Biliary Tract and Liver Complications in Polycystic Kidney Disease

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Supplemental Table 1: Management of biliary tract disease and serious liver

complications in patients with polycystic kidney disease treated by Oxford Kidney

Unit

Complication	Total number of admissions (number of patients)	Management	Number of Admissions (number of patients)
Biliary tract disease comp	olications		
Biliary sepsis (including cholecystitis and cholangitis	90 (21)	Antibiotics	90 (21)
Cholelithiasis ± Choledocholithiasis	26 (21)	Ursodeoxycholic acid	2 (2)
Choledocholitilidais		*ERCP with:	
		- Stone removal	21 (11)
		- Sphincterotomy	13 (5)
		- Stent	8 (3)
		- Sludge trawled	4 (4)
		Percutaneous cholecystostomy	1 (1)
		Laparoscopic/open cholecystectomy	8 (8)
		Biliary bypass	1 (1)
Serious liver complication	IS		
Infected liver cyst and/or abscess	22 (12)	Antibiotics	22 (22)
		Ultrasound-guided cyst aspiration	3 (3)
Liver cyst de-roofing	4 (4)		
Extrinsic compression		ERCP and stent	1 (1)
from liver cysts	1 (1)	Liverhierev	1 (1)
Abnormal liver architecture/focal	1 (1)	Liver biopsy	1 (1)
cholangitis			
Refractory ascites	1 (1)		
Liver hemorrhage	1 (1)	Partial hepatectomy	1 (1)
Liver failure	2 (2)	Liver transplant	2 (2)
Subphrenic abscess	1 (1)	Drainage and antibiotics	1 (1)

ERCP = Endoscopic retrograde cholangiopancreatography

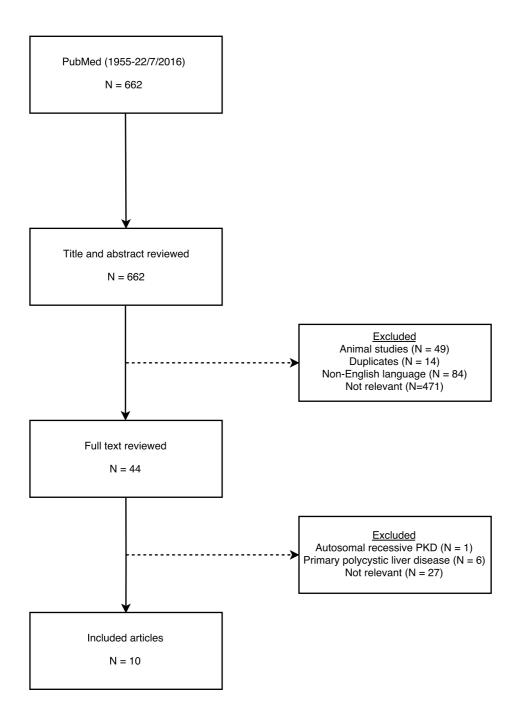
Supplemental Table 2: Diagnostic and procedural codes used to define biliary tract

