

**Late diagnosis of chronic liver disease in a community cohort (UK Biobank):
determinants and impact on subsequent survival**

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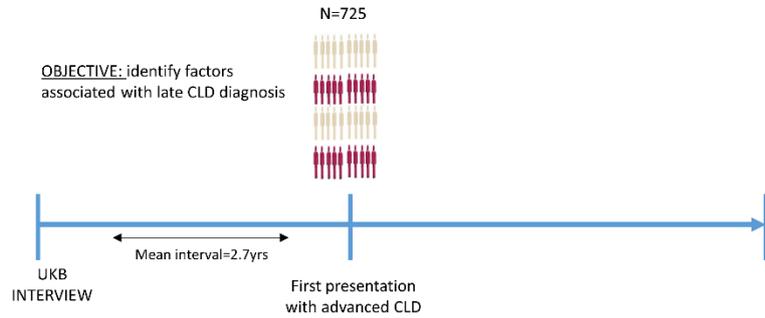
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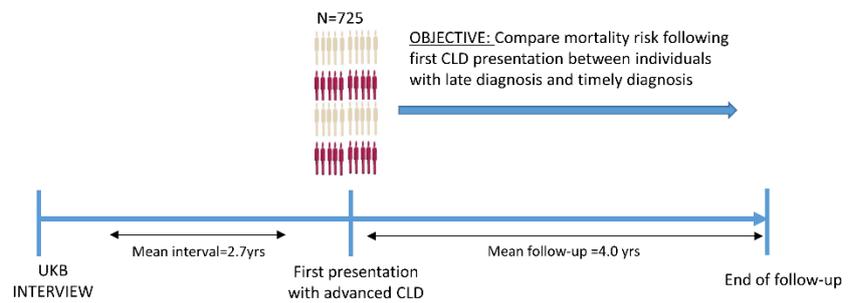
SUPPLEMENTARY TABLES, FIGURES AND APPENDICES

