | 137 | 61 |
| Range | 0.00-0.41 | 0.00-0.23 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.04 (0.00-0.10) | <0.001 | 137 | 61 |
| Range | 0.00-0.71 | 0.00-0.28 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.01) | 0.010 | 137 | 61 |
| Range | 0.00-0.06 | 0.00-0.07 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.02 (0.00-0.05) | 0.316 | 137 | 61 |
| Range | 0.00-0.41 | 0.00-0.14 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.01 (0.00-0.03) | 0.501 | 137 | 61 |
| Range | 0.00-0.24 | 0.00-0.07 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | 0.292 | 137 | 61 |
| Range | 0.00-0.17 | 0.00-0.10 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.098 | 137 | 61 |
| Range | 0.00-0.02 | 0.00-0.00 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 0.13 (0.03-0.33) | 6.35 (4.51-9.24) | <0.001 | 137 | 61 |
| Range | 0.00-1.98 | 2.15-14.82 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.06) | 1.18 (0.60-2.54) | <0.001 | 137 | 61 |
| Range | 0.00-0.83 | 0.07-8.58 | | | |
| GUDCA | | | | | |
| Median (IQR) | 0.09 (0.03-0.22) | 4.82 (2.79-6.50) | <0.001 | 137 | 61 |
| Range | 0.00-1.71 | 1.36-9.59 | | | |

| | NN PSC | NY PSC | p-value | NN PSC (n) | NY PSC (n) |
|-------------------------------|-------------------|---------------------|---------|------------|------------|
| TUDCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.09 (0.06-0.18) | <0.001 | 137 | 61 |
| Range | 0.00-0.17 | 0.02-0.92 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.86 (0.62-0.94) | 0.74 (0.63-0.87) | 0.015 | 137 | 61 |
| Range | 0.13-1.00 | 0.28-0.99 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.89 (0.67-0.97) | 0.90 (0.65-0.98) | 0.803 | 137 | 61 |
| Range | 0.09-1.00 | 0.27-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.93 (0.76-0.98) | 0.82 (0.69-0.94) | 0.015 | 137 | 61 |
| Range | 0.12-1.00 | 0.37-0.99 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.66 (0.38-0.83) | 0.45 (0.29-0.63) | 0.006 | 102 | 64 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.70 (0.50-0.86) | 0.58 (0.49-0.75) | 0.026 | 80 | 44 |
| Range | 0.00-1.00 | 0.25-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.26 (0.00-0.50) | 0.22 (0.00-0.57) | 0.659 | 76 | 36 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.88 (0.69-0.97) | 0.77 (0.65-0.88) | 0.007 | 129 | 61 |
| Range | 0.00-1.00 | 0.27-0.99 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 6.60 (3.59-10.24) | 21.59 (12.74-33.80) | <0.001 | 136 | 61 |
| Range | 0.58-93.11 | 4.30-85.82 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 6.00 (3.60-9.38) | 8.62 (5.64-12.70) | <0.001 | 135 | 57 |
| Range | 0.50-70.33 | 2.59-26.00 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 6.53 (3.34-11.17) | 9.17 (6.35-13.78) | 0.002 | 136 | 61 |
| Range | 0.38-92.17 | 1.58-35.11 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.09 (2.54-8.00) | 8.31 (5.00-10.81) | <0.001 | 83 | 44 |
| Range | 0.30-44.50 | 2.00-45.00 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 2.58 (1.08-6.75) | 5.60 (4.18-8.67) | 0.035 | 30 | 23 |
| Range | 0.50-17.00 | 0.67-22.00 | | | |

| | NN PSC | NY PSC | p-value | NN PSC (n) | NY PSC (n) |
|--------------------------------|--------------------|---------------------|----------------|-------------------|-------------------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 3.50 (3.25-3.75) | na | na | 2 | 0 |
| Range | 3.00-4.00 | na | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 10.50 (5.00-22.00) | 46.45 (29.94-64.75) | <0.001 | 73 | 61 |
| Range | 0.71-124.00 | 7.09-145.00 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.25 (0.17-0.38) | 0.07 (0.03-0.12) | <0.001 | 137 | 61 |
| Range | 0.04-0.79 | 0.00-0.39 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.48 (0.38-0.61) | 0.12 (0.10-0.17) | <0.001 | 137 | 61 |
| Range | 0.14-0.93 | 0.04-0.40 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.11 (0.00-0.26) | 0.06 (0.01-0.12) | 0.111 | 137 | 61 |
| Range | 0.00-0.64 | 0.00-0.26 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.01 (0.00-0.02) | 0.026 | 137 | 61 |
| Range | 0.00-0.12 | 0.00-0.08 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.408 | 137 | 61 |
| Range | 0.00-0.05 | 0.00-0.01 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.03 (0.01-0.07) | 0.70 (0.59-0.77) | <0.001 | 137 | 61 |
| Range | 0.00-0.29 | 0.42-0.89 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.50 (0.31-0.80) | 0.51 (0.33-0.75) | 0.913 | 137 | 61 |
| Range | 0.07-3.77 | 0.05-3.09 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 1.16 (0.45-5.25) | 0.73 (0.29-3.27) | 0.092 | 102 | 54 |
| Range | 0.09-822.00 | 0.09-305.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 9.33 (4.00-23.00) | 0.20 (0.14-0.27) | <0.001 | 129 | 61 |
| Range | 0.66-422.00 | 0.04-0.94 | | | |
| Total BA* | | | | | |
| Median (IQR) | 4.54 (2.37-7.83) | 2.93 (1.87-4.28) | 0.001 | 137 | 61 |
| Range | 0.59-16.10 | 0.61-8.92 | | | |
| Total BA (conj. frac.)* | | | | | |
| Median (IQR) | 0.85 (0.61-0.94) | 0.71 (0.54-0.86) | 0.005 | 137 | 61 |
| Range | 0.12-1.00 | 0.29-0.99 | | | |

| | Control | NN PSC | p-value | NN PSC (n) | NY PSC (n) |
|------------------------------|-------------------|-------------------|---------|---------------|---------------|
| Total BA (G:T ratio)* | | | | | |
| Median (IQR) | 6.43 (3.48-10.00) | 9.33 (6.65-13.92) | <0.001 | 136 | 61 |
| Range | 0.58-90.89 | 2.54-36.50 | | | |
| CA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.25 (0.18-0.39) | 0.24 (0.12-0.32) | 0.131 | 136 | 61 |
| Range | 0.04-0.79 | 0.02-0.73 | | | |
| CDCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.51 (0.40-0.65) | 0.44 (0.30-0.56) | 0.010 | 136 | 61 |
| Range | 0.14-0.93 | 0.16-0.86 | | | |
| DCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.12 (0.00-0.29) | 0.24 (0.03-0.41) | 0.008 | 136 | 61 |
| Range | 0.00-0.65 | 0.00-0.58 | | | |
| LCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.03 (0.00-0.06) | <0.001 | 136 | 61 |
| Range | 0.00-0.12 | 0.00-0.28) | | | |
| HDCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.01 (0.00-0.01) | 0.098 | 136 | 61 |
| Range | 0.00-0.06 | 0.00-0.05 | | | |

*Values with UDCA and its conjugated forms (GUDCA and TUDCA) removed from the analysis;
 NN PSC: Normal total bile acid, No UDCA treatment; NY PSC: Normal total bile acid, Yes UDCA treatment

Supplementary Table 4. Bile acids in HN and HY PSC patients.

| | HN PSC | HY PSC | p-value | HN PSC (n) | HY PSC (n) |
|----------------------------|---------------------|----------------------|---------|------------|------------|
| Age in years | | | | | |
| Median (IQR) | 47.50 (32.21-59.69) | 49.13 (34.11-60.88) | 0.758 | 63 | 115 |
| Range | 20.31-79.68 | 10.74-77.56 | | | |
| Sex (% Male) | 54.0 | 60.9 | 0.372 | 63 | 115 |
| Total BA | | | | | |
| Median (IQR) | 38.73 (23.61-63.57) | 48.69 (28.84-116.70) | 0.022 | 63 | 115 |
| Range | 18.53-291.62 | 17.81-646.47 | | | |
| CA (total) | | | | | |
| Median (IQR) | 18.65 (10.26-32.42) | 4.20 (1.89-13.54) | <0.001 | 63 | 115 |
| Range | 3.65-224.36 | 0.34-192.53 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.04-0.17) | 0.07 (0.03-0.22) | 0.701 | 63 | 115 |
| Range | 0.01-10.65 | 0.00-5.72 | | | |
| GCA | | | | | |
| Median (IQR) | 11.67 (5.27-17.57) | 3.33 (1.56-10.12) | <0.001 | 63 | 115 |
| Range | 2.44-165.50 | 0.19-151.29 | | | |
| TCA | | | | | |
| Median (IQR) | 7.60 (2.74-16.16) | 0.53 (0.15-2.94) | <0.001 | 63 | 115 |
| Range | 0.47-58.61 | 0.00-41.19 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 14.21 (9.36-24.92) | 6.22 (3.96-16.37) | <0.001 | 63 | 115 |
| Range | 3.53-71.89 | 1.05-141.73 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.21) | 0.25 (0.08-0.66) | <0.001 | 63 | 115 |
| Range | 0.00-14.78 | 0.01-7.27 | | | |
| GCDCA | | | | | |
| Median (IQR) | 7.80 (5.56-16.44) | 4.73 (3.04-13.17) | <0.001 | 63 | 115 |
| Range | 2.16-39.30 | 0.85-119.44 | | | |
| TCDCA | | | | | |
| Median (IQR) | 5.22 (3.09-10.93) | 0.98 (0.35-3.01) | <0.001 | 63 | 115 |
| Range | 0.35-42.03 | 0.04-27.78 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.87 (0.18-3.19) | 1.15 (0.22-2.71) | 0.995 | 63 | 115 |
| Range | 0.00-24.36 | 0.00-18.32 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.03 (0.01-0.24) | 0.13 (0.01-0.51) | 0.006 | 63 | 115 |
| Range | 0.00-2.63 | 0.00-2.92 | | | |

| | HN PSC | HY PSC | p-value | HN PSC (n) | HY PSC (n) |
|----------------------------|------------------|---------------------|---------|------------|------------|
| GDCA | | | | | |
| Median (IQR) | 0.40 (0.08-1.84) | 0.78 (0.14-1.82) | 0.458 | 63 | 115 |
| Range | 0.00-14.96 | 0.00-15.49 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.34 (0.08-1.08) | 0.15 (0.02-0.34) | 0.001 | 63 | 115 |
| Range | 0.00-8.55 | 0.00-3.41 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.04 (0.02-0.12) | 0.18 (0.02-0.66) | 0.002 | 63 | 115 |
| Range | 0.00-1.15 | 0.00-2.85 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.05 (0.00-0.15) | <0.001 | 63 | 115 |
| Range | 0.00-0.67 | 0.00-0.96 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.02 (0.01-0.06) | 0.09 (0.01-0.36) | <0.001 | 63 | 115 |
| Range | 0.00-0.31 | 0.00-2.14 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.02 (0.01-0.04) | 0.01 (0.00-0.08) | 0.951 | 63 | 115 |
| Range | 0.00-0.17 | 0.00-0.56 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.01 (0.00-0.03) | 0.01 (0.00-0.06) | 0.358 | 63 | 115 |
| Range | 0.00-0.28 | 0.00-0.73 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.01) | 0.00 (0.00-0.03) | 0.328 | 63 | 115 |
| Range | 0.00-0.11 | 0.00-0.15 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | 0.662 | 63 | 115 |
| Range | 0.00-0.17 | 0.00-0.73 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00-0.00 | 0.100 | 63 | 115 |
| Range | 0.00-0.07 | 0.00-0.03 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 0.45 (0.15-0.91) | 31.10 (19.71-63.93) | <0.001 | 63 | 115 |
| Range | 0.01-2.03 | 8.87-537.71 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.03) | 3.87 (1.56-6.83) | <0.001 | 63 | 115 |
| Range | 0.00-0.36 | 0.24-52.33 | | | |
| GUDCA | | | | | |
| Median (IQR) | 0.29 (0.08-0.73) | 27.12 (14.82-52.66) | <0.001 | 63 | 115 |
| Range | 0.01-1.71 | 2.72-472.47 | | | |

| | HN PSC | HY PSC | p-value | HN PSC (n) | HY PSC (n) |
|-------------------------------|------------------|--------------------|---------|------------|------------|
| TUDCA | | | | | |
| Median (IQR) | 0.07 (0.02-0.20) | 1.20 (0.49-3.75) | <0.001 | 63 | 115 |
| Range | 0.00-0.68 | 0.09-51.06 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.99 (0.98-1.00) | 0.91 (0.82-0.97) | <0.001 | 63 | 115 |
| Range | 0.24-1.00 | 0.37-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 1.00 (0.99-1.00) | 0.99 (0.91-1.00) | <0.001 | 63 | 115 |
| Range | 0.24-1.00 | 0.18-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 1.00 (0.99-1.00) | 0.97 (0.90-0.99) | <0.001 | 63 | 115 |
| Range | 0.24-1.00 | 0.39-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.97 (0.93-0.99) | 0.85 (0.69-0.94) | <0.001 | 61 | 107 |
| Range | 0.67-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.87 (0.80-1.00) | 0.74 (0.63-0.84) | <0.001 | 55 | 93 |
| Range | 0.33-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.41 (0.00-0.67) | 0.11 (0.00-0.61) | 0.516 | 37 | 71 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.98 (0.92-1.00) | 0.90 (0.79-0.97) | <0.001 | 63 | 115 |
| Range | 0.42-1.00 | 0.28-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 1.81 (0.99-2.62) | 12.52 (7.62-23.15) | <0.001 | 63 | 115 |
| Range | 0.37-9.61 | 1.67-67.52 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 1.69 (0.96-2.80) | 6.25 (3.93-10.48) | <0.001 | 63 | 114 |
| Range | 0.27-9.23 | 0.62-30.00 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.76 (0.99-2.83) | 6.28 (4.05-10.21) | <0.001 | 63 | 115 |
| Range | 0.36-10.69 | 0.69-22.86 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 1.27 (0.71-2.13) | 6.02 (3.45-9.35) | <0.001 | 55 | 94 |
| Range | 0.22-11.33 | 0.59-22.00 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 1.00 (0.68-2.94) | 4.25 (2.40-7.80) | <0.001 | 42 | 65 |
| Range | 0.10-11.00 | 0.89-36.00 | | | |

| | HN PSC | HY PSC | p-value | HN PSC (n) | HY PSC (n) |
|--------------------------------|----------------------|---------------------|---------|------------|------------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.00 (0.81-1.25) | 6.25 (3.88-8.62) | 0.044 | 6 | 2 |
| Range | 0.71-1.40 | 1.50-11.00 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 3.0 (1.76-6.82) | 23.01 (13.57-38.67) | <0.001 | 58 | 115 |
| Range | 0.14-26.67 | 3.22-102.82 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.50 (0.35-0.65) | 0.10 (0.05-0.17) | <0.001 | 63 | 115 |
| Range | 0.13-0.79 | 0.01-0.44 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.40 (0.29-0.49) | 0.14 (0.11-0.19) | <0.001 | 63 | 115 |
| Range | 0.15-0.85 | 0.04-0.42 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.03 (0.00-0.09) | 0.02 (0.00-0.06) | 0.217 | 63 | 115 |
| Range | 0.00-0.48 | 0.00-0.21 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.01) | 0.021 | 63 | 115 |
| Range | 0.00-0.06 | 0.00-0.04 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.531 | 63 | 115 |
| Range | 0.00-0.02 | 0.00-0.01 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.68 (0.59-0.77) | <0.001 | 63 | 115 |
| Range | 0.00-0.10 | 0.40-0.91 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 1.17 (0.69-2.10) | 0.57 (0.38-1.09) | <0.001 | 63 | 115 |
| Range | 0.15-5.17 | 0.06-4.43 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 21.96 (3.34-129.27) | 3.37 (1.03-31.84) | <0.001 | 61 | 107 |
| Range | 0.42-2002.00 | 0.19-1681.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 31.84 (13.96-109.23) | 0.21 (0.15-0.31) | <0.001 | 63 | 115 |
| Range | 3.62-1310.00 | 0.004-0.97 | | | |
| Total BA* | | | | | |
| Median (IQR) | 38.02 (22.96-62.69) | 14.63 (7.75-36.40) | <0.001 | 63 | 115 |
| Range | 17.10-290.60 | 2.41-313.39 | | | |
| Total BA (conj. frac.)* | | | | | |
| Median (IQR) | 0.99 (0.98-1.00) | 0.94 (0.86-0.99) | <0.001 | 63 | 115 |
| Range | 0.24-1.00 | 0.32-1.00 | | | |

| | Control | NN PSC | p-value | HN PSC (n) | HY PSC (n) |
|------------------------------|------------------|-------------------|---------|---------------|---------------|
| Total BA (G:T ratio)* | | | | | |
| Median (IQR) | 1.79 (0.98-2.59) | 6.49 (3.96-10.44) | <0.001 | 63 | 115 |
| Range | 0.37-9.31 | 0.67-23.86 | | | |
| CA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.50 (0.35-0.65) | 0.31 (0.21-0.45) | <0.001 | 63 | 115 |
| Range | 0.13-0.81 | 0.05-0.81 | | | |
| CDCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.41 (0.30-0.50) | 0.47 (0.38-0.64) | 0.002 | 63 | 115 |
| Range | 0.16-0.87 | 0.18-0.93 | | | |
| DCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.03 (0.00-0.10) | 0.09 (0.01-0.23) | 0.026 | 63 | 115 |
| Range | 0.00-0.50 | 0.00-0.51 | | | |
| LCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.01 (0.00-0.03) | <0.001 | 63 | 115 |
| Range | 0.00-0.06 | 0.00-0.20 | | | |
| HDCA (frac. BA pool)* | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.017 | 63 | 115 |
| Range | 0.00-0.02 | 0.00-0.0 | | | |

*Values with UDCA and its conjugated forms (GUDCA and TUDCA) removed from the analysis;

HN PSC: High total bile acid, No UDCA treatment; HY PSC: High total bile acid, Yes UDCA treatment

Supplementary Table 5. Bile acids in NN and HN PSC patients.