disease, serious liver complications and extra-renal complications

ICD-10 (ICD-9) codes	ICD-10 descriptions	OPCS-4 codes	OPCS-4 descriptions	
Biliary tract disease	descriptions	codes	descriptions	
K80.0-K80.2 (574.0, 547.1,	Gallbladder calculi – with or	J20.2	Closure of cholecystotomy	
574.2, 574.6-574.9, 575) K82.1-K82.3 (575.2-575.5)	without cholecystitis Hydrops of gallbladder,	J21.1-J21.3, J24.1-J24.9, J26.1	Open and percutaneous removal of calculus from gallbladder and drainage o gallbladder	
	perforation or fistula			
K82.8-K82.9 (575.8, 575.9)	Other diseases of the gallbladder	J18.1-J18.9	Partial/Total cholecystectomy and exploration of common bile duct	
K80.3-K80.5 (574.3-574.5, 574.6-574.9)	Calculi in bile ducts with/without cholecystitis or cholangitis	J25.8, J25.9, J26.1, J26.8, J26.9	Other gallbladder and calculus procedures	
		J24.1-J24.8	Percutaneous treatments to stones	
K80.8, K81.0, K81.1, K81.8, K81.9 (575.0, 575.1)	Other cholelithiasis, cholecystitis	J41.1, J76.1	Endoscopic retrograde extraction of calculus from bile duct	
K83.0 (576.1)	Cholangitis	J33.1-J34.3, J35.1-J35.9,		
K83.1-K83.3 (576.2)	Obstruction of bile duct	J38.1-J39.1 J38.1-J39.1	Sphincterotomy/-plasty	
K83.8-K83.9 (576.8, 576.9)	Other diseases of the biliary tract	J48.5-J49.2	Percutaneous drainage of liver/gallbladder, t-tube insertion	
K74.3-K74.5 (571.6)	Biliary cirrhosis	J43.3	Endoscopic retrograde cholangiopancreatography and collectio of bile	
K85 (577.0)	Acute pancreatitis			
		J42.3	Endoscopic retrograde removal of calculus from pancreatic duct	
Serious liver complication K74.0-K74.2	Hepatic fibrosis,	J02.1-J02.9	Liver resection	
	Sclerosis	J08.1, J08.2	Investigation of liver and gallbladder	
K74.6 (571.5)	Other and unspecified cirrhosis of liver	Y06.2	Deroofing of cyst of organ	
K76.9 (571.9)	Liver disease, unspecified	J08.8, J08.9	Unspecified therapeutic endoscopic	
K75.0 (572.0)	Abscess of liver		operations on liver using laparoscope	
Z94.4	Liver transplant status	J01.1-J01.3, J01.5-J01.9	Transplantation of liver	
T86.4	Liver transplant failure and rejection			
End-stage renal disease				
Complex algorithm				
Cerebral aneurysm I60 (430)	Subarachnoid haemorrhage	L33-L34	Operation on cerebral aneurysm	
Other abdominal wall hernia K41 (551.0, 552.0, 553.0)	Femoral hernia	T22-T23	Femoral hernia repair	
K42 (551.1, 552.1, 553.1)	Umbilical hernia	T24	Umbilical hernia repair	
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595)	Urinary tract infections			
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595)	Urinary tract infections Mitral valve regurgitation	K25, K30.1	Mitral valve repair	
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595) Cardiac valve disease		K25, K30.1 K26, K30.2	Mitral valve repair Aortic valve repair	
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595) Cardiac valve disease I34.0 (424.0)	Mitral valve regurgitation		·	
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595) Cardiac valve disease I34.0 (424.0) I34.1 (424.0)	Mitral valve regurgitation Mitral valve prolapse		·	
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595) Cardiac valve disease I34.0 (424.0) I34.1 (424.0) I34.2 (394.0) I35.1 (424.1) I35.0 (424.1)	Mitral valve regurgitation Mitral valve prolapse Mitral valve stenosis		·	
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595) Cardiac valve disease I34.0 (424.0) I34.1 (424.0) I34.2 (394.0) I35.1 (424.1) I35.0 (424.1)	Mitral valve regurgitation Mitral valve prolapse Mitral valve stenosis Aortic valve regurgitation		·	
Urinary tract infections N10, N13.6, N15.1, N30, N39.0 (590, 595) Cardiac valve disease 134.0 (424.0) 134.1 (424.0) 134.2 (394.0) 135.1 (424.1) 135.0 (424.1) Breast cancer	Mitral valve regurgitation Mitral valve prolapse Mitral valve stenosis Aortic valve regurgitation		·	

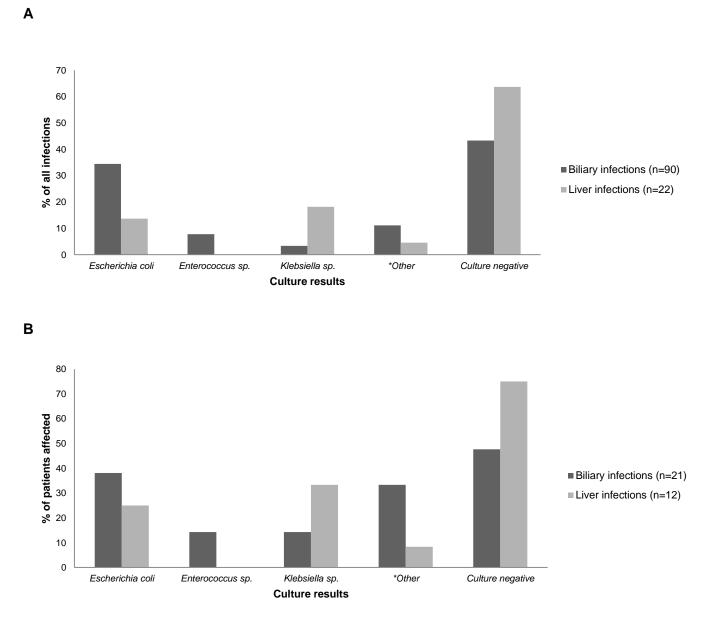
ICD-10 (ICD-9)	ICD-10	OPCS-4	OPCS-4
codes	descriptions	codes	descriptions
Aortic or other aneurysms			
171.1-171.2 (441.1-441.2)	Thoracic aortic aneurysm	L18-L19, L27-L28	Abdominal aneurysm repair
171.0 (441.0)	Aortic dissection	L48-49	lliac artery aneurysm repair
171.3-171.6 (441.3-441.9)	Abdominal aortic aneurysm		
172 (442)	Other aneurysm		
Hiatus hernia and gastroesoph	nageal reflux disease		
K44, Q40.1, Q79.0 (551.3, 552.3, 553.3, 750.6, 756.6)	Diaphragmatic hernia		
K20-K21 (530.1-530.2)	Gastro-oesophageal reflux disease or oesophagitis		
Renal stones	alcoace of ecceptingine		
N20-N23 (592, 594)	Urolithiasis		
ICD = International Classification	of Disease. OPCS= Office of Popu	lation Censuses and Survey	s' Classification of Interventions and Procedures.

