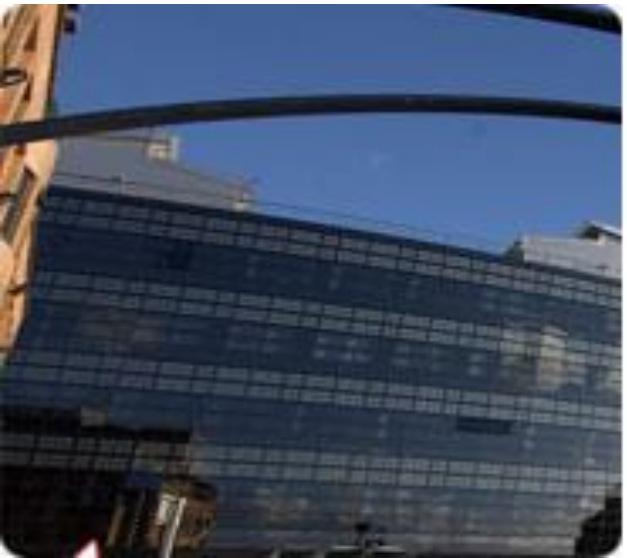
Autoimmune Hepatitis: Defining the need for Liver Transplantation

Michael A Heneghan, MD, MMedSc, FRCPI.

Institute of Liver Studies,

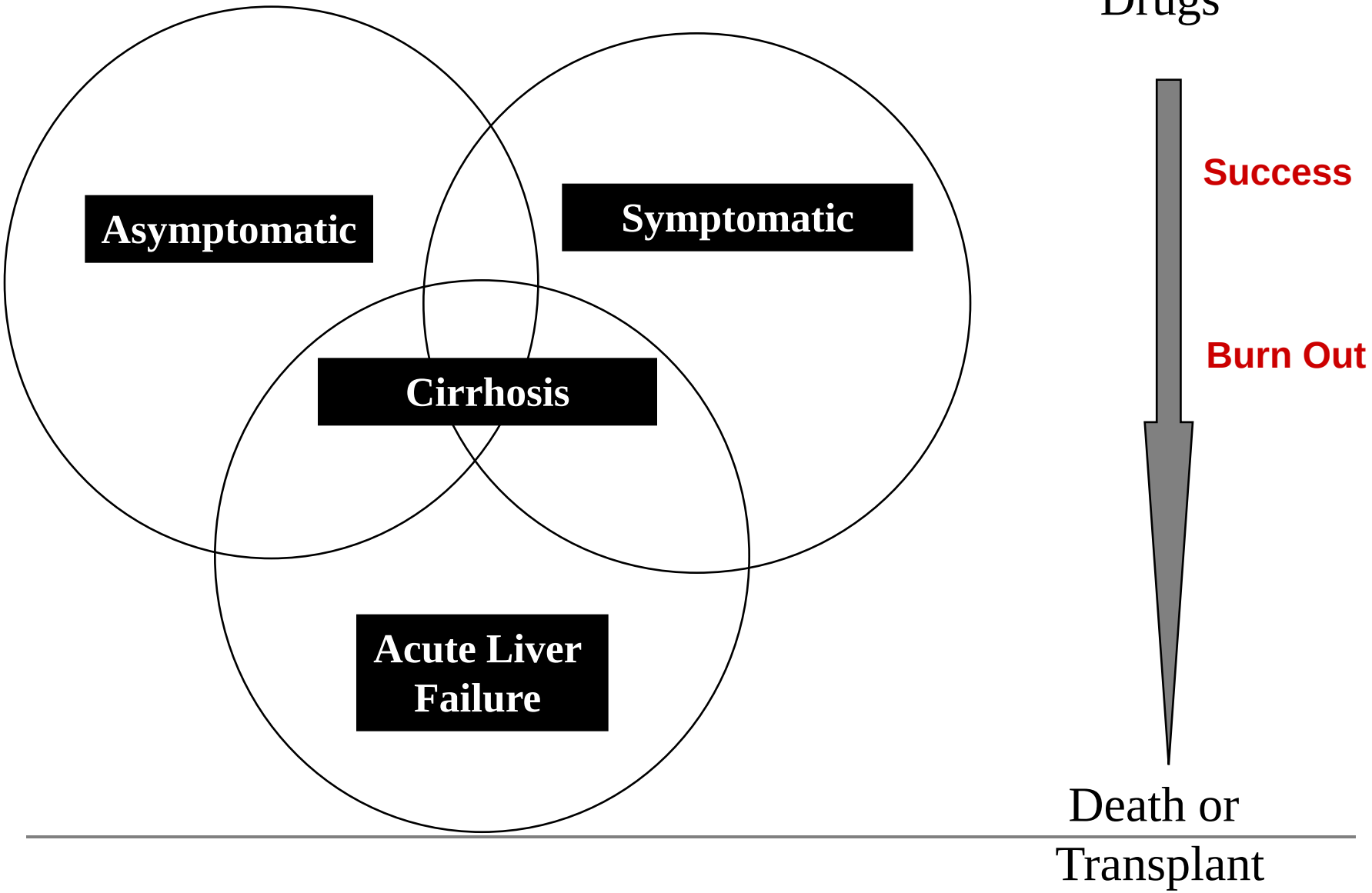
King's College Hospital, London



Outline

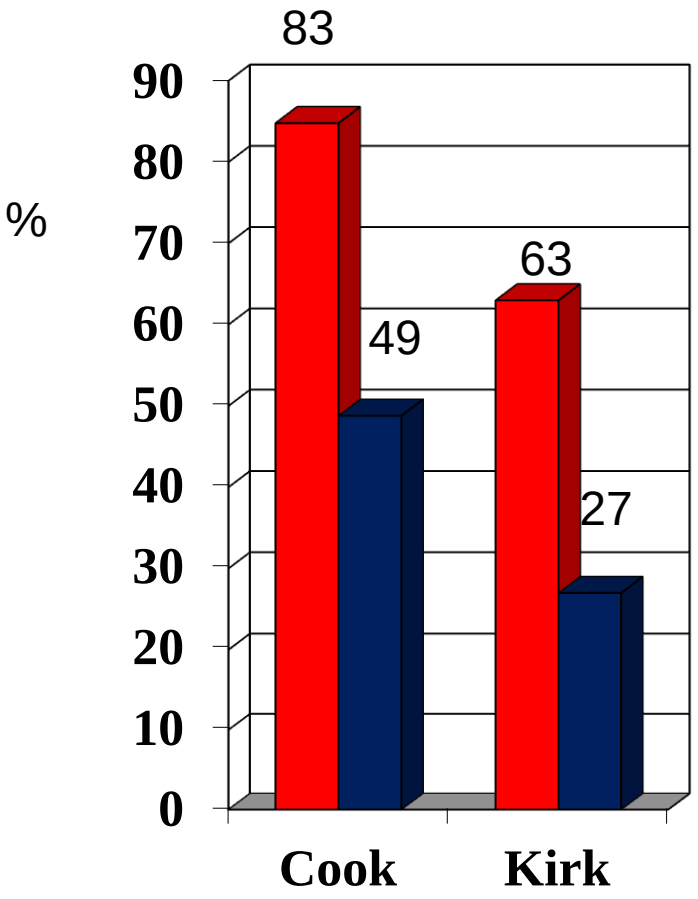
- Autoimmune Hepatitis Background
- Concordance with treatment
- Indications for transplant
  - Standard
  - HCC
- Special situations
  - Acute Severe AIH
- Retransplantation

AIH a Chameleon Disease



Heneghan MA et al. Lancet 2013;282:1433-44.

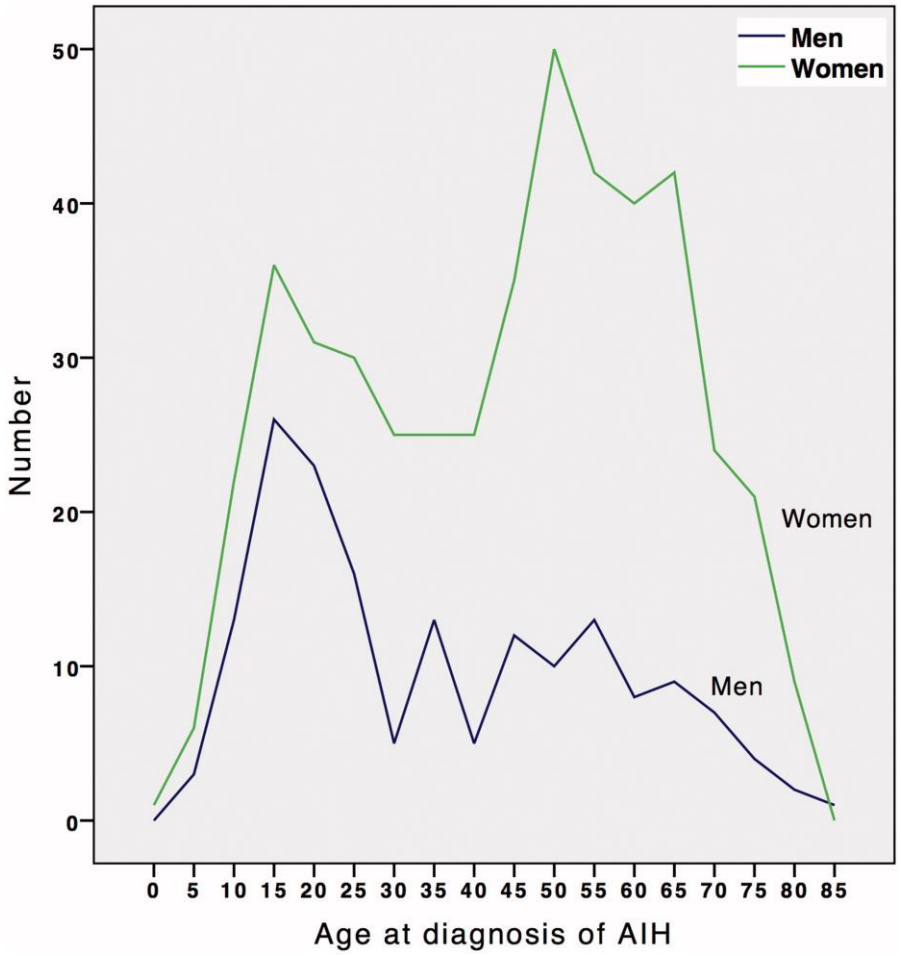
Probability of Survival with Steroid Therapy



