

**Supplementary table 1:** Univariate analysis using un-imputed data and multivariate analysis using 10 imputed data sets, of factors at **diagnosis** associated with **10 year risk** of transplantation or death

Factor	Univariable Analysis		Multivariable Analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Female	0.83 (0.64,1.07)	0.157		
Age at diagnosis	1.01 (1.01,1.02)	0.001	1.02 (1.01,1.03)	0.001
Extra-hepatic biliary disease	1.76 (1.34,2.31)	<0.001	1.45 (1.09,1.92)	0.010
IBD presence	0.94 (0.65,1.37)	0.766		
Autoimmune disease	1.16 (0.84,1.60)	0.353		
Smoker	1.03 (0.79,1.34)	0.846		
Bilirubin				
35 -49	2.92 (1.67,5.11)	<0.001	1.92 (1.07,3.45)	0.030
50+	4.88 (3.52,6.75)	<0.001	2.50 (1.66,3.75)	0.000
ALP ratio				
1.5 - <2.5	1.15 (0.72,1.82)		1.15 (0.75,1.78)	0.519
2.5+	2.04 (1.46,2.85)	<0.001	1.70 (1.16,2.50)	0.007
ALT	1.02 (1.00,1.03)	0.030		
Albumin	0.92 (0.89,0.94)	<0.001	0.97 (0.94,1.00)	0.075
Haemoglobin	0.85 (0.79,0.92)	<0.001	0.99 (0.98,1.00)	0.037
Platelets group				
150 - 199	0.37 (0.21,0.66)	0.001	0.63 (0.36,1.11)	0.106
200 - 399	0.24 (0.16,0.37)	<0.001	0.40 (0.25,0.63)	0.000
400+	0.24 (0.14,0.41)	<0.001	0.24 (0.13,0.45)	0.000
Eosinophils	1.00 (0.82,1.21)	0.964		
Sodium	0.91 (0.87,0.96)	0.001		
Creatinine >120	1.75 (0.77,3.96)	0.181		
IgG	1.03 (0.95,1.12)	0.478		

IBD; Inflammatory bowel disease, ALP; Alkaline Phosphatase ALT; Alanine Transaminase, IgG; immunoglobulins

**Supplementary Table 2:** Change in mean biochemistry from baseline ( $t_0$ ) to year 2 ( $t_2$ ) for all patients within derivation cohort (positive result indicates increase in value). Values are mean unless otherwise stated.

Variable	Change from baseline	p-value
ALT	-43.99 (-52.53,-35.44)	<0.001
Albumin	0.39 (-0.09,0.87)	0.1102
Bilirubin	0.18 (-4.99,5.34)	0.9457
Platelets	-29.86 (-38.98,-20.73)	<0.001
ALP (ratio)	-1.77 (2.01,-1.54)	<0.001

**Supplementary table 3:** Event rates in four groups defined according to long-term risk score in the derivation and validation cohorts

Risk Group	Score (RS <sub>LT</sub> )	Derivation Cohort		Validation Cohort	
		No. of individuals	Observed event rate (%)	No. of individuals	Observed event rate (%)
1	RS <sub>LT</sub> < -2.019879	216	13 (6.0%)	105	3 (2.9%)
2	-2.019879 < RS <sub>LT</sub> < -1.463874	215	18 (8.4%)	77	8 (10.4%)
3	-1.463874 < RS <sub>LT</sub> < -0.8146346	215	41 (19.1%)	60	12 (20.0%)
4	-0.8146346 < RS <sub>LT</sub> < 2.737384	215	120 (55.8%)	94	45 (47.9%)

**Supplementary table 4:** HLA genotype and association with outcome using a test for trend across 0, 1 and 2 copies of each HLA allele

Allele	HR (95% CI)	p-value
<i>HLA-B*08:01</i>	1.24 (1.05,1.47)	0.013
<i>HLA-DR*03:01</i>	1.33 (1.13,1.58)	0.001
<i>HLA-DR*04:01</i>	1.03 (0.67,1.57)	0.903
<i>HLA-DR*07:01</i>	0.88 (0.63,1.24)	0.466
<i>HLA-DR*13:01</i>	0.85 (0.62,1.16)	0.304
<i>HLA-DR*15:01</i>	1.23 (0.96,1.58)	0.096

