

Figure S1 Flow diagram for the inclusion and exclusion of patients in the study.

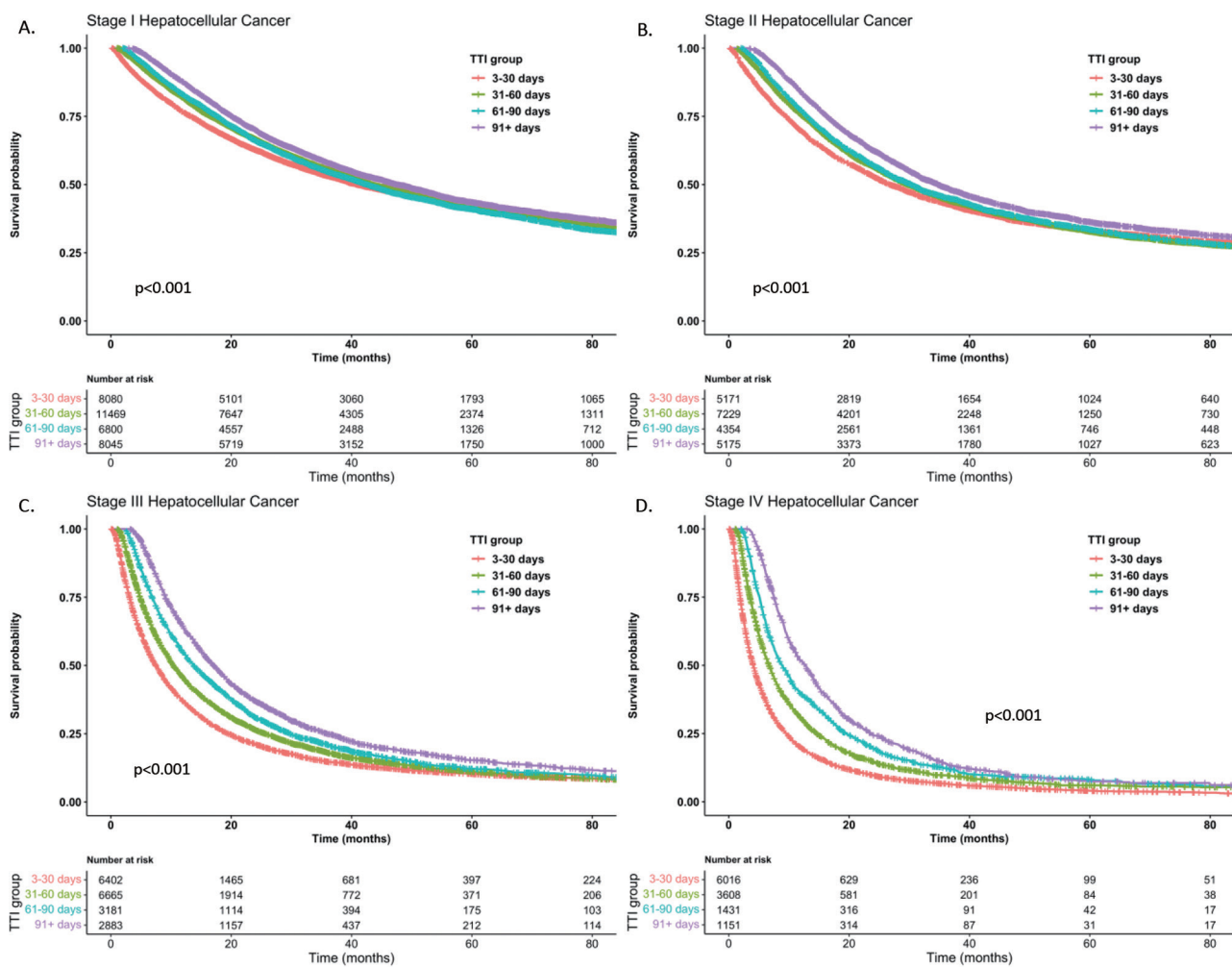


Figure S2 Kaplan-Meier survival analysis for patients with stage I (A), II (B), III (C), and IV (D) hepatocellular carcinoma, stratified by time from diagnosis to initiation of definitive therapy. P values calculated by log-rank test. TTI, time to treatment initiation.