Supplementary Figure 1. Schematic of analysis #1 and analysis #2

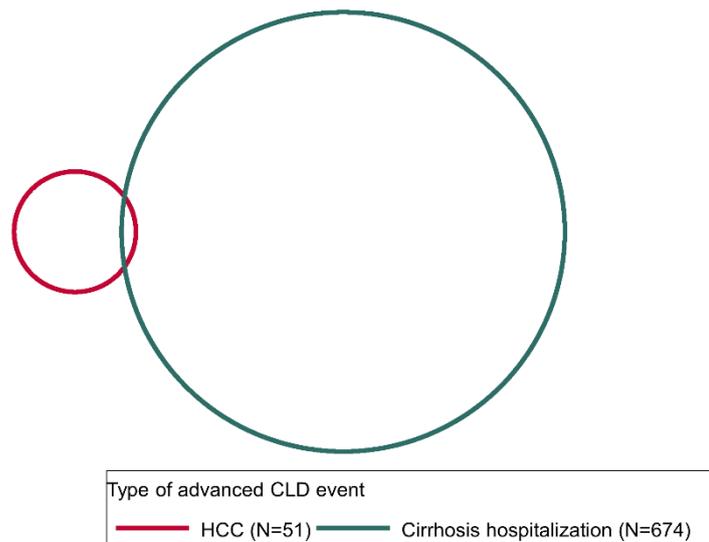
ANALYSIS#1



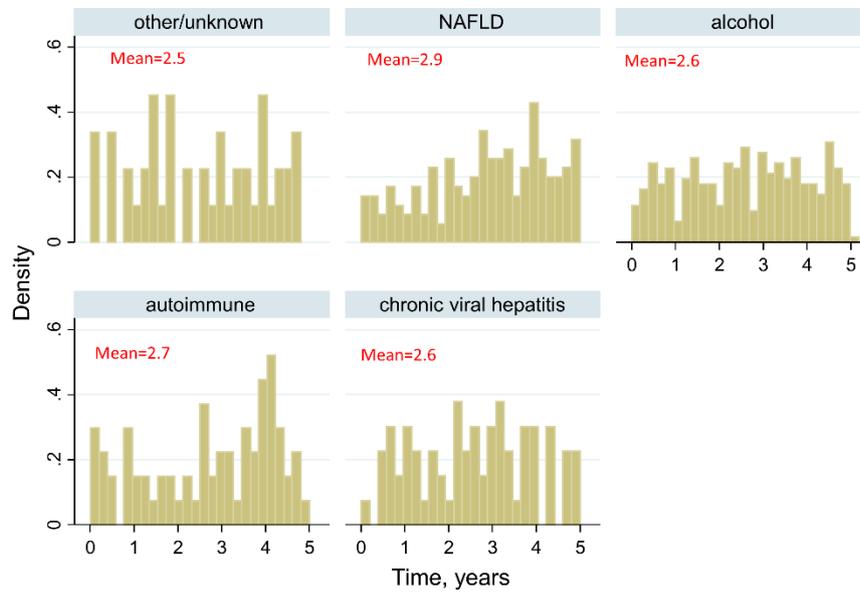
ANALYSIS#2



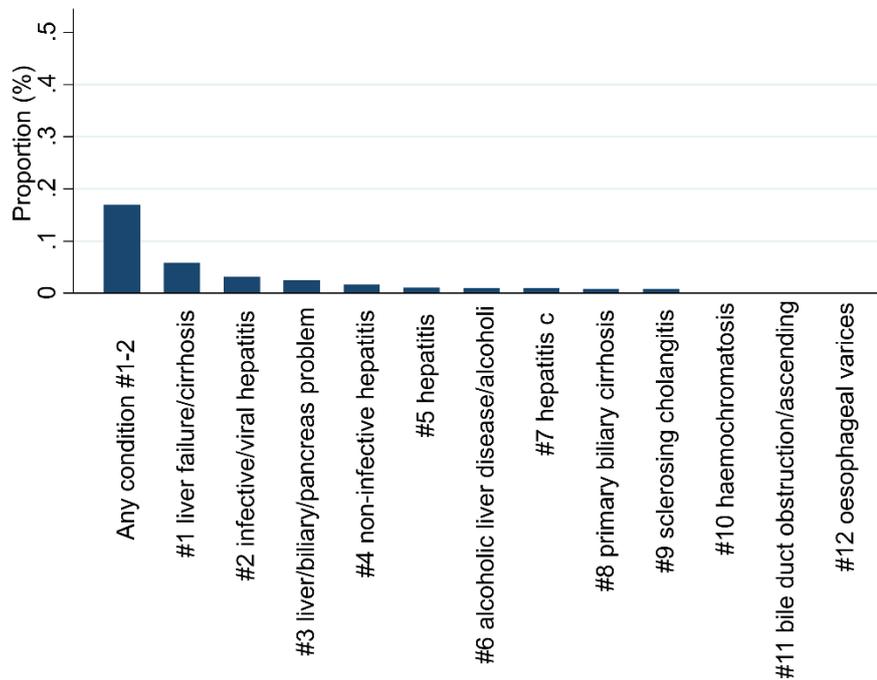
Supplementary Figure 2. Type of first advanced CLD event: Venn diagram (N=725)