Mean time to death
11 months versus 23 months

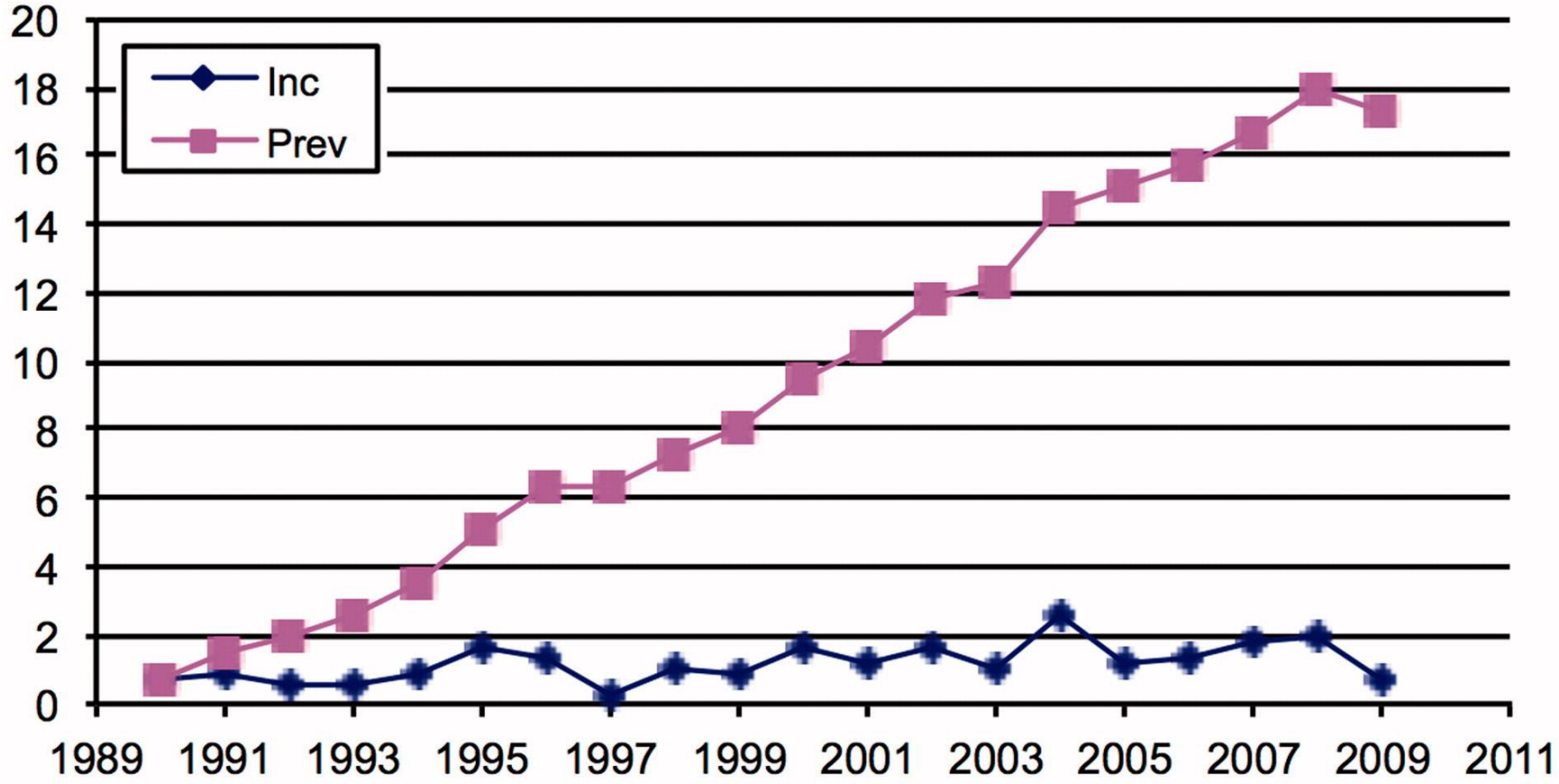
Cook et al. Q J Med 1971;158:159-85
Kirk et al. Gut 1980;21:78-83

Age at diagnosis in AIH: Swedish Registry



Daniellsen Borssen et al. Scand J Gastro 2017:52:1022-28

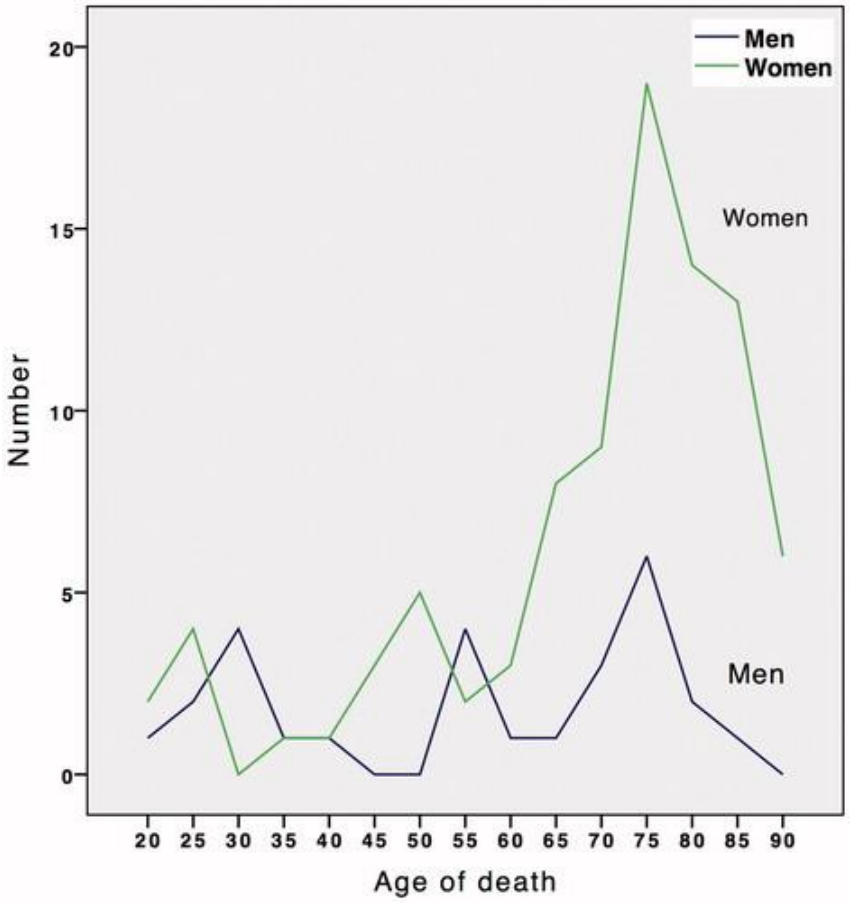
Incidence and Prevalence data 1989-2009

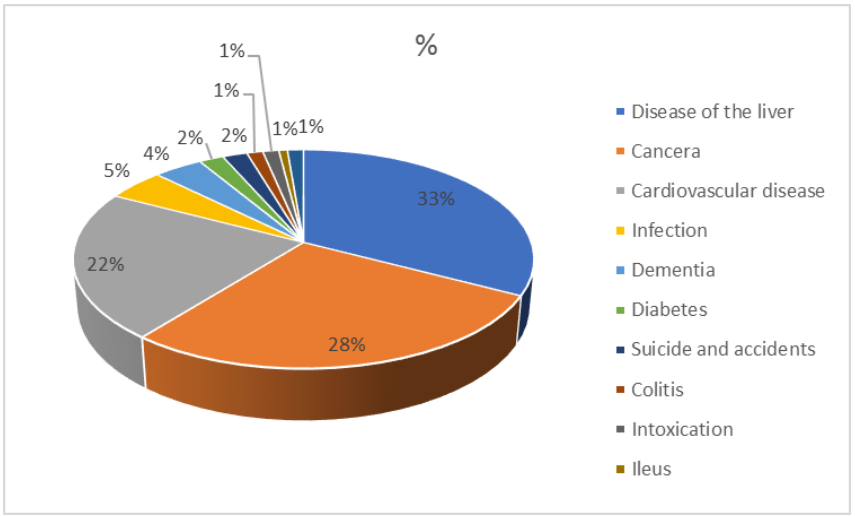


Prevalence of AIH
17.3/100,000 inhabitants in 2009
(22.4/100,000 for women and 11.9/100,000 for men)