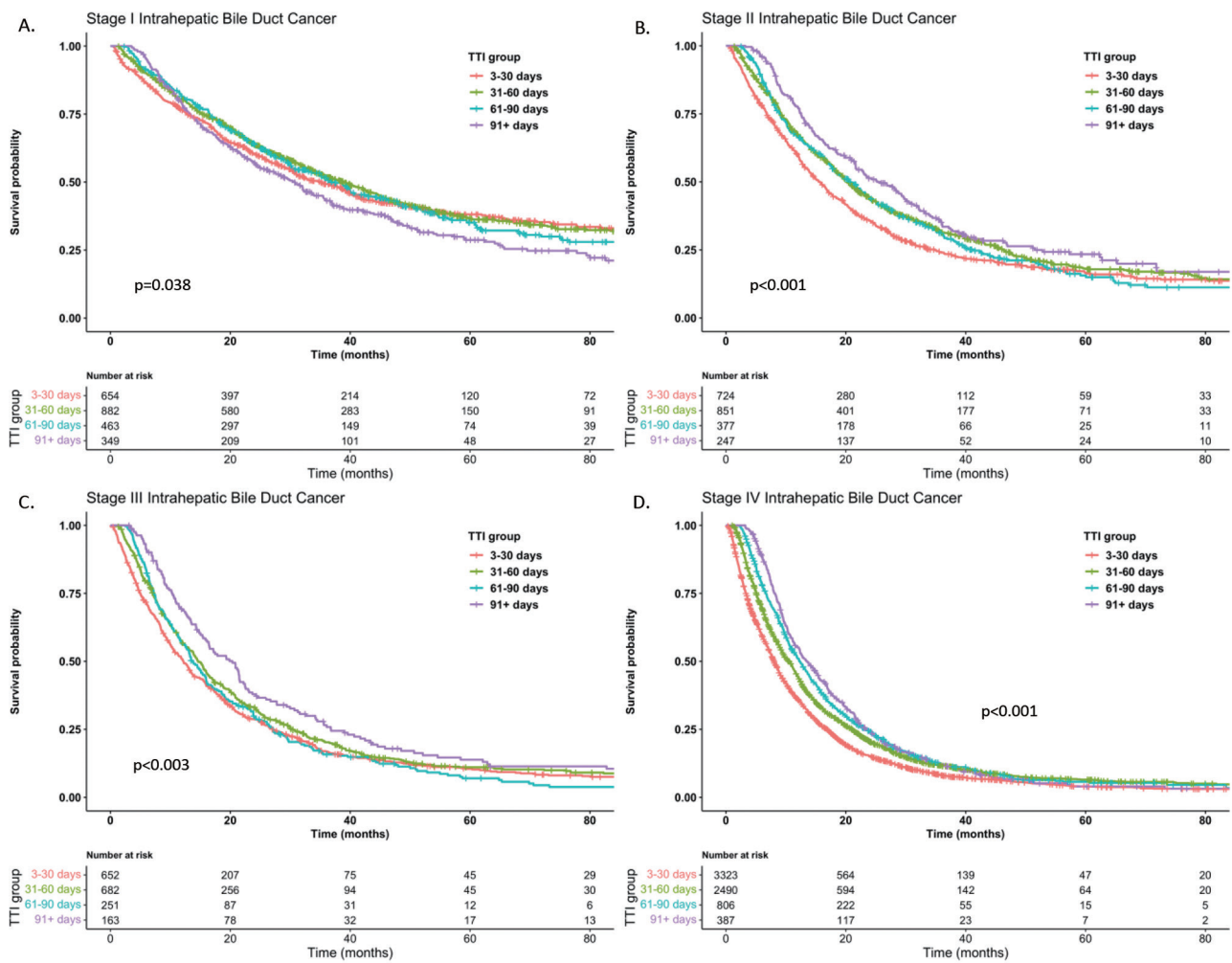


Figure S3 Kaplan-Meier survival analysis for patients with stage I (A), II (B), III (C), and IV (D) intrahepatic bile duct cholangiocarcinoma or adenocarcinoma, stratified by time from diagnosis to initiation of definitive therapy. P values calculated by log-rank test. TTI, time to treatment initiation.