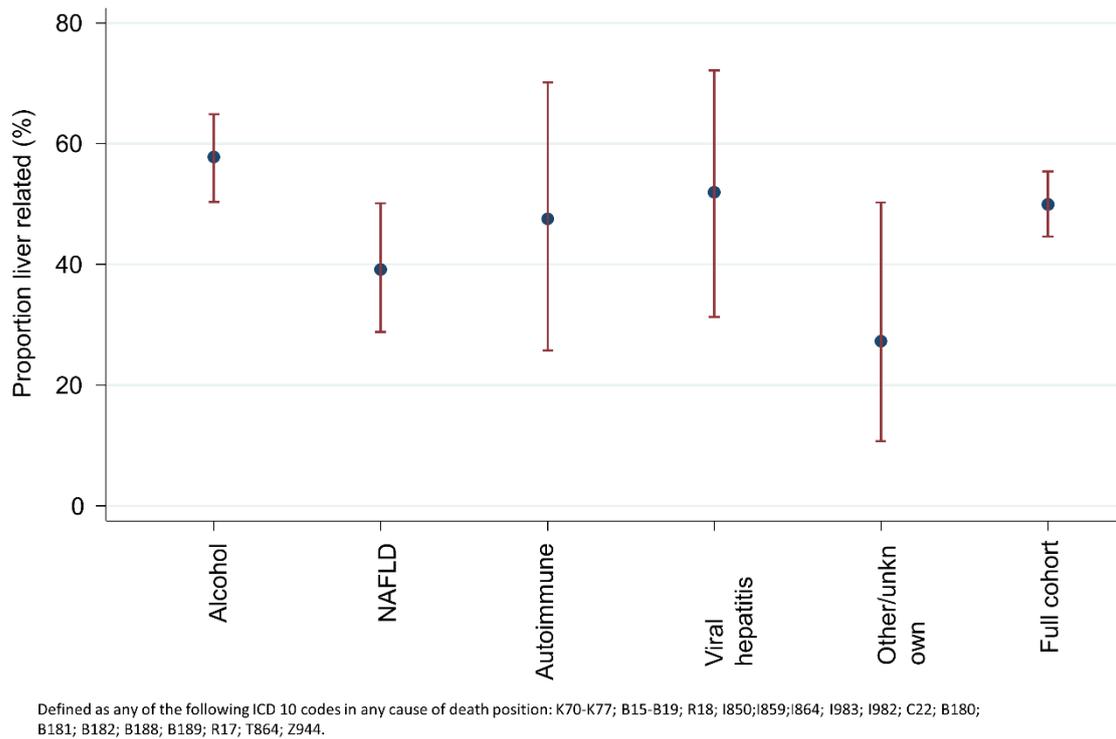
Supplementary Figure 3. Time between UK biobank recruitment and first advanced CLD event, by aetiology (N=725)



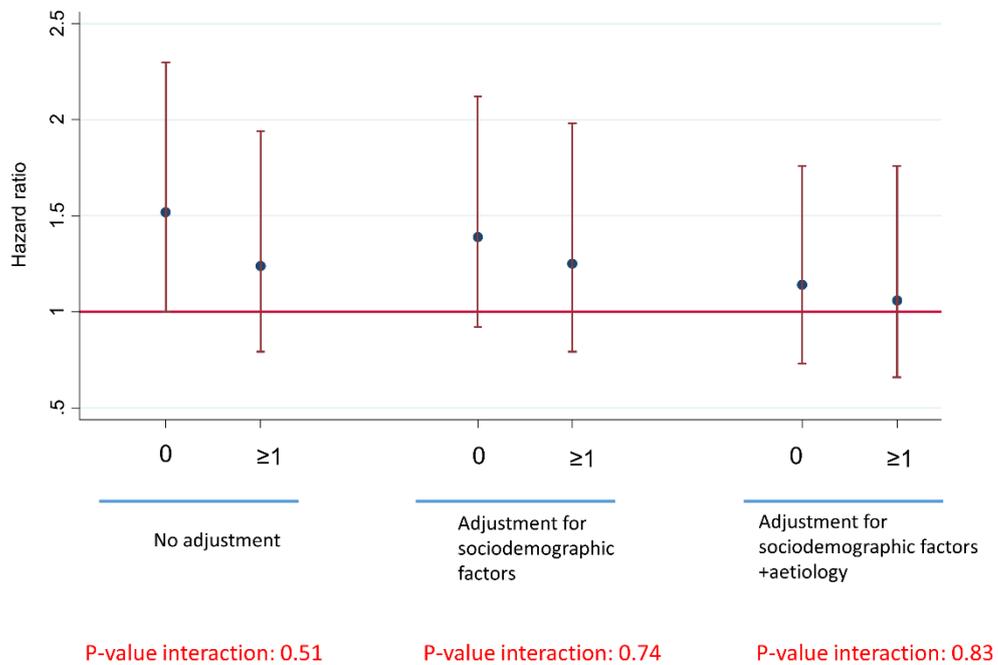
Supplementary Figure 4. Frequency of specific chronic liver disease conditions reported at UK biobank recruitment (N=725)