Daniellsen Borssen et al. Scand J Gastro 2017:52:1022-28

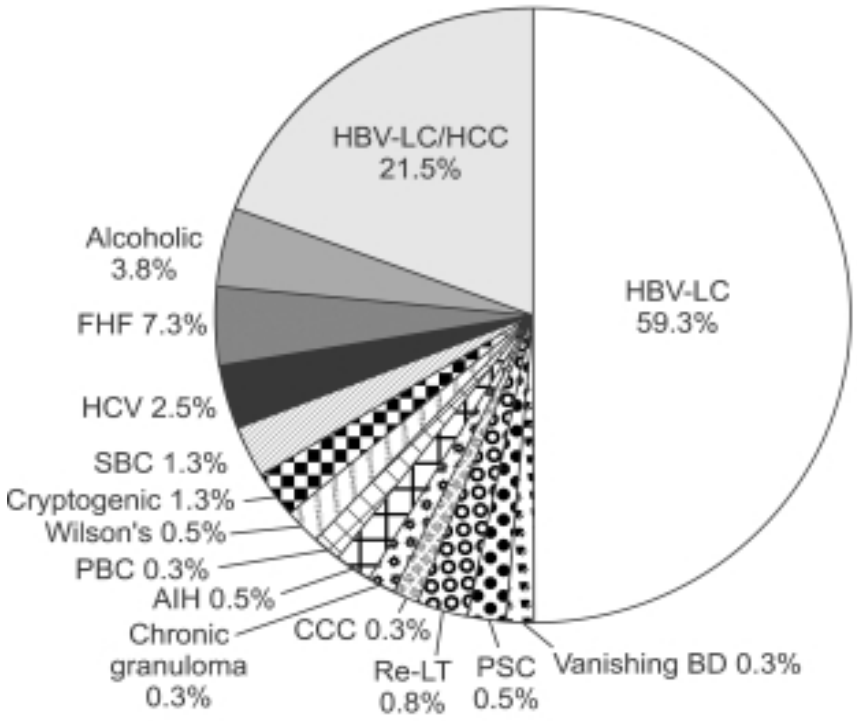
Age and Causes of death in AIH



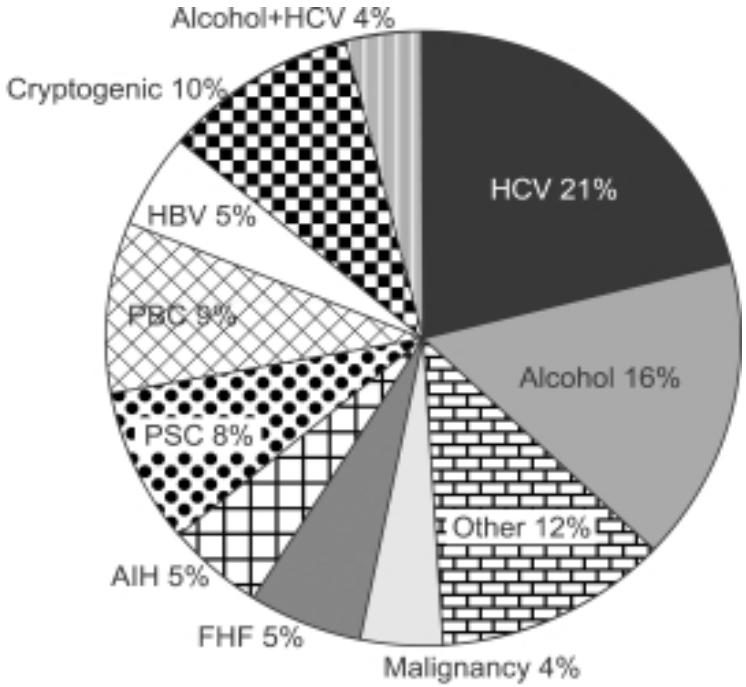


Daniellsen Borssen et al. Scand J Gastro 2017:52:1022-28

AIH as an indication for Transplant



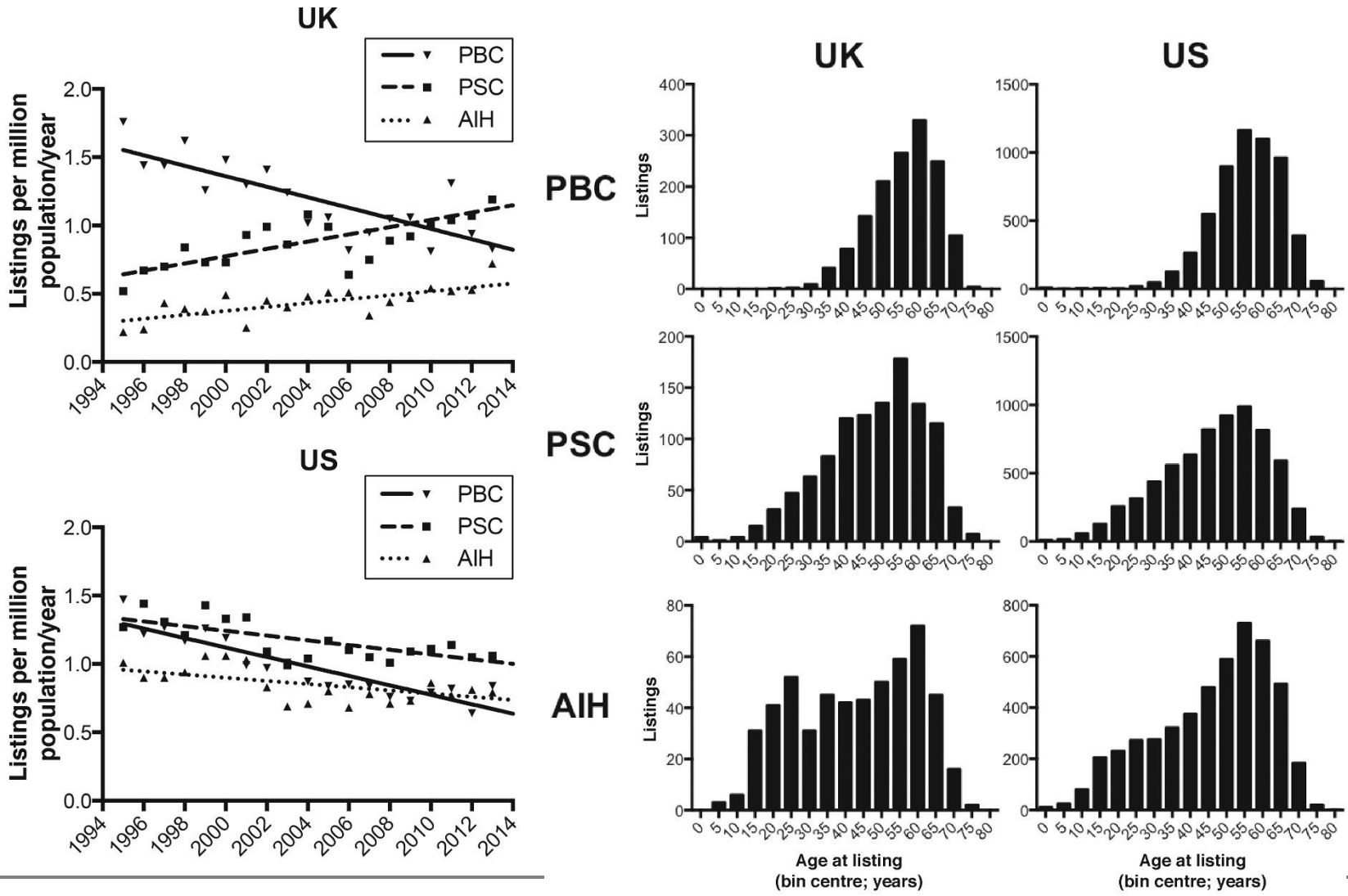
Asan Medical Center



United States

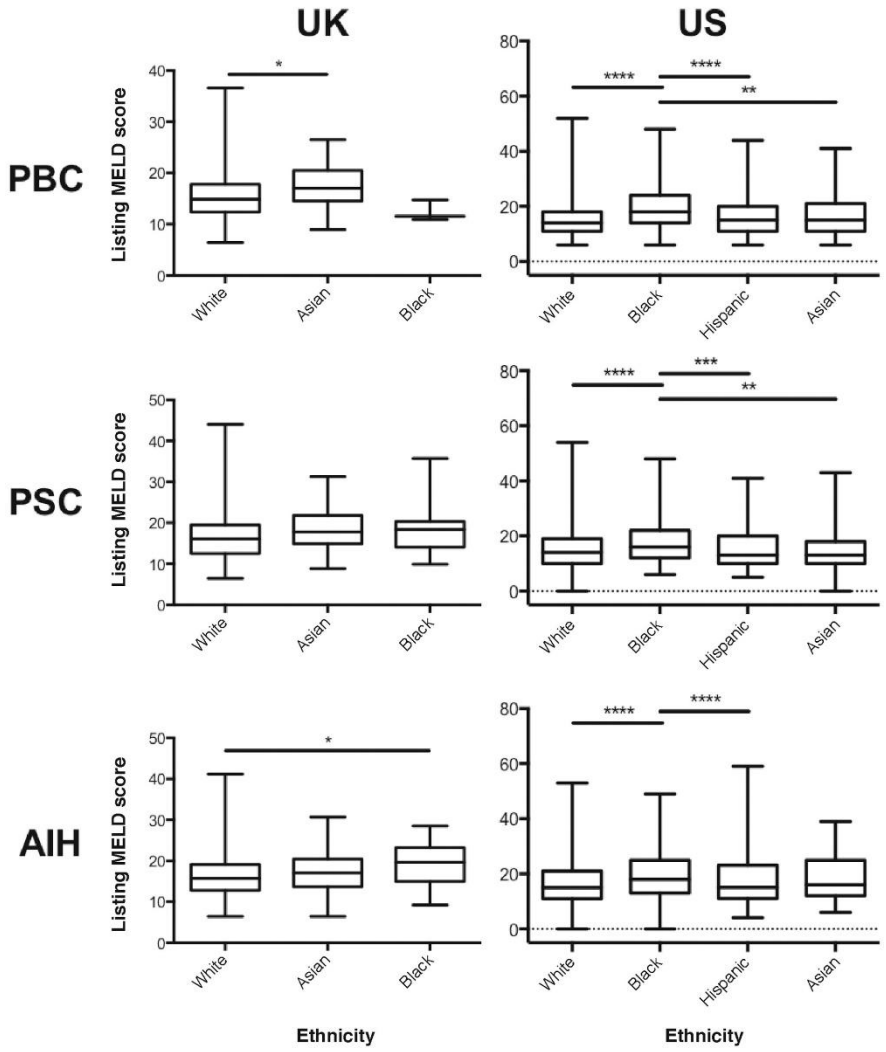
Moon & Lee, Gut & Liver 2009;3:145-65.

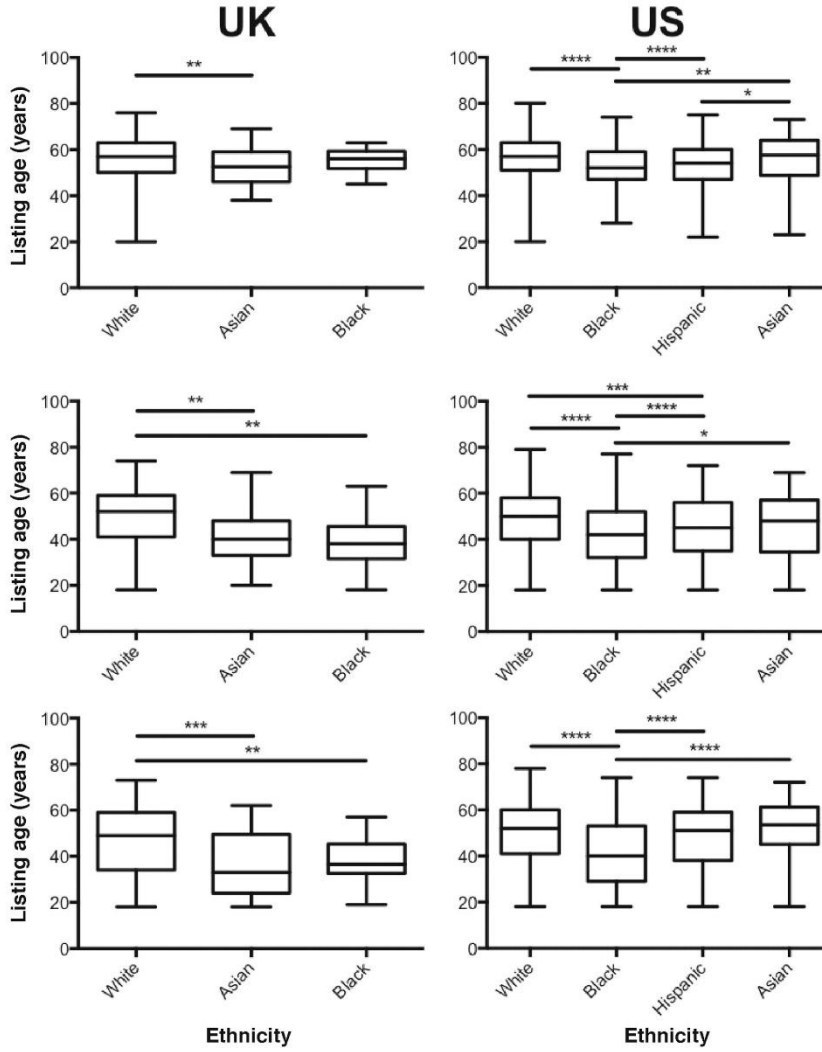
Listing characteristics in AILD: USA v UK



Webb et al. Clin Gastro Hepatology 2018 16, 278-287.