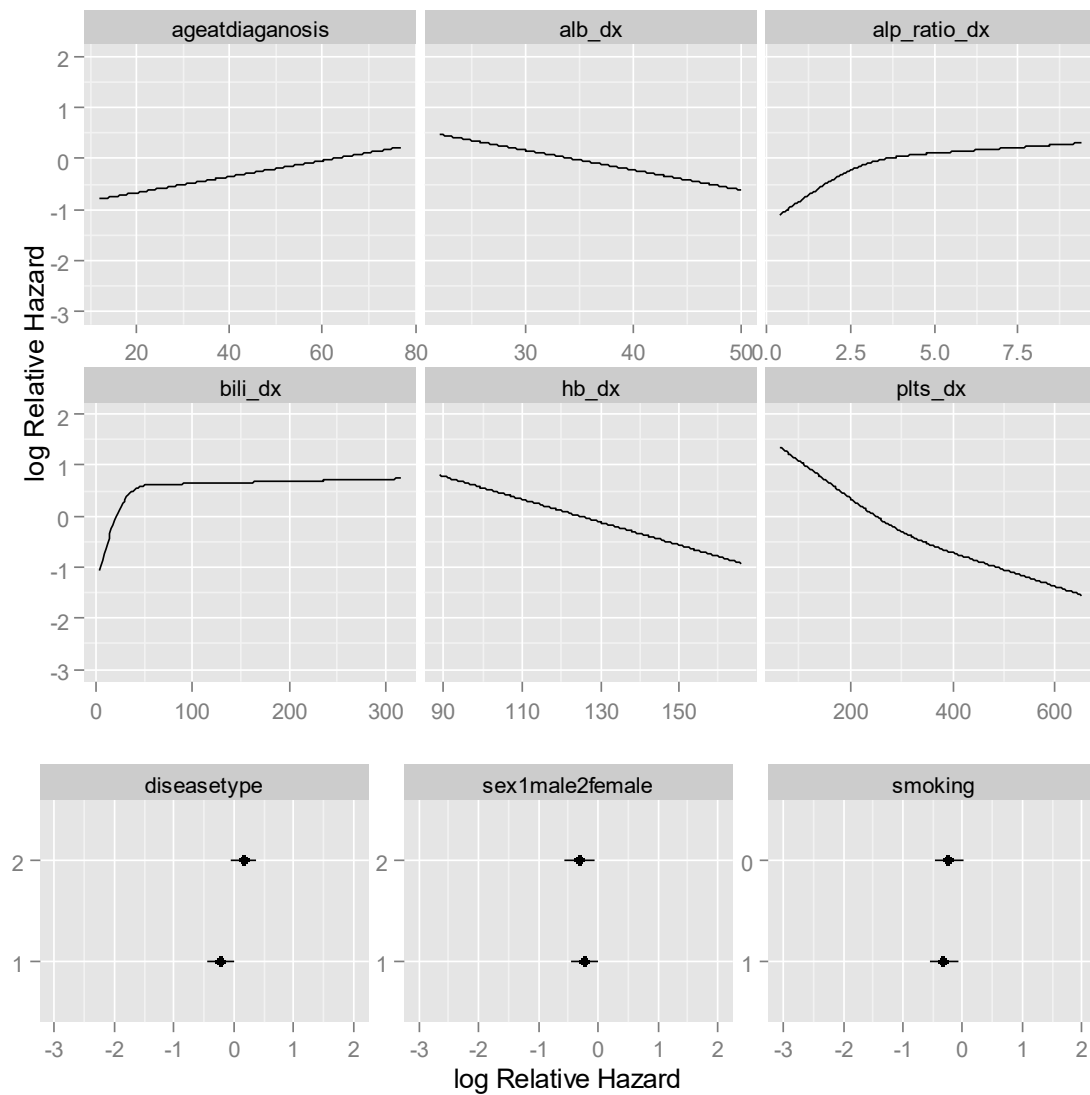
**Supplementary table 5:** Association between HLA-DR\*03:01 genotype and clinical characteristics (standard deviation of continuous variables in brackets)

No. of alleles	HLA-DR*03:01			p-value
	0	1	2	
Age	47.6 (15.9)	46.6 (13.8)	40.8 (15.4)	0.007
Bilirubin	28 (57)	48 (92)	34 (54)	0.059
ALP ratio	2.6 (1.9)	2.8 (2.1)	2.8 (2.1)	0.612
Albumin	40 (6)	39 (6)	37 (8)	0.068
Haemoglobin	134 (18)	134 (18)	129 (14)	0.324

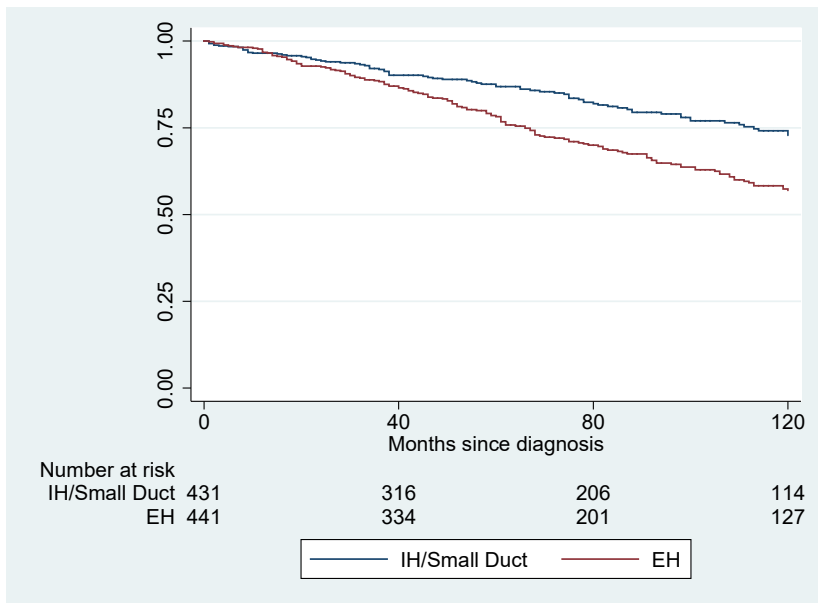
Platelet count	298 (128)	298 (141)	297 (133)	0.998
Female	35.2	32.9	40.7	0.561
Disease type (EH disease)	50.1	56.6	49.1	0.404

ALP; Alkaline Phosphatase ALT; Alanine Transaminase, IgG; immunoglobulins, EH; extra-hepatic biliary

**Supplementary figure 1:** Cubic splines demonstrating relationship between each variable and log of the relative hazard ratio.



**Supplementary figure 2:** Kaplan-Meier survival curve for presence of extra-hepatic (EH) biliary disease (red line) versus intra-hepatic biliary (IH) or small duct disease (blue line) at diagnosis



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