

Cancer classifications	Topography code	Morphology codes
Hepatocellular carcinoma	C22.0 & C22.1	8170-8175
Other Specified Carcinoma	C22.0	8012-8013,8124,8142,8161-8162, 8180,8190,8211,8240,8246,8249,8255, 8290,8310,8323,8337,8440,8450,8453,8470- 8471,8500,8503,8510,8521,8550,8574,8576
Poorly Specified Carcinoma	C22.0	8010,8020,8021,8022,8031,8046,8050
Hepatoblastoma	C22.0	8970
Hemangiosarcoma	C22.0	9120
Hemangioendothelioma	C22.0	9130,9133
Other Sarcoma	C22.0	8800-8805,8810,8815,8830,8850,8852,8890, 8891,8894-8896,8900,8910,8920,8935,8936, 8940,8963,8990,9040,9041,9124,9150,9180, 9220,9260,9364,9473,9500,9540,9560
Embryonal Sarcoma	C22.0	8991
Germ Cell Tumors	C22.0	9064,9070,9071,9080,9100
Melanomas, Carcinosarcomas	C22.0	8720,8980
Cholangiocarcinoma	C22.1 & C22.0 (intrahepatic)	8032-8033, 8041, 8070-8071, 8140-8141, 8160, 8260, 8480, 8481, 8490, 8560
	C24.0 (extrahepatic)	8032-8033, 8041, 8070-8071, 8140-8141, 8160, 8260, 8480, 8481, 8490, 8560
Other intrahepatic bile duct cancers	C22.1	All morphology codes except 8170-8175, 8032-8033, 8041, 8070-8071, 8140-8141, 8160, 8260, 8480, 8481, 8490, 8560
Other Extrahepatic bile duct cancers	C24.0	All morphology codes except 8032-8033, 8041, 8070-8071, 8140-8141, 8160, 8260, 8480, 8481, 8490, 8560
Malignant neoplasms of the gallbladder	C23	All morphology codes*

Ampulla of Vater	C24.1	All morphology codes*
Overlapping lesions of biliary tract	C24.8	All morphology codes*
Biliary tract, NOS	C24.9	All morphology codes*

*Except Kaposi's sarcoma: 9140, Mesothelioma: 9050-9055, Poorly specified malignancies: 8000-8005, Hematologic Malignancies: 9590-9989

Supplementary Table 2. RRs for HBV and HCC, HCV and HCC, and PSC and cholangiocarcinoma adjusted for year of transplant

Variable	Outcome	Original unadjusted estimates			Adjusted for year of transplant			
		RR	LCL	UCL	RR	LCL	UCL	
HBV	Active	HCC	3.24	1.31	6.89	3.73	1.50	8.03
	Resolved	HCC	1.79	0.85	3.41	2.13	1.00	4.11
	Unknown	HCC	1.04	0.40	2.22	1.20	0.46	2.57
HCV	Seropositive	HCC	10.01	5.88	16.93	12.92	7.47	22.23
	Unknown	HCC	1.65	0.72	3.34	1.88	0.81	3.82
PSC	Non-liver	Cholangiocarcinoma	12.26	4.13	36.40	12.41	4.17	37.01

Supplementary Tables 3. Association between cholangiocarcinoma and azathioprine stratified by year of transplant

Year of transplant	Azathioprine	No. Cases	RR	LCL	UCL
All years	No	24	1.00		
	Yes	18	1.99	1.05	3.70
1987-1994	No	3	1.00		
	Yes	12	1.54	0.47	6.89
1995-1999	No	6	1.00		
	Yes	5	2.80	0.78	9.64
2000-2004	No	12	1.00		
	Yes	1	1.41	0.08	7.33
2005-2008	No	3	---	---	---
	Yes	0			

Supplemental Table 4. Association of hepatocellular carcinoma (HCC) and cholangiocarcinoma with immunosuppressive medication by type of solid organ transplant

