

Supplementary Table 1 Routes to diagnosis according to patient and tumour characteristics in cohort diagnosed with cholangiocarcinoma 2006-2017

Characteristics	Route to Diagnosis					P-value ^a	
	EP	TWW referral ¹	GP referral	Othe ²	Unkno wn	EP other routes	TWW other routes
Total patients (<i>n</i> , %)	11715 (49.6)	3253 (13.8)	4835 (20.5)	3181 (13.5)	648 (2.7)		
Age at diagnosis (yr)							
0-44	214 (43.9)	26 (5.3)	118 (24.2)	110 (22.5)	20 (4.1)	< 0.001	< 0.001
45-54	528 (41.2)	162 (12.6)	301 (23.5)	249 (19.4)	42 (3.3)		
55-64	1342 (38.7)	516 (14.9)	810 (23.4)	675 (19.5)	123 (3.5)		
65-74	2700 (42.8)	1016 (16.1)	1430 (22.6)	999 (15.8)	170 (2.7)		
75-84	4049 (53.2)	1079 (14.2)	1476 (19.4)	820 (10.8)	182 (2.4)		
> 84	2882 (64.4)	454 (10.1)	700 (15.6)	328 (7.3)	111 (2.5)		
Gender							
Male	5452 (47.5)	1599 (13.9)	2408 (21.0)	1697 (14.8)	310 (2.7)	< 0.001	0.446
Female	6263 (51.5)	1654 (13.6)	2427 (19.9)	1484 (12.2)	338 (2.8)		
Year of diagnosis							
2006	813 (51.3)	157 (9.9)	295 (18.6)	269 (17.0)	51 (3.2)	0.004	< 0.001
2007	771 (50.1)	156 (10.1)	311 (20.2)	254 (16.5)	48 (3.1)		
2008	886 (51.2)	181 (10.5)	326 (18.8)	279 (16.1)	60 (3.5)		
2009	970 (52.0)	204 (10.9)	338 (18.1)	298 (16.0)	57 (3.1)		
2010	983 (50.4)	231 (11.8)	381 (19.5)	308 (15.8)	49 (2.5)		
2011	975 (49.3)	233 (11.8)	445 (22.5)	276 (14.0)	48 (2.4)		

Characteristics		Route to Diagnosis					P-value ^a	
		EP	TWW referral ¹	GP referral	Othe ²	Unkno wn	EP other routes	<i>vs</i> TWW <i>vs</i> other routes
	2012	968 (48.5)	288 (14.4)	440 (22.0)	257 (12.9)	44 (2.2)		
	2013	1073 (50.9)	313 (14.8)	455 (21.6)	242 (11.5)	27 (1.3)		
	2014	1042 (50.6)	288 (14.0)	443 (21.5)	237 (11.5)	50 (2.4)		
	2015	1081 (48.8)	361 (16.3)	461 (20.8)	268 (12.1)	46 (2.1)		
	2016	1080 (47.7)	379 (16.8)	500 (22.1)	239 (10.6)	64 (2.8)		
	2017	1073 (46.0)	462 (19.8)	440 (18.9)	254 (10.9)	104 (4.5)		
Stage at diagnosis	1	141 (37.4)	73 (19.4)	94 (24.9)	59 (15.6)	10 (2.7)	< 0.001	< 0.001
	2	294 (33.7)	156 (17.9)	234 (26.8)	173 (19.8)	16 (1.8)		
	3	165 (38.4)	87 (20.2)	97 (22.6)	70 (16.3)	11 (2.6)		
	4	2336 (47.5)	942 (19.2)	994 (20.2)	537 (10.9)	109 (2.2)		
	Unstaged	8779 (51.5)	1995 (11.7)	3416 (20.1)	2342 (13.7)	502 (2.9)		
Performance status at diagnosis	0	228 (32.1)	166 (23.3)	180 (25.3)	113 (15.9)	24 (3.4)	< 0.001	< 0.001
	1	337 (39.5)	215 (25.2)	197 (23.1)	90 (10.5)	15 (1.8)		
	2+	540 (57.8)	179 (19.2)	139 (14.9)	65 (7.0)	11 (1.2)		
	Not recorded	10610 (50.2)	2693 (12.7)	4319 (20.4)	2913 (13.8)	598 (2.8)		
Tumour sub-type	CCA Other	752 (50.1)	202 (13.5)	289 (19.3)	221 (14.7)	36 (2.4)	< 0.001	0.651
	eCCA	2031 (46.2)	589 (13.4)	959 (21.8)	724 (16.5)	97 (2.2)		