| | NN PSC | HN PSC | p-value | NN PSC (n) | HN PSC (n) |
|----------------------------|---------------------|---------------------|----------------|-------------------|-------------------|
| Age in years | | | | | |
| Median (IQR) | 51.14 (32.76-61.38) | 47.50 (32.21-59.69) | 0.741 | 137 | 63 |
| Range | 11.82-78.53 | 20.31-79.68 | | | |
| Sex (% Male) | 59.1 | 54.0 | 0.493 | 137 | 63 |
| Total BA | | | | | |
| Median (IQR) | 4.98 (2.45-8.50) | 38.73 (23.61-63.57) | <0.001 | 137 | 63 |
| Range | 0.59-16.35 | 18.53-291.62 | | | |
| CA (total) | | | | | |
| Median (IQR) | 1.00 (0.46-2.12) | 18.65 (10.26-32.42) | <0.001 | 137 | 63 |
| Range | 0.04-10.09 | 3.65-224.36) | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.23) | 0.07 (0.04-0.17) | 0.937 | 137 | 63 |
| Range | 0.00-2.99 | 0.01-10.65 | | | |
| GCA | | | | | |
| Median (IQR) | 0.52 (0.27-1.44) | 11.67 (5.27-17.57) | <0.001 | 137 | 63 |
| Range | 0.02-6.74 | 2.44-165.50 | | | |
| TCA | | | | | |
| Median (IQR) | 0.09 (0.04-0.34) | 7.60 (2.74-16.16) | <0.001 | 137 | 63 |
| Range | 0.00-3.67 | 0.47-58.61 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 2.14 (1.22-4.11) | 14.21 (9.36-24.92) | <0.001 | 137 | 63 |
| Range | 0.16-10.18 | 3.53-71.89 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.14 (0.05-0.46) | 0.07 (0.03-0.21) | 0.025 | 137 | 63 |
| Range | 0.00-5.23 | 0.00-14.78 | | | |
| GCDCA | | | | | |
| Median (IQR) | 1.47 (0.69-2.44) | 7.80 (5.56-16.44) | <0.001 | 137 | 63 |
| Range | 0.10-8.29 | 2.16-39.30 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.20 (0.08-0.61) | 5.22 (3.09-10.93) | <0.001 | 137 | 63 |
| Range | 0.00-3.25 | 0.35-42.03 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.39 (0.00-1.26) | 0.87 (0.18-3.19) | <0.001 | 137 | 63 |
| Range | 0.00-7.81 | 0.00-24.36 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.09 (0.00-0.40) | 0.03 (0.01-0.24) | 0.237 | 137 | 63 |
| Range | 0.00-5.99 | 0.00-2.63 | | | |

| | NN PSC | HN PSC | p-value | NN PSC (n) | HN PSC (n) |
|----------------------------|------------------|------------------|----------------|-----------------------|-----------------------|
| GDCA | | | | | |
| Median (IQR) | 0.13 (0.00-0.56) | 0.40 (0.08-1.84) | <0.001 | 137 | 63 |
| Range | 0.00-2.41 | 0.00-14.96 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.03 (0.00-0.12) | 0.34 (0.08-1.08) | <0.001 | 137 | 63 |
| Range | 0.00-1.35 | 0.00-8.55 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.02 (0.00-0.06) | 0.04 (0.02-0.12) | <0.001 | 137 | 63 |
| Range | 0.00-1.18 | 0.00-1.15 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.01 (0.00-0.02) | 0.521 | 137 | 63 |
| Range | 0.00-0.41 | 0.00-0.67 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.02 (0.01-0.06) | 0.005 | 137 | 63 |
| Range | 0.00-0.71 | 0.00-0.31 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.02 (0.01-0.04) | <0.001 | 137 | 63 |
| Range | 0.00-0.06 | 0.00-0.17 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.03) | 0.996 | 137 | 63 |
| Range | 0.00-0.41 | 0.00-0.28 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.01 (0.00-0.01) | 0.460 | 137 | 63 |
| Range | 0.00-0.24 | 0.00-0.11 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | 0.747 | 137 | 63 |
| Range | 0.00-0.17 | 0.00-0.17 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.012 | 137 | 63 |
| Range | 0.00-0.02 | 0.00-0.07 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 0.13 (0.03-0.33) | 0.45 (0.15-0.91) | <0.001 | 137 | 63 |
| Range | 0.00-1.98 | 0.01-2.03 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.06) | 0.01 (0.00-0.03) | 0.080 | 137 | 63 |
| Range | 0.00-0.83 | 0.00-0.36 | | | |
| GUDCA | | | | | |
| Median (IQR) | 0.09 (0.03-0.22) | 0.29 (0.08-0.73) | <0.001 | 137 | 63 |
| Range | 0.00-1.71 | 0.01-1.71 | | | |

| | NN PSC | HN PSC | p-value | NN PSC (n) | HN PSC (n) |
|-------------------------------|-------------------|------------------|----------------|-----------------------|-----------------------|
| TUDCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.07 (0.02-0.20) | <0.001 | 137 | 63 |
| Range | 0.00-0.17 | 0.00-0.68 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.86 (0.62-0.94) | 0.99 (0.98-1.00) | <0.001 | 137 | 63 |
| Range | 0.13-1.00 | 0.24-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.89 (0.67-0.97) | 1.00 (0.99-1.00) | <0.001 | 137 | 63 |
| Range | 0.09-1.00 | 0.24-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.93 (0.76-0.98) | 1.00 (0.99-1.00) | <0.001 | 137 | 63 |
| Range | 0.12-1.00 | 0.24-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.66 (0.38-0.83) | 0.97 (0.93-0.99) | <0.001 | 102 | 61 |
| Range | 0.00-1.00 | 0.67-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.70 (0.50-0.86) | 0.87 (0.80-1.00) | <0.001 | 80 | 55 |
| Range | 0.00-1.00 | 0.33-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.26 (0.00-0.50) | 0.41 (0.00-0.67) | 0.137 | 76 | 37 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.88 (0.69-0.97) | 0.98 (0.92-1.00) | <0.001 | 129 | 63 |
| Range | 0.00-1.00 | 0.42-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 6.60 (3.59-10.24) | 1.81 (0.99-2.62) | <0.001 | 136 | 63 |
| Range | 0.58-93.11 | 0.37-9.61 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 6.00 (3.60-9.38) | 1.69 (0.96-2.80) | <0.001 | 135 | 63 |
| Range | 0.50-70.33 | 0.27-9.23 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 6.53 (3.34-11.17) | 1.76 (0.99-2.83) | <0.001 | 136 | 63 |
| Range | 0.38-92.17 | 0.36-10.69 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.09 (2.54-8.00) | 1.27 (0.71-2.13) | <0.001 | 83 | 55 |
| Range | 0.30-44.50 | 0.22-11.33 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 2.58 (1.08-6.75) | 1.00 (0.68-2.94) | 0.004 | 30 | 42 |
| Range | 0.50-17.00 | 0.10-11.00 | | | |

| | NN PSC | HN PSC | p-value | NN PSC (n) | HN PSC (n) |
|-----------------------------|--------------------|---------------------|----------------|-----------------------|-----------------------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 3.50 (3.25-3.75) | 1.00 (0.81-1.25) | 0.044 | 2 | 6 |
| Range | 3.00-4.00 | 0.71-1.40 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 10.50 (5.00-22.00) | 3.00 (1.76-6.82) | <0.001 | 73 | 58 |
| Range | 0.71-124.00 | 0.14-26.67 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.25 (0.17-0.38) | 0.50 (0.35-0.64) | <0.001 | 137 | 63 |
| Range | 0.04-0.79 | 0.13-0.79 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.48 (0.38-0.61) | 0.40 (0.29-0.49) | <0.001 | 137 | 63 |
| Range | 0.14-0.93 | 0.15-0.85 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.11 (0.00-0.26) | 0.03 (0.00-0.09) | 0.111 | 137 | 63 |
| Range | 0.00-0.64 | 0.00-0.48 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.167 | 137 | 63 |
| Range | 0.00-0.12 | 0.00-0.06 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.005 | 137 | 63 |
| Range | 0.00-0.05 | 0.00-0.02 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.03 (0.01-0.07) | 0.01 (0.00-0.02) | <0.001 | 137 | 63 |
| Range | 0.00-0.29 | 0.00-0.10 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.50 (0.31-0.80) | 1.17 (0.69-2.10) | <0.001 | 137 | 63 |
| Range | 0.07-3.77 | 0.15-5.17 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 1.16 (0.45-5.25) | 21.96 (3.34-129.27) | <0.001 | 102 | 61 |
| Range | 0.09-822.00 | 0.42-2002.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 9.33 (4.00-23.00) | 31.84 (13.96-109.2) | <0.001 | 129 | 63 |
| Range | 0.66-422.00 | 3.62-1310.00 | | | |

NN PSC: Normal total bile acids, No UDCA treatment; HN PSC: High total bile acids, No UDCA treatment

Supplementary Table 6. Bile acids in NY and HY PSC patients.

| | NY PSC | HY PSC | p-value | NY PSC (n) | HY PSC (n) |
|----------------------------|---------------------|---------------------|---------|------------|------------|
| Age in years | | | | | |
| Median (IQR) | 43.92 (33.74-54.55) | 49.13 (34.11-60.88) | 0.088 | 61 | 115 |
| Range | 10.13-72.71 | 10.74-77.56 | | | |
| Sex (% Male) | 50.8 | 60.9 | 0.199 | 61 | 115 |
| Total BA | | | | | |
| Median (IQR) | 9.79 (6.73-14.02) | 48.69 (28.84-116.7) | <0.001 | 61 | 115 |
| Range | 3.06-17.51 | 17.81-646.47 | | | |
| CA (total) | | | | | |
| Median (IQR) | 0.60 (0.31-1.28) | 4.20 (1.89-13.54) | <0.001 | 61 | 115 |
| Range | 0.04-5.47 | 0.34-192.53 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.04 (0.02-0.15) | 0.07 (0.03-0.22) | 0.061 | 61 | 115 |
| Range | 0.00-0.90 | 0.00-5.72 | | | |
| GCA | | | | | |
| Median (IQR) | 0.35 (0.18-0.88) | 3.33 (1.56-10.12) | <0.001 | 61 | 115 |
| Range | 0.03-4.77 | 0.19-151.29 | | | |
| TCA | | | | | |
| Median (IQR) | 0.05 (0.02-0.13) | 0.53 (0.15-2.94) | <0.001 | 61 | 115 |
| Range | 0.00-0.66 | 0.00-41.19 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 1.19 (0.73-1.92) | 6.22 (3.96-16.37) | <0.001 | 61 | 115 |
| Range | 0.18-4.58 | 1.05-141.73 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.17 (0.07-0.44) | 0.25 (0.08-0.66) | 0.109 | 61 | 115 |
| Range | 0.01-1.73 | 0.01-7.27 | | | |
| GCDCA | | | | | |
| Median (IQR) | 0.85 (0.50-1.24) | 4.73 (3.04-13.17) | <0.001 | 61 | 115 |
| Range | 0.10-3.39 | 0.85-119.44 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.07 (0.04-0.18) | 0.98 (0.35-3.01) | <0.001 | 61 | 115 |
| Range | 0.01-0.79 | 0.04-27.78 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.62 (0.09-1.22) | 1.15 (0.22-2.71) | <0.001 | 61 | 115 |
| Range | 0.00-3.35 | 0.00-18.32 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.28 (0.04-0.56) | 0.13 (0.01-0.51) | 0.331 | 61 | 115 |
| Range | 0.00-1.32 | 0.00-2.92 | | | |

| | NY PSC | HY PSC | p-value | NY PSC (n) | HY PSC (n) |
|----------------------------|------------------|---------------------|---------|------------|------------|
| GDCA | | | | | |
| Median (IQR) | 0.19 (0.04-0.50) | 0.78 (0.14-1.82) | <0.001 | 61 | 115 |
| Range | 0.00-2.10 | 0.00-15.49 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.02 (0.00-0.08) | 0.15 (0.02-0.34) | <0.001 | 61 | 115 |
| Range | 0.00-0.50 | 0.00-3.41 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.09 (0.00-0.19) | 0.18 (0.02-0.66) | 0.005 | 61 | 115 |
| Range | 0.00-0.53 | 0.00-2.85 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.03 (0.00-0.07) | 0.05 (0.00-0.15) | 0.060 | 61 | 115 |
| Range | 0.00-0.23 | 0.00-0.96 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.04 (0.00-0.10) | 0.09 (0.01-0.36) | 0.004 | 61 | 115 |
| Range | 0.00-0.28 | 0.00-2.14 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.01 (0.00-0.08) | <0.001 | 61 | 115 |
| Range | 0.00-0.07 | 0.00-0.56 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.02 (0.00-0.05) | 0.01 (0.00-0.06) | 0.841 | 61 | 115 |
| Range | 0.00-0.14 | 0.00-0.73 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.03) | 0.00 (0.00-0.03) | 0.978 | 61 | 115 |
| Range | 0.00-0.07 | 0.00-0.15 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | 0.237 | 61 | 115 |
| Range | 0.00-0.10 | 0.00-0.73 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.036 | 61 | 115 |
| Range | 0.00-0.00 | 0.00-0.03 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 6.35 (4.51-9.24) | 31.10 (19.71-63.93) | <0.001 | 61 | 115 |
| Range | 2.15-14.82 | 8.87-537.71 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 1.18 (0.60-2.54) | 3.87 (1.56-6.83) | <0.001 | 61 | 115 |
| Range | 0.07-8.58 | 0.24-52.33 | | | |
| GUDCA | | | | | |
| Median (IQR) | 4.84 (2.79-6.50) | 27.12 (14.82-52.66) | <0.001 | 61 | 115 |
| Range | 1.36-9.59 | 2.72-472.47 | | | |

| | NY PSC | HY PSC | p-value | NY PSC (n) | HY PSC (n) |
|-------------------------------|---------------------|--------------------|---------|------------|------------|
| TUDCA | | | | | |
| Median (IQR) | 0.09 (0.06-0.18) | 1.20 (0.49-3.75) | <0.001 | 61 | 115 |
| Range | 0.02-0.92 | 0.09-51.06 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.74 (0.63-0.87) | 0.91 (0.82-0.97) | <0.001 | 61 | 115 |
| Range | 0.28-0.99 | 0.37-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.90 (0.65-0.98) | 0.99 (0.91-1.00) | <0.001 | 61 | 115 |
| Range | 0.27-1.00 | 0.18-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.82 (0.69-0.94) | 0.97 (0.90-0.99) | <0.001 | 61 | 115 |
| Range | 0.37-0.99 | 0.39-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.45 (0.29-0.63) | 0.85 (0.69-0.94) | <0.001 | 54 | 107 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.58 (0.49-0.75) | 0.74 (0.63-0.84) | <0.001 | 44 | 93 |
| Range | 0.25-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.22 (0.00-0.57) | 0.11 (0.00-0.61) | 0.986 | 36 | 71 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.77 (0.65-0.88) | 0.90 (0.79-0.97) | <0.001 | 61 | 115 |
| Range | 0.27-0.99 | 0.28-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 21.59 (12.74-33.80) | 12.52 (7.62-23.15) | <0.001 | 61 | 115 |
| Range | 4.30-85.82 | 1.67-67.52 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 8.62 (5.64-12.70) | 6.25 (3.93-10.48) | 0.016 | 57 | 114 |
| Range | 2.59-26.00 | 0.62-30.00 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 9.17 (6.35-13.78) | 6.28 (4.05-10.21) | <0.001 | 61 | 115 |
| Range | 1.58-35.11 | 0.69-22.86 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 8.31 (5.00-10.81) | 6.02 (3.45-9.35) | 0.011 | 44 | 94 |
| Range | 2.00-45.00 | 0.59-22.00 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 5.60 (4.18-8.67) | 4.25 (2.40-7.80) | 0.277 | 23 | 65 |
| Range | 0.67-22.00 | 0.89-36.00 | | | |

| | NY PSC | HY PSC | p-value | NY PSC (n) | HY PSC (n) |
|-----------------------------|---------------------|---------------------|---------|------------|------------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | na | 6.25 (3.88-8.62) | na | 0 | 2 |
| Range | na | 1.50-11.00 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 46.45 (29.94-64.75) | 23.01 (13.57-38.67) | <0.001 | 61 | 115 |
| Range | 7.09-145.00 | 3.22-102.82 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.07 (0.03-0.12) | 0.10 (0.05-0.17) | 0.034 | 61 | 115 |
| Range | 0.00-0.39 | 0.01-0.44 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.12 (0.10-0.17) | 0.14 (0.11-0.19) | 0.186 | 61 | 115 |
| Range | 0.04-0.40 | 0.04-0.42 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.06 (0.01-0.12) | 0.02 (0.00-0.06) | 0.003 | 61 | 115 |
| Range | 0.00-0.26 | 0.00-0.21 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.00 (0.00-0.01) | 0.034 | 61 | 115 |
| Range | 0.00-0.08 | 0.00-0.04 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.002 | 61 | 115 |
| Range | 0.00-0.01 | 0.00-0.01 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.70 (0.59-0.77) | 0.68 (0.59-0.77) | 0.873 | 61 | 115 |
| Range | 0.42-0.89 | 0.40-0.91 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.51 (0.33-0.75) | 0.57 (0.38-1.09) | 0.068 | 61 | 115 |
| Range | 0.05-3.09 | 0.06-4.43 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 0.73 (0.29-3.27) | 3.37 (1.03-31.84) | <0.001 | 54 | 107 |
| Range | 0.09-305.00 | 0.19-1681.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 0.20 (0.14-0.27) | 0.21 (0.15-0.31) | 0.260 | 61 | 115 |
| Range | 0.04-0.94 | 0.04-0.97 | | | |

NY PSC: Normal total bile acids, Yes UDCA treatment; HY PSC: High total bile acids, Yes UDCA treatment

Supplementary Table 7. Bile acids in Control and No IBD PSC patients.