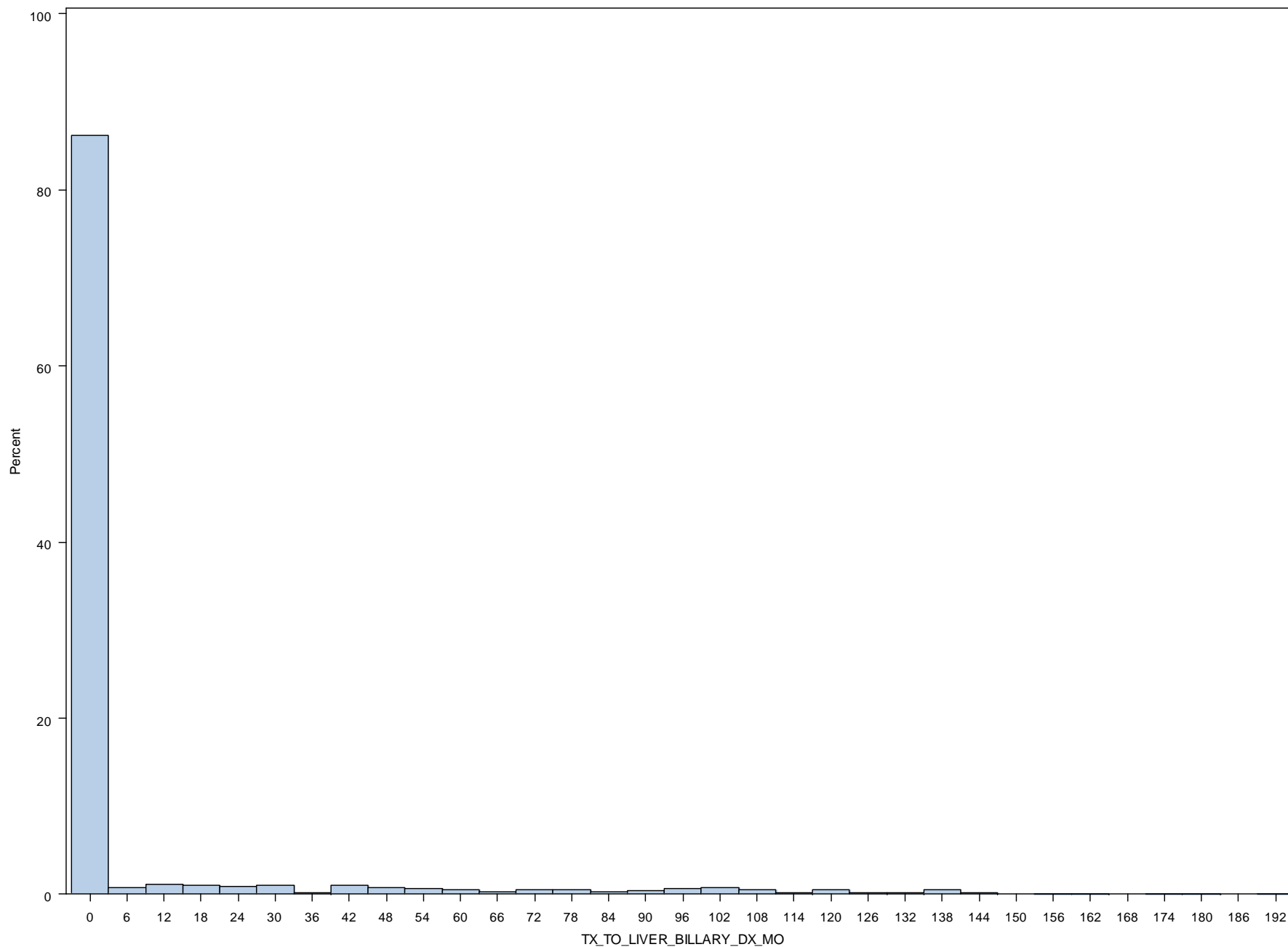
Medication	Organ type	No. Cases	HCC			No. Cases	Cholangiocarcinoma		
			RR*	LCL	UCL		RR*	LCL	UCL
Any induction therapy	All	27	0.92	0.56	1.49	14	0.99	0.49	1.93
	Liver	2	0.60	0.10	1.99	0	---	---	---
	Non-liver	25	0.96	0.56	1.63	14	1.16	0.55	2.46
cyclosporine	All	49	1.35	0.87	2.11	25	1.49	0.79	2.88
	Liver	15	1.90	0.92	3.95	7	1.90	0.64	5.61
	Non-liver	34	1.10	0.65	1.92	18	1.36	0.64	3.08
tacrolimus	All	30	0.71	0.44	1.12	13	0.59	0.29	1.14
	Liver	16	0.71	0.35	1.49	8	0.84	0.29	2.57
	Non-liver	14	0.70	0.37	1.26	5	0.43	0.14	1.04
azathioprine	All	29	1.32	0.83	2.07	18	1.99	1.05	3.70
	Liver	8	1.44	0.60	3.12	4	1.58	0.43	4.76
	Non-liver	21	1.32	0.75	2.27	14	2.39	1.12	5.13
mycophenolate mofetil or MMF	All	31	0.70	0.44	1.09	15	0.67	0.34	1.27
	Liver	4	0.35	0.10	0.90	5	1.33	0.40	3.93
	Non-liver	27	0.85	0.50	1.44	10	0.46	0.20	0.99
mTOR inhibitors	All	1	0.24	0.01	1.07	1	0.49	0.03	2.27
	Liver	0	---	---	---	0	---	---	---
	Non-liver	1	0.31	0.02	1.39	1	0.63	0.04	2.96
steroids	All	81	1.78	0.80	5.06	39	1.42	0.51	5.87
	Liver	28	1.54	0.46	9.54	14	---	---	---
	Non-liver	53	1.93	0.71	7.91	25	0.92	0.32	3.88