MELD & Age at listing (Ethnic Influence)





Webb et al. Clin Gastro Hepatology 2018 16, 278-287.

Concordance with Therapy

Acne: Important at diagnosis and during treatment

HRQOL Depression, Anxiety in Adult AIH

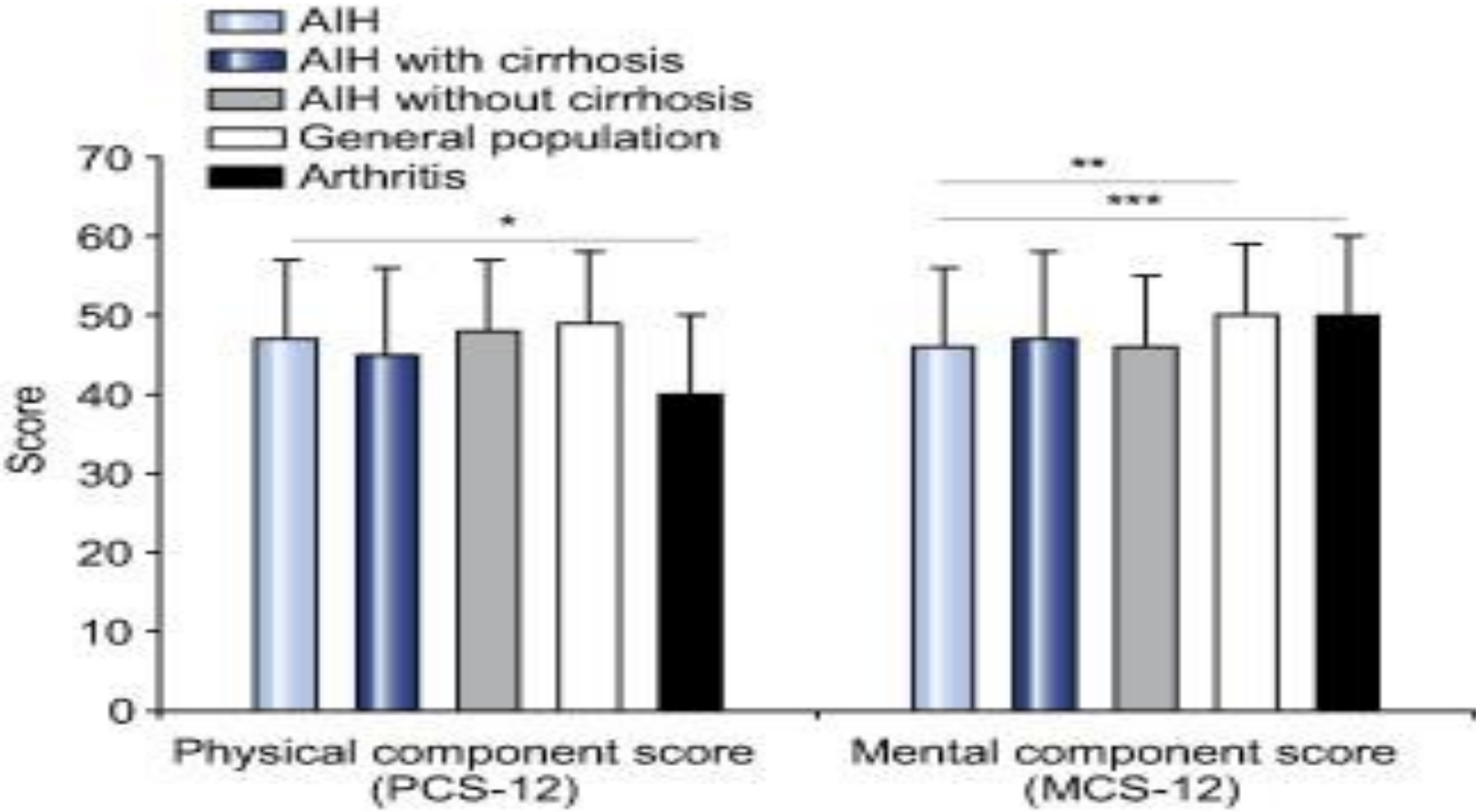
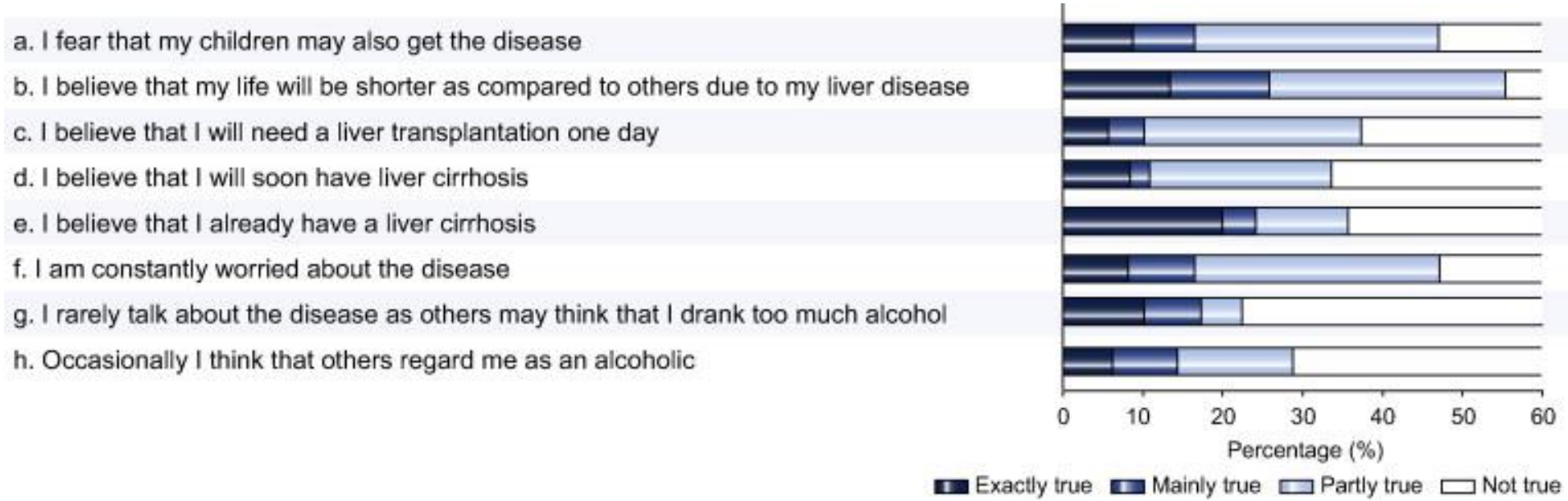


Fig. 1 Health-related quality of life in patients with autoimmune hepatitis. Physical (PCS-12) and mental (MCS-12) component score of patients with AIH, patients with AIH with and without liver cirrhosis, arthritis (n = 695)