| | Control | No IBD PSC | p-value | Con (n) | No IBD PSC (n) |
|----------------------------|---------------------|---------------------|----------------|----------------|-----------------------|
| Age in years | | | | | |
| Median (IQR) | 56.40 (48.49-65.29) | 55.82 (43.32-61.82) | 0.032 | 302 | 65 |
| Range | 19.28-86.12 | 14.25-79.68 | | | |
| Sex (% Male) | 58.3 | 49.2 | 0.182 | 302 | 65 |
| Tot BA / UDCA Group | | | | | |
| NN - # (%) | na | 19 (29.2) | na | na | 65 |
| NY - # (%) | na | 10 (15.4) | | | |
| HN - # (%) | na | 13 (20.0) | | | |
| HY - # (%) | na | 23 (35.4) | | | |
| Total BA | | | | | |
| Median (IQR) | 1.90 (1.02-3.52) | 23.57 (7.71-45.45) | <0.001 | 302 | 65 |
| Range | 0.19-17.79 | 0.88-646.47 | | | |
| CA (total) | | | | | |
| Median (IQR) | 0.22 (0.11-0.49) | 1.84 (0.86-8.72) | <0.001 | 302 | 65 |
| Range | 0.01-6.43 | 0.13-68.19 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.04 (0.02-0.12) | 0.05 (0.03-0.12) | 0.169 | 302 | 65 |
| Range | 0.00-5.23 | 0.00-4.02 | | | |
| GCA | | | | | |
| Median (IQR) | 0.12 (0.05-0.25) | 1.11 (0.45-5.13) | <0.001 | 302 | 65 |
| Range | 0.01-5.84 | 0.06-53.99 | | | |
| TCA | | | | | |
| Median (IQR) | 0.02 (0.01-0.04) | 0.30 (0.07-2.09) | <0.001 | 302 | 65 |
| Range | 0.00-1.50 | 0.00-30.29 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 0.63 (0.33-1.39) | 3.85 (2.14-9.80) | <0.001 | 302 | 65 |
| Range | 0.05-10.77 | 0.30-141.73 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.23) | 0.16 (0.05-0.47) | <0.001 | 302 | 65 |
| Range | 0.00-5.28 | 0.01-7.27 | | | |
| GCDCA | | | | | |
| Median (IQR) | 0.42 (0.21-0.88) | 2.99 (1.32-6.33) | <0.001 | 302 | 65 |
| Range | 0.02-5.38 | 0.18-119.44 | | | |
| TCDC | | | | | |
| Median (IQR) | 0.05 (0.03-0.11) | 0.56 (0.16-2.77) | <0.001 | 302 | 65 |
| Range | 0.00-2.49 | 0.02-42.03 | | | |

| | Control | No IBD PSC | p-value | Con (n) | No IBD PSC (n) |
|----------------------------|------------------|-------------------|---------|---------|----------------|
| DCA (total) | | | | | |
| Median (IQR) | 0.65 (0.36-1.21) | 1.43 (0.76-2.23) | <0.001 | 302 | 65 |
| Range | 0.00-8.26 | 0.00-24.36 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.33 (0.19-0.58) | 0.29 (0.09-0.65) | 0.263 | 302 | 65 |
| Range | 0.00-4.49 | 0.00-3.63 | | | |
| GDCA | | | | | |
| Median (IQR) | 0.21 (0.10-0.46) | 0.64 (0.35-1.07) | <0.001 | 302 | 65 |
| Range | 0.00-5.94 | 0.00-15.49 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.04 (0.02-0.08) | 0.15 (0.05-0.31) | <0.001 | 302 | 65 |
| Range | 0.00-1.13 | 0.00-8.55 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.03 (0.02-0.05) | 0.10 (0.06-0.21) | <0.001 | 302 | 65 |
| Range | 0.00-0.42 | 0.00-2.85 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.03 (0.01-0.07) | <0.001 | 302 | 65 |
| Range | 0.00-0.21 | 0.00-0.29 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.05 (0.02-0.13) | <0.001 | 302 | 65 |
| Range | 0.00-0.19 | 0.00-2.14 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.01 (0.00-0.03) | <0.001 | 302 | 65 |
| Range | 0.00-0.07 | 0.00-0.42 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.03 (0.01-0.05) | 0.02 (0.00-0.05) | 0.322 | 302 | 65 |
| Range | 0.00-0.29 | 0.00-0.17 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.01-0.03) | 0.02 (0.00-0.04) | 0.448 | 302 | 65 |
| Range | 0.00-0.11 | 0.00-0.13 | | | |
| GHDCa | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.003 | 302 | 65 |
| Range | 0.00-0.11 | 0.00-0.06 | | | |
| THDCa | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | <0.001 | 302 | 65 |
| Range | 0.00-0.09 | 0.00-0.07 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 0.13 (0.07-0.27) | 3.33 (0.29-18.37) | <0.001 | 302 | 65 |
| Range | 0.00-2.15 | 0.02-537.71 | | | |

| | Control | No IBD PSC | p-value | Con (n) | No IBD PSC (n) |
|-------------------------------|-------------------|-------------------|---------|---------|----------------|
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.01-0.06) | 0.12 (0.02-2.29) | <0.001 | 302 | 65 |
| Range | 0.00-0.92 | 0.00-52.33 | | | |
| GUDCA | | | | | |
| Median (IQR) | 0.09 (0.05-0.19) | 1.73 (0.24-15.78) | <0.001 | 302 | 65 |
| Range | 0.00-1.78 | 0.01-472.47) | | | |
| TUDCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.01) | 0.14 (0.03-0.52) | <0.001 | 302 | 65 |
| Range | 0.00-0.25 | 0.00-35.47 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.64 (0.49-0.79) | 0.92 (0.74-0.98) | <0.001 | 302 | 65 |
| Range | 0.11-0.97 | 0.20-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.75 (0.53-0.89) | 0.97 (0.83-1.00) | <0.001 | 302 | 65 |
| Range | 0.02-1.00 | 0.09-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.87 (0.70-0.94) | 0.96 (0.79-0.99) | <0.001 | 302 | 65 |
| Range | 0.19-1.00 | 0.29-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.44 (0.29-0.60) | 0.78 (0.52-0.93) | <0.001 | 299 | 63 |
| Range | 0.00-1.00 | 0.18-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.50 (0.40-0.69) | 0.71 (0.54-0.80) | <0.001 | 274 | 62 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.20 (0.00-0.50) | 0.00 (0.00-0.41) | 0.275 | 261 | 48 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.83 (0.67-0.94) | 0.90 (0.75-0.97) | 0.068 | 301 | 65 |
| Range | 0.00-1.00 | 0.28-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 7.66 (4.89-11.17) | 8.09 (2.80-18.65) | 0.959 | 300 | 65 |
| Range | 0.91-139.00 | 0.62-69.38 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 6.00 (3.50-9.00) | 5.12 (2.33-9.54) | 0.171 | 263 | 64 |
| Range | 0.83-31.00 | 0.50-27.00 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 8.00 (5.33-12.13) | 5.43 (2.37-9.74) | <0.001 | 298 | 65 |
| Range | 1.00-100.00 | 0.67-35.50 | | | |

| | Control | No IBD PSC | p-value | Con (n) | No IBD PSC (n) |
|-----------------------------|--------------------|--------------------|---------|---------|----------------|
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.50 (3.74-8.00) | 5.09 (2.17-8.60) | 0.263 | 272 | 61 |
| Range | 0.50-61.00 | 0.50-45.00 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 2.00 (1.00-4.25) | 3.00 (1.50-7.00) | 0.062 | 79 | 37 |
| Range | 0.50-13.00 | 0.50-36.00 | | | |
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.22 (1.00-3.00) | 0.71 (0.71-0.71) | 0.137 | 5 | 1 |
| Range | 1.00-4.00 | 0.71-0.71 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 10.00 (5.00-18.00) | 13.81 (6.47-31.96) | 0.073 | 177 | 59 |
| Range | 1.00-95.00 | 0.14-101.14 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.13 (0.08-0.17) | 0.12 (0.05-0.28) | 0.691 | 302 | 65 |
| Range | 0.02-0.55 | 0.01-0.79 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.35 (0.27-0.45) | 0.23 (0.13-0.38) | <0.001 | 302 | 65 |
| Range | 0.06-0.75 | 0.04-0.79 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.37 (0.24-0.47) | 0.08 (0.03-0.19) | <0.001 | 302 | 65 |
| Range | 0.00-0.78 | 0.00-0.64 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.02 (0.01-0.03) | 0.01 (0.00-0.01) | <0.001 | 302 | 65 |
| Range | 0.00-0.13 | 0.00-0.04 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.01-0.02) | 0.00 (0.00-0.00) | <0.001 | 302 | 65 |
| Range | 0.00-0.14 | 0.00-0.03 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.07 (0.04-0.12) | 0.43 (0.02-0.70) | 0.024 | 302 | 65 |
| Range | 0.00-0.39 | 0.00-0.89 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.38 (0.24-0.54) | 0.51 (0.30-0.91) | 0.002 | 302 | 65 |
| Range | 0.06-3.10 | 0.06-5.17 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 0.36 (0.19-0.73) | 1.18 (0.44-5.94) | <0.001 | 299 | 63 |
| Range | 0.04-103.00 | 0.12-698.25 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 3.00 (1.78-5.07) | 0.48 (0.19-11.13) | 0.031 | 302 | 65 |
| Range | 0.44-35.00 | 0.05-414.18 | | | |

Supplementary Table 8. Bile acids in No IBD and UC PSC patients.

| | No IBD PSC | UC PSC | p-value | No IBD PSC (n) | UC PSC (n) |
|----------------------------|---------------------|---------------------|---------|----------------|------------|
| Age in years | | | | | |
| Median (IQR) | 55.82 (43.32-61.82) | 47.61 (31.69-61.33) | 0.044 | 65 | 231 |
| Range | 14.25-79.68 | 10.74-77.56 | | | |
| Sex (% Male) | | | | | |
| | 49.2 | 61.9 | 0.066 | 65 | 231 |
| Tot BA / UDCA Group | | | | | |
| NN - # (%) | 19 (29.2) | 83 (35.9) | 0.706 | 65 | 231 |
| NY - # (%) | 10 (15.4) | 38 (16.5) | | | |
| HN - # (%) | 13 (20.0) | 37 (16.0) | | | |
| HY - # (%) | 23 (35.4) | 73 (31.6) | | | |
| Total BA | | | | | |
| Median (IQR) | 23.57 (7.71-45.45) | 15.93 (5.90-39.39) | 0.206 | 65 | 231 |
| Range | 0.88-646.47 | 1.00-530.95 | | | |
| CA (total) | | | | | |
| Median (IQR) | 1.84 (0.86-8.72) | 2.21 (0.81-8.82) | 0.691 | 65 | 231 |
| Range | 0.13-68.19 | 0.04-224.36 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.05 (0.03-0.12) | 0.07 (0.03-0.24) | 0.244 | 65 | 231 |
| Range | 0.00-4.02 | 0.00-10.65 | | | |
| GCA | | | | | |
| Median (IQR) | 1.11 (0.45-5.13) | 1.74 (0.51-5.36) | 0.682 | 65 | 231 |
| Range | 0.06-53.99 | 0.03-165.50 | | | |
| TCA | | | | | |
| Median (IQR) | 0.30 (0.07-2.09) | 0.25 (0.07-1.67) | 0.957 | 65 | 231 |
| Range | 0.00-30.29 | 0.00-58.61 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 3.85 (2.14-9.80) | 3.91 (1.52-9.02) | 0.426 | 65 | 231 |
| Range | 0.30-141.73 | 0.29-120.63) | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.16 (0.05-0.47) | 0.14 (0.06-0.38) | 0.539 | 65 | 231 |
| Range | 0.01-7.27 | 0.00-14.78 | | | |
| GCDCA | | | | | |
| Median (IQR) | 2.99 (1.32-6.33) | 2.71 (1.14-6.53) | 0.648 | 65 | 231 |
| Range | 0.18-119.44 | 0.21-92.80 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.56 (0.16-2.77) | 0.45 (0.13-1.71) | 0.360 | 65 | 231 |
| Range | 0.02-42.03 | 0.01-35.85 | | | |

| | No IBD PSC | UC PSC | p-value | No IBD PSC (n) | UC PSC (n) |
|----------------------------|-------------------|-------------------|---------|----------------|------------|
| DCA (total) | | | | | |
| Median (IQR) | 1.43 (0.76-2.23) | 0.48 (0.01-1.54) | <0.001 | 65 | 231 |
| Range | 0.00-24.36 | 0.00-16.23 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.29 (0.09-0.65) | 0.06 (0.00-0.41) | <0.001 | 65 | 231 |
| Range | 0.00-3.63 | 0.00-5.99 | | | |
| GDCA | | | | | |
| Median (IQR) | 0.64 (0.35-1.07) | 0.19 (0.01-0.84) | <0.001 | 65 | 231 |
| Range | 0.00-15.49 | 0.00-10.84 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.15 (0.05-0.31) | 0.04 (0.00-0.18) | <0.001 | 65 | 231 |
| Range | 0.00-8.55 | 0.00-4.02 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.10 (0.06-0.21) | 0.03 (0.00-0.14) | <0.001 | 65 | 231 |
| Range | 0.00-2.85 | 0.00-2.18 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.03 (0.01-0.07) | 0.01 (0.00-0.04) | <0.001 | 65 | 231 |
| Range | 0.00-0.29 | 0.00-0.88 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.05 (0.02-0.13) | 0.01 (0.00-0.08) | <0.001 | 65 | 231 |
| Range | 0.00-2.14 | 0.00-1.63 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.03) | 0.00 (0.00-0.01) | 0.009 | 65 | 231 |
| Range | 0.00-0.42 | 0.00-0.43 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.02 (0.00-0.05) | 0.01 (0.00-0.04) | 0.006 | 65 | 231 |
| Range | 0.00-0.17 | 0.00-0.28 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.00-0.04) | 0.00 (0.00-0.02) | 0.001 | 65 | 231 |
| Range | 0.00-0.13 | 0.00-0.14 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.01) | 0.372 | 65 | 231 |
| Range | 0.00-0.06 | 0.00-0.17 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.051 | 65 | 231 |
| Range | 0.00-0.07 | 0.00-0.05 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 3.33 (0.29-18.37) | 1.82 (0.13-18.98) | 0.163 | 65 | 231 |
| Range | 0.02-537.71 | 0.00-355.15 | | | |

| | No IBD PSC | UC PSC | p-value | No IBD PSC (n) | UC PSC (n) |
|-------------------------------|-------------------|-------------------|---------|----------------|------------|
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.12 (0.02-2.29) | 0.17 (0.01-2.25) | 0.328 | 65 | 231 |
| Range | 0.00-52.33 | 0.00-19.26 | | | |
| GUDCA | | | | | |
| Median (IQR) | 1.73 (0.24-15.78) | 1.31 (0.09-13.86) | 0.200 | 65 | 231 |
| Range | 0.01-472.47) | 0.00-297.47 | | | |
| TUDCA | | | | | |
| Median (IQR) | 0.14 (0.03-0.52) | 0.08 (0.01-0.53) | 0.072 | 65 | 231 |
| Range | 0.00-35.47 | 0.00-51.06 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.92 (0.74-0.98) | 0.90 (0.76-0.98) | 0.855 | 65 | 231 |
| Range | 0.20-1.00 | 0.24-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.97 (0.83-1.00) | 0.97 (0.85-0.99) | 0.652 | 65 | 231 |
| Range | 0.09-1.00 | 0.18-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.96 (0.79-0.99) | 0.95 (0.85-0.99) | 0.961 | 65 | 231 |
| Range | 0.29-1.00 | 0.24-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.78 (0.52-0.93) | 0.81 (0.55-0.96) | 0.307 | 63 | 187 |
| Range | 0.18-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.71 (0.54-0.80) | 0.75 (0.57-0.87) | 0.089 | 62 | 146 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.00 (0.00-0.41) | 0.33 (0.00-0.61) | 0.020 | 48 | 121 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.90 (0.75-0.97) | 0.90 (0.77-0.98) | 0.790 | 65 | 225 |
| Range | 0.28-1.00 | 0.00-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 8.09 (2.80-18.65) | 9.01 (4.08-18.02) | 0.578 | 65 | 231 |
| Range | 0.62-69.38 | 0.37-67.52 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 5.12 (2.33-9.54) | 6.00 (3.08-9.56) | 0.311 | 64 | 230 |
| Range | 0.50-27.00 | 0.27-30.00 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 5.43 (2.37-9.74) | 6.28 (2.93-10.32) | 0.247 | 65 | 231 |
| Range | 0.67-35.50 | 0.36-51.00 | | | |

| | No IBD PSC | UC PSC | p-value | No IBD PSC (n) | UC PSC (n) |
|-----------------------------|--------------------|--------------------|---------|----------------|------------|
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.09 (2.17-8.60) | 4.69 (1.96-9.00) | 0.648 | 61 | 153 |
| Range | 0.50-45.00 | 0.29-44.50 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 3.00 (1.50-7.00) | 3.00 (1.80-7.00) | 0.881 | 37 | 91 |
| Range | 0.50-36.00 | 0.10-25.00 | | | |
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 0.71 (0.71-0.71) | 1.40 (1.00-4.00) | 0.143 | 1 | 5 |
| Range | 0.71-0.71 | 0.75-11.00 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 13.81 (6.47-31.96) | 20.23 (7.58-37.57) | 0.324 | 59 | 185 |
| Range | 0.14-101.14 | 0.33-124.00 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.12 (0.05-0.28) | 0.19 (0.10-0.38) | 0.022 | 65 | 231 |
| Range | 0.01-0.79 | 0.00-0.79 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.23 (0.13-0.38) | 0.28 (0.14-0.47) | 0.211 | 65 | 231 |
| Range | 0.04-0.79 | 0.04-0.83 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.08 (0.03-0.19) | 0.02 (0.00-0.12) | <0.001 | 65 | 231 |
| Range | 0.00-0.64 | 0.00-0.56 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.00-0.01) | 0.00 (0.00-0.01) | <0.001 | 65 | 231 |
| Range | 0.00-0.04 | 0.00-0.08 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.005 | 65 | 231 |
| Range | 0.00-0.03 | 0.00-0.04 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.43 (0.02-0.70) | 0.18 (0.01-0.67) | 0.226 | 65 | 231 |
| Range | 0.00-0.89 | 0.00-0.91 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.51 (0.30-0.91) | 0.67 (0.40-1.16) | 0.012 | 65 | 231 |
| Range | 0.06-5.17 | 0.05-4.43 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 1.18 (0.44-5.94) | 3.12 (0.90-60.92) | <0.001 | 63 | 187 |
| Range | 0.12-698.25 | 0.09-2002.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 0.48 (0.19-11.13) | 1.44 (0.21-18.25) | 0.317 | 65 | 225 |
| Range | 0.05-414.18 | 0.04-1310.00 | | | |

Supplementary Table 9. Bile acids in No IBD and CD PSC patients.