Supplemental Figure 1: PubMed literature search for biliary tract disease and serious liver complications in autosomal dominant polycystic kidney disease



Search terms included polycystic kidney disease (PKD), polycystic liver disease (PLD), hepatic complications, gallstones, cholecystitis, gallbladder and other specific treatments for PLD and PKD.

Supplemental Figure 2: Organisms identified during biliary tract and liver infections in patients with polycystic kidney disease treated by Oxford Kidney Unit by; admissions (panel A), and by patient (panel B)



* Other infections include: *Pseudomonas aeruginosa* (liver=1, biliary=3), *Serratia marcesens* (biliary=2), extended spectrum beta lactamase (biliary=2), *Enterococcus* sp. (biliary=2), *Proteus* sp. (biliary=1). The 90 biliary infections occurred in a total of 21 patients and the 22 liver infections occurred in a total of 12 patients.

Supplemental Figure 3: Association between polycystic kidney disease and risk of hospitalisation for different disease by diagnostic position in all–England Hospital Episode Statistics 1998–2012 (sensitivity analysis)

All patients

	Number of ev	ents (% per year)	Number of ev	ents (% per year))	Primary and secondary diagn	
Outcome	Polycystic kidney disease (n=23,454)	Hospital controls (n=6,412,754)	Polycystic kidney disease (n=23,454)	Hospital controls (n=6,412,754)		Primary diagno Rate ratio (95% CI)	sis only Rate ratio (95% CI)
Cerebral aneurysm	311 (0.14%)	12,867 (0.02%)	283 (0.13%)	11,262 (0.02%)		5.95 (5.31–6.66)	6.25 (5.55–7.03)
Serious liver complication	767 (0.31%)	37,232 (0.07%)	314 (0.13%)	15,310 (0.03%)		4.67 (4.35–5.02)	4.64 (4.15–5.19)
Other abdominal wall hernia	1,050 (0.46%)	60,963 (0.11%)	867 (0.38%)	52,567 (0.09%)		4.22 (3.97–4.49)	4.08 (3.82–4.37)
Urinary tract infections	5,897 (3.21%)	546,411 (1.01%)	3,570 (1.86%)	275,893 (0.50%)	۳.	3.19 (3.11–3.27)	3.71 (3.59–3.84)
Cardiac valve disease	1,305 (0.53%)	125,584 (0.23%)	370 (0.14%)	40,448 (0.07%)	■	2.34 (2.22–2.47)	1.88 (1.69–2.08)
Biliary tract disease	2,617 (1.31%)	319,621 (0.59%)	1,704 (0.85%)	266,019 (0.49%)	-	2.24 (2.16–2.33)	1.74 (1.66–1.82)
Diverticular disease	3,151 (1.38%)	354,432 (0.65%)	1,511 (0.64%)	175,350 (0.32%)	8	2.12 (2.05–2.20)	2.02 (1.92–2.13)
Inguinal hernia	1,225 (0.43%)	174,625 (0.32%)	1,046 (0.36%)	165,553 (0.30%)	2	1.35 (1.27–1.42)	1.21 (1.14–1.29)
					0.5 1 2 t Rate ratio	5 10	

CI = confidence intervals. Outcomes include admissions with relevant diagnostic codes in either any diagnostic position or primary diagnostic position only, or any relevant procedural codes. Adjusted for age at entry as a continuous variable (using both linear and quadratic terms), sex, ethnicity, quintile of patients' Index of Multiple Deprivation score, region of residence, calendar year of first recorded admission and comorbidities (grouped into vascular, cancer and diabetes).