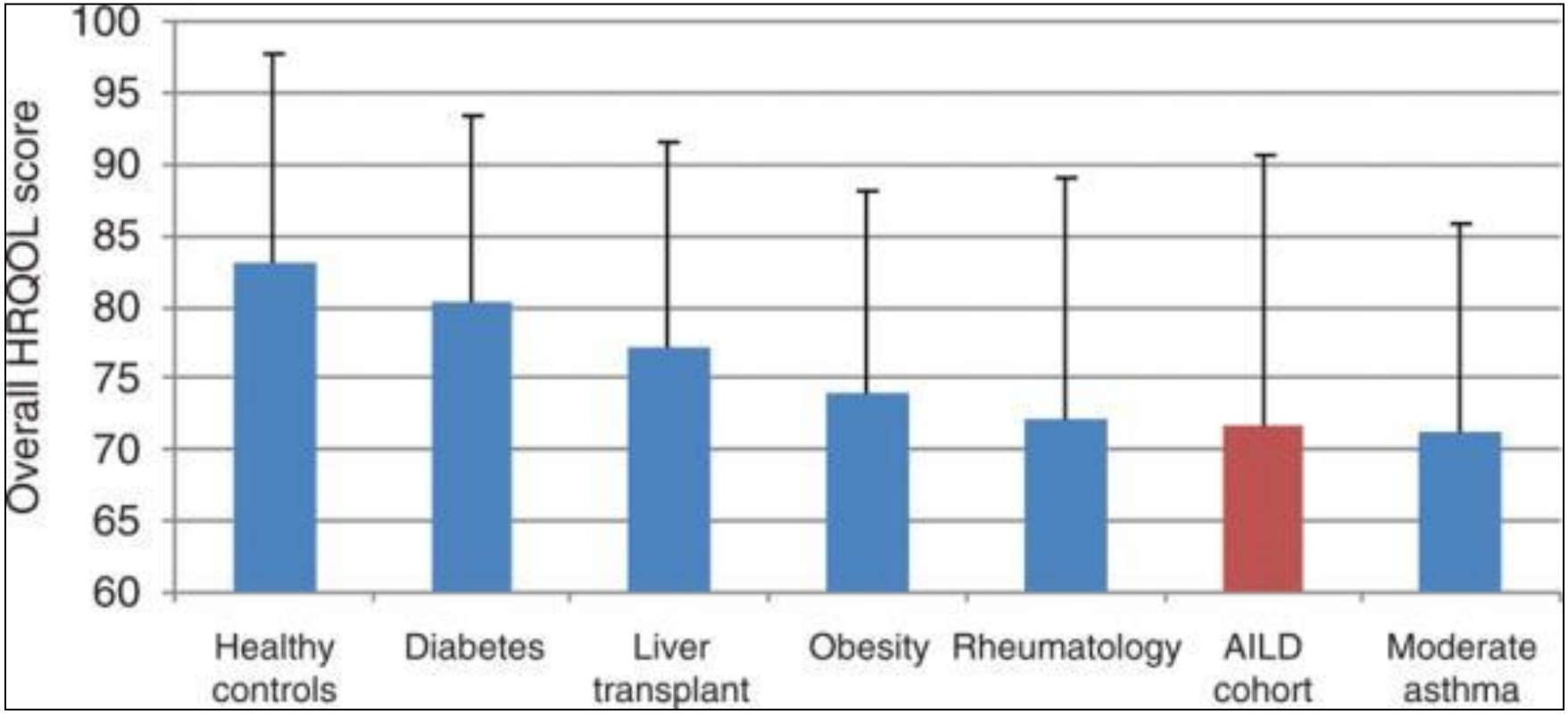
Schramm et al. J Hepatol 2014:60:618-24

Ad-hoc questions in relation to patient fears



Schramm et al. J Hepatol 2014:60:618-24

Quality of Life in Children with AIH



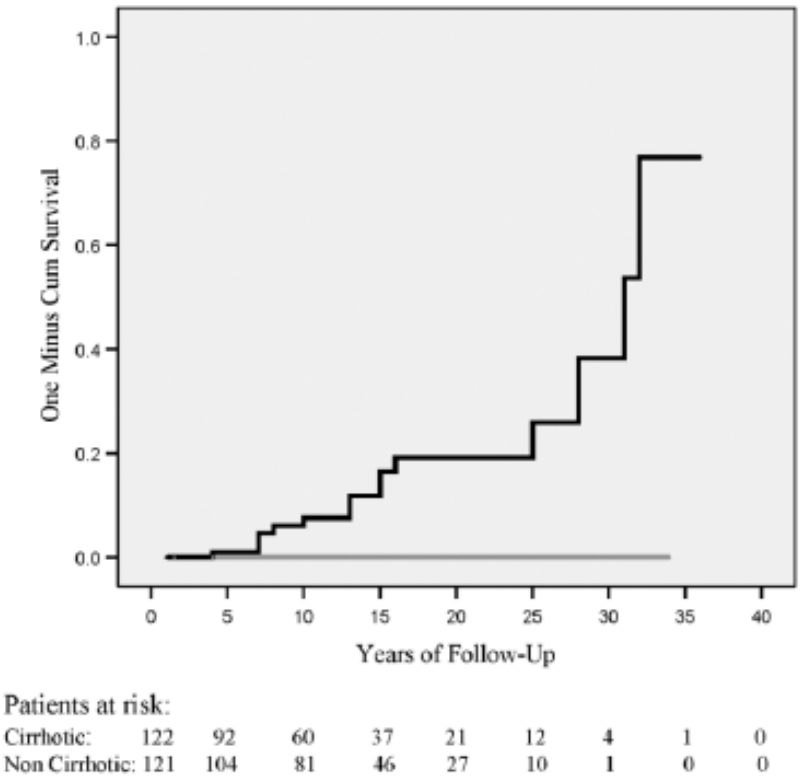
40 Patients:Single-center US based study

Gulati et al. JPGN 2013:57:444-450,

Indications for Transplant

- Standard
- HCC
- Acute/Subacute Liver Failure
- Retransplantation: Disease Recurrence

Risk factors for HCC development in AIH



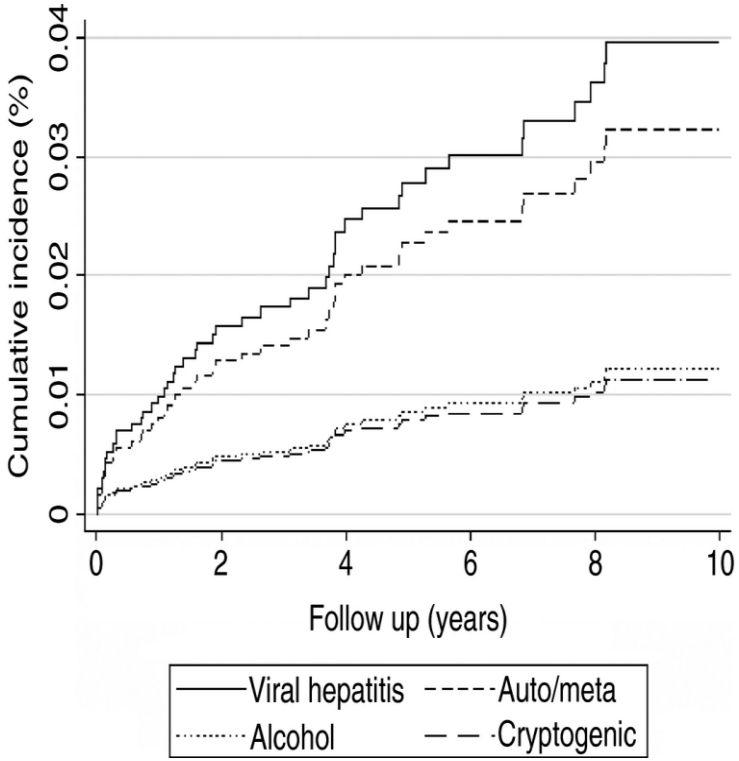
Features At Presentation	Hazard Ratio (CI)	p
Jaundice	**0.26 (0.052-1.32)**	**0.105**
Variceal Bleed	**8.41 (1.75-40.47)**	**0.008**
Cirrhotic	**8.01 (1.64-39.07)**	**0.001**

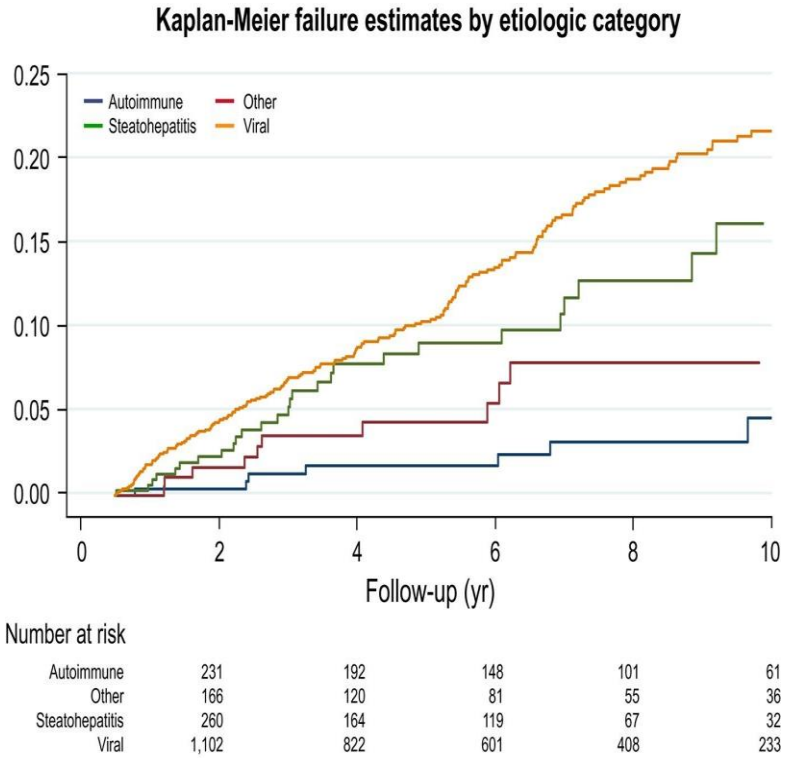
10.9/1000 yrs follow-up
6.2% of all patients
12.3% of cirrhotic
Male = Female

After 9yrs of cirrhosis

Yeoman AD et al. Hepatology 2008

Risk of HCC in different aetiologies of cirrhosis: a population-based cohort study

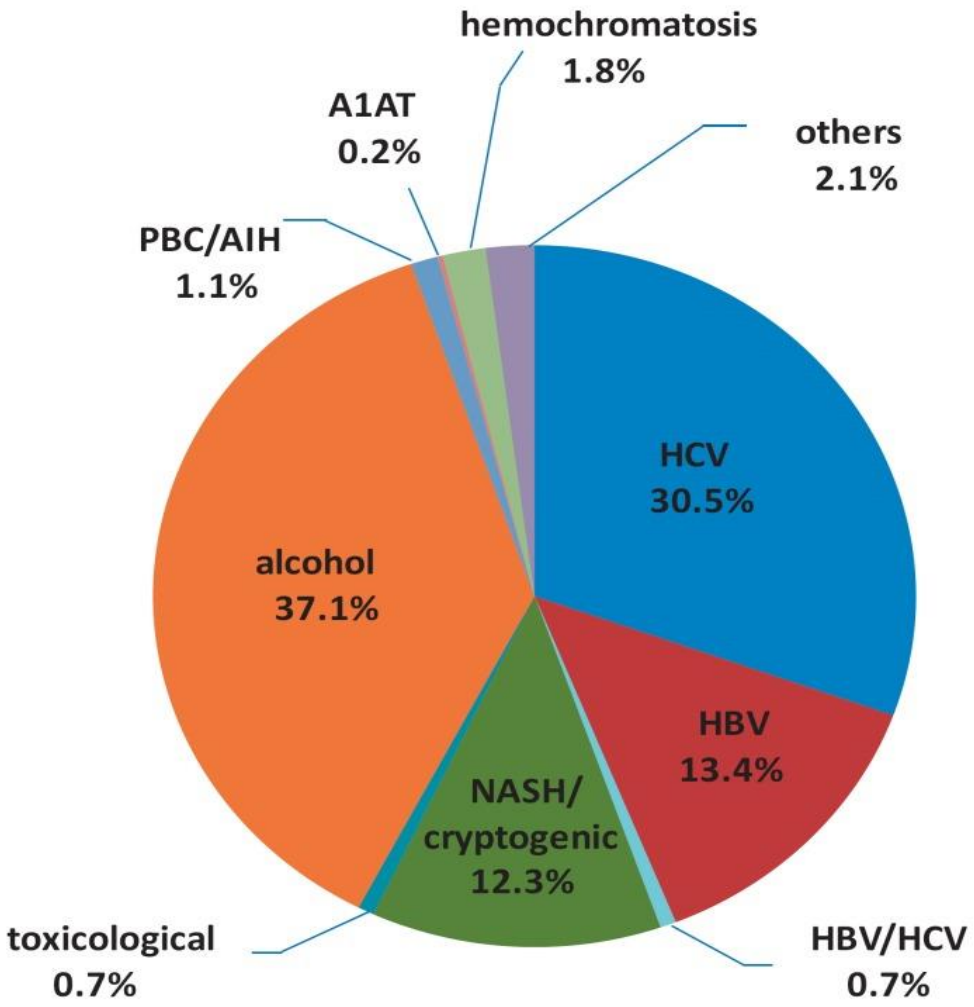




West et al. AP&T 2017;45:983-990.