| | No IBD PSC | CD PSC | p-value | No IBD PSC (n) | CD PSC (n) |
|----------------------------|---------------------|---------------------|---------|----------------|------------|
| Age in years | | | | | |
| Median (IQR) | 55.82 (43.32-61.82) | 48.17 (38.38-55.93) | 0.150 | 65 | 26 |
| Range | 14.25-79.68 | 10.13-71.10 | | | |
| Sex (% Male) | 49.2 | 38.5 | 0.352 | 65 | 26 |
| Tot BA / UDCA Group | | | | | |
| NN - # (%) | 19 (29.2) | 17 (65.4) | 0.003 | 65 | 26 |
| NY - # (%) | 10 (15.4) | 5 (19.2) | | | |
| HN - # (%) | 13 (20.0) | 3 (11.5) | | | |
| HY - # (%) | 23 (35.4) | 1 (3.8) | | | |
| Total BA | | | | | |
| Median (IQR) | 23.57 (7.71-45.45) | 6.79 (3.08-12.15) | <0.001 | 65 | 26 |
| Range | 0.88-646.47 | 0.59-124.14 | | | |
| CA (total) | | | | | |
| Median (IQR) | 1.84 (0.86-8.72) | 0.98 (0.41-1.54) | 0.015 | 65 | 26 |
| Range | 0.13-68.19 | 0.04-31.62 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.05 (0.03-0.12) | 0.12 (0.03-0.28) | 0.127 | 65 | 26 |
| Range | 0.00-4.02 | 0.01-0.76 | | | |
| GCA | | | | | |
| Median (IQR) | 1.11 (0.45-5.13) | 0.54 (0.16-1.24) | 0.009 | 65 | 26 |
| Range | 0.06-53.99 | 0.02-19.29 | | | |
| TCA | | | | | |
| Median (IQR) | 0.30 (0.07-2.09) | 0.07 (0.02-0.22) | 0.010 | 65 | 26 |
| Range | 0.00-30.29 | 0.00-20.10 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 3.85 (2.14-9.80) | 2.21 (0.91-4.99) | 0.021 | 65 | 26 |
| Range | 0.30-141.73 | 0.16-24.66 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.16 (0.05-0.47) | 0.31 (0.08-0.63) | 0.318 | 65 | 26 |
| Range | 0.01-7.27 | 0.00-5.23 | | | |
| GCDCA | | | | | |
| Median (IQR) | 2.99 (1.32-6.33) | 1.35 (0.37-3.32) | 0.007 | 65 | 26 |
| Range | 0.18-119.44 | 0.10-17.57 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.56 (0.16-2.77) | 0.12 (0.04-0.69) | 0.008 | 65 | 26 |
| Range | 0.02-42.03 | 0.00-15.94 | | | |

| | No IBD PSC | CD PSC | p-value | No IBD PSC (n) | CD PSC (n) |
|----------------------------|-------------------|------------------|---------|----------------|------------|
| DCA (total) | | | | | |
| Median (IQR) | 1.43 (0.76-2.23) | 0.81 (0.15-2.20) | 0.063 | 65 | 26 |
| Range | 0.00-24.36 | 0.00-11.70 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.29 (0.09-0.65) | 0.37 (0.03-0.66) | 0.598 | 65 | 26 |
| Range | 0.00-3.63 | 0.00-3.67 | | | |
| GDCA | | | | | |
| Median (IQR) | 0.64 (0.35-1.07) | 0.17 (0.05-0.85) | 0.009 | 65 | 26 |
| Range | 0.00-15.49 | 0.00-7.51 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.15 (0.05-0.31) | 0.02 (0.00-0.25) | 0.014 | 65 | 26 |
| Range | 0.00-8.55 | 0.00-3.41 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.10 (0.06-0.21) | 0.03 (0.01-0.09) | 0.001 | 65 | 26 |
| Range | 0.00-2.85 | 0.00-1.44 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.03 (0.01-0.07) | 0.01 (0.00-0.02) | 0.001 | 65 | 26 |
| Range | 0.00-0.29 | 0.00-0.41 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.05 (0.02-0.13) | 0.01 (0.01-0.06) | 0.005 | 65 | 26 |
| Range | 0.00-2.14 | 0.00-0.71 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.03) | 0.00 (0.00-0.01) | 0.017 | 65 | 26 |
| Range | 0.00-0.42 | 0.00-0.56 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.02 (0.00-0.05) | 0.01 (0.00-0.05) | 0.701 | 65 | 26 |
| Range | 0.00-0.17 | 0.00-0.41 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.00-0.04) | 0.01 (0.00-0.03) | 0.719 | 65 | 26 |
| Range | 0.00-0.13 | 0.00-0.24 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.01) | 0.311 | 65 | 26 |
| Range | 0.00-0.06 | 0.00-0.17 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.291 | 65 | 26 |
| Range | 0.00-0.07 | 0.00-0.01 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 3.33 (0.29-18.37) | 0.49 (0.12-1.15) | 0.005 | 65 | 26 |
| Range | 0.02-537.71 | 0.00-60.88 | | | |

| | No IBD PSC | CD PSC | p-value | No IBD PSC (n) | CD PSC (n) |
|-------------------------------|-------------------|-------------------|---------|----------------|------------|
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.12 (0.02-2.29) | 0.06 (0.01-0.40) | 0.135 | 65 | 26 |
| Range | 0.00-52.33 | 0.00-6.51 | | | |
| GUDCA | | | | | |
| Median (IQR) | 1.73 (0.24-15.78) | 0.24 (0.06-0.73) | 0.003 | 65 | 26 |
| Range | 0.01-472.47) | 0.00-54.41 | | | |
| TUDCA | | | | | |
| Median (IQR) | 0.14 (0.03-0.52) | 0.02 (0.00-0.05) | <0.001 | 65 | 26 |
| Range | 0.00-35.47 | 0.00-4.77 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.92 (0.74-0.98) | 0.75 (0.47-0.91) | 0.014 | 65 | 26 |
| Range | 0.20-1.00 | 0.28-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.97 (0.83-1.00) | 0.85 (0.55-0.96) | 0.006 | 65 | 26 |
| Range | 0.09-1.00 | 0.25-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.96 (0.79-0.99) | 0.87 (0.59-0.93) | 0.015 | 65 | 26 |
| Range | 0.29-1.00 | 0.24-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.78 (0.52-0.93) | 0.58 (0.23-0.80) | 0.042 | 63 | 24 |
| Range | 0.18-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.71 (0.54-0.80) | 0.75 (0.50-0.89) | 0.386 | 62 | 21 |
| Range | 0.00-1.00 | 0.33-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.00 (0.00-0.41) | 0.00 (0.00-0.41) | 0.737 | 48 | 17 |
| Range | 0.00-1.00 | 0.00-0.67 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.90 (0.75-0.97) | 0.81 (0.60-0.92) | 0.032 | 65 | 24 |
| Range | 0.28-1.00 | 0.27-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 8.09 (2.80-18.65) | 8.19 (4.70-20.57) | 0.818 | 65 | 25 |
| Range | 0.62-69.38 | 0.46-85.82 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 5.12 (2.33-9.54) | 6.29 (3.07-10.25) | 0.453 | 64 | 23 |
| Range | 0.50-27.00 | 0.57-22.80 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 5.43 (2.37-9.74) | 7.85 (3.81-13.20) | 0.126 | 65 | 25 |
| Range | 0.67-35.50 | 0.36-67.00 | | | |

| | No IBD PSC | CD PSC | p-value | No IBD PSC (n) | CD PSC (n) |
|-----------------------------|--------------------|---------------------|---------|----------------|------------|
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.09 (2.17-8.60) | 6.86 (5.09-8.60) | 0.456 | 61 | 19 |
| Range | 0.50-45.00 | 0.22-23.50 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 3.00 (1.50-7.00) | 4.25 (0.79-8.21) | 0.733 | 37 | 8 |
| Range | 0.50-36.00 | 0.20-13.00 | | | |
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 0.71 (0.71-0.71) | 3.00 (3.00-3.00) | 0.317 | 1 | 1 |
| Range | 0.71-0.71 | 3.00-3.00 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 13.81 (6.47-31.96) | 21.00 (11.41-51.25) | 0.310 | 59 | 17 |
| Range | 0.14-101.14 | 0.42-145.00 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.12 (0.05-0.28) | 0.17 (0.12-0.27) | 0.404 | 65 | 26 |
| Range | 0.01-0.79 | 0.01-0.56 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.23 (0.13-0.38) | 0.39 (0.25-0.56) | 0.004 | 65 | 26 |
| Range | 0.04-0.79 | 0.08-0.85 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.08 (0.03-0.19) | 0.12 (0.04-0.22) | 0.404 | 65 | 26 |
| Range | 0.00-0.64 | 0.00-0.61 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.00-0.01) | 0.01 (0.00-0.01) | 0.626 | 65 | 26 |
| Range | 0.00-0.04 | 0.00-0.12 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.01) | 0.463 | 65 | 26 |
| Range | 0.00-0.03 | 0.00-0.05 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.43 (0.02-0.70) | 0.05 (0.04-0.20) | 0.150 | 65 | 26 |
| Range | 0.00-0.89 | 0.00-0.83 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.51 (0.30-0.91) | 0.38 (0.26-0.71) | 0.366 | 65 | 26 |
| Range | 0.06-5.17 | 0.15-1.45 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 1.18 (0.44-5.94) | 1.03 (0.40-5.40) | 0.812 | 63 | 24 |
| Range | 0.12-698.25 | 0.09-182.50 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 0.48 (0.19-11.13) | 4.27 (0.87-11.00) | 0.189 | 65 | 24 |
| Range | 0.05-414.18 | 0.09-50.65 | | | |

Supplementary Table 10. Bile acids in No IBD and Indeterminate IBD PSC patients.

| | No IBD PSC | Ind IBD PSC | p-value | No IBD PSC (n) | Ind IBD PSC (n) |
|----------------------------|---------------------|---------------------|---------|----------------|-----------------|
| Age in years | | | | | |
| Median (IQR) | 55.82 (43.32-61.82) | 47.03 (29.80-59.11) | 0.187 | 65 | 25 |
| Range | 14.25-79.68 | 18.90-78.53 | | | |
| Sex (% Male) | 49.2 | 52.0 | 0.814 | 65 | 25 |
| Tot BA / UDCA Group | | | | | |
| NN - # (%) | 19 (29.2) | 11 (44.0) | 0.465 | 65 | 25 |
| NY - # (%) | 10 (15.4) | 4 (16.0) | | | |
| HN - # (%) | 13 (20.0) | 5 (20.0) | | | |
| HY - # (%) | 23 (35.4) | 5 (20.0) | | | |
| Total BA | | | | | |
| Median (IQR) | 23.57 (7.71-45.45) | 12.06 (6.73-38.40) | 0.184 | 65 | 25 |
| Range | 0.88-646.47 | 0.96-53.68 | | | |
| CA (total) | | | | | |
| Median (IQR) | 1.84 (0.86-8.72) | 1.85 (0.60-7.10) | 0.564 | 65 | 25 |
| Range | 0.13-68.19 | 0.16-25.90 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.05 (0.03-0.12) | 0.04 (0.03-0.14) | 0.910 | 65 | 25 |
| Range | 0.00-4.02 | 0.01-2.65 | | | |
| GCA | | | | | |
| Median (IQR) | 1.11 (0.45-5.13) | 1.26 (0.33-4.17) | 0.525 | 65 | 25 |
| Range | 0.06-53.99 | 0.07-12.90 | | | |
| TCA | | | | | |
| Median (IQR) | 0.30 (0.07-2.09) | 0.15 (0.03-2.10) | 0.452 | 65 | 25 |
| Range | 0.00-30.29 | 0.01-12.74 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 3.85 (2.14-9.80) | 4.68 (1.48-8.18) | 0.675 | 65 | 25 |
| Range | 0.30-141.73 | 0.70-24.40 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.16 (0.05-0.47) | 0.14 (0.04-0.56) | 0.708 | 65 | 25 |
| Range | 0.01-7.27 | 0.01-3.68 | | | |
| GCDCA | | | | | |
| Median (IQR) | 2.99 (1.32-6.33) | 3.14 (1.00-5.53) | 0.656 | 65 | 25 |
| Range | 0.18-119.44 | 0.36-16.22 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.56 (0.16-2.77) | 0.42 (0.13-2.06) | 0.441 | 65 | 25 |
| Range | 0.02-42.03 | 0.03-8.40 | | | |

| | No IBD PSC | Ind IBD PSC | p-value | No IBD PSC (n) | Ind IBD PSC (n) |
|----------------------------|-------------------|------------------|---------|----------------|-----------------|
| DCA (total) | | | | | |
| Median (IQR) | 1.43 (0.76-2.23) | 0.61 (0.24-2.34) | 0.073 | 65 | 25 |
| Range | 0.00-24.36 | 0.00-6.13 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.29 (0.09-0.65) | 0.12 (0.02-0.39) | 0.054 | 65 | 25 |
| Range | 0.00-3.63 | 0.00-3.06 | | | |
| GDCA | | | | | |
| Median (IQR) | 0.64 (0.35-1.07) | 0.33 (0.08-1.27) | 0.091 | 65 | 25 |
| Range | 0.00-15.49 | 0.00 – 4.71 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.15 (0.05-0.31) | 0.08 (0.01-0.32) | 0.239 | 65 | 25 |
| Range | 0.00-8.55 | 0.00-1.35 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.10 (0.06-0.21) | 0.04 (0.01-0.11) | 0.005 | 65 | 25 |
| Range | 0.00-2.85 | 0.00-1.13 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.03 (0.01-0.07) | 0.01 (0.00-0.03) | 0.002 | 65 | 25 |
| Range | 0.00-0.29 | 0.00-0.96 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.05 (0.02-0.13) | 0.01 (0.00-0.05) | 0.008 | 65 | 25 |
| Range | 0.00-2.14 | 0.00-0.30 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.01 (0.00-0.03) | 0.00 (0.00-0.03) | 0.237 | 65 | 25 |
| Range | 0.00-0.42 | 0.00-0.11 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.02 (0.00-0.05) | 0.01 (0.00-0.04) | 0.224 | 65 | 25 |
| Range | 0.00-0.17 | 0.00-0.15 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.02 (0.00-0.04) | 0.01 (0.00-0.03) | 0.178 | 65 | 25 |
| Range | 0.00-0.13 | 0.00-0.15 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.850 | 65 | 25 |
| Range | 0.00-0.06 | 0.00-0.06 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.723 | 65 | 25 |
| Range | 0.00-0.07 | 0.00-0.02 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 3.33 (0.29-18.37) | 0.67 (0.21-7.33) | 0.254 | 65 | 25 |
| Range | 0.02-537.71 | 0.01-44.31 | | | |

| | No IBD PSC | Ind IBD PSC | p-value | No IBD PSC (n) | Ind IBD PSC (n) |
|-------------------------------|-------------------|-------------------|---------|----------------|-----------------|
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.12 (0.02-2.29) | 0.06 (0.01-0.76) | 0.238 | 65 | 25 |
| Range | 0.00-52.33 | 0.00-5.65 | | | |
| GUDCA | | | | | |
| Median (IQR) | 1.73 (0.24-15.78) | 0.49 (0.20-4.89) | 0.266 | 65 | 25 |
| Range | 0.01-472.47) | 0.01-39.65 | | | |
| TUDCA | | | | | |
| Median (IQR) | 0.14 (0.03-0.52) | 0.07 (0.02-0.17) | 0.161 | 65 | 25 |
| Range | 0.00-35.47 | 0.00-2.63 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.92 (0.74-0.98) | 0.94 (0.78-0.97) | 0.811 | 65 | 25 |
| Range | 0.20-1.00 | 0.21-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.97 (0.83-1.00) | 0.95 (0.88-0.99) | 0.488 | 65 | 25 |
| Range | 0.09-1.00 | 0.15-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.96 (0.79-0.99) | 0.97 (0.84-0.99) | 0.853 | 65 | 25 |
| Range | 0.29-1.00 | 0.24-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.78 (0.52-0.93) | 0.83 (0.59-0.94) | 0.565 | 63 | 23 |
| Range | 0.18-1.00 | 0.20-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.71 (0.54-0.80) | 0.75 (0.58-0.96) | 0.151 | 62 | 19 |
| Range | 0.00-1.00 | 0.15-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.00 (0.00-0.41) | 0.00 (0.00-0.53) | 0.558 | 48 | 15 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.90 (0.75-0.97) | 0.92 (0.78-0.98) | 0.766 | 65 | 25 |
| Range | 0.28-1.00 | 0.44-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 8.09 (2.80-18.65) | 8.47 (2.41-22.54) | 0.989 | 65 | 25 |
| Range | 0.62-69.38 | 0.62-93.11 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 5.12 (2.33-9.54) | 5.19 (2.87-9.27) | 0.671 | 64 | 25 |
| Range | 0.50-27.00 | 0.66-70.33 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 5.43 (2.37-9.74) | 4.54 (2.33-12.08) | 0.715 | 65 | 25 |
| Range | 0.67-35.50 | 0.56-92.17 | | | |

| | No IBD PSC | Ind IBD PSC | p-value | No IBD PSC (n) | Ind IBD PSC (n) |
|-----------------------------|--------------------|--------------------|---------|----------------|-----------------|
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.09 (2.17-8.60) | 4.05 (2.00-7.74) | 0.462 | 61 | 18 |
| Range | 0.50-45.00 | 0.59-14.00 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 3.00 (1.50-7.00) | 1.45 (1.00-5.00) | 0.131 | 37 | 9 |
| Range | 0.50-36.00 | 0.33-8.00 | | | |
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 0.71 (0.71-0.71) | 1.50 (1.50-1.50) | 0.317 | 1 | 1 |
| Range | 0.71-0.71 | 1.50-1.50 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 13.81 (6.47-31.96) | 15.37 (4.33-29.00) | 0.840 | 59 | 21 |
| Range | 0.14-101.14 | 2.41-87.17 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.12 (0.05-0.28) | 0.23 (0.10-0.33) | 0.240 | 65 | 25 |
| Range | 0.01-0.79 | 0.02-0.67 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.23 (0.13-0.38) | 0.43 (0.18-0.57) | 0.023 | 65 | 25 |
| Range | 0.04-0.79 | 0.08-0.74 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.08 (0.03-0.19) | 0.07 (0.01-0.12) | 0.240 | 65 | 25 |
| Range | 0.00-0.64 | 0.00-0.55 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.01 (0.00-0.01) | 0.00 (0.00-0.01) | 0.010 | 65 | 25 |
| Range | 0.00-0.04 | 0.00-0.04 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.317 | 65 | 25 |
| Range | 0.00-0.03 | 0.00-0.01 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.43 (0.02-0.70) | 0.06 (0.02-0.59) | 0.479 | 65 | 25 |
| Range | 0.00-0.89 | 0.01-0.89 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.51 (0.30-0.91) | 0.53 (0.34-0.72) | 0.960 | 65 | 25 |
| Range | 0.06-5.17 | 0.11-2.14 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 1.18 (0.44-5.94) | 2.71 (0.89-16.38) | 0.139 | 63 | 23 |
| Range | 0.12-698.25 | 0.18-1295.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 0.48 (0.19-11.13) | 7.78 (0.27-18.80) | 0.075 | 65 | 25 |
| Range | 0.05-414.18 | 0.09-75.00 | | | |

Supplementary Table 11. Bile acids in cirrhotic and non-cirrhotic PSC patients.