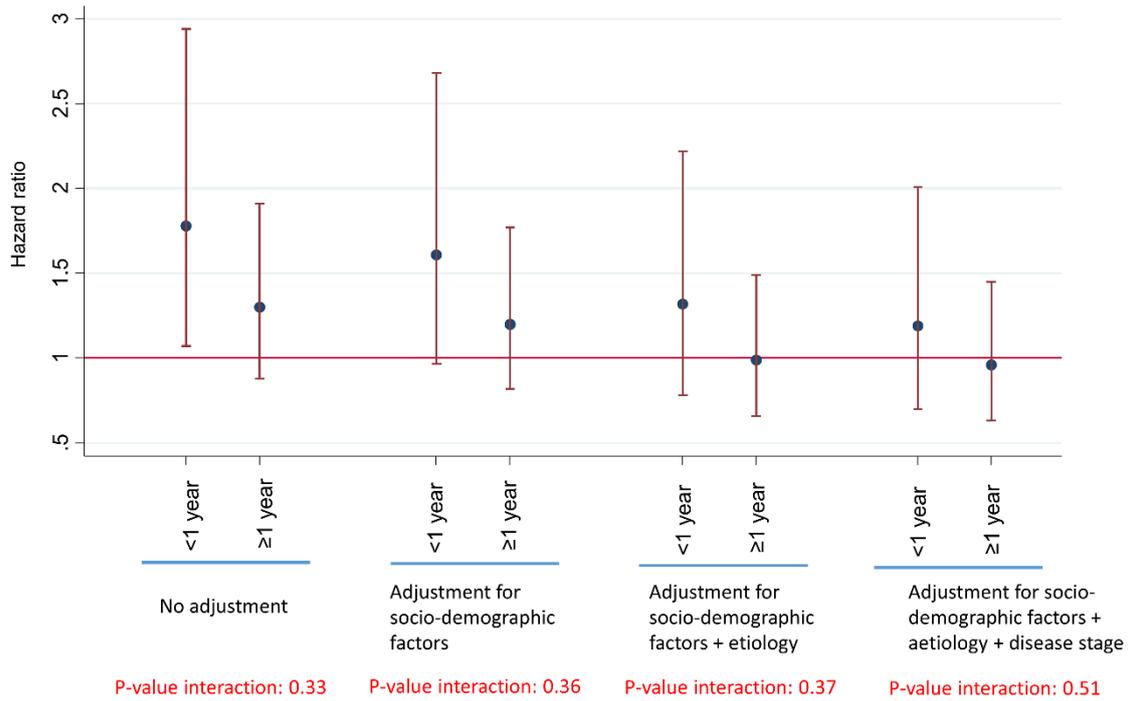
Supplementary Figure 5. Proportion of all-cause deaths that are liver related (N=342).