Sharma et al. J Hep 2017 EPUB

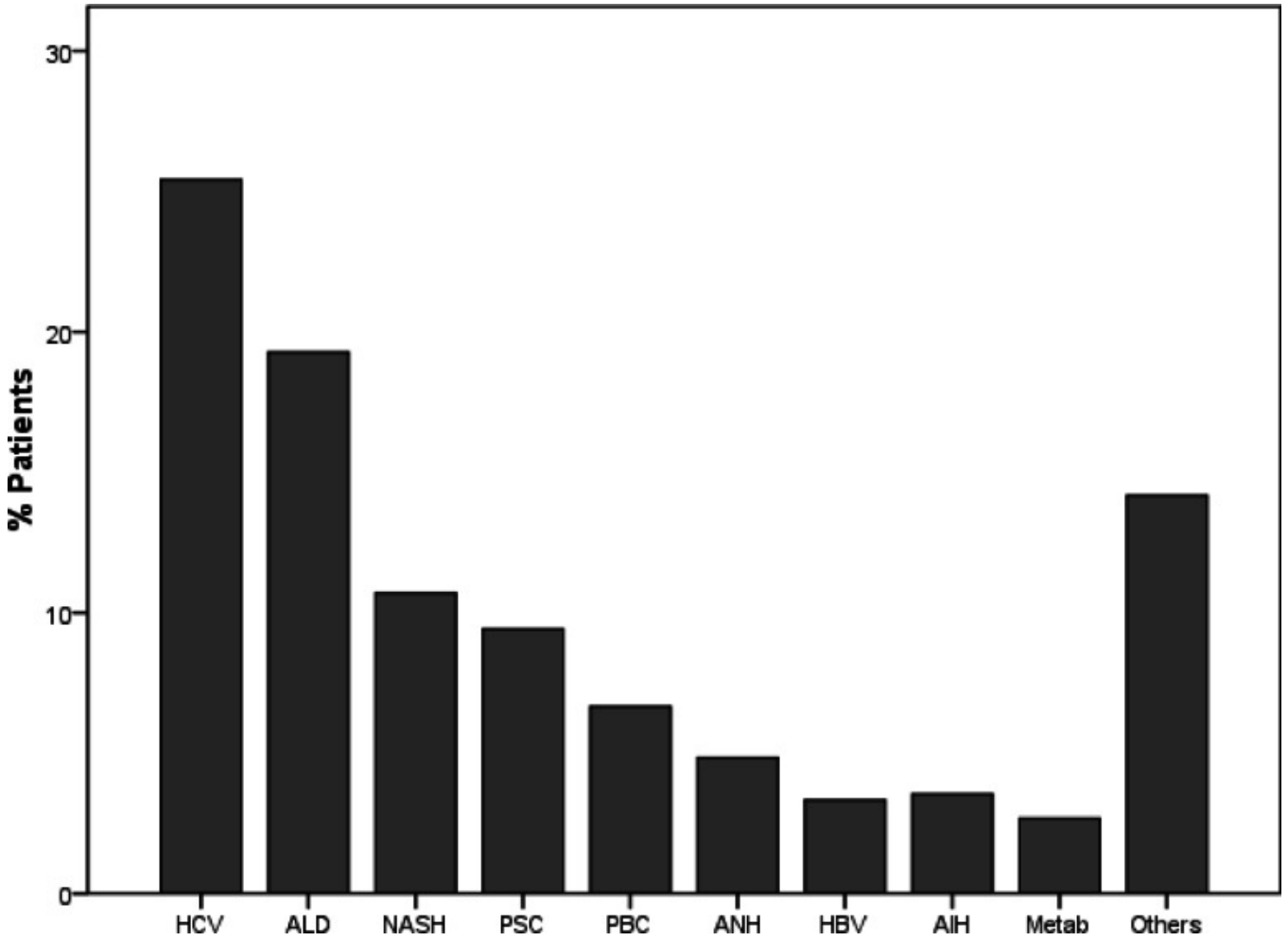
HCC as an indication for Liver Tx in AIH



523 HCCs Transplanted
At Univ of Bonn

Strassburg CP. Visc Med 2016;32:36371.

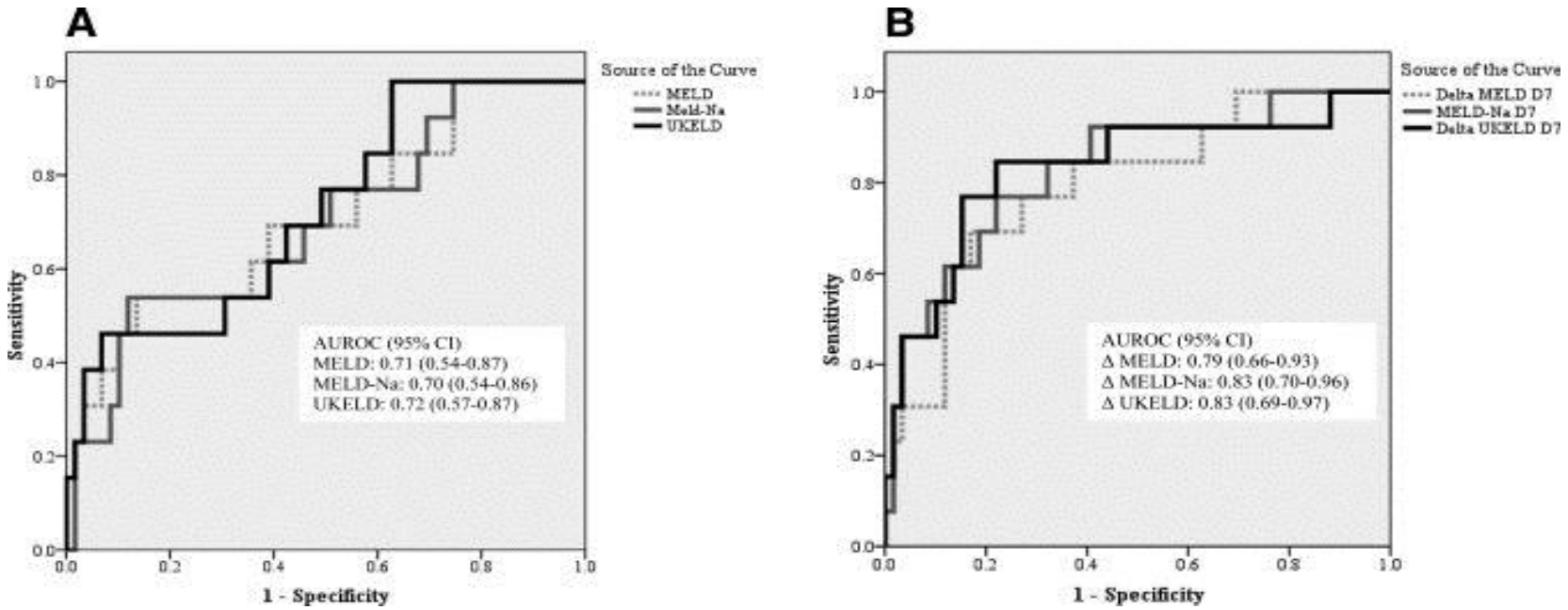
AIH: Less risk of de-novo malignancy post-transplant (SRTR data 1987-2009)



Zhou et al. Plos One 2016

Acute/Subacute Liver Failure

Utility of Liver Specific Scoring Systems in icteric presentations of AIH



Day 0	Change in Scores after 7 days Rx

Yeoman et al. Hepatology 2011;53:926-34.

Admission Parameters associated with failure to respond in icteric presentations of AIH. (N = 72)

- 18% Treatment Failure

Bilirubin	(451 vs 262)	p=0.02
INR	(1.62 vs 1.33)	p= 0.005
MELD score	(26 vs 20)	p=0.02
MELD-Na	(27 vs 22)	p=0.03
UKELD score	(59 vs 57)	p=0.01
Cirrhosis		NS
Creatinine		NS
Age at Dx		NS

Yeoman et al. Hepatology 2011;53:926-34.

Acute severe AIH. (Fulminant AIH)

- INR > 1.8
- No underlying chronic liver disease

- 42 patients (30 index presentation) 12 excluded

- Of 30 index patients, 21 received steroids
- 48% of treated patients transplanted
- All untreated patients transplanted

Yeoman et al. J Hepatol 2014;61:876-82.

Proposed Severe Autoimmune Hepatitis Histological Patterns USALF

Pattern of MHN	Characteristic Features
MHN 1	Panlobular necrosis and neocholangiolar proliferation
MHN 2	MHN1 plus regenerative nodules “submassive necrosis”
MHN 3	Severe acute hepatitis: Interface hepatitis, multilobular and bridging necrosis
MHN 4	MHN 1 with centrilobular haemorrhagic necrosis
MHN 5	Confluent necrosis superimposed on chronic hepatitis

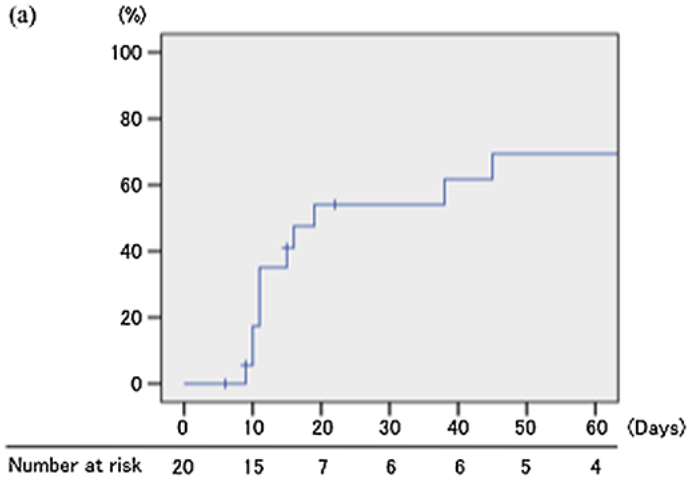
MHN = Massive Hepatocellular Necrosis
Suggested that type 4 and 5 most common