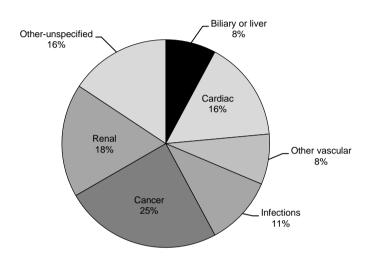
Supplemental Figure 4: Association between polycystic kidney disease and risk of hospitalisation for different diseases by diagnostic position in all–England Hospital Episode Statistics 1998–2012 (sensitivity analysis)

Treated end-stage renal disease patients

Number of events (% per year)		Number of events (% per year)		Primary and secondary diagnosis			
Outcome	Polycystic kidney disease (n=5,813)	Other primary renal diagnosis (n=62,519)	Polycystic kidney disease (n=5,813)	Other primary renal diagnosis (n=62,519)		Primary diagno Rate ratio (95% CI)	sis only Rate ratio (95% CI)
Cerebral aneurysm	37 (0.13%)	150 (0.06%)	32 (0.11%)	118 (0.05%)		2.23 (1.53–3.26)	2.44 (1.61–3.68)
Serious liver complication	197 (0.70%)	1,561 (0.62%)	61 (0.21%)	314 (0.12%)		1.15 (0.98–1.33)	1.67 (1.26–2.23)
Other abdominal wall hernia	365 (1.23%)	1,242 (0.50%)	295 (0.93%)	943 (0.38%)		2.47 (2.19–2.80)	2.45 (2.14–2.81)
Urinary tract infections	1,369 (6.29%)	11,268 (4.93%)	874 (3.64%)	6,373 (2.66%)	-	1.28 (1.20–1.35)	1.37 (1.27–1.47)
Cardiac valve disease	366 (1.47%)	4,128 (1.63%)	108 (0.36%)	951 (0.38%)	-	0.90 (0.81–1.00)	0.95 (0.78–1.17)
Biliary tract disease	494 (1.92%)	4,014 (1.61%)	321 (1.16%)	2,237 (0.89%)		1.19 (1.08–1.31)	1.30 (1.15–1.47)
Diverticular disease	738 (2.70%)	4,069 (1.64%)	321 (1.01%)	1,559 (0.62%)		1.65 (1.52–1.79)	1.62 (1.43–1.84)
Inguinal hernia	269 (1.00%)	1,490 (0.59%)	230 (0.82%)	1,240 (0.49%)	-8-	1.70 (1.49–1.95)	1.67 (1.44–1.93)
					0.5 1 2 5 Rate ratio	5 10	

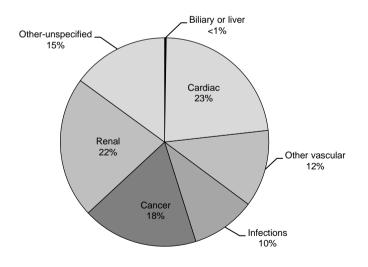
CI = confidence intervals. Outcomes include admissions with relevant diagnostic codes in either any diagnostic position or primary diagnostic position only, or any relevant procedural codes. Adjusted for age at entry as a continuous variable (using both linear and quadratic terms), sex, ethnicity, quintile of patients' Index of Multiple Deprivation score, region of residence, calendar year of renal replacement therapy start and comorbidities (grouped into vascular, cancer and diabetes).

Supplemental Figure 5: Underlying causes of death in all people with polycystic kidney disease by; prior biliary tract or serious liver complication (panel A), or without such complications

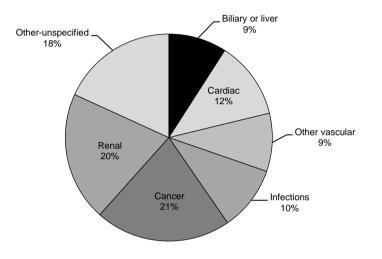


A: (1,128 deaths in 3,136 patients)

B: (6,192 deaths in 20,318 patients)



Supplemental Figure 6: Underlying causes of death in all people with polycystic kidney disease and prior biliary tract or serious liver complications in; females (panel A), or males (panel B)



A: Females (509 deaths in 1,580 patients)

B: Males (619 deaths in 1,556 patients)