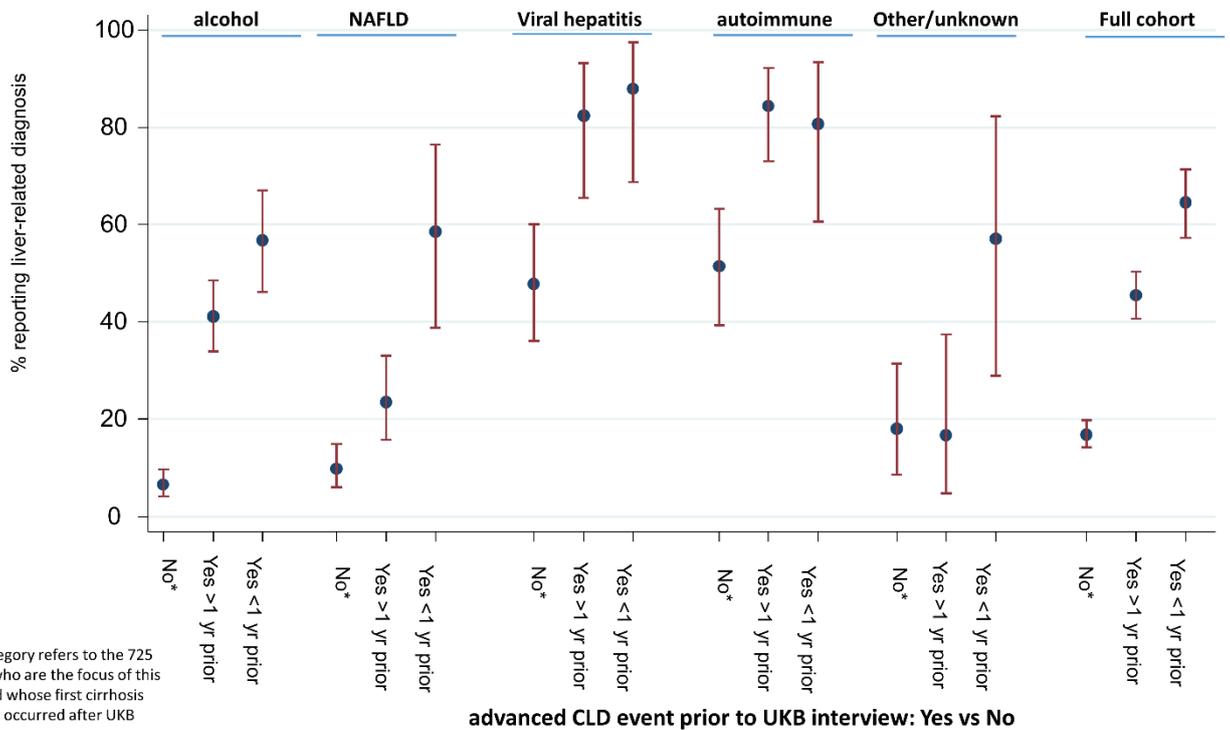
Supplementary Figure 6. Association between late CLD diagnosis and subsequent mortality according to number of CLD complications recorded at index advanced CLD event.



Supplementary Figure 7. Association between late CLD diagnosis and mortality, within and after 1 year of the advanced CLD event.



Supplementary Figure 8. Self-reported diagnosis of chronic liver disease for participants with a first advanced CLD event prior to UKB interview (N=598), and those with first advanced CLD event after UKB interview (N=725).



* This category refers to the 725 patients who are the focus of this study, and whose first cirrhosis admission occurred after UKB interview

eTable 1. ICD 10 and OPCS4 codes used to define liver cirrhosis. Cirrhosis was defined as the presence of any one of these codes in any diagnostic position