| | Non-cirrhotic | Cirrhotic | p-value | NC (n) | Cir (n) |
|----------------------------|----------------------|----------------------|----------------|---------------|----------------|
| Age in years | | | | | |
| Median (IQR) | 47.99 (32.95-59.36) | 55.37 (33.51-61.41) | 0.143 | 340 | 60 |
| Range | 10.13-80.48 | 17.27-79.68 | | | |
| Sex (% Male) | 58.5 | 53.3 | 0.453 | 340 | 60 |
| Total BA | | | | | |
| Median (IQR) | 13.50 (5.38-32.27) | 48.84 (22.67-119.16) | <0.001 | 340 | 60 |
| Range | 0.54-291.62 | 1.86-646.47 | | | |
| CA (total) | | | | | |
| Median (IQR) | 1.80 (0.64-6.38) | 13.34 (3.04-32.12) | <0.001 | 340 | 60 |
| Range | 0.04-224.36 | 0.46-192.53 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.06 (0.03-0.20) | 0.08 (0.03-0.26) | 0.766 | 340 | 60 |
| Range | 0.00-10.65 | 0.01-9.85 | | | |
| GCA | | | | | |
| Median (IQR) | 1.33 (0.41-4.53) | 8.07 (1.96-18.62) | <0.001 | 340 | 60 |
| Range | 0.01-165.50 | 0.18-151.29 | | | |
| TCA | | | | | |
| Median (IQR) | 0.18 (0.05-1.23) | 4.19 (0.49-11.65) | <0.001 | 340 | 60 |
| Range | 0.00-58.61 | 0.01-41.19 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 3.53 (1.37-80.3) | 14.80 (4.69-42.63) | <0.001 | 340 | 60 |
| Range | 0.10-71.89 | 0.73-268.56 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.16 (0.05-0.46) | 0.11 (0.05-0.46) | 0.823 | 340 | 60 |
| Range | 0.00-14.78 | 0.01-9.35 | | | |
| GCDCA | | | | | |
| Median (IQR) | 2.39 (0.97-5.39) | 7.88 (2.95-23.59) | <0.001 | 340 | 60 |
| Range | 0.02-47.74 | 0.51-214.48 | | | |
| TCDC | | | | | |
| Median (IQR) | 0.36 (0.11-1.32) | 5.07 (1.11-11.79) | <0.001 | 340 | 60 |
| Range | 0.00-35.85 | 0.01-52.46 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.66 (0.02-1.78) | 0.55 (0.17-1.57) | 0.540 | 340 | 60 |
| Range | 0.00-24.36 | 0.00-9.94 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.13 (0.01-0.46) | 0.03 (0.01-0.19) | 0.032 | 340 | 60 |
| Range | 0.00-5.99 | 0.00-3.63 | | | |

| | Non-cirrhotic | Cirrhotic | p-value | NC (n) | Cir (n) |
|----------------------------|-------------------|-------------------|---------|--------|---------|
| GDCA | | | | | |
| Median (IQR) | 0.27 (0.01-1.03) | 0.31 (0.08-0.83) | 0.483 | 340 | 60 |
| Range | 0.00-15.49 | 0.00-8.20 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.05 (0.00-0.25) | 0.17 (0.04-0.32) | 0.007 | 340 | 60 |
| Range | 0.00-8.55 | 0.00-3.44 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.04 (0.00-0.13) | 0.06 (0.02-0.26) | 0.006 | 340 | 60 |
| Range | 0.00-2.18 | 0.00-2.85 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.07) | 0.151 | 340 | 60 |
| Range | 0.00-0.96 | 0.00-0.70 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.02 (0.00-0.08) | 0.02 (0.01-0.14) | 0.070 | 340 | 60 |
| Range | 0.00-1.63 | 0.00-2.14 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.01 (0.00-0.06) | <0.001 | 340 | 60 |
| Range | 0.00-0.56 | 0.00-0.42 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.03) | 0.310 | 340 | 60 |
| Range | 0.00-0.41 | 0.00-0.73 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.03) | 0.00 (0.00-0.01) | 0.125 | 340 | 60 |
| Range | 0.00-0.24 | 0.00-0.13 | | | |
| GHDCa | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.204 | 340 | 60 |
| Range | 0.00-0.17 | 0.00-0.73 | | | |
| THDCa | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.018 | 340 | 60 |
| Range | 0.00-0.07 | 0.00-0.01 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 2.00 (0.19-14.29) | 1.09 (0.22-33.79) | 0.207 | 340 | 60 |
| Range | 0.00-194.12 | 0.00-537.71 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.17 (0.01-2.00) | 0.14 (0.01-2.33) | 0.784 | 340 | 60 |
| Range | 0.00-26.13 | 0.00-52.33 | | | |
| GUDCA | | | | | |
| Median (IQR) | 1.62 (0.12-12.06) | 0.88 (0.09-30.72) | 0.239 | 340 | 60 |
| Range | 0.00-175.83 | 0.00-472.47 | | | |

| | Non-cirrhotic | Cirrhotic | p-value | NC (n) | Cir (n) |
|-------------------------------|-------------------|------------------|---------|--------|---------|
| TUDCA | | | | | |
| Median (IQR) | 0.08 (0.01-0.47) | 0.17 (0.04-2.63) | <0.001 | 340 | 60 |
| Range | 0.00-18.60 | 0.00-51.06 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.89 (0.72-0.97) | 0.98 (0.88-0.99) | <0.001 | 340 | 60 |
| Range | 0.13-1.00 | 0.20-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.96 (0.82-0.99) | 0.99 (0.96-1.00) | <0.001 | 340 | 60 |
| Range | 0.09-1.00 | 0.09-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.94 (0.82-0.99) | 0.99 (0.93-1.00) | <0.001 | 340 | 60 |
| Range | 0.09-1.00 | 0.24-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.77 (0.50-0.93) | 0.95 (0.80-0.99) | <0.001 | 286 | 59 |
| Range | 0.00-1.00 | 0.18-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.75 (0.55-0.86) | 0.79 (0.57-1.00) | 0.081 | 231 | 55 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.20 (0.00-0.52) | 0.33 (0.00-0.67) | 0.314 | 199 | 32 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.88 (0.74-0.97) | 0.97 (0.86-0.99) | 0.002 | 333 | 59 |
| Range | 0.00-1.00 | 0.46-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 9.04 (4.44-18.55) | 3.80 (1.77-9.92) | <0.001 | 339 | 60 |
| Range | 0.47-93.11 | 0.37-55.50 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 6.00 (3.38-9.67) | 2.44 (1.42-5.80) | <0.001 | 333 | 60 |
| Range | 0.47-70.33 | 0.27-22.96 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 6.46 (3.27-10.71) | 2.52 (1.74-5.60) | <0.001 | 339 | 60 |
| Range | 0.38-92.17 | 0.36-51.00 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 5.47 (2.61-8.75) | 2.17 (1.29-3.98) | <0.001 | 241 | 51 |
| Range | 0.29-45.00 | 0.22-38.50 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 3.82 (2.00-7.00) | 1.45 (1.00-2.85) | <0.001 | 132 | 37 |
| Range | 0.50-36.00 | 0.10-12.00 | | | |

| | Non-cirrhotic | Cirrhotic | p-value | NC (n) | Cir (n) |
|-------------------------------|--------------------|---------------------|---------|--------|---------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.37 (1.00-2.62) | 1.00 (1.00-1.00) | 0.382 | 10 | 2 |
| Range | 0.71-11.00 | 1.00-1.00 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 21.00 (8.88-38.21) | 7.55 (4.25-18.05) | <0.001 | 276 | 54 |
| Range | 0.14-145.00 | 0.33-89.15 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.17 (0.08-0.34) | 0.26 (0.12-0.43) | 0.008 | 340 | 60 |
| Range | 0.00-0.79 | 0.01-0.76 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.26 (0.14-0.45) | 0.31 (0.20-0.50) | 0.136 | 340 | 60 |
| Range | 0.04-0.93 | 0.06-0.88 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.05 (0.00-0.14) | 0.01 (0.00-0.04) | 0.026 | 340 | 60 |
| Range | 0.00-0.64 | 0.00-0.46 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | 0.992 | 340 | 60 |
| Range | 0.00-0.12 | 0.00-0.06 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.039 | 340 | 60 |
| Range | 0.00-0.05 | 0.00-0.02 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.21 (0.03-0.68) | 0.08 (0.01-0.60) | 0.029 | 340 | 60 |
| Range | 0.00-0.97 | 0.00-0.88 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.59 (0.34-1.07) | 0.66 (0.44-1.45) | 0.106 | 340 | 60 |
| Range | 0.05-5.26 | 0.06-4.43 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 1.91 (0.59-17.09) | 19.69 (2.81-162.95) | <0.001 | 286 | 59 |
| Range | 0.09-3796.67 | 0.36-2002.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 1.36 (0.21-11.07) | 5.27 (0.30-36.10) | 0.017 | 333 | 59 |
| Range | 0.04-1310.00 | 0.06-422.00 | | | |
| Bile acid / UDCA group | | | <0.001 | 319 | 57 |
| NN | 127 (39.8%) | 10 (17.5%) | | | |
| NY | 60 (18.8%) | 1 (1.8%) | | | |
| HN | 41 (12.9%) | 22 (38.6%) | | | |
| HY | 91 (28.5%) | 24 (42.1%) | | | |

Supplementary Table 12. Bile acids in autoimmune hepatitis (AIH) overlap and non-overlap large duct PSC patients.

| | non-overlap "Large duct" PSC | AIH overlap | p-value | No (n) | AIH (n) |
|----------------------------|---------------------------------|---------------------|---------|--------|---------|
| Age in years | | | | | |
| Median (IQR) | 48.83 (33.42-60.14) | 45.84 (25.23-64.63) | 0.716 | 362 | 14 |
| Range | 10.13-80.48 | 19.44-67.75 | | | |
| Sex (% Male) | 57.2 | 57.1 | 0.998 | 362 | 14 |
| Total BA | | | | | |
| Median (IQR) | 16.34 (5.89-45.87) | 25.92 (12.76-55.13) | 0.234 | 362 | 14 |
| Range | 0.54-646.47 | 2.56-184.74 | | | |
| CA (total) | | | | | |
| Median (IQR) | 2.12 (0.76-10.54) | 2.26 (1.12-5.25) | 0.894 | 362 | 14 |
| Range | 0.04-224.36 | 0.18-110.08 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.23) | 0.04 (0.02-0.11) | 0.347 | 362 | 14 |
| Range | 0.00-10.65 | 0.01-0.77 | | | |
| GCA | | | | | |
| Median (IQR) | 1.70 (0.46-6.41) | 1.96 (0.69-3.87) | 0.975 | 362 | 14 |
| Range | 0.01-165.50 | 0.16-51.45 | | | |
| TCA | | | | | |
| Median (IQR) | 0.27 (0.07-2.57) | 0.27 (0.08-1.27) | 0.911 | 362 | 14 |
| Range | 0.00-58.57 | 0.01-58.61 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 4.09 (1.69-10.26) | 4.50 (3.06-8.57) | 0.660 | 362 | 14 |
| Range | 0.10-268.56 | 0.73-71.89 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.15 (0.05-0.46) | 0.29 (0.14-0.63) | 0.170 | 362 | 14 |
| Range | 0.00-14.78 | 0.01-1.55 | | | |
| GCDCA | | | | | |
| Median (IQR) | 2.87 (1.10-7.18) | 3.59 (1.81-5.57) | 0.651 | 362 | 14 |
| Range | 0.02-214.48 | 0.40-36.01 | | | |
| TCDC A | | | | | |
| Median (IQR) | 0.49 (0.13-2.25) | 0.62 (0.20-2.17) | 0.678 | 362 | 14 |
| Range | 0.00-52.46 | 0.06-35.85 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.65 (0.03-1.73) | 1.43 (0.32-2.02) | 0.279 | 362 | 14 |
| Range | 0.00-24.36 | 0.00-6.45 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.09 (0.01-0.41) | 0.38 (0.07-0.54) | 0.160 | 362 | 14 |
| Range | 0.00-5.99 | 0.00-0.85 | | | |

| | Non-overlap | AIH overlap | p-value | No (n) | AIH (n) |
|----------------------------|--------------------|--------------------|----------------|---------------|----------------|
| GDCA | | | | | |
| Median (IQR) | 0.28 (0.02-0.93) | 0.65 (0.10-1.36) | 0.386 | 362 | 14 |
| Range | 0.00-15.49 | 0.00-4.16 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.06 (0.00-0.29) | 0.11 (0.01-0.39) | 0.350 | 362 | 14 |
| Range | 0.00-8.55 | 0.00-1.98 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.04 (0.00-0.15) | 0.10 (0.01-0.24) | 0.379 | 362 | 14 |
| Range | 0.00-2.85 | 0.00-1.71 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.04 (0.00-0.06) | 0.160 | 362 | 14 |
| Range | 0.00-0.96 | 0.00-0.55 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.02 (0.00-0.09) | 0.03 (0.00-0.13) | 0.672 | 362 | 14 |
| Range | 0.00-2.14 | 0.00-1.03 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.01 (0.00-0.02) | 0.440 | 362 | 14 |
| Range | 0.00-0.56 | 0.00-0.13 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.07) | 0.341 | 362 | 14 |
| Range | 0.00-0.73 | 0.00-0.09 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.01 (0.00-0.03) | 0.872 | 362 | 14 |
| Range | 0.00-0.24 | 0.00-0.09 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.01 (0.00-0.01) | 0.101 | 362 | 14 |
| Range | 0.00-0.73 | 0.00-0.05 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.894 | 362 | 14 |
| Range | 0.00-0.07 | 0.00-0.04 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 1.80 (0.17-18.69) | 8.73 (1.47-24.76) | 0.106 | 362 | 14 |
| Range | 0.00-537.71 | 0.03-78.99 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.15 (0.01-2.03) | 2.79 (0.14-5.47) | 0.060 | 362 | 14 |
| Range | 0.00-52.33 | 0.00-16.90 | | | |
| GUDCA | | | | | |
| Median (IQR) | 1.41 (0.11-13.86) | 5.80 (1.08-15.36) | 0.124 | 362 | 14 |
| Range | 0.00-472.47 | 0.02-66.92 | | | |

| | Non-overlap | AIH overlap | p-value | No (n) | AIH (n) |
|-------------------------------|--------------------|--------------------|----------------|---------------|----------------|
| TUDCA | | | | | |
| Median (IQR) | 0.08 (0.01-0.53) | 0.28 (0.10-0.70) | 0.114 | 362 | 14 |
| Range | 0.00-51.06 | 0.01-8.13 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.91 (0.74-0.98) | 0.84 (0.68-0.93) | 0.371 | 362 | 14 |
| Range | 0.13-1.00 | 0.63-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.97 (0.84-0.99) | 0.98 (0.89-0.99) | 0.591 | 362 | 14 |
| Range | 0.09-1.00 | 0.44-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.96 (0.83-0.99) | 0.91 (0.77-0.98) | 0.449 | 362 | 14 |
| Range | 0.12-1.00 | 0.57-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.81 (0.54-0.96) | 0.71 (0.51-0.81) | 0.359 | 313 | 13 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.75 (0.57-0.88) | 0.68 (0.33-0.79) | 0.099 | 258 | 11 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.25 (0.00-0.55) | 0.59 (0.06-0.97) | 0.111 | 205 | 10 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.90 (0.75-0.97) | 0.80 (0.74-0.96) | 0.394 | 354 | 14 |
| Range | 0.00-1.00 | 0.58-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 8.26 (3.39-17.30) | 11.42 (5.03-20.53) | 0.612 | 361 | 14 |
| Range | 0.37-93.11 | 0.92-47.57 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 5.53 (2.64-9.00) | 5.82 (2.98-11.86) | 0.663 | 356 | 14 |
| Range | 0.27-70.33 | 0.88-21.30 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 5.68 (2.77-10.33) | 5.75 (2.67-9.27) | 0.684 | 361 | 14 |
| Range | 0.36-92.17 | 0.97-16.33 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 4.69 (2.08-8.20) | 4.82 (3.07-6.57) | 0.900 | 265 | 11 |
| Range | 0.22-44.50 | 0.63-18.38 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 3.00 (1.45-6.00) | 5.05 (1.66-6.25) | 0.657 | 153 | 8 |
| Range | 0.10-36.00 | 1.00-7.92 | | | |

| | Non-overlap | AIH overlap | p-value | No (n) | AIH (n) |
|-------------------------------|--------------------|--------------------|----------------|---------------|----------------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.33 (1.00-2.25) | 0.75 (0.75-0.75) | 0.185 | 11 | 1 |
| Range | 0.71-11.00 | 0.75-0.75 | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 17.44 (7.00-34.58) | 27.54 (8.80-35.44) | 0.552 | 299 | 14 |
| Range | 0.14-145.00 | 1.11-62.84 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.19 (0.09-0.37) | 0.08 (0.04-0.18) | 0.066 | 362 | 14 |
| Range | 0.00-0.79 | 0.03-0.60 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.27 (0.15-0.45) | 0.17 (0.12-0.36) | 0.141 | 362 | 14 |
| Range | 0.04-0.88 | 0.06-0.55 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.03 (0.00-0.14) | 0.06 (0.01-0.10) | 0.743 | 362 | 14 |
| Range | 0.00-0.64 | 0.00-0.23 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.01) | 0.538 | 362 | 14 |
| Range | 0.00-0.12 | 0.00-0.06 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.385 | 362 | 14 |
| Range | 0.00-0.05 | 0.00-0.01 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.17 (0.02-0.66) | 0.65 (0.18-0.72) | 0.096 | 362 | 14 |
| Range | 0.00-0.91 | 0.00-0.88 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.63 (0.35-1.15) | 0.51 (0.34-0.86) | 0.374 | 362 | 14 |
| Range | 0.05-5.26 | 0.15-1.53 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 2.72 (0.81-27.51) | 1.08 (0.76-3.56) | 0.448 | 313 | 14 |
| Range | 0.09-3796.67 | 0.28-1650.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 1.88 (0.22-14.22) | 0.27 (0.17-3.66) | 0.159 | 354 | 14 |
| Range | 0.04-1310.00 | 0.06-462.67 | | | |
| Bile acid / UDCA group | | | 0.185 | 342 | 13 |
| NN | 128 (37.4%) | 1 (7.7%) | | | |
| NY | 52 (15.2%) | 3 (23.1%) | | | |
| HN | 58 (17.0%) | 3 (23.1%) | | | |
| HY | 104 (30.4%) | 6 (46.2%) | | | |

Supplementary Table 13. Bile acids in small duct (SD) and large duct (LD) PSC patients.