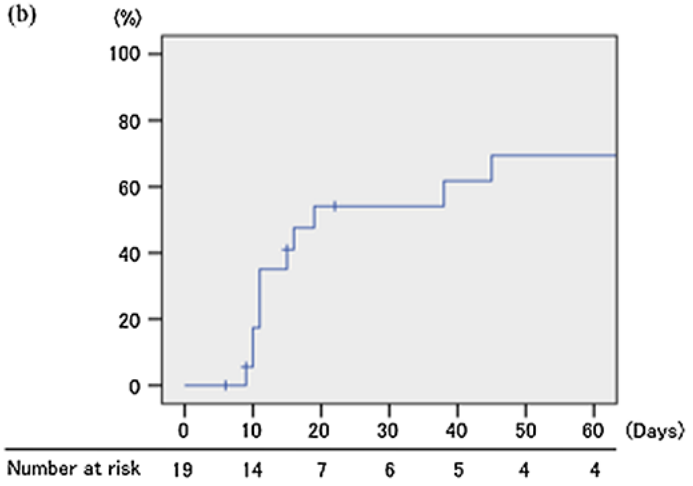
ASAIH: Untreated v Treated

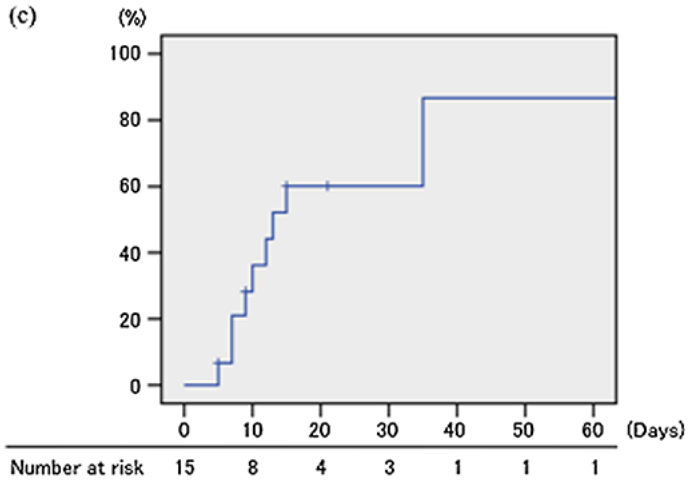
Parameter	Untreated n=9	Treated n=21	p value
Bilirubin µmol/l (3-20)	477	461	0.98
AST mmol/l (10-50)	779	556	0.33
Globulin (g/l) (25-35)	30	47	0.09
Admission INR (0.9-1.2)	2.8	2.2	0.07
Peak INR (0.9-1.2)	3.2	2.46	0.049
Creatinine µmol/l (45-120)	104	97	0.27
MELD Score	34	28	0.02
UKELD Score	65	62	0.17
IAIHG Score	15	15	0.91
AutoAbs >1:80	67%	57%	0.69
No. Transplant	100%	48%	0.01
Death	22%	19%	0.99

Yeoman et al. J Hepatol 2014;61:876-82.

Analysis of infectious complications and timing for emergency LT in AIH ALF







Cumulative incidence rate of infectious complication in first 60 days from Dx of severe disease (a),
introduction of CS (b)
onset of grade 2 hepatic coma (c)

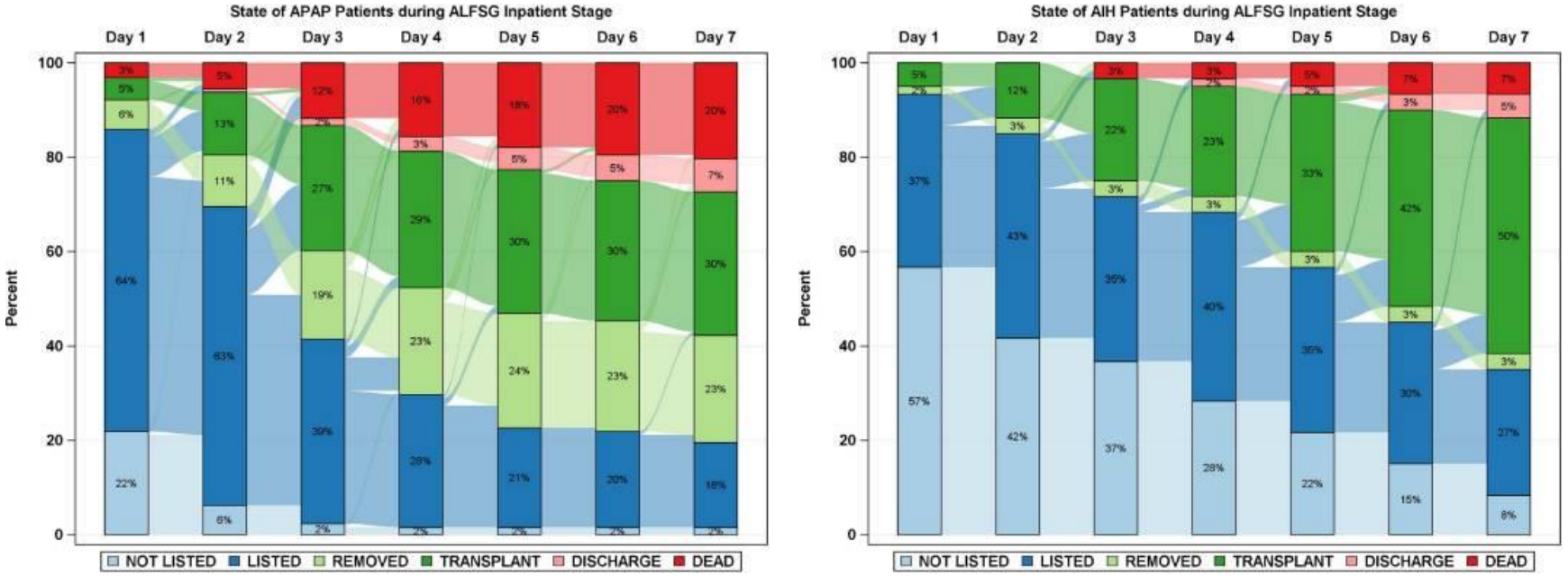
Fujiwara et al. J Hepato-Biliary-Pancreatic Sciences 2016;23:212-9.

Outcome following Listing for Liver Tx in Acute Liver Failure (US ALFSG). Outcome to day 21.

	N	SS (N=117)	Died (N=108)	LT (N=392)	P-Value
Patient Demographics					
Age (years)	617	35.5(12.5)	40.1(14.9)	39.8(13.9)	0.008
Gender (% Female)	617	83(71)	75(69)	263(67)	0.70
Race	617				0.014
Caucasian		91(78)	86(80)	261(67)	
African-American		11(9)	10(9)	75(19)	
Other		15(13)	12(11)	56(14)	
Weight (kg)	591	73.43(18.43)	76.88(20.73)	81.68(21.85)	<0.001
Etiology *(N=614; SS = 117, Died = 107‡, LT = 390)*					
Acetaminophen	173	70(60)	41(38)	62(16)	
Drug Induced Liver Injury	95	11(9)	21(20)	63(16)	
Autoimmune Hepatitis	83	6(5)	6(6)	71(18)	
Hepatitis B	66	6(5)	13(12)	47(12)	
Indeterminate	114	15(13)	15(14)	84(22)	
Other△	83	9(8)	11(10)	63(16)	

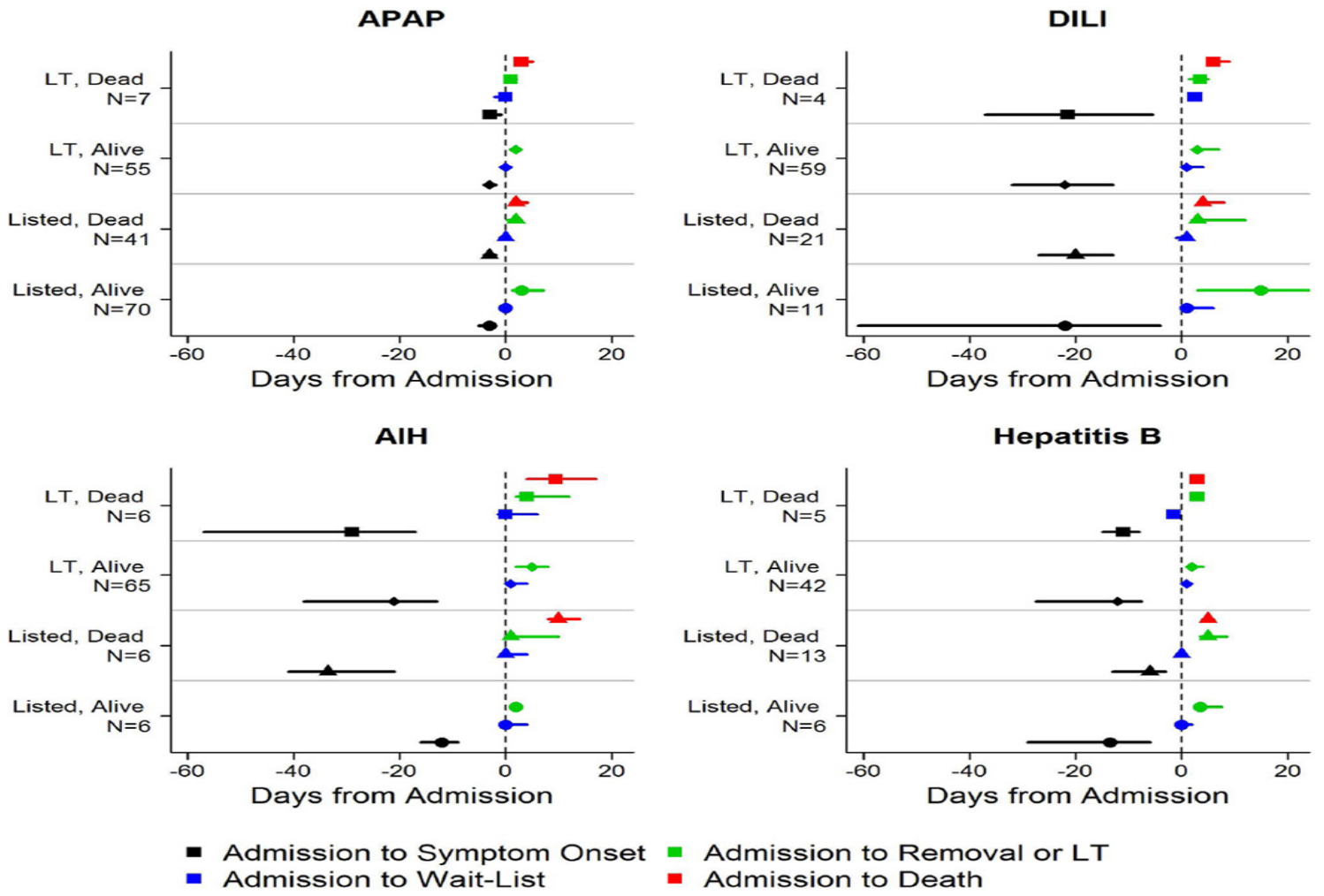
Reddy KR & ALFSG Liver Transpl 2016

Outcome following Listing for Liver Tx in Acute Liver Failure (US ALFSG). Outcome to day 21.