*Adjusted for gender, age, and race

Supplemental Table 5. Comparison of independent models for risk factors for hepatocellular carcinoma versus mutually adjusted models. All models adjusted for gender, age, race/ethnicity, and type of organ transplanted.

	Independent models			Mutually adjusted models		
	OR	LCL	UCL	OR	LCL	UCL
HBV						
Uninfected	1.0			1.0		
Active	3.2	1.3	6.9	2.3	0.7	5.7
Resolved	1.8	0.8	3.4	1.0	0.5	2.0
Unknown	1.0	0.4	2.2	2.3	0.5	7.8
HCV						
Negative	1.0			1.0		
Positive	10.0	5.9	16.9	12.3	7.0	22.2
Unknown	1.7	0.7	3.3	0.9	0.2	4.1
BMI						
Underweight	2.5	0.9	5.9	4.4	1.3	11.4
Normal	1.0			1.0		
Overweight	0.8	0.5	1.3	0.9	0.5	1.6
Obese	0.6	0.3	1.2	0.5	0.2	1.1
Diabetes						
No	1.0			1.0		
Insulin-dependent	1.3	0.6	2.5	1.5	0.7	3.0
Non-insulin-dependent	2.5	1.2	4.8	2.9	1.4	5.6
Unknown dependency	3.9	0.6	13.1	3.4	0.6	11.4
Unknown	0.3	0.02	1.5	0.3	0.02	1.5

Supplemental Figure 1. Distribution of hepatobiliary cancer cases by months from transplant to the diagnosis of hepatobiliary cancer.



The large proportion (>80%) of cases diagnosed within 6 months of transplantation is consistent with delayed diagnoses of cancers that were present before transplantation.

Supplemental Methods. Subjects were considered HCV seropositive based on enzyme immunoassay for HCV antibodies.¹¹ Only 0.13% of the cohort was positive for anti-HBc and unknown for HBsAg. Of those positive for anti-HBc (N=35118), 29634 (84%) were negative for HBsAg, 4823 (14%) were positive for HBsAg, and 661 (2%) were unknown. Therefore, recipients who were positive for anti-HBc and unknown for HBsAg were likely negative for HBsAg. In addition, most people with an HBV-related reason for transplant had active (65%) or resolved (17%) infection. Similarly, 81.0% of people with an HCV-related reason for transplant were HCV seropositive, suggesting our classification is generally accurate.