Code type	Code	Description
ICD 10 (reflecting hospital discharge diagnoses)	K70.3	Alcoholic cirrhosis of liver
	K71.7	Toxic liver disease with fibrosis and cirrhosis of liver
	K72.1	Chronic hepatic failure
	K74.4	Secondary biliary cirrhosis
	K74.5	Biliary cirrhosis, unspecified
	K74.6	Other and unspecified cirrhosis of liver
	K76.6	Portal hypertension
	I85.0; I85.9; I98.2	Esophageal varices
OPCS4 (reflecting procedure performed during hospital admission)	I86.4	Gastric varices
	J06.1	Tranjugular intrahepatic insertion of stent into portal vein
	J06.2	Transjugular intrahepatic insertion of stent graft into portal vein
	T46.1	Paracentesis abdominis for ascites
	T46.2	Drainage of ascites NEC
	G10.4	Local ligation of varices of oesophagus
	G10.8	Other specified open operations on varices of oesophagus
	G10.9	Unspecified open operations on varices of oesophagus
	G14.4	Fibreoptic endoscopic injection sclerotherapy to varices of oesophagus
	G17.4	Endoscopic injection sclerotherapy to varices of oesophagus using rigid oesophagoscope
G43.7	Fibreoptic endoscopic rubber band ligation of upper gastrointestinal tract varices	

eTable 2. Criteria used to assign liver disease aetiology

Etiology	Criteria
Viral hepatitis	#1. record of hospital admission for chronic hepatitis B/C *
Autoimmune	#2. record of hospital episode for autoimmune liver disease†
Alcohol liver disease	#3. record of alcohol-related hospital admission §
	#4. report consuming >26 units/week on average, in the past 12 months at UKB interview ‡
	#5. reporting diagnosis of alcohol dependency at UK biobank interview
Non alcoholic fatty liver disease	#6. BMI ≥30 at UKB interview
	#7. waist-hip ratio >0.9 (males) or >0.85 (females)
	#8. report diagnosis of diabetes at UKB interview

*defined according to the presence of any one of the following viral hepatitis-related ICD 9/10 codes: B16-B19; 070.2-070.9.

† defined according to the presence of any one of the following autoimmune liver disease-related ICD 9/10 codes: K75.4; K74.3; K74.5; 571.42; 571.6

§ defined according to the presence of any one of the following ICD 9/10 codes that are wholly attributable to alcohol: E24.4; E51.2; F10; G31.2; G62.1; G72.1; I42.6; K29.2; K70; K85.2; K86.0; O35.4; P04.3; Q86.0; R78.0; T51.0; T51.1; T51.9; X45; X65; Y15; Y57.3; Y90; Y91; Z50.2; Z71.4; Z72.1; 264.1; 303.9; 305.0; 291.8 291.0; 291.3; 291.5; 291.9; 291.1; 291.2; 357.5; 425.5; 535.3; 571.0; 571.1; 571.2; 571.3; 760.7; 759.8; 790.3; 980.0; 980.1; 980.9; E8600; E8601; E8602; E8609; E9473.

‡ corresponds to estimated risk threshold for cirrhosis development; Bellentani S, et al. Gut 1997; 41:845-850.

eTable 3. International Classification of Disease (ICD) codes used to define liver cirrhosis complications at first cirrhosis hospital admission			
Complication event	ICD 10 code	ICD 10 code description	Source/previous use
Ascites	R18	Ascites	Ratib et al. Am J Gastroenterol. 2014;
Bleeding varices	I85.0	Oesophageal varices with bleeding	Ratib et al. Am J Gastroenterol. 2014;
	I98.3	Oesophageal varices with bleeding in disease classified elsewhere	
Infection	A41.9	Sepsis, unspecified	Asrani et al. Am J Gastroenterol 2019;114:98-106.
	R65.2	Systemic inflammatory response syndrome of non-infectious origin without organ failure	Asrani et al. Am J Gastroenterol 2019;114:98-106.
	K67	Disorders of peritoneum in infectious diseases classified elsewhere	
	L03	Cellulitis	
	H66.0	Acute suppurative otitis media	
	A04	Other bacterial intestinal infections	
	A49	Bacterial infection of unspecified site.	
	J10-J18	Influenza and pneumonia	
	K83.0	cholangitis	
	Renal dysfunction	N28.9	
N17.9		Acute renal failure, unspecified	Asrani et al. Am J Gastroenterol 2019