Table S1 Histology and ICD-10 codes included in each cancer cohort

Cancer type	Included histology codes (SEER ICD-0-3)	Included ICD-10 codes
Extrahepatic bile duct	8140–8147	C24.0 - Malignant neoplasm of extrahepatic bile duct
	8160–8163	C24.1 - Malignant neoplasm of ampulla of Vater C24.8 - Malignant neoplasm of overlapping sites of biliary tract C24.9 - Malignant neoplasm of biliary tract, unspecified
Pancreas	8450-8455	8140-8148 C25.0 - Malignant neoplasm of head of pancreas
	8470-8471	8210-8211 C25.1 - Malignant neoplasm of body of pancreas
	8480-8481	8260-8263 C25.2 - Malignant neoplasm of tail of pancreas
	8500	8310 C25.3 - Malignant neoplasm of pancreatic duct
	8503	8323 C25.4 - Malignant neoplasm of endocrine pancreas
	8570-8576	8440-8441 C25.7 - Malignant neoplasm of other parts of pancreas C25.8 - Malignant neoplasm of overlapping sites of pancreas C25.9 - Malignant neoplasm of pancreas, unspecified
Liver	8170-8175	C22.0 - Liver cell carcinoma
Intrahepatic bile duct	8140-8147	C22.1 - Intrahepatic bile duct carcinoma
	8160-8163	

Table S2 Time to treatment initiation by cancer stage

Cancer type and stage	Median TTI in days (IQR)	Number treated in each time frame, n (%)			
		3-30 d	31-60 d	61-90 d	91+ d
EHBD					
Stage I	32 (20–53)	2,202 (47)	1,574 (34)	534 (11)	373 (8)
Stage II	29 (17–46)	4,782 (53)	2,915 (33)	821 (9)	456 (5)
Stage III	30 (17–49)	2,025 (50)	1,323 (33)	409 (10)	270 (7)
Stage IV	32 (20–53)	2,919 (47)	2,095 (34)	789 (13)	447 (7)
All	31 (18–49)	11,928 (50)	7,907 (33)	2,553 (11)	1,546 (7)
Pancreas					
Stage I	29 (19–47)	7,709 (52)	4,794 (32)	1,404 (10)	871 (6)
Stage II	26 (16–40)	36,626 (61)	18,312 (30)	3,778 (6)	1,812 (3)
Stage III	29 (19–44)	13,181 (53)	8,363 (34)	2,080 (8)	1,061 (4)
Stage IV	24 (15–38)	51,287 (64)	22,706 (28)	4,670 (6)	2,060 (3)
All	26 (16–40)	108,803 (60)	54,175 (30)	11,932 (7)	5,804 (3)
Liver					
Stage I	54 (33–87)	8,891 (23)	13,160 (34)	7,843 (20)	9,065 (23)
Stage II	55 (33–88)	5,652 (23)	8,143 (33)	4,962 (20)	5,848 (24)
Stage III	43 (25–70)	6,917 (33)	7,460 (35)	3,628 (17)	3,209 (15)
Stage IV	32 (16–55)	6,674 (49)	4,112 (30)	1,644 (12)	1,307 (10)
All	48 (28–79)	28,134 (29)	32,875 (33)	18,077 (18)	19,429 (20)
IHBD					
Stage I	47 (29–72)	761 (27)	1,038 (37)	557 (20)	423 (15)
Stage II	42 (27–65)	861 (33)	1,028 (39)	446 (17)	304 (12)
Stage III	38 (23–58)	687 (37)	740 (40)	263 (14)	173 (9)
Stage IV	33 (21–50)	3,952 (47)	3,086 (36)	960 (11)	489 (6)
All	37 (22–58)	6,261 (40)	5,892 (37)	2,226 (14)	1,389 (9)

TTI, time to treatment initiation; IQR, interquartile range; d, days; IHBD, intrahepatic bile duct; EHBD, extrahepatic bile duct.