Characteristics		Route to Diagnosis					P-value ^a	
		EP	TWW referral ¹	GP referral	Othe ²	Unkno wn	EP other routes	<i>vs</i> TWW <i>vs</i> other routes
Tumour morphology	iCCA	8932 (50.4)	2462 (13.9)	3587 (20.2)	2236 (12.6)	515 (2.9)		
	Adenomas and adenocarcinomas	10701 (49.0)	3049 (14.0)	4532 (20.8)	2939 (13.5)	610 (2.8)	< 0.001	0.002
	Other	1014 (56.3)	204 (11.3)	303 (16.8)	242 (13.4)	38 (2.1)		
English Index of Multiple Deprivation, income component	Quintile 1 (least deprived)	2005 (44.6)	659 (14.7)	996 (22.2)	676 (15.1)	155 (3.5)	< 0.001	0.011
	Quintile 2	2328 (46.9)	713 (14.4)	1091 (22.0)	687 (13.8)	147 (3.0)		
	Quintile 3	2359 (48.9)	678 (14.1)	994 (20.6)	676 (14.0)	116 (2.4)		
	Quintile 4	2498 (52.7)	632 (13.3)	901 (19.0)	590 (12.4)	121 (2.6)		
	Quintile 5 (most deprived)	2525 (54.8)	571 (12.4)	853 (18.5)	552 (12.0)	109 (2.4)		
Charlson Comorbidity Index	0	8306 (47.5)	2694 (15.4)	3588 (20.5)	2356 (13.5)	547 (3.1)	< 0.001	< 0.001
	1	1556 (53.5)	315 (10.8)	607 (20.9)	380 (13.1)	48 (1.7)		
	2	893 (54.8)	145 (8.9)	328 (20.1)	236 (14.5)	28 (1.7)		
	3+	960 (59.8)	99 (6.2)	312 (19.4)	209 (13.0)	25 (1.6)		
Underlying liver disease	No	10904 (49.6)	3095 (14.1)	4451 (20.3)	2889 (13.2)	628 (2.9)	0.48	< 0.001
	Yes	811 (48.7)	158 (9.5)	384 (23.1)	292 (17.5)	20 (1.2)		

Characteristics	Route to Diagnosis					P-value ^a	
	EP	TWW referral ¹	GP referral	Othe ²	Unkno wn	EP other routes	vs TWW other routes
Cancer Alliance at diagnosis	638 (52.4)	117 (9.6)	264 (21.7)	174 (14.3)	25 (2.1)	< 0.001	< 0.001
Cheshire and Merseyside							
East Midlands	1023 (47.3)	325 (15.0)	491 (22.7)	276 (12.8)	49 (2.3)		
East of England - North	667 (51.4)	203 (15.6)	253 (19.5)	127 (9.8)	48 (3.7)		
East of England - South	690 (51.0)	150 (11.1)	272 (20.1)	192 (14.2)	48 (3.6)		
Greater Manchester	702 (54.9)	149 (11.7)	240 (18.8)	165 (12.9)	22 (1.7)		
Humber, Coast and Vale	457 (53.0)	137 (15.9)	180 (20.9)	69 (8.0)	19 (2.2)		
Kent and Medway	316 (47.6)	80 (12.0)	135 (20.3)	110 (16.6)	23 (3.5)		
Lancashire and South Cumbria	447 (52.4)	129 (15.1)	143 (16.8)	111 (13.0)	23 (2.7)		
North Central London	197 (48.3)	37 (9.1)	84 (20.6)	71 (17.4)	19 (4.7)		

Characteristics	Route to Diagnosis					P-value ^a	
	EP	TWW referral ¹	GP referral	Othe ²	Unkno wn	EP other routes	vs TWW other routes
North East London	271 (54.4)	59 (11.8)	80 (16.1)	75 (15.1)	13 (2.6)		
North West and South West London	550 (49.6)	93 (8.4)	228 (20.6)	190 (17.1)	48 (4.3)		
Northern Peninsula Somerset, Wiltshire, and Gloucestershire	900 (49.0)	319 (17.4)	357 (19.5)	223 (12.2)	36 (2.0)		
Avon and Gloucestershire	362 (38.1)	127 (13.4)	270 (28.4)	172 (18.1)	19 (2.0)		
South East London	595 (50.0)	178 (14.9)	228 (19.1)	158 (13.3)	32 (2.7)		
South East London	260 (52.3)	66 (13.3)	93 (18.7)	58 (11.7)	20 (4.0)		
South Yorkshire and Bassetlaw	386 (58.9)	100 (15.3)	96 (14.7)	65 (9.9)	8 (1.2)		
Surrey and Sussex	625 (46.2)	173 (12.8)	308 (22.7)	196 (14.5)	52 (3.8)		

Characteristics	Route to Diagnosis					P-value ^a	
	EP	TWW referral ¹	GP referral	Othe ²	Unkno wn	EP other routes	vs TWW vs other routes
Thames Valley	270 (45.8)	86 (14.6)	110 (18.6)	100 (16.9)	24 (4.1)		
Wessex	560 (45.7)	232 (18.9)	234 (19.1)	170 (13.9)	29 (2.4)		
West Midlands	1220 (47.4)	319 (12.4)	600 (23.3)	363 (14.1)	71 (2.8)		
West Yorkshire and Harrogate	579 (54.7)	174 (16.4)	169 (16.0)	116 (11.0)	20 (1.9)		

¹TWW - Two Week Wait, urgent GP referrals with a suspicion of cancer.

²Other includes: DCO - Diagnosis by death certificate only, Inpatient elective and other outpatient.

^aP-value calculated using Pearson's chi-squared test.

EP: Emergency Presentation; iCCA: Intrahepatic cholangiocarcinoma; eCCA: Extrahepatic cholangiocarcinoma.