| | large duct PSC | small duct PSC | p-value | LD (n) | SD (n) |
|----------------------------|---------------------|---------------------|---------|--------|--------|
| Age in years | | | | | |
| Median (IQR) | 48.83 (33.42-60.14) | 38.20 (29.06-50.11) | 0.013 | 362 | 26 |
| Range | 10.13-80.48 | 11.82-68.15 | | | |
| Sex (% Male) | 57.2 | 65.4 | 0.413 | 362 | 26 |
| Total BA | | | | | |
| Median (IQR) | 16.34 (5.89-45.87) | 11.36 (5.95-28.85) | 0.184 | 362 | 26 |
| Range | 0.54-646.47 | 0.88-60.71 | | | |
| CA (total) | | | | | |
| Median (IQR) | 2.12 (0.76-10.54) | 1.18 (0.37-5.82) | 0.020 | 362 | 26 |
| Range | 0.04-224.36 | 0.30-24.40 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.07 (0.03-0.23) | 0.04 (0.02-0.08) | 0.034 | 362 | 26 |
| Range | 0.00-10.65 | 0.01-0.50 | | | |
| GCA | | | | | |
| Median (IQR) | 1.70 (0.46-6.41) | 0.92 (0.26-2.66) | 0.064 | 362 | 26 |
| Range | 0.01-165.50 | 0.06-13.69 | | | |
| TCA | | | | | |
| Median (IQR) | 0.27 (0.07-2.57) | 0.12 (0.03-0.44) | 0.040 | 362 | 26 |
| Range | 0.00-58.57 | 0.00-4.92 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 4.09 (1.69-10.26) | 3.35 (1.19-5.82) | 0.114 | 362 | 26 |
| Range | 0.10-268.56 | 0.30-24.40 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.15 (0.05-0.46) | 0.13 (0.07-0.38) | 0.773 | 362 | 26 |
| Range | 0.00-14.78 | 0.02-1.67 | | | |
| GCDCA | | | | | |
| Median (IQR) | 2.87 (1.10-7.18) | 2.06 (0.86-4.46) | 0.183 | 362 | 26 |
| Range | 0.02-214.48 | 0.18-19.54 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.49 (0.13-2.25) | 0.33 (0.07-0.94) | 0.117 | 362 | 26 |
| Range | 0.00-52.46 | 0.02-8.04 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.65 (0.03-1.73) | 0.64 (0.01-1.71) | 0.565 | 362 | 26 |
| Range | 0.00-24.36 | 0.00-5.98 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.09 (0.01-0.41) | 0.30 (0.00-0.44) | 0.545 | 362 | 26 |
| Range | 0.00-5.99 | 0.00-1.23 | | | |

| | large duct PSC | small duct PSC | p-value | LD (n) | SD (n) |
|----------------------------|-------------------|-------------------|---------|--------|--------|
| GDCA | | | | | |
| Median (IQR) | 0.28 (0.02-0.93) | 0.23 (0.01-1.02) | 0.605 | 362 | 26 |
| Range | 0.00-15.49 | 0.00-4.76 | | | |
| TDCA | | | | | |
| Median (IQR) | 0.06 (0.00-0.29) | 0.04 (0.00-0.12) | 0.160 | 362 | 26 |
| Range | 0.00-8.55 | 0.00-0.59 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.04 (0.00-0.15) | 0.04 (0.00-0.13) | 0.752 | 362 | 26 |
| Range | 0.00-2.85 | 0.00-0.60 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.06) | 0.666 | 362 | 26 |
| Range | 0.00-0.96 | 0.00-0.23 | | | |
| GLCA | | | | | |
| Median (IQR) | 0.02 (0.00-0.09) | 0.01 (0.00-0.07) | 0.686 | 362 | 26 |
| Range | 0.00-2.14 | 0.00-0.33 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.00 (0.00-0.01) | 0.300 | 362 | 26 |
| Range | 0.00-0.56 | 0.00-0.15 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.04) | 0.668 | 362 | 26 |
| Range | 0.00-0.73 | 0.00-0.12 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.01 (0.00-0.03) | 0.310 | 362 | 26 |
| Range | 0.00-0.24 | 0.00-0.08 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.555 | 362 | 26 |
| Range | 0.00-0.73 | 0.00-0.04 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.176 | 362 | 26 |
| Range | 0.00-0.07 | 0.00-0.00 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 1.80 (0.17-18.69) | 3.56 (0.23-11.21) | 0.954 | 362 | 26 |
| Range | 0.00-537.71 | 0.02-52.22 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.15 (0.01-2.03) | 0.51 (0.01-1.49) | 0.792 | 362 | 26 |
| Range | 0.00-52.33 | 0.00-5.84 | | | |
| GUDCA | | | | | |
| Median (IQR) | 1.41 (0.11-13.86) | 2.62 (0.19-9.51) | 0.869 | 362 | 26 |
| Range | 0.00-472.47 | 0.01-44.53 | | | |

| | large duct PSC | small duct PSC | p-value | LD (n) | SD (n) |
|-------------------------------|-------------------|--------------------|---------|--------|--------|
| TUDCA | | | | | |
| Median (IQR) | 0.08 (0.01-0.53) | 0.10 (0.00-0.29) | 0.498 | 362 | 26 |
| Range | 0.00-51.06 | 0.00-2.61 | | | |
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.91 (0.74-0.98) | 0.87 (0.74-0.93) | 0.317 | 362 | 26 |
| Range | 0.13-1.00 | 0.51-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.97 (0.84-0.99) | 0.95 (0.88-0.99) | 0.811 | 362 | 26 |
| Range | 0.09-1.00 | 0.37-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.96 (0.83-0.99) | 0.91 (0.81-0.98) | 0.164 | 362 | 26 |
| Range | 0.12-1.00 | 0.45-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.81 (0.54-0.96) | 0.63 (0.42-0.83) | 0.049 | 313 | 20 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.75 (0.57-0.88) | 0.62 (0.47-0.79) | 0.041 | 258 | 18 |
| Range | 0.00-1.00 | 0.25-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.25 (0.00-0.55) | 0.00 (0.00-0.31) | 0.072 | 205 | 18 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.90 (0.75-0.97) | 0.88 (0.80-0.96) | 0.864 | 354 | 26 |
| Range | 0.00-1.00 | 0.50-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 8.26 (3.39-17.30) | 10.64 (5.99-17.69) | 0.133 | 361 | 26 |
| Range | 0.37-93.11 | 2.07-69.38 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 5.53 (2.64-9.00) | 6.00 (4.17-10.56) | 0.105 | 356 | 25 |
| Range | 0.27-70.33 | 2.08-14.00 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 5.68 (2.77-10.33) | 6.79 (4.58-10.42) | 0.301 | 361 | 26 |
| Range | 0.36-92.17 | 2.02-31.00 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 4.69 (2.08-8.20) | 8.06 (4.13-10.67) | 0.036 | 265 | 17 |
| Range | 0.22-44.50 | 1.83-45.00 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 3.00 (1.45-6.00) | 3.86 (1.40-7.00) | 0.583 | 153 | 9 |
| Range | 0.10-36.00 | 1.00-14.00 | | | |

| | large duct PSC | small duct PSC | p-value | LD (n) | SD (n) |
|-------------------------------|--------------------|---------------------|---------|--------|--------|
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.33 (1.00-2.25) | NA | NA | 11 | 0 |
| Range | 0.71-11.00 | NA | | | |
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 17.44 (7.00-34.58) | 29.78 (19.47-44.73) | 0.019 | 299 | 19 |
| Range | 0.14-145.00 | 5.91-101.14 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.19 (0.09-0.37) | 0.12 (0.06-0.28) | 0.054 | 362 | 26 |
| Range | 0.00-0.79 | 0.02-0.62 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.27 (0.15-0.45) | 0.26 (0.14-0.47) | 0.780 | 362 | 26 |
| Range | 0.04-0.88 | 0.05-0.93 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.03 (0.00-0.14) | 0.08 (0.00-0.13) | 0.828 | 362 | 26 |
| Range | 0.00-0.64 | 0.00-0.39 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.01 (0.00-0.01) | 0.421 | 362 | 26 |
| Range | 0.00-0.12 | 0.00-0.04 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.232 | 362 | 26 |
| Range | 0.00-0.05 | 0.00-0.03 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.17 (0.02-0.66) | 0.53 (0.04-0.66) | 0.417 | 362 | 26 |
| Range | 0.00-0.91 | 0.00-0.86 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.63 (0.35-1.15) | 0.48 (0.30-0.64) | 0.044 | 362 | 26 |
| Range | 0.05-5.26 | 0.07-2.31 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 2.72 (0.81-27.51) | 0.80 (0.38-4.20) | 0.030 | 313 | 20 |
| Range | 0.09-3796.67 | 0.16-520.00 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 1.88 (0.22-14.22) | 0.41 (0.22-9.28) | 0.504 | 354 | 26 |
| Range | 0.04-1310.00 | 0.07-375.67 | | | |
| Bile acid / UDCA group | | | 0.245 | 342 | 23 |
| NN | 128 (37.4%) | 8 (34.8%) | | | |
| NY | 52 (15.2%) | 7 (30.4%) | | | |
| HN | 58 (17.0%) | 2 (8.7%) | | | |
| HY | 104 (30.4%) | 6 (26.1%) | | | |

Supplementary Table 14. Univariate time to event (hepatic decompensation) analyses.

| Parameter | HR (95% CI) | p-value | c-stat | n |
|---------------------------------------|---------------------|----------------|---------------|----------|
| Age (per 10 years) | 1.50 (1.24-1.83) | <0.001 | 0.69 | 400 |
| Male sex | 0.75 (0.43-1.30) | 0.302 | 0.52 | 400 |
| IBD type (vs. No IBD) | | | | 347 |
| Indeterminate IBD | 0.75 (0.21-2.70) | 0.66 | 0.53 | |
| Crohn's Disease (CD) | 0.25 (0.03-1.96) | 0.19 | 0.53 | |
| Ulcerative colitis (UC) | 0.78 (0.39-1.57) | 0.49 | 0.53 | |
| PSC subtypes (vs. non-subtype) | | | | 400 |
| Cirrhotic | 5.29 (3.02-9.25) | <0.001 | 0.66 | |
| Small duct disease | 0.24 (0.03-1.75) | 0.16 | 0.53 | |
| AIH overlap | 2.94 (1.17-7.40) | 0.02 | 0.53 | |
| Total bile acids | | | | |
| Total | 1.15 (1.11-1.18) | <0.001 | 0.80 | 400 |
| Total (excluding UDCA) | 1.15 (1.11-1.19) | <0.001 | 0.80 | 400 |
| Conjugated fraction | 10.90 (3.47-34.24) | <0.001 | 0.72 | 400 |
| G:T conjugation ratio | 0.47 (0.30-0.72) | <0.001 | 0.69 | 399 |
| CA | | | | |
| Total | 1.06 (1.04-1.08) | <0.001 | 0.80 | 400 |
| Unconjugated | 0.98 (0.90-1.06) | 0.60 | 0.56 | 400 |
| GCA | 1.05 (1.03-1.07) | <0.001 | 0.79 | 400 |
| TCA | 1.03 (1.02-1.03) | <0.001 | 0.82 | 400 |
| Conjugated fraction | 42.27 (5.09-351.22) | <0.001 | 0.77 | 400 |
| G:T conjugation ratio | 0.30 (0.17-0.53) | <0.001 | 0.72 | 393 |
| Fraction of bile acid pool | 1.31 (1.04-1.65) | 0.02 | 0.55 | 400 |
| CDCA | | | | |
| Total | 1.16 (1.11-1.20) | <0.001 | 0.80 | 400 |
| Unconjugated | 0.98 (0.87-1.11) | 0.75 | 0.53 | 400 |
| GCDCA | 1.13 (1.09-1.16) | <0.001 | 0.78 | 400 |
| TCDCA | 1.09 (1.07-1.11) | <0.001 | 0.83 | 400 |
| Conjugated fraction | 12.68 (3.30-48.76) | <0.001 | 0.75 | 400 |
| G:T conjugation ratio | 0.20 (0.10-0.39) | <0.001 | 0.74 | 399 |
| Fraction of bile acid pool | 0.74 (0.50-1.11) | 0.14 | 0.54 | 400 |
| DCA | | | | |
| Total | 1.02 (0.91-1.15) | 0.71 | 0.56 | 400 |
| Unconjugated | 0.71 (0.48-1.06) | 0.09 | 0.56 | 400 |
| GDCA | 1.02 (0.94-1.11) | 0.58 | 0.56 | 400 |
| TDCA | 1.03 (0.99-1.07) | 0.18 | 0.70 | 400 |
| Conjugated fraction | 7.35 (3.04-17.73) | <0.001 | 0.71 | 345 |
| G:T conjugation ratio | 0.24 (0.12-0.45) | <0.001 | 0.74 | 292 |
| Fraction of bile acid pool | 0.08 (0.02-0.39) | <0.001 | 0.61 | 400 |

| Parameter | HR (95% CI) | p-value | c-stat | n |
|--|-------------------|---------|--------|-----|
| LCA | | | | |
| Total | 1.12 (1.07-1.17) | <0.001 | 0.66 | 400 |
| Unconjugated | 1.12 (1.08-1.15) | <0.001 | 0.62 | 400 |
| GLCA | 1.06 (1.02-1.10) | 0.01 | 0.62 | 400 |
| TLCA | 1.05 (1.03-1.08) | <0.001 | 0.75 | 400 |
| Conjugated fraction | 1.08 (0.71-1.65) | 0.70 | 0.53 | 286 |
| G:T conjugation ratio | 0.55 (0.33-0.91) | 0.02 | 0.65 | 169 |
| Fraction of bile acid pool | 1.00 (0.65-1.53) | 0.99 | 0.49 | 400 |
| HDCA | | | | |
| Total | 0.98 (0.75-1.29) | 0.90 | 0.52 | 400 |
| Unconjugated | 1.06 (0.83-1.36) | 0.65 | 0.49 | 400 |
| GHCA | 0.94 (0.80-1.11) | 0.47 | 0.52 | 400 |
| THCA | na (0.00-na) | Na | na | 400 |
| Conjugated fraction | 0.81 (0.46-1.42) | 0.46 | 0.52 | 231 |
| G:T conjugation ratio | na (0.00-na) | Na | na | 12 |
| Fraction of bile acid pool | 0.17 (0.04-0.76) | 0.02 | 0.59 | 400 |
| UDCA | | | | |
| Total | 1.04 (1.03-1.06) | <0.001 | 0.66 | 400 |
| Unconjugated | 1.05 (1.02-1.08) | <0.001 | 0.57 | 400 |
| GUDCA | 1.04 (1.02-1.05) | <0.001 | 0.65 | 400 |
| TUDCA | 1.02 (1.01-1.02) | <0.001 | 0.75 | 400 |
| Conjugated fraction | 4.18 (1.97-8.87) | <0.001 | 0.66 | 392 |
| G:T conjugation ratio | 0.30 (0.17-0.54) | <0.001 | 0.72 | 330 |
| Fraction of bile acid pool | 1.22 (0.81-1.83) | 0.34 | 0.50 | 400 |
| High total BA (>17.79 μmol/L) | 8.00 (3.60-17.77) | <0.001 | 0.72 | 400 |
| UDCA treatment (predicted) | 1.65 (0.94-2.90) | 0.08 | 0.57 | 376 |
| CA:CDCA Ratio | 1.19 (1.05-1.35) | 0.01 | 0.62 | 400 |
| CA:DCA Ratio | 1.00 (1.00-1.00) | 0.67 | 0.71 | 345 |
| Bilirubin (total) | 1.15 (1.09-1.21) | <0.001 | 0.77 | 370 |
| Alkaline phosphatase (AP) | | | | |
| AP x ULN (upper limit of normal) | 1.21 (1.10-1.33) | <0.001 | 0.70 | 375 |
| AP > 1.0 x ULN | 7.93 (2.47-25.51) | <0.001 | 0.65 | 375 |
| AP > 1.5 x ULN | 2.81 (1.51-5.23) | 0.001 | 0.64 | 375 |

Supplementary Table 15. Univariate event rate (hepatic decompensation) by quartiles analyses.

| Parameter | Quartile of parameter value | | | |
|----------------------------|-----------------------------|-------|-------|-------|
| | Q1 | Q2 | Q3 | Q4 |
| Total bile acids | | | | |
| Total | 3.18 | 4.42 | 14.56 | 45.51 |
| Total (excluding UDCA) | 1.07 | 9.56 | 12.35 | 45.75 |
| Conjugated fraction | 3.20 | 11.79 | 15.32 | 31.71 |
| G:T conjugation ratio | 26.13 | 15.83 | 14.48 | 4.29 |
| CA | | | | |
| Total | 1.05 | 3.27 | 21.90 | 40.81 |
| Unconjugated | 17.71 | 17.58 | 13.66 | 10.89 |
| GCA | 1.04 | 5.59 | 20.26 | 38.52 |
| TCA | 0.00 | 4.43 | 18.42 | 44.10 |
| Conjugated fraction | 2.05 | 8.18 | 15.19 | 41.70 |
| G:T conjugation ratio | 37.62 | 13.21 | 8.24 | 3.35 |
| Fraction of bile acid pool | 10.26 | 17.94 | 11.83 | 19.66 |
| CDCA | | | | |
| Total | 4.21 | 7.55 | 9.99 | 47.97 |
| Unconjugated | 20.91 | 9.83 | 17.19 | 12.34 |
| GCDCA | 3.12 | 9.83 | 14.88 | 38.55 |
| TCDCA | 0.00 | 7.52 | 13.81 | 48.07 |
| Conjugated fraction | 0.00 | 14.13 | 14.85 | 34.74 |
| G:T conjugation ratio | 34.84 | 20.37 | 4.31 | 3.30 |
| Fraction of bile acid pool | 16.40 | 17.64 | 16.50 | 9.23 |
| DCA | | | | |
| Total | 4.44 | 18.72 | 23.18 | 14.15 |
| Unconjugated | 11.47 | 30.51 | 8.68 | 11.40 |
| GDCA | 5.61 | 18.67 | 21.63 | 14.22 |
| TDCA | 2.21 | 5.38 | 25.99 | 29.62 |
| Conjugated fraction | 3.38 | 14.82 | 35.28 | 9.36 |
| G:T conjugation ratio | 36.66 | 17.59 | 4.43 | 3.42 |
| Fraction of bile acid pool | 8.11 | 37.57 | 14.33 | 2.27 |
| LCA | | | | |
| Total | 5.53 | 13.34 | 13.41 | 28.74 |
| Unconjugated | 10.80 | 12.59 | 11.28 | 25.80 |
| GLCA | 8.04 | 11.84 | 15.13 | 25.52 |
| TLCA | 1.06 | 8.21 | 10.36 | 44.74 |
| Conjugated fraction | 19.95 | 15.60 | 19.56 | 5.43 |
| G:T conjugation ratio | 38.75 | 18.80 | 3.35 | 2.22 |
| Fraction of bile acid pool | 4.39 | 30.18 | 15.04 | 12.42 |
| HDCA | | | | |
| Total | 11.03 | 20.91 | 11.53 | 16.72 |
| Unconjugated | 11.09 | 16.61 | 19.70 | 12.55 |
| GHCA | 14.84 | 5.29 | 28.01 | 12.79 |

| Parameter | Quartile of parameter value | | | |
|----------------------------|-----------------------------|-------|-------|-------|
| | Q1 | Q2 | Q3 | Q4 |
| HDCA (cont.) | | | | |
| THDCA | 13.26 | 18.92 | 6.87 | 21.08 |
| Conjugated fraction | 15.01 | 16.07 | 5.83 | 23.05 |
| G:T conjugation ratio | 29.81 | 25.55 | 5.58 | 3.08 |
| Fraction of bile acid pool | 6.72 | 31.92 | 15.32 | 7.79 |
| UDCA | | | | |
| Total | 11.91 | 10.76 | 6.51 | 33.66 |
| Unconjugated | 19.19 | 4.68 | 11.36 | 24.87 |
| GUDCA | 15.53 | 8.07 | 3.25 | 36.78 |
| TUDCA | 4.16 | 10.69 | 11.48 | 37.41 |
| Conjugated fraction | 3.11 | 12.29 | 24.77 | 21.43 |
| G:T conjugation ratio | 34.27 | 21.17 | 5.64 | 3.07 |
| Fraction of bile acid pool | 21.46 | 4.50 | 19.11 | 15.12 |
| CA:CDCA Ratio | 6.85 | 9.69 | 16.79 | 26.52 |
| CA:DCA Ratio | 2.24 | 14.33 | 36.40 | 9.37 |

Event rate calculated as Number of Events / Person Years

Supplementary Table 16. Variables and relative influence on GBM Model

| Variable | Relative Influence | Influence direction[#] |
|----------------------------|---------------------------|--|
| Age (per decade) | 14.684 | Increase |
| TUDCA | 14.475 | Increase |
| TCDCA | 12.421 | Increase |
| TLCA | 8.865 | Increase |
| TCA | 8.603 | Increase |
| TBA | 4.234 | Increase |
| DCA (fraction of BA pool) | 3.606 | Decrease |
| GDCA | 3.023 | Decrease |
| CDCA (total) | 2.890 | Increase |
| LCA (total) | 2.462 | Increase |
| LCA (conjugated fraction) | 2.198 | Decrease |
| CA (fraction of BA pool) | 1.831 | Increase |
| GCDCA | 1.814 | Increase |
| CA (conjugated fraction) | 1.775 | Increase |
| GUDCA | 1.739 | Increase |
| TDCA | 1.421 | Decrease |
| TBA (conjugated fraction) | 1.386 | Increase |
| CA (total) | 1.356 | Increase |
| DCA (conjugated fraction) | 1.207 | Increase |
| UDCA (fraction of BA pool) | 1.191 | Decrease |
| UDCA (total) | 1.123 | Increase |
| CDCA (conjugated fraction) | 1.086 | Decrease |
| GLCA | 0.947 | Decrease |
| GCA | 0.873 | Decrease |
| UDCA (conjugated fraction) | 0.849 | Increase |
| DCA (total) | 0.787 | Decrease |
| LCA (fraction of BA pool) | 0.659 | Increase |
| CDCA (unconjugated) | 0.576 | Increase |
| UDCA (unconjugated) | 0.451 | Decrease |
| HDCA (unconjugated) | 0.426 | Increase |
| CDCA (fraction of BA pool) | 0.361 | Decrease |
| CA (unconjugated) | 0.144 | Decrease |
| HDCA (fraction of BA pool) | 0.121 | Decrease |
| HDCA (total) | 0.102 | Increase |
| Male sex | 0.100 | Decrease |
| DCA (unconjugated) | 0.070 | Decrease |
| GHDCa | 0.038 | Increase |
| HDCA (conjugated fraction) | 0.000 | Decrease |
| THDCA | 0.000 | Decrease |
| UDCA use (calculated) | 0.000 | Increase |

Increase or decreased risk of hepatic decompensation with increase in value of variable based on visualization of functional form plots. For instance, increased TUDCA concentration increased risk in the model whereas increased GDCA concentration lowered the risk.