Table S3 Cox proportional hazards regression for overall survival sensitivity analysis: unadjusted model

Cancer type and stage	Time to treatment initiation (days)			
	3-30	31-60	61-90	>90
EHBD				
Stage I	REF	1.19 [1.08–1.30]*	1.44 [1.27–1.63]*	1.61 [1.39–1.86]*
Stage II	REF	1.11 [1.04–1.17]*	1.25 [1.14–1.37]*	1.22 [1.09–1.38]*
Stage III	REF	1.15 [1.06–1.25]*	1.32 [1.17–1.50]*	1.19 [1.02–1.38]*
Stage IV	REF	0.78 [0.73–0.83]*	0.73 [0.67–0.80]*	0.61 [0.54–0.68]*
Pancreas				
Stage I	REF	1.12 [1.07–1.17]*	1.25 [1.16–1.33]*	1.02 [0.94–1.12]
Stage II	REF	1.06 [1.04–1.08]*	1.14 [1.10–1.18]*	1.03 [0.98–1.09]
Stage III	REF	0.99 [0.96–1.02]	1.02 [0.97–1.07]	0.84 [0.79–0.90]*
Stage IV	REF	0.81 [0.80–0.82]*	0.72 [0.70–0.74]*	0.62 [0.59–0.65]*
Liver				
Stage I	REF	0.96 [0.92–0.99]*	0.97 [0.93–1.02]	0.87 [0.84–0.91]*
Stage II	REF	0.95 [0.91–0.99]*	0.93 [0.88–0.98]*	0.82 [0.78–0.86]*
Stage III	REF	0.82 [0.79–0.85]*	0.69 [0.66–0.73]*	0.59 [0.56–0.62]*
Stage IV	REF	0.70 [0.67–0.73]*	0.56 [0.53–0.60]*	0.46 [0.43–0.49]*
IHBD				
Stage I	REF	0.93 [0.81–1.06]	0.99 [0.85–1.16]	1.17 [0.99–1.37]
Stage II	REF	0.83 [0.74–0.92]*	0.86 [0.74–0.99]*	0.70 [0.59–0.83]*
Stage III	REF	0.88 [0.79–0.99]*	0.97 [0.83–1.13]	0.72 [0.60–0.86]*
Stage IV	REF	0.79 [0.75–0.84]*	0.71 [0.65–0.77]*	0.66 [0.59–0.74]*

*, P value <0.05. Covariates included in hazard regression: none. REF, reference group; TTI, time to treatment initiation; IHBD, intrahepatic bile duct; EHBD, extrahepatic bile duct.

Table S4 Cox proportional hazards regression for overall survival sensitivity analysis: adjusted for patient factors only

Cancer type and stage	Time to treatment initiation (days)			
	3-30	31-60	61-90	>90
EHBD				
Stage I	REF	1.13 [1.03–1.24]*	1.34 [1.17–1.53]*	1.54 [1.33–1.79]*
Stage II	REF	1.06 [1.00–1.13]	1.18 [1.07–1.30]*	1.13 [1.00–1.29]*
Stage III	REF	1.12 [1.03–1.22]*	1.31 [1.15–1.50]*	1.19 [1.02–1.39]*
Stage IV	REF	0.77 [0.72–0.82]*	0.72 [0.65–0.78]*	0.59 [0.52–0.66]*
Pancreas				
Stage I	REF	1.08 [1.03–1.13]*	1.19 [1.11–1.28]*	0.98 [0.90–1.08]
Stage II	REF	1.04 [1.02–1.06]*	1.10 [1.06–1.15]*	1.01 [0.95–1.07]
Stage III	REF	0.99 [0.96–1.02]	1.01 [0.96–1.06]	0.84 [0.78–0.90]*
Stage IV	REF	0.80 [0.79–0.82]*	0.71 [0.68–0.73]*	0.61 [0.58–0.64]*
Liver				
Stage I	REF	0.93 [0.89–0.96]*	0.94 [0.90–0.98]*	0.88 [0.84–0.92]*
Stage II	REF	0.92 [0.88–0.96]*	0.89 [0.85–0.94]*	0.81 [0.77–0.85]*
Stage III	REF	0.81 [0.78–0.84]*	0.68 [0.65–0.71]*	0.58 [0.55–0.61]*
Stage IV	REF	0.69 [0.66–0.73]*	0.55 [0.52–0.59]*	0.45 [0.42–0.49]*
IHBD				
Stage I	REF	0.91 [0.79–1.04]	0.92 [0.78–1.08]	1.11 [0.94–1.32]
Stage II	REF	0.80 [0.71–0.90]*	0.82 [0.70–0.95]*	0.65 [0.55–0.78]*
Stage III	REF	0.84 [0.74–0.95]*	0.90 [0.76–1.06]	0.66 [0.54–0.80]*
Stage IV	REF	0.77 [0.73–0.82]*	0.68 [0.63–0.74]*	0.63 [0.56–0.71]*