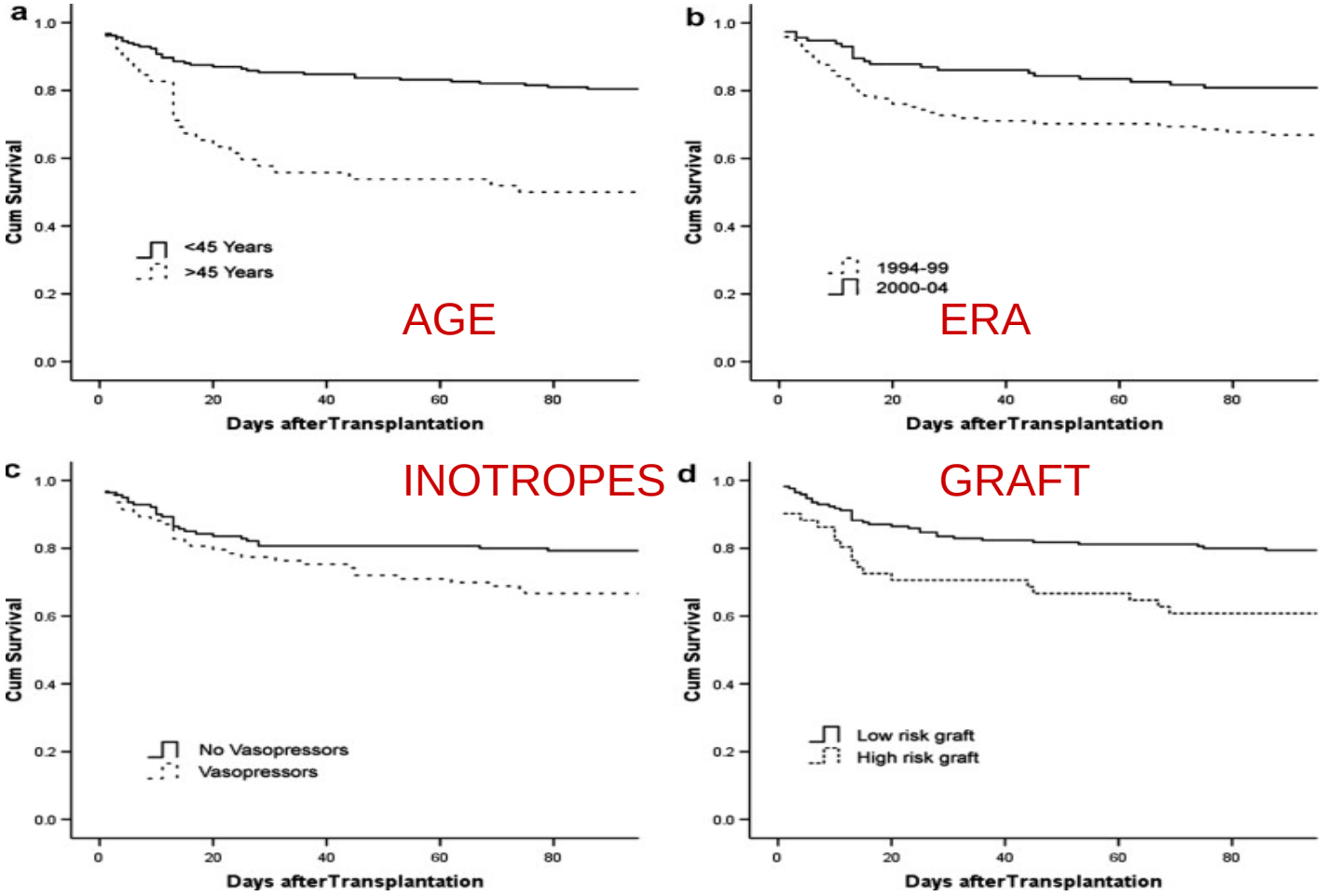


Reddy KR & ALFSG Liver Transpl 2016

Time to event following Listing



Factors associated with Poor prognosis following LT in ALF



Bernal W et al J Hepatol 2009;50:306-13.

Pattern of Late Mortality in Liver Transplant Recipients in the United Kingdom

TABLE 2. Cox regression analysis for death after yr 1 in the UK Transplant cohort (n=4483)

Variable	HR	SE	95% CI	Wald statistic	*df*	*P*
Recipient age	1.01[a]	0.004	1.00–1.01	3.48	1	0.06
Donor age	1.01[a]	0.003	1.00–1.01	3.86	1	0.05
Gender	1.05	0.09	0.88–1.26	0.31	1	0.58
Casue				131.17	9	<0.0001
PBC[b]						
PSC	1.28	0.19	0.88–1.86	1.67	1	0.20
ALD	2.10	0.15	1.56–2.82	24.01	1	<0.0001
AIH or cryptogenic	1.68	0.16	1.22–2.32	10.00	1	0.002
HCV	2.51	0.16	1.84–3.43	33.92	1	<0.0001
HBV	1.09	0.27	0.65–1.84	0.10	1	0.75
ALF	1.08	0.20	0.73–1.58	0.15	1	0.70
HCC	4.19	0.15	3.12–5.63	90.15	1	<0.0001
Metabolic liver disease	1.38	0.26	0.83–2.28	1.57	1	0.21
Other	1.80	0.24	1.12–2.88	5.88	1	0.02

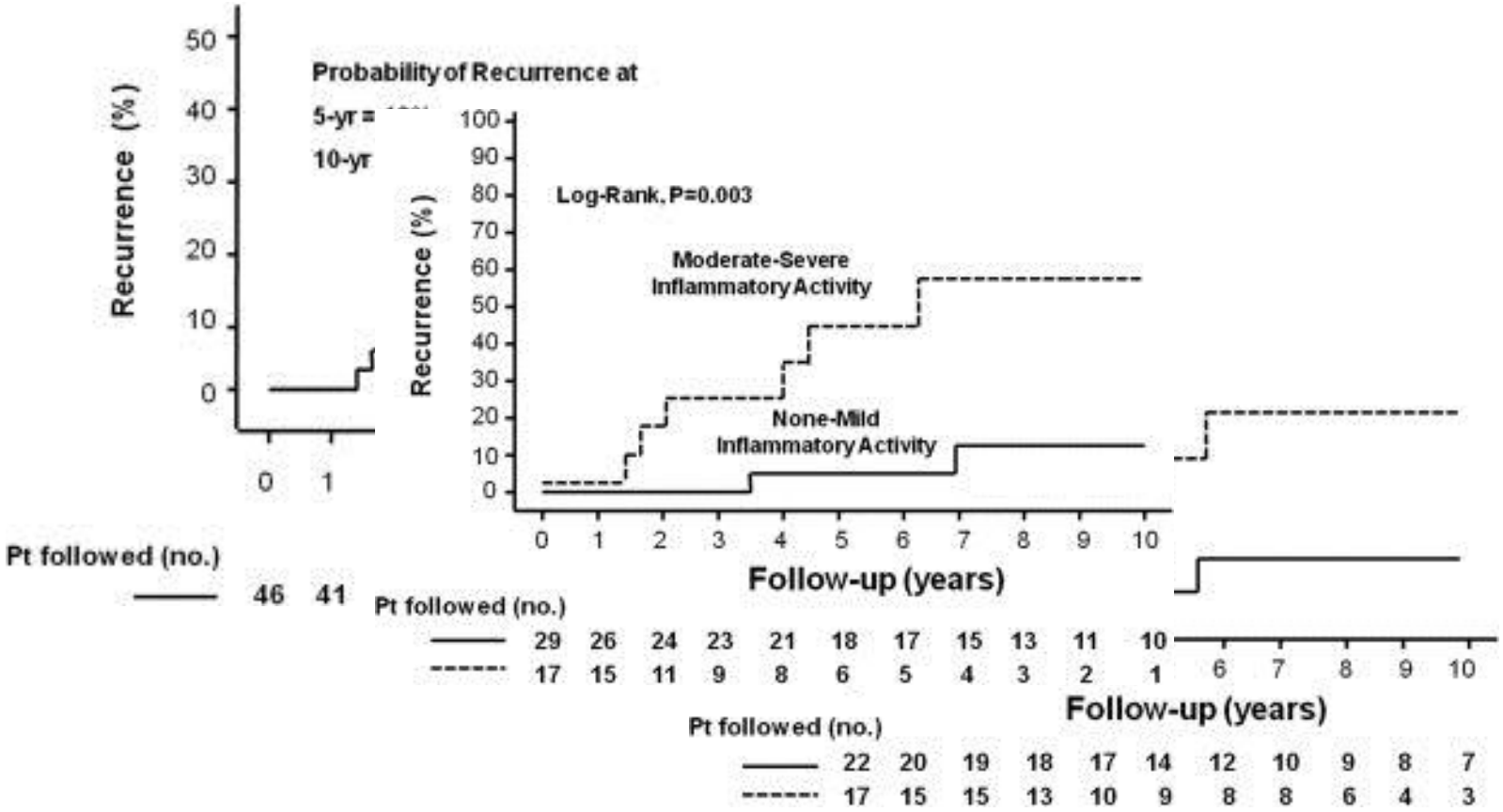
[a] Per year of age.
[b] Baseline category.
HR, hazard ratio; SE, standard error; CI, confidence interval; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; ALD, alcohol-related liver disease; AIH, autoimmune hepatitis; HCV, hepatitis C virus; HBV, hepatitis B virus; ALF, acute liver failure; HCC, hepatocellular carcinoma.

TRANSPLANTATION

Cox regression analysis for death after yr 1 in the UK Transplant cohort (n=4483)

Gelson, W et al. Transplantation 2011;91:1240-1244.

Risk factors for recurrence of AIH after LTx



Montano-Loza et al. Liver Transpl 2009;15:1254-61

Conclusions

- AIH: Ongoing indication for LT
- Chamelion disease
- Disease recurrence
- Steroid doses in ASAIH ?