Overall accuracy of a group of clinical markers (but some may not be included in our list)
Single lab parameters predict biopsy results – univariate and multivariate

2) What is the accuracy of laboratory and clinical markers vs liver biopsy for the diagnosis of a) alcoholic liver disease vs other disease b) alcohol related hepatitis vs decompensated cirrhosis [including alcohol-related hepatitis with decompensated cirrhosis vs alcohol-related without decompensated cirrhosis								
Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Thabut D, Naveau S, Charlotte F et al. The diagnostic value of biomarkers (AshTest) for the prediction of alcoholic steato-hepatitis in patients with chronic alcoholic liver disease. *Journal of Hepatology.* 2006; 44(6):1175-1185. Ref ID: 1973	Retrospective case series	N=225 N=70 training group N=62 validation group one N=93 validation group two	Patients with an alcohol intake >50 g/d with available serum and liver biopsy Training group: age at biopsy 54 yrs, male:female 12:31, Maddrey ≥ 32 44%, duration between biopsy and serum, 4.5 days alcoholic hepatitis features: necrosis and polynuclear neutrophils 60%, hepatocellular necrosis 74%, polynuclear neutrophils 61%, Mallory bodies 69%, ballooning 87%; alcoholic hepatitis grade: severe 34%; cirrhosis predicted by biopsy 81%, cirrhosis predicted by FibroTest 77%, steatosis 89%, markers (means): AST 200 IU/L, ALT 101 IU/L, total bilirubin 120 mol/L, GGT 373 U/L, Maddrey discriminant function, 35.4 AST/ALT ratio 2.3 Validation group 1 age at biopsy 54 yrs, male:female 19:17, Maddrey ≥ 32 27%, duration between biopsy and serum 0, alcoholic hepatitis features: necrosis and polynuclear neutrophils 19%, hepatocellular necrosis 25%, polynuclear neutrophils 31%, Mallory bodies 27%, ballooning 31%; alcoholic hepatitis grade: severe 5%; cirrhosis predicted by biopsy 90%, cirrhosis predicted by FibroTest 74%, steatosis 47%, markers: AST 69 IU/L, ALT 49 IU/L, total bilirubin 98 mmol/L, GGT 154 U/L, Maddrey discriminant function 26.9, AST/ALT ratio 2.0 Validation group 2 age at biopsy 47 yrs ,	Liver biopsy			Alcoholic steato-hepatitis (ASH) defined by the presence of both polymorphnucleat neutrophil infiltrate (PMN) and hepatocellular necrosis ASH features: necrosis, PMN, Mallory bodies and ballooning	

			male:female 68:25, Maddrey ≥ 32 5%, duration between biopsy and serum 6.5 days, alcoholic hepatitis features: necrosis and polynuclear neutrophils 24%, hepatocellular necrosis 54%, polynuclear neutrophils 31%, Mallory bodies 26%, ballooning 39%; alcoholic hepatitis grade: severe 17%; cirrhosis predicted by biopsy 25%, cirrhosis predicted by FibroTest 31%, steatosis 96%, markers: AST 100 IU/L, ALT 74 IU/L, total bilirubin 42 mmol/L, GGT 2.0 U/L, Maddrey discriminant function 9.8, AST/ALT ratio 1.7					
847		N=300	Patients with liver disease including: N=52 alcoholic liver disease (N=37 biopsy) N=36 chronic active hepatitis (N=24 biopsy)					
Talley NJ, Roth A, Woods J et al. Diagnostic value of liver biopsy in alcoholic liver disease. *Journal of Clinical Gastroenterology*. 1988; 10(6):647-650.		N=108	Patients with a clinical diagnosis of diffuse liver disease prebiopsy underwent, for the first time, percutaneous liver biopsy Patients were considered to have chronic liver disease if they had two or more of spider nevi, palmar erythema, hepatomegaly, ascites, splenomegaly and testicular atrophy Patient population: prebiopsy diagnosis of alcoholic liver disease N=35, median age 53 yrs, 69% male Prebiopsy non-alcoholic liver disease N=73: median age 49 yrs, male 56%	Percutaneous liver biopsy	Clinical diagnosis Included: Bilirubin, alanine aminotransferase (ALT), aspirate aminotransferase (AST), gamma glutamyltransferase (GGT), serum alkaline phosphatise, albumin	NA	Accuracy	None reported
Effect There was a significant association between the prebiopsy clinical diagnosis of alcoholic liver disease and the diagnosis of alcoholic liver disease at histology ($p<0.01$): 25 patients clinical and biopsy proven diagnosis of alcoholic liver disease (ALD) 5 patients with a clinical diagnosis of non-alcoholic liver disease but a biopsy proven diagnosis of alcoholic liver disease								

A clinical diagnosis of ALD compared with liver histology had a sensitivity of 79% and a specificity of 98%

van Ness M, Diehl AM. Is liver biopsy useful in the evaluation of patients with chronically elevated liver enzymes? *Annals of Internal Medicine.* 1989; 111(6):473. Ref ID 1689		N=90	Patients with elevated liver associated enzymes. Patients with previously undiagnosed liver disease were included if at least one liver-associated enzyme (ASP, ALT, AP, GGT) was elevated to 1.5 times the upper limit of normal for 3 months or more Exclusion criteria: if required laparoscopic biopsy for staging of malignancy or previous biopsy Patient population: male:female 51:39, mean age 46 yrs, mean prothrombin time 11 seconds	Post-biopsy diagnosis Percutaneous liver biopsy Investigator examined biopsies blind to the clinical work The final diagnosis was based on the histological diagnosis plus all other clinical/lab test results	Pre-biopsy (clinical diagnosis Immediately before the biopsy, one investigator reviewed the complete non-invasive work and results of the laboratory tests and imaging studies The complete blood count, platelet count, prothrombin time and partial thromboplastine time were measured within 3 days before the biopsy	NA	Accuracy	US Navy Health Sciences and Education and Training Command Grant

Effect

The accuracy of clinical assessment correlated with the degree of transaminase elevation for all diagnostic groups. Patients with more elevated levels of alanine aminotransferase were more likely to be correctly diagnosed using noninvaive clinical tests alone than those in whom alanine aminotransferase levels were only slightly increased. The PPV of the clinical diagnosis was 58% (N=40; 95%CI 43 to 73%) for patients with alanine aminotransferase values one to 1.5 times the upper limit of normal; 80% (N=30; 95%CI 66 to 96%) for those with alanine aminotransferase values 1.5 to 3 times the upper limit of normal, and 95% (N=20; 95%CI 85 to 100%) for those with alanine transferase levels greater than three time the upper limit of normal.

Results	Final diagnostic group			
	Alcohol (N=23)	Fatty liver (N=27)	Chronic necroinflammatory disease (N=26)	Misc (N=24)
Positive predictive value	88 (95%CI 75 to 100)	56 (37 to 75)	81 (66 to 96)	65 (46 to 84)
Negative predictive value	97 (90 to 100)	90 (79 to 100)	92 (82 to 100)	87 (75 to 100)
Sensitivity	91 (79 to 100)	59 (40 to 78)	81 (66 to 96)	63 (44 to 82)
Specificity	96 (88 to 100)	89 (77 to 100)	92 (82 to 100)	91 (80 to 100)