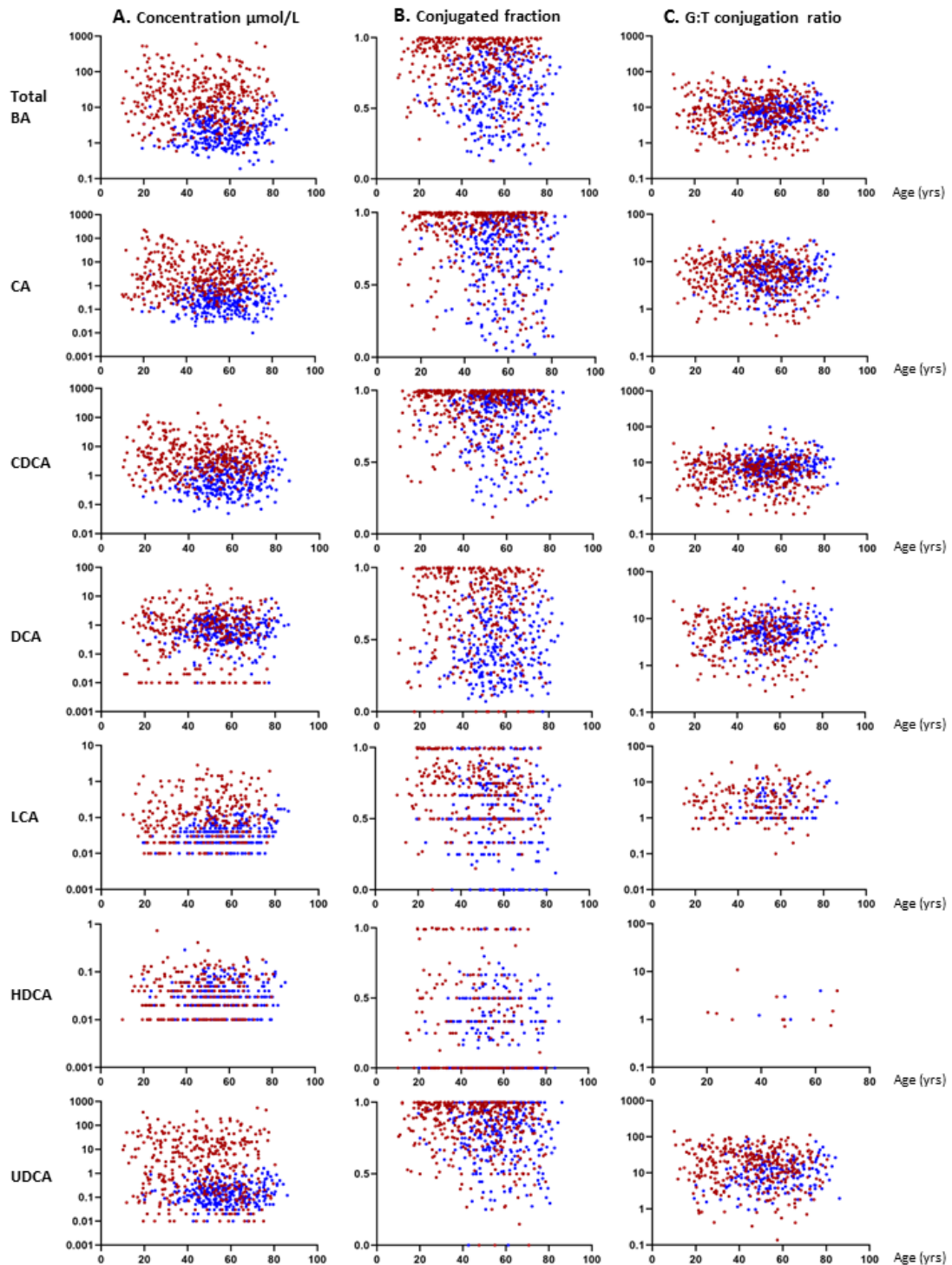
Supplementary Table 17. Bile acids in PSC patients: Derivation and Validation cohorts.

| | PSC (derivation) | PSC (validation) | p-value | PSC Der (n) | PSC Val (n) |
|----------------------------|--------------------|--------------------|---------|-------------|-------------|
| Total BA | | | | | |
| Median (IQR) | 16.34 (6.04-44.31) | 14.31 (5.12-59.30) | 0.895 | 400 | 108 |
| Range | 0.54-646.47 | 0.74-457.45 | | | |
| CA (total) | | | | | |
| Median (IQR) | 2.09 (0.73-10.01) | 3.01 (1.26-20.19) | 0.019 | 400 | 108 |
| Range | 0.04-224.36 | 0.15-251.95 | | | |
| CA (unconjugated) | | | | | |
| Median (IQR) | 0.06 (0.03-0.22) | 0.04 (0.02-0.09) | 0.003 | 400 | 108 |
| Range | 0.00-10.65 | 0.00-3.92 | | | |
| GCA | | | | | |
| Median (IQR) | 1.60 (0.44-6.12) | 2.03 (0.98-15.33) | 0.010 | 400 | 108 |
| Range | 0.01-165.50 | 0.11-192.78 | | | |
| TCA | | | | | |
| Median (IQR) | 0.25 (0.06-2.44) | 0.42 (0.14-6.64) | 0.003 | 400 | 108 |
| Range | 0.00-58.61 | 0.01-149.57 | | | |
| CDCA (total) | | | | | |
| Median (IQR) | 4.09 (1.61-9.81) | 4.30 (1.86-12.04) | 0.482 | 400 | 108 |
| Range | 0.10-268.56 | 0.31-125.26 | | | |
| CDCA (unconjugated) | | | | | |
| Median (IQR) | 0.15 (0.05-0.46) | 0.07 (0.02-0.20) | <0.001 | 400 | 108 |
| Range | 0.00-14.78 | 0.01-5.13 | | | |
| GCDCA | | | | | |
| Median (IQR) | 2.87 (1.10-6.90) | 2.77 (1.30-7.63) | 0.672 | 400 | 108 |
| Range | 0.02-214.48 | 0.19-87.38 | | | |
| TCDCA | | | | | |
| Median (IQR) | 0.47 (0.13-2.12) | 0.92 (0.30-3.98) | 0.003 | 400 | 108 |
| Range | 0.00-52.46 | 0.02-67.72 | | | |
| DCA (total) | | | | | |
| Median (IQR) | 0.66 (0.03-1.76) | 0.61 (0.16-1.79) | 0.702 | 400 | 108 |
| Range | 0.00-24.36 | 0.00-20.69 | | | |
| DCA (unconjugated) | | | | | |
| Median (IQR) | 0.10 (0.01-0.44) | 0.05 (0.00-0.16) | 0.025 | 400 | 108 |
| Range | 0.00-5.99 | 0.00-2.96 | | | |
| GDCA | | | | | |
| Median (IQR) | 0.28 (0.02-0.96) | 0.38 (0.10-1.13) | 0.158 | 400 | 108 |
| Range | 0.00-15.49 | 0.00-16.97 | | | |

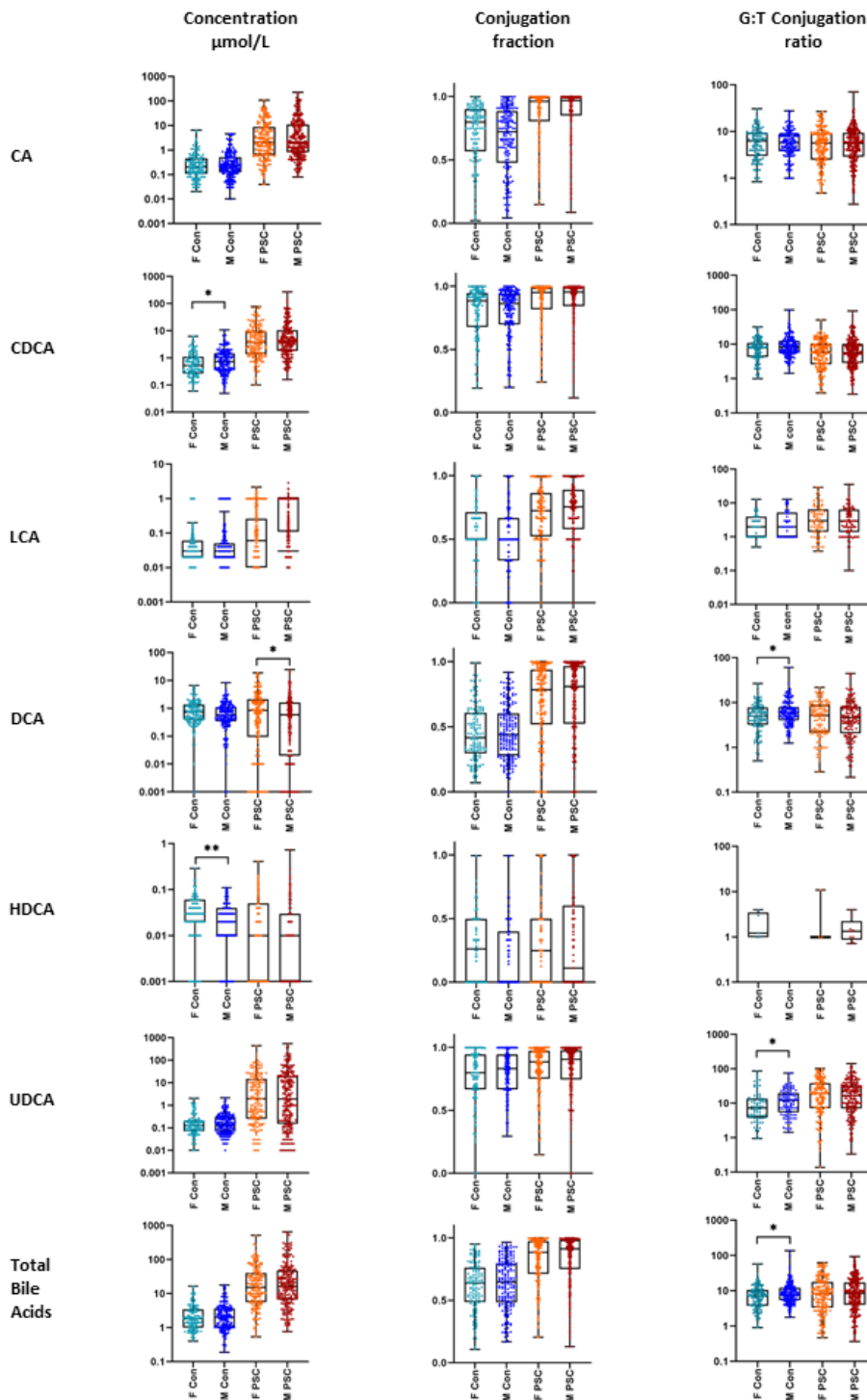
| | PSC (derivation) | PSC (validation) | p-value | PSC Der (n) | PSC Val (n) |
|----------------------------|-------------------|-------------------|---------|-------------|-------------|
| TDCA | | | | | |
| Median (IQR) | 0.06 (0.00-0.27) | 0.07 (0.01-0.25) | 0.266 | 400 | 108 |
| Range | 0.00-8.55 | 0.00-3.71 | | | |
| LCA (total) | | | | | |
| Median (IQR) | 0.04 (0.00-0.15) | 0.02 (0.00-0.05) | 0.010 | 400 | 108 |
| Range | 0.00-2.85 | 0.00-1.82 | | | |
| LCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.02) | 0.043 | 400 | 108 |
| Range | 0.00-0.96 | 0.00-0.23) | | | |
| GLCA | | | | | |
| Median (IQR) | 0.02 (0.00-0.09) | 0.00 (0.00-0.00) | <0.001 | 400 | 108 |
| Range | 0.00-2.14 | 0.00-1.38 | | | |
| TLCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.02) | 0.01 (0.00-0.02) | 0.037 | 400 | 108 |
| Range | 0.00-0.56) | 0.00-0.26 | | | |
| HDCA (total) | | | | | |
| Median (IQR) | 0.01 (0.00-0.04) | 0.01 (0.00-0.03) | 0.117 | 400 | 108 |
| Range | 0.00-0.73 | 0.00-0.18 | | | |
| HDCA (unconjugated) | | | | | |
| Median (IQR) | 0.01 (0.00-0.02) | 0.00 (0.00-0.02) | 0.063 | 400 | 108 |
| Range | 0.00-0.24 | 0.00-0.16 | | | |
| GHDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.004 | 400 | 108 |
| Range | 0.00-0.73 | 0.00-0.09 | | | |
| THDCA | | | | | |
| Median (IQR) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.065 | 400 | 108 |
| Range | 0.00-0.07 | 0.00-0.10 | | | |
| UDCA (total) | | | | | |
| Median (IQR) | 1.95 (0.19-18.27) | 0.36 (0.09-10.56) | 0.039 | 400 | 108 |
| Range | 0.00-537.71 | 0.00-308.01 | | | |
| UDCA (unconjugated) | | | | | |
| Median (IQR) | 0.17 (0.01-2.02) | 0.05 (0.00-0.53) | <0.001 | 400 | 108 |
| Range | 0.00-52.33 | 0.00-17.16 | | | |
| GUDCA | | | | | |
| Median (IQR) | 1.53 (0.12-13.52) | 0.27 (0.06-9.42) | 0.063 | 400 | 108 |
| Range | 0.00-472.47 | 0.00-278.90 | | | |
| TUDCA | | | | | |
| Median (IQR) | 0.09 (0.01-0.52) | 0.06 (0.01-0.60) | 0.428 | 400 | 108 |
| Range | 0.00-51.06 | 0.00-44.90 | | | |

| | PSC (derivation) | PSC (validation) | p-value | PSC Der (n) | PSC Val (n) |
|-------------------------------|-------------------------|-------------------------|----------------|--------------------|--------------------|
| Total BA (conj. frac.) | | | | | |
| Median (IQR) | 0.91 (0.74-0.98) | 0.95 (0.88-0.99) | <0.001 | 400 | 108 |
| Range | 0.13-1.00 | 0.23-1.00 | | | |
| CA (conj. frac.) | | | | | |
| Median (IQR) | 0.97 (0.85-0.99) | 0.98 (0.94-1.00) | <0.001 | 400 | 108 |
| Range | 0.09-1.00 | 0.185-1.00 | | | |
| CDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.95 (0.83-0.99) | 0.98 (0.92-1.00) | <0.001 | 400 | 108 |
| Range | 0.12-1.00 | 0.23-1.00 | | | |
| DCA (conj. frac.) | | | | | |
| Median (IQR) | 0.80 (0.52-0.95) | 0.92 (0.74-0.98) | <0.001 | 345 | 95 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| LCA (conj. frac.) | | | | | |
| Median (IQR) | 0.75 (0.56-0.87) | 0.71 (0.40-0.88) | 0.069 | 286 | 77 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| HDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.22 (0.00-0.55) | 0.00 (0.00-0.48) | 0.134 | 231 | 55 |
| Range | 0.00-1.00 | 0.00-1.00 | | | |
| UDCA (conj. frac.) | | | | | |
| Median (IQR) | 0.90 (0.75-0.97) | 0.95 (0.86-1.00) | <0.001 | 392 | 105 |
| Range | 0.00-1.00 | 0.23-1.00 | | | |
| Total BA (G:T ratio) | | | | | |
| Median (IQR) | 8.36 (3.57-17.44) | 4.70 (2.55-8.21) | <0.001 | 399 | 108 |
| Range | 0.37-93.11 | 0.45-57.86 | | | |
| CA (G:T ratio) | | | | | |
| Median (IQR) | 5.56 (2.72-9.23) | 4.71 (2.25-8.07) | 0.038 | 393 | 108 |
| Range | 0.27-70.33 | 0.49-19.00 | | | |
| CDCA (G:T ratio) | | | | | |
| Median (IQR) | 5.76 (2.80-10.30) | 3.24 (1.83-5.53) | <0.001 | 399 | 108 |
| Range | 0.36-92.17 | 0.37-21.00 | | | |
| DCA (G:T ratio) | | | | | |
| Median (IQR) | 4.90 (2.13-8.26) | 4.97 (2.82-9.25) | 0.290 | 292 | 89 |
| Range | 0.22-45.00 | 0.68-30.29 | | | |
| LCA (G:T ratio) | | | | | |
| Median (IQR) | 3.00 (1.40-6.22) | 2.43 (1.00-5.00) | 0.174 | 169 | 23 |
| Range | 0.10-36.00 | 0.50-11.57 | | | |
| HDCA (G:T ratio) | | | | | |
| Median (IQR) | 1.17 (1.00-1.88) | 1.50 (1.50-1.80) | 0.336 | 12 | 5 |
| Range | 0.71-11.00 | 1.00-2.67 | | | |

| | PSC (derivation) | PSC (validation) | p-value | PSC Der (n) | PSC Val (n) |
|-----------------------------|-------------------------|-------------------------|----------------|------------------------|------------------------|
| UDCA (G:T ratio) | | | | | |
| Median (IQR) | 18.40 (7.25-35.75) | 9.26 (4.45-18.00) | <0.001 | 330 | 83 |
| Range | 0.14-145.00 | 0.27-107.33 | | | |
| CA (frac. BA pool) | | | | | |
| Median (IQR) | 0.18 (0.08-0.36) | 0.29 (0.18-0.44) | <0.001 | 400 | 108 |
| Range | 0.01-0.79 | 0.02-0.87 | | | |
| CDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.26 (0.15-0.46) | 0.32 (0.19-0.46) | 0.153 | 400 | 108 |
| Range | 0.04-0.93 | 0.09-0.79 | | | |
| DCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.04 (0.01-0.14) | 0.03 (0.01-0.15) | 0.532 | 400 | 108 |
| Range | 0.00-0.64 | 0.00-0.54 | | | |
| LCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.004 | 400 | 108 |
| Range | 0.00-0.12 | 0.00-0.05 | | | |
| HDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.00 (0.00-0.01) | 0.00 (0.00-0.00) | 0.064 | 400 | 108 |
| Range | 0.00-0.05 | 0.00-0.04 | | | |
| UDCA (frac. BA pool) | | | | | |
| Median (IQR) | 0.18 (0.02-0.66) | 0.05 (0.01-0.47) | <0.001 | 400 | 108 |
| Range | 0.00-0.91 | 0.00-0.84 | | | |
| CA:CDCA ratio | | | | | |
| Median (IQR) | 0.60 (0.35-1.12) | 0.89 (0.49-1.60) | <0.001 | 400 | 108 |
| Range | 0.05-5.26 | 0.13-7.15 | | | |
| CA:DCA ratio | | | | | |
| Median (IQR) | 2.60 (0.79-26.43) | 4.47 (1.38-32.18) | 0.101 | 345 | 95 |
| Range | 0.09-3796.67 | 0.09-1683.67 | | | |
| CDCA:LCA+HDCA+UDCA | | | | | |
| Median (IQR) | 1.57 (0.22-13.81) | 5.93 (0.38-22.31) | 0.002 | 392 | 105 |
| Range | 0.04-1310.00 | 0.12-673.13 | | | |

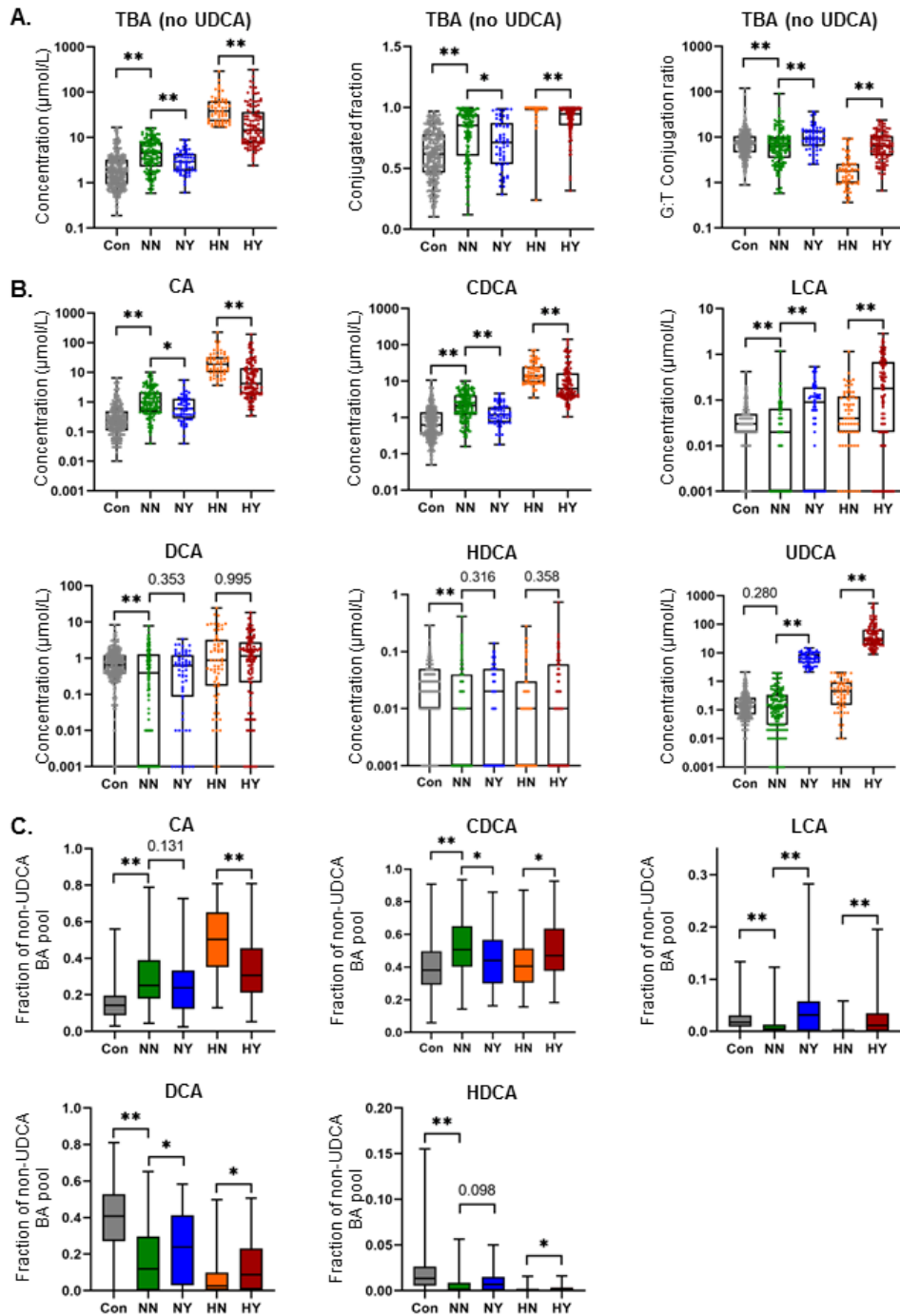
Supplementary Figure 1. Bile acids by age in PSC and controls.**Supplementary Figure 1.** Plots showing bile acid (A) concentration, (B) conjugated fraction and (C) G:T conjugation ratio (Y axis) by age in years (X axis). Red dots indicate PSC patients and blue dots indicate controls.

Supplementary Figure 2. Bile acids by sex in PSC and controls.

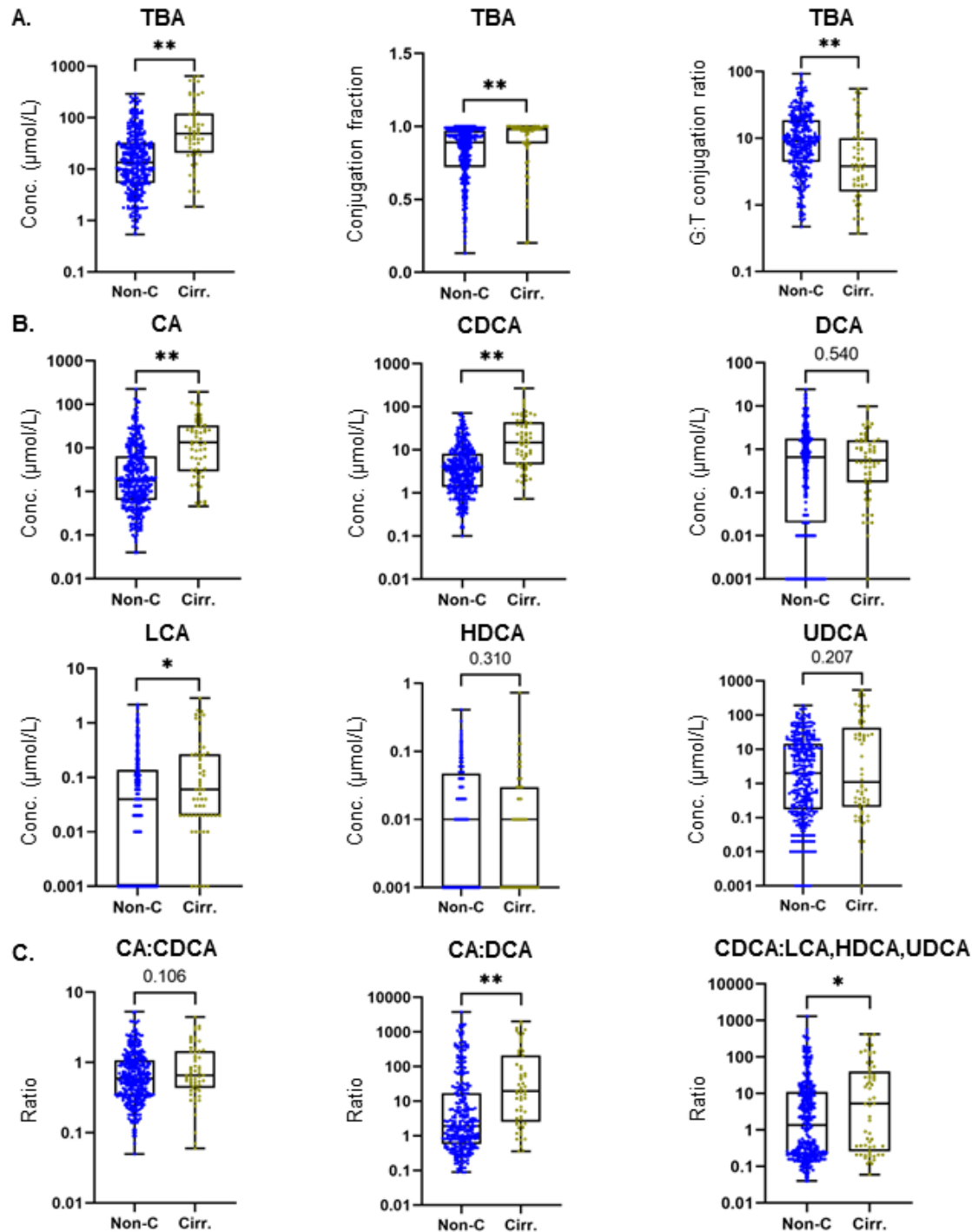


Supplementary Figure 2. Plots showing bile acid (A) concentration, (B) conjugated fraction and (C) G:T conjugation ratio by comparing values in females to males within PSC and control groups. *p<0.05, **p<0.01.

Supplementary Figure 3. Bile acids in controls and PSC patients by bile acid group.



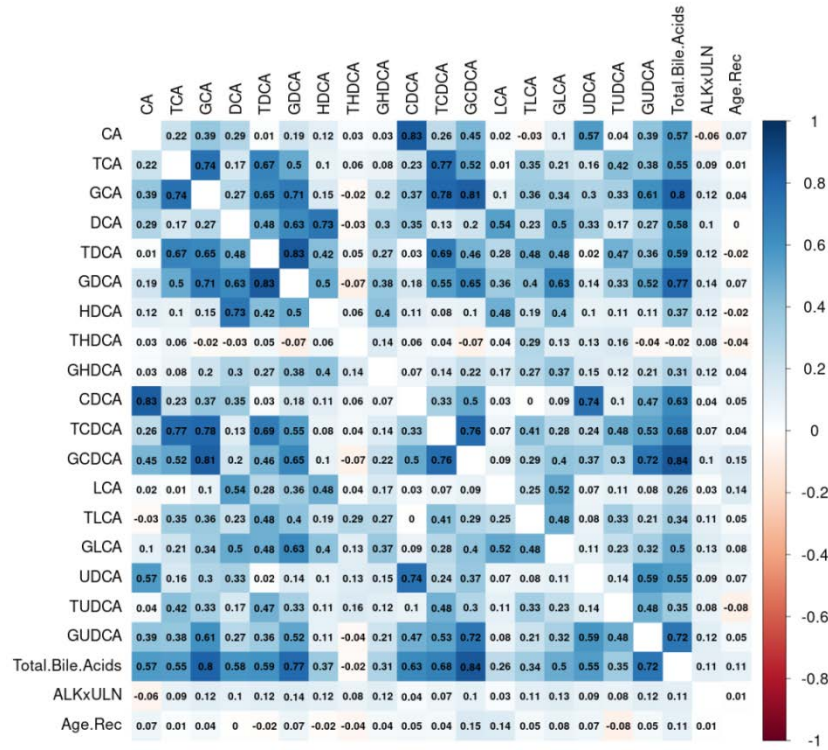
Supplementary Figure 3. Plots showing (A) concentration, conjugation fraction, and G:T conjugation ratio of total bile acids (TBA) with UDCA, GUDCA and TUDCA removed; (B) concentration of bile acid “families” (i.e., the sum of conjugated and unconjugated forms); and (C) bile acid “families” as a fraction of the non-UDCA BA pool in controls (Con) and PSC patients separated by BA group. NN: normal TBA, no UDCA; NY: normal TBA, yes UDCA; HN: high TBA, no UDCA; HY: high TBA, yes UDCA. * $p < 0.05$, ** $p < 0.001$

Supplementary Figure 4. Bile acids in cirrhotic and non-cirrhotic PSC patients

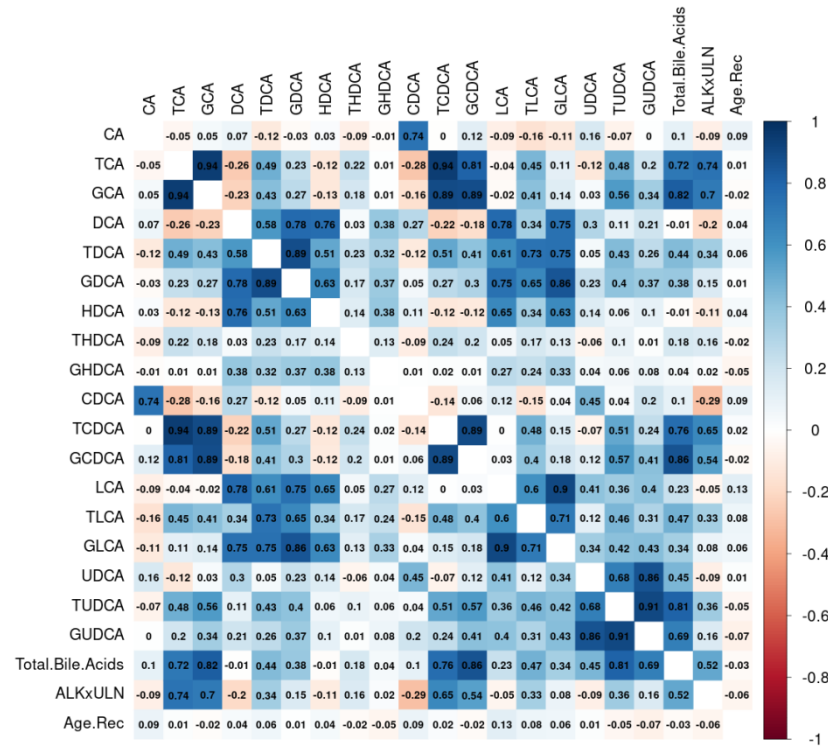
Supplementary Figure 4. Plots showing (A) concentration, conjugation fraction and G:T conjugation ratio of total bile acid (TBA); (B) concentration of bile acid “families” (i.e., total of conjugated and unconjugated forms); and (C) bile acid ratios in PSC patients who were non-cirrhotic (Non-C) or cirrhotic (Cirr.) at time of sample collection. * $p < 0.05$, ** $p < 0.001$

Supplementary Figure 5. BA correlation plots in PSC and controls.

A. Controls



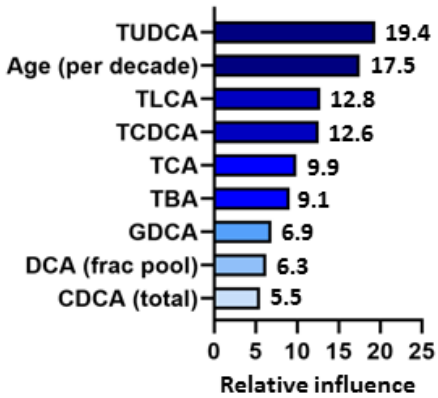
B. PSC



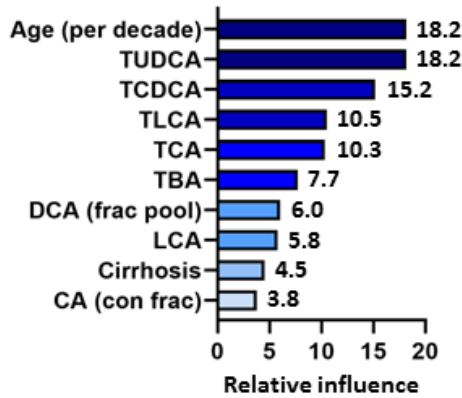
Supplementary Figure 5. Spearman correlation plots of BA concentrations in (A) controls and (B) PSC patients. Dark blue values indicate high correlation whereas red values indicate low correlation.

Supplementary Figure 6. Alternate GBM models using BA profiles

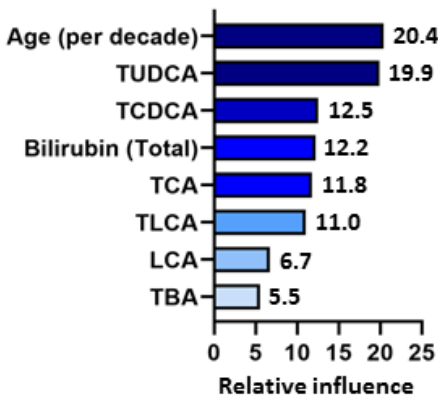
A. Remove SD and AIH patients from GBM model – Concordance = 0.95



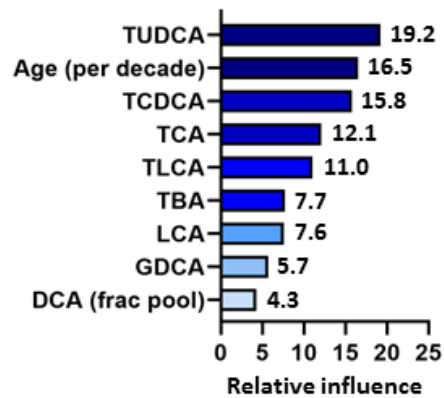
B. Add Cirrhosis phenotype to GBM model – Concordance = 0.95



C. Add Bilirubin (Total) to GBM model Concordance = 0.95



D. Add ALP (times upper limit of normal) to GBM model – Concordance = 0.96



Supplementary Figure 6. Alternate GBM models using BA profiles with (A) PSC patients with small duct (SD) disease and/or having overlapping autoimmune hepatitis (AIH) removed, (B) cirrhosis phenotype (yes/no) added to the model, (C) Bilirubin (total) added to the model, and (D) alkaline phosphatase (ALP) added to the model.