*, P value <0.05. Covariates included in hazard regression: age (<65 vs. ≥65), sex, race, Hispanic ethnicity, patient insurance, and Charlson-Deyo score. REF, reference group; TTI, time to treatment initiation; IHBD, intrahepatic bile duct; EHBD, extrahepatic bile duct.

Table S5 Cox proportional hazards regression for overall survival sensitivity analysis: adjusted for facility factors only

Cancer type and stage	Time to treatment initiation (days)			
	3-30	31-60	61-90	>90
EHBD				
Stage I	REF	1.23 [1.13–1.35]*	1.52 [1.34–1.74]*	1.74 [1.50–2.02]*
Stage II	REF	1.11 [1.04–1.18]*	1.25 [1.13–1.37]*	1.25 [1.10–1.41]*
Stage III	REF	1.14 [1.05–1.25]*	1.39 [1.22–1.58]*	1.22 [1.05–1.42]*
Stage IV	REF	0.80 [0.75–0.85]*	0.76 [0.69–0.83]*	0.63 [0.56–0.70]*
Pancreas				
Stage I	REF	1.12 [1.07–1.18]*	1.25 [1.16–1.34]*	1.04 [0.95–1.14]
Stage II	REF	1.07 [1.05–1.09]*	1.13 [1.08–1.17]*	1.05 [1.00–1.11]
Stage III	REF	0.98 [0.95–1.01]	0.99 [0.94–1.04]	0.82 [0.77–0.88]*
Stage IV	REF	0.82 [0.81–0.83]*	0.71 [0.69–0.74]*	0.61 [0.58–0.64]*
Liver				
Stage I	REF	0.96 [0.92–1.00]*	0.98 [0.93–1.02]*	0.89 [0.86–0.93]*
Stage II	REF	0.94 [0.90–0.99]*	0.94 [0.89–0.99]*	0.84 [0.80–0.88]*
Stage III	REF	0.83 [0.79–0.86]*	0.69 [0.66–0.73]*	0.60 [0.57–0.63]*
Stage IV	REF	0.69 [0.66–0.72]*	0.56 [0.52–0.59]*	0.46 [0.43–0.49]*
IHBD				
Stage I	REF	0.97 [0.84–1.11]	1.02 [0.87–1.19]	1.23 [1.04–1.46]*
Stage II	REF	0.80 [0.71–0.90]*	0.87 [0.75–1.00]	0.71 [0.60–0.85]*
Stage III	REF	0.91 [0.81–1.02]	1.02 [0.87–1.20]	0.73 [0.60–0.89]*
Stage IV	REF	0.79 [0.75–0.84]*	0.70 [0.65–0.77]*	0.67 [0.59–0.75]*

*, P value <0.05. Covariates included in hazard regression: year of diagnosis (before or after 2013), geographic region, facility urbanicity, and facility type. REF, reference group; TTI, time to treatment initiation; IHBD, intrahepatic bile duct; EHBD, extrahepatic bile duct.

Table S6 Cox proportional hazards regression for overall survival sensitivity analysis: fully-adjusted model with age and year of diagnosis as continuous variables

Cancer type and stage	Time to treatment initiation (days)			
	3-30	31-60	61-90	>90
EHBD				
Stage I	REF	1.14 [1.04–1.25]*	1.33 [1.16–1.53]*	1.55 [1.33–1.81]*
Stage II	REF	1.06 [0.99–1.13]	1.15 [1.05–1.27]*	1.09 [0.96–1.24]
Stage III	REF	1.11 [1.02–1.21]*	1.35 [1.19–1.55]*	1.21 [1.04–1.42]*
Stage IV	REF	0.79 [0.74–0.84]*	0.74 [0.67–0.81]*	0.60 [0.53–0.68]*
Pancreas				
Stage I	REF	1.05 [1.00–1.11]*	1.24 [1.14–1.35]*	0.95 [0.86–1.04]
Stage II	REF	1.03 [1.01–1.06]*	1.06 [1.02–1.11]*	1.01 [0.95–1.07]
Stage III	REF	0.96 [0.93–0.99]*	0.95 [0.90–1.00]	0.79 [0.73–0.85]*
Stage IV	REF	0.81 [0.79–0.82]*	0.69 [0.67–0.72]*	0.59 [0.56–0.62]*
Liver				
Stage I	REF	0.93 [0.90–0.97]*	0.94 [0.90–0.99]*	0.91 [0.87–0.95]*
Stage II	REF	0.92 [0.88–0.96]*	0.91 [0.86–0.95]*	0.82 [0.78–0.86]*
Stage III	REF	0.81 [0.78–0.84]*	0.68 [0.65–0.72]*	0.58 [0.55–0.61]*
Stage IV	REF	0.69 [0.66–0.73]*	0.55 [0.52–0.59]*	0.45 [0.42–0.49]*
IHBD				
Stage I	REF	0.92 [0.80–1.06]	0.92 [0.77–1.08]	1.15 [0.96–1.37]
Stage II	REF	0.78 [0.69–0.88]*	0.82 [0.71–0.96]*	0.67 [0.55–0.80]*
Stage III	REF	0.87 [0.77–0.99]*	0.98 [0.82–1.16]	0.66 [0.53–0.82]*
Stage IV	REF	0.76 [0.72–0.81]*	0.67 [0.61–0.73]*	0.61 [0.54–0.69]*

*, P value <0.05. Covariates included in hazard regression: age (continuous), sex, year of diagnosis (continuous), race, Hispanic ethnicity, geographic region, facility urbanicity, patient insurance, facility type, and Charlson-Deyo score. REF, reference group; TTI, time to treatment initiation; IHBD, intrahepatic bile duct; EHBD, extrahepatic bile duct.

Table S7 Cox proportional hazards regression for overall survival sensitivity analysis: fully-adjusted model with time to treatment initiation as a binary variable, split points at 30 and 60 days

Cancer type and stage	Time to treatment initiation (days)			
	3-30	>30	3-60	>60
EHBD				
Stage I	REF	1.27 [1.17–1.39]*	REF	1.39 [1.25–1.54]*
Stage II	REF	1.09 [1.03–1.16]*	REF	1.13 [1.05–1.22]*
Stage III	REF	1.17 [1.08–1.27]*	REF	1.25 [1.12–1.38]*
Stage IV	REF	0.75 [0.71–0.79]*	REF	0.76 [0.71–0.82]*
Pancreas				
Stage I	REF	1.09 [1.04–1.14]*	REF	1.08 [1.02–1.14]*
Stage II	REF	1.05 [1.03–1.07]*	REF	1.05 [1.02–1.09]*
Stage III	REF	0.96 [0.93–0.99]*	REF	0.92 [0.88–0.96]*
Stage IV	REF	0.77 [0.76–0.78]*	REF	0.71 [0.69–0.73]*
Liver				
Stage I	REF	0.92 [0.89–0.96]*	REF	0.95 [0.93–0.98]*
Stage II	REF	0.88 [0.85–0.92]*	REF	0.90 [0.87–0.93]*
Stage III	REF	0.72 [0.69–0.74]*	REF	0.71 [0.68–0.73]*
Stage IV	REF	0.60 [0.58–0.63]*	REF	0.59 [0.56–0.62]*
IHBD				
Stage I	REF	0.98 [0.86–1.12]	REF	1.08 [0.96–1.21]
Stage II	REF	0.78 [0.70–0.87]*	REF	0.89 [0.79–1.00]*
Stage III	REF	0.86 [0.77–0.97]*	REF	0.90 [0.79–1.03]
Stage IV	REF	0.73 [0.69–0.77]*	REF	0.75 [0.70–0.81]*

*, P value <0.05. Covariates included in hazard regression: age (<65 vs. ≥65), sex, year of diagnosis (before or after 2013), race, Hispanic ethnicity, geographic region, facility urbanicity, patient insurance, facility type, and Charlson-Deyo score. REF, reference group; TTI, time to treatment initiation; IHBD, intrahepatic bile duct; EHBD, extrahepatic bile duct.