

Supplementary Materials

Supplementary Table 1. Full disease diagnosis codes, procedure codes, drug codes, and laboratory criteria for each clinical outcome

Supplementary Table 2. Subgroup analysis

Supplementary Table 3. Subgroup analysis (among COVID-19+CLD group)

Supplementary Table 1 Full disease diagnosis codes, procedure codes, drug codes, and laboratory criteria for each clinical outcome

Chronic liver disease	ICD-9-CM dx	ICD-9-CM px	Drugs	Laboratory
Viral hepatitis B	070.3 070.30 070.31 070.32 070.33		Lamivudine; Telbivudine; Adefovir; Entecavir; Tenofovir disoproxil fumarate; Tenofovir alafenamide; Pegylated interferon alpha 2a (subcutaneous injection)	Positive hepatitis B surface antigen (HBsAg+)
Viral hepatitis C	070.54 070.7 070.70 V02.62		Boceprevir; Pegylated interferon alpha 2b (subcutaneous injection); Velpatasvir; Glecaprevir; Ledipasvir; Grazoprevir; Voxilaprevir; Ribavirin; Sofosbuvir; Pibrentasvir; Elbasvir;	
Unspecified viral hepatitis, chronic hepatitis, other chronic hepatitis, liver disease	070.9 571.4 571.40 571.41 571.49			

Fatty liver disease	571.8 571.9	
Alcoholic liver disease	571.0 571.2 571.3	
Alcoholic hepatitis	571.1	
Wilson's disease	275.1	Trientine; Zinc sulphate
Autoimmune hepatitis	571.42	
Primary biliary cholangitis	571.6	Ursodeoxycholic acid
& Primary sclerosing cholangitis		

Clinical Outcomes	ICD-9-CM dx	ICD-9-CM px	Drugs	Laboratory
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Adverse hepatic outcomes

Cirrhosis	571 571.5 571.6 275.1 275.03 571.5 572.3 456.1 456.21		Aminoleban (oral); Vitamin K (oral)	FIB-4 > 3.25
Hepatocellular carcinoma	155.0			
Liver decompensation				
Hepatic encephalopathy	coma/ 070.2 070.20 070.21 070.22 070.23 070.44 070.71 070.6 572.2			

Hepatorenal syndrome	572.4			Terlipressin	(intravenous injection)
Ascites	789.5 789.59		54.91		
Liver failure	570 572.8 782.4				
Variceal bleeding	456.0 456.20 571.5		42.91 44.91 39.1		
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Treatment for HCC	ICD-9-CM dx		ICD-9-CM px	Drugs	Laboratory
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Curative treatment to HCC					
Hepatic resection			50.22 50.3 50.4		
Liver transplantation	V42.7		50.5 50.51 50.59	Basiliximab	(intravenous injection)
Radiofrequency ablation of liver			50.23 50.24 50.25 50.26 50.29 50.94		
Non-curative treatment to HCC					

Transarterial		38.86	
chemoembolization			
Radiotherapy to liver	V58.0		
Systemic chemotherapy or immunotherapy	V58.11 V58.12	99.25	Nivolumab (intravenous); Pembrolizumab (intravenous); Atezolizumab (intravenous); Sorafenib (oral); Lenvatinib (oral); Regorafenib (oral); Ipilimumab (intravenous); Bevacizumab (intravenous); Cabozantinib (oral)
Palliative care	V66.7		Morphine (oral or intravenous)

Note: FIB-4 = Fibrosis 4

Supplementary Table 2 Subgroup analysis

Outcomes	COVID-19 patients (N=55,163)						Control (N=55,163)						COVID-19 patients vs Control		
	Cumulative incidence			Crude incidence rate (Events / 10,000 person-years)			Cumulative incidence			Crude incidence rate (Events / 10,000 person-years)					
	N	Neve nts	Rate	Estimate	95% CI	Person- years	N	Neve nts	Rate	Estimate	95% CI	Person- years	IRR ¹	95% CI	P-value
Hepatocellular carcinoma															
Overall	53,912	211	0.39%	64.2	(55.8, 73.5)	32,870	53,912	276	0.51%	54.0	(47.8, 60.8)	51,087	1.19	(0.99, 1.42)	0.06
Age ≤ 50	15,266	17	0.11%	17.0	(9.9, 27.3)	9,983	15,266	20	0.13%	13.2	(8.1, 20.4)	15,109	1.29	(0.67, 2.46)	0.45
Age > 50	35,122	161	0.46%	76.5	(65.2, 89.3)	21,033	35,122	269	0.77%	81.6	(72.2, 92.0)	32,956	0.94	(0.77, 1.14)	0.52
With cirrhosis	1,095	31	2.83%	533.2	(362.3, 756.8)	581	1,095	260	2.39%	284.1	(185.6, 416.3)	915	1.88 ^a	(1.11, 3.17)	0.02

Without cirrhosis	50,305	167	0.33%	53.9	(46.0, 62.7)	30,975	50,305	260	0.52%	54.1	(47.7, 61.1)	48,044	1.00	(0.82, 1.21)	0.97
HBV	21,182	168	0.79%	144.8	(123.7, 168.4)	11,602	21,181	221	1.04%	118.4	(103.3, 135.0)	18,671	1.22 ^a	(1.00, 1.50)	0.05
Other causes of CLD	30,127	30	0.10%	15.1	(10.2, 21.5)	19,876	30,120	35	0.12%	11.6	(8.1, 16.1)	30,241	1.30	(0.80, 2.12)	0.29
With multi-organ dysfunction	19,394	91	0.47%	84.1	(67.7, 103.2)	10,826	19,394	97	0.50%	56.0	(45.4, 68.3)	17,319	1.50 ^b	(1.13, 2.00)	0.005
Without multi-organ dysfunction	31,820	106	0.33%	51.3	(42.0, 62.1)	20,657	31,820	176	0.55%	55.9	(47.9, 64.8)	31,482	0.92	(0.72, 1.17)	0.49
Fully vaccinated	27,157	69	0.25%	55.6	(43.2, 70.3)	12,420	27,157	109	0.40%	46.3	(38.1, 55.9)	23,519	1.20	(0.89, 1.62)	0.24
Not-fully vaccinated/ unvaccinated	24,161	126	0.52%	66.7	(55.5, 79.4)	18,902	24,161	155	0.64%	60.9	(51.7, 71.3)	25,441	1.09	(0.86, 1.38)	0.45
Year of 2020	2,368	7	0.30%	13.7	(5.5, 28.2)	5,110	2,368	29	1.22%	44.5	(29.8, 64.0)	6,512	0.31 ^b	(0.13, 0.70)	0.005
Year of 2021	371	0	0.00%	0.0	NA	630	371	2	0.54%	29.5	(3.6, 106.5)	679	NA	NA	NA

Year of 2022	51,1	204	0.40	75.2	(65.2, 86.3)	27,1	51,1	245	0.48	55.	(49.0,	43,8	1.3	(1.12,	0.00
	73		%			29	73		%	8	63.3)	97	5 ^b	1.62)	2
All-cause mortality															
Overall	55,1	2,2	4.12	676.5	(648.9,	33,6	55,1	1,60	2.90	306	(291.4,	52,2	2.2	(2.07,	<0.0
	63	73	%		704.9)	01	63	0	%	.2	321.6)	58	1 ^b	2.36)	01
Age ≤ 50	15,4	68	0.44	67.4	(52.3, 85.4)	10,0	15,3	107	0.70	70.	(57.8,	15,1	0.9	(0.70,	0.76
	82		%			94	15		%	6	85.3)	62	5	1.29)	5
Age > 50	39,6	2,2	5.56	938.0	(899.3,	23,5	36,9	1,25	3.40	362	(342.7,	34,7	2.5	(2.41,	<0.0
	81	05	%		978.0)	07	91	8	%	.4	383.0)	12	9 ^b	2.78)	01
With cirrhosis	1,89	191	10.0	1910.	(1,649.5,	1,00	1,51	117	7.72	915	(756.8,	1,27	2.0	(1.65,	<0.0
	7		7%	9	2,201.9)	0	5		%	.1	1,096.8)	8	9 ^b	2.64)	01
Without cirrhosis	53,2	2,0	3.91	638.6	(611.5,	32,6	50,9	1,25	2.47	257	(243.8,	48,7	2.4	(2.31,	<0.0
	65	82	%		666.7)	01	31	6	%	.9	272.5)	06	8 ^b	2.66)	01
HBV	23,7	1,2	5.23	955.5	(903.1,	13,0	22,0	781	3.54	400	(372.6,	19,5	2.3	(2.18,	<0.0
	83	43	%		1,010.2)	09	82		%	.2	429.3)	14	9 ^b	2.61)	01
Other causes of CLD	31,3	1,0	3.28	500.2	(470.1,	20,5	30,2	595	1.97	195	(180.2,	30,4	2.5	(2.31,	<0.0
	80	30	%		531.7)	92	62		%	.6	211.9)	22	6 ^b	2.83)	01
With multi-organ dysfunction	22,7	1,8	8.07	1458.	(1,392.4,	12,5	20,2	970	4.78	535	(502.7,	18,1	2.7	(2.52,	<0.0
	64	36	%	3	1,526.6)	90	74		%	.9	570.7)	01	2 ^b	2.94)	01

Without multi-organ dysfunction	32,399	437	1.35%	208.0	(188.9, 228.4)	21,011	32,083	458	1.43%	144.0	(131.1, 157.8)	31,803	1.4	(1.27, 1.65)	<0.001
Fully vaccinated	27,631	209	0.76%	165.4	(143.8, 189.4)	12,634	27,566	259	0.94%	108.3	(95.6, 122.4)	23,904	1.5	(1.27, 1.83)	<0.001
Not-fully vaccinated/ unvaccinated	27,530	2,063	7.49%	984.0	(942.0, 1,027.4)	20,966	24,775	1,080	4.36%	414.9	(390.5, 440.4)	26,030	2.3	(2.20, 2.56)	<0.001
Year of 2020	2,397	130	5.42%	251.4	(210.0, 298.5)	5,171	2,397	197	8.22%	298.5	(258.3, 343.2)	6,600	0.8	(0.67, 1.05)	0.132
Year of 2021	375	18	4.80%	282.2	(167.3, 446.1)	638	375	20	5.33%	291.7	(178.2, 450.5)	686	0.9	(0.51, 1.84)	0.920
Year of 2022	52,391	2,125	4.06%	764.6	(732.4, 797.8)	27,792	52,391	1,383	2.64%	307.5	(291.5, 324.2)	44,972	2.4	(2.32, 2.66)	<0.001
Adverse hepatic outcome															
Overall	52,114	2,407	4.62%	789.3	(758.1, 821.5)	30,495	52,114	2,183	4.19%	453.5	(434.7, 473.0)	48,133	1.7	(1.64, 1.85)	<0.001
Age ≤ 50	14,964	187	1.25%	193.9	(167.1, 223.8)	9,643	14,964	275	1.84%	187.7	(166.2, 211.3)	14,647	1.0	(0.86, 1.25)	0.73

Age > 50	33,9	1,8	5.48	962.8	(919.5,	19,2	33,9	1,72	5.07	557	(531.3,	30,8	1.7	(1.62,	<0.0
	15	58	%		1,007.6)	99	15	1	%	.4	584.3)	78	3 ^b	1.85)	01
HBV	20,4	1,2	6.29	1207.	(1,142.8,	10,6	20,4	1,19	5.82	684	(646.3,	17,3	1.7	(1.63,	<0.0
	50	86	%	9	1,275.8)	47	50	1	%	.6	724.6)	97	6 ^b	1.91)	01
Other causes of CLD	29,3	1,0	3.41	536.9	(504.2,	18,6	29,3	833	2.83	287	(268.7,	28,9	1.8	(1.70,	<0.0
	83	03	%		571.2)	80	83		%	.9	308.1)	34	7 ^b	2.05)	01
With multi-organ dysfunction	18,1	1,2	6.84	1304.	(1,232.6,	9,53	18,1	989	5.44	631	(592.9,	15,6	2.0	(1.90,	<0.0
	96	44	%	1	1,378.6)	9	96		%	.6	672.3)	58	6 ^b	2.25)	01
Without multi-organ dysfunction	31,4	976	3.11	494.7	(464.2,	19,7	31,4	1,09	3.50	361	(340.4,	30,4	1.3	(1.25,	<0.0
	25		%		526.7)	29	25	9	%	.4	383.4)	09	7 ^b	1.49)	01
Fully vaccinated	26,4	556	2.10	464.6	(426.8,	11,9	26,4	741	2.80	328	(304.9,	22,5	1.4	(1.27,	<0.0
	98		%		504.9)	67	98		%	.1	352.6)	84	2 ^b	1.58)	01
Not-fully vaccinated/ unvaccinated	23,2	1,6	7.11	961.6	(915.8,	17,2	23,2	1,31	5.67	556	(527.0,	23,6	1.7	(1.60,	<0.0
	78	55	%		1,009.1)	11	78	9	%	.6	587.5)	96	3 ^b	1.86)	01
Year of 2020	2,32	270	11.6	598.3	(529.1,	4,51	2,32	221	9.51	366	(319.4,	6,03	1.6	(1.36,	<0.0
	3		2%		674.1)	3	3		%	.0	417.6)	8	3 ^b	1.97)	01
Year of 2021	369	34	9.21	597.0	(413.4,	570	369	25	6.78	389	(252.0,	642	1.5	(0.90,	0.12
			%		834.2)				%	.3	574.7)	3		2.62)	

Year of 2022	49,4	2,1	4.26	827.5	(792.5,	25,4	49,4	1,93	3.92	467	(446.7,	41,4	1.7	(1.66,	<0.0
	22	03	%		863.7)	13	22	7	%	.3	488.6)	53	7 ^b	1.89)	01
Liver decompensation															
Overall	53,5	326	0.61	99.9	(89.4,	32,6	53,5	374	0.70	73.	(66.4,	50,7	1.3	(1.17,	<0.0
	52		%		111.4)	17	52		%	7	81.6)	25	6 ^b	1.57)	01
Age ≤ 50	15,0	38	0.25	38.6	(27.3, 53.0)	9,84	15,0	60	0.40	40.	(30.7,	14,9	0.9	(0.64,	0.85
	87		%			0	87		%	2	51.8)	20	6	1.44)	
Age > 50	35,7	237	0.66	110.9	(97.2,	21,3	35,7	284	0.79	84.	(75.1,	33,5	1.3	(1.10,	0.00
	55		%		126.0)	69	55		%	7	95.1)	45	1 ^b	1.56)	2
With cirrhosis	639	35	5.48	1090.	(759.3,	321	639	33	5.16	622	(428.2,	531	1.7	(1.09,	0.02
			%	1	1,516.1)				%	.0	873.5)		5 ^a	2.83)	
Without cirrhosis	50,5	251	0.50	80.7	(71.0, 91.3)	31,1	50,5	302	0.60	62.	(55.7,	48,2	1.2	(1.09,	0.00
	73		%			16	73		%	6	70.0)	77	9 ^b	1.52)	3
HBV	21,3	188	0.88	161.0	(138.8,	11,6	21,3	201	0.94	106	(92.7,	18,7	1.5	(1.23,	<0.0
	15		%		185.7)	79	13		%	.9	122.8)	98	1 ^b	1.84)	01
Other causes of CLD	29,7	111	0.37	56.5	(46.5, 68.1)	19,6	29,7	148	0.50	49.	(41.9,	29,8	1.1	(0.89,	0.30
	44		%			31	44		%	6	58.3)	37	4	1.46)	
With multi-organ dysfunction	19,2	166	0.86	155.0	(132.3,	10,7	19,2	163	0.85	95.	(81.0,	17,1	1.6	(1.31,	<0.0
	22		%		180.4)	11	22		%	0	110.7)	59	3 ^b	2.03)	01

Without multi-organ dysfunction	31,7	127	0.40	61.6	(51.4, 73.3)	20,6	31,7	214	0.67	68.	(59.3,	31,4	0.9	(0.73,	0.37
	74		%			14	74		%	1	77.9)	26	0	1.13)	
Fully vaccinated	27,0	81	0.30	65.5	(52.0, 81.4)	12,3	27,0	111	0.41	47.	(39.0,	23,4	1.3	(1.04,	0.03
	43		%			66	43		%	4	57.1)	29	8 ^a	1.84)	
Not-fully vaccinated/ unvaccinated	23,9	209	0.87	111.6	(97.0,	18,7	23,9	238	0.99	94.	(82.8,	25,2	1.1	(0.98,	0.08
	80		%		127.8)	30	80		%	4	107.2)	06	8	1.42)	
Year of 2020	2,34	7	0.30	13.8	(5.6, 28.5)	5,06	2,34	54	2.30	83.	(62.9,	6,44	0.1	(0.07,	<0.0
	8		%			9	8		%	8	109.3)	4	6 ^b	0.36)	01
Year of 2021	365	2	0.55	32.4	(3.9, 116.9)	618	365	6	1.64	90.	(33.0,	667	0.3	(0.07,	0.21
			%						%	0	195.8)		6	1.79)	
Year of 2022	50,8	317	0.62	117.7	(105.1,	26,9	50,8	314	0.62	72.	(64.3,	43,6	1.6	(1.40,	<0.0
	39		%		131.4)	30	39		%	0	80.4)	14	3 ^b	1.91)	01
Palliative care															
Overall	53,3	924	1.73	285.8	(267.7,	32,3	53,3	904	1.70	179	(167.5,	50,5	1.6	(1.46,	<0.0
	20		%		304.8)	32	20		%	.0	191.0)	10	0 ^b	1.75)	01
Age ≤ 50	14,9	79	0.53	80.8	(64.0,	9,77	14,9	96	0.64	64.	(52.5,	14,8	1.2	(0.93,	0.15
	81		%		100.7)	3	81		%	8	79.2)	10	5	1.68)	
Age > 50	35,7	707	1.98	333.3	(309.2,	21,2	35,7	661	1.85	197	(182.5,	33,5	1.6	(1.52,	<0.0
	32		%		358.8)	12	32		%	.3	212.9)	06	9 ^b	1.88)	01

With cirrhosis	1,33	47	3.53	688.7	(506.0,	682	1,33	41	3.08	369	(265.0,	1,11	1.8	(1.22,	0.00
	1		%		915.9)		1		%	.3	501.0)	0	6 ^b	2.84)	4
Without cirrhosis	49,6	809	1.63	266.2	(248.2,	30,3	49,6	737	1.48	155	(144.4,	47,4	1.7	(1.55,	<0.0
	55		%		285.2)	92	55		%	.4	167.1)	14	1 ^b	1.89)	01
HBV	21,2	568	2.68	492.1	(452.4,	11,5	21,2	514	2.42	274	(251.5,	18,7	1.7	(1.59,	<0.0
	29		%		534.3)	43	29		%	.7	299.5)	10	9 ^b	2.02)	01
Other causes of CLD	29,6	285	0.96	146.4	(129.9,	19,4	29,6	246	0.83	82.	(72.7,	29,7	1.7	(1.49,	<0.0
	60		%		164.4)	66	60		%	7	93.7)	42	7 ^b	2.10)	01
With multi-organ dysfunction	19,1	492	2.57	463.9	(423.8,	10,6	19,1	425	2.22	248	(225.8,	17,0	1.8	(1.64,	<0.0
	62		%		506.8)	05	62		%	.9	273.8)	73	6 ^b	2.12)	01
Without multi-organ dysfunction	31,6	355	1.12	173.7	(156.1,	20,4	31,6	395	1.25	126	(114.0,	31,3	1.3	(1.19,	<0.0
	81		%		192.8)	36	81		%	.1	139.2)	14	8 ^b	1.59)	01
Fully vaccinated	27,0	171	0.63	138.4	(118.4,	12,3	27,0	230	0.85	98.	(86.1,	23,3	1.4	(1.15,	<0.0
	14		%		160.8)	56	14		%	4	111.9)	80	1 ^b	1.71)	01
Not-fully vaccinated/ unvaccinated	23,8	660	2.76	356.2	(329.6,	18,5	23,8	532	2.23	211	(194.0,	25,1	1.6	(1.50,	<0.0
	88		%		384.5)	28	88		%	.6	230.4)	37	8 ^b	1.89)	01
Year of 2020	2,35	103	4.38	207.9	(169.7,	4,95	2,35	104	4.42	161	(131.8,	6,44	1.2	(0.98,	0.07
	2		%		252.2)	4	2		%	.4	195.5)	6	9	1.70)	

Year of 2021	367	13	3.54	211.7	(112.7,	614	367	9	2.45	134	(61.6,	668	1.5	(0.67,	0.30
			%		362.0)				%	.8	255.8)		7	3.70)	
Year of 2022	50,6	808	1.60	301.9	(281.4,	26,7	50,6	791	1.56	182	(169.8,	43,3	1.6	(1.50,	<0.0
	01		%		323.5)	64	01		%	.3	195.4)	97	6 ^b	1.83)	01

Note: CLD = chronic liver disease; HCC = hepatocellular carcinoma; IRR = incidence rate ratio; CI = confidence interval

¹ IRR >1 (or <1) indicates COVID-19 patients had higher (lower) risk of clinical outcome compared to the matched control group.

^{a,b} IRR is considered statistically significant, with ^a indicates p<0.05 and ^b indicates p<0.01

Supplementary Table 3. Subgroup analysis (among COVID-19+CLD group)

Outcomes	Hospitalized patients (N=4,827)					Non-hospitalized patients (N=4,827)					Hospitalized patients vs Non-hospitalized patients		
	Cumulative incidence (Events / 10,000 person-years)					Cumulative incidence (Events / 10,000 person-years)							
	Number of events	Rate %	Estimate	95% CI	Person-years	Number of events	Rate %	Estimate	95% CI	Person-years	IRR ¹	95% CI	P-value
Hepatocellular carcinoma	3	0.07 %	7.9	(1.6, 23.2)	3,774	2	0.04 %	4.8	(0.6, 17.5)	4,131	1.64	(0.27, 9.83)	0.587
All-cause mortality	41	0.85 %	97.4	(69.9, 132.1)	4,209	31	0.64 %	72.0	(48.9, 102.2)	4,305	1.35	(0.85, 2.16)	0.205
Adverse hepatic outcomes	103	2.28 %	288.8	(235.8, 350.3)	3,566	100	2.22 %	254.1	(206.8, 309.1)	3,935	1.14	(0.86, 1.50)	0.371
Liver decompensation	5	0.11 %	13.3	(4.3, 31.0)	3,762	0	0.00 %	0.0	NA	4,121	NA	NA	NA

Palliative care	42	0.93	114.0	(82.2,	3,684	29	0.64	71.2	(47.7,	4,07	1.6	(0.99,	0.05
		%		154.1)			%		102.3)	1	0	2.58)	3

Outcomes	Antiviral users² (N=7,818)					Non-users (N=7,818)					Antiviral users vs Non-users		
	Cumulative incidence		Crude incidence rate (Events / person-years)		rate	Cumulative incidence		Crude incidence rate (Events / person-years)		rate			
	Number of events	Rate	Estimate	95% CI	Person-years	Number of events	Rate	Estimate	95% CI	Person-years	IRR ¹	95% CI	P-value
Hepatocellular carcinoma	1	0.01%	3.3	(0.1, 18.2)	3,062	1	0.01%	2.1	(0.1, 11.8)	4,726	1.54	(0.10, 24.66)	0.759
All-cause mortality	26	0.3%	84.8	(55.4, 124.3)	3,066	56	0.72%	118.3	(89.4, 153.6)	4,734	0.72	(0.45, 1.14)	0.161
Adverse hepatic outcomes	65	0.8%	220.9	(170.5, 281.6)	2,942	56	0.72%	120.9	(91.3, 157.0)	4,633	1.83	(1.28, 2.62)	0.001
Liver decompensation	1	0.01%	3.3	(0.1, 18.2)	3,059	2	0.03%	4.2	(0.5, 15.3)	4,725	0.77	(0.07, 8.52)	0.833

Palliative care	32	0.4	106.3	(72.7,	3,01	32	0.41	68.2	(46.6,	4,695	1.5	(0.95,	0.07
		1%		150.1)	0		%		96.2)		6	2.55)	6

Note: IRR = incidence rate ratio; CI = confidence interval

¹ IRR >1 (or <1) indicates hospitalized patients (or antiviral users) had higher (lower) risk of clinical outcome compared to the matched non-hospitalized patients (or non-users). IRR was estimated only if the total number of events in the two comparison groups were greater than 1

² Antiviral users were defined as patients who received any of the following antiviral medications: (i) molnupiravir, (ii) nirmatrelvir/ritonavir, or (iii) remdesivir

^{a,b} IRR is considered statistically significant, with ^a indicates p<0.05 and ^b indicates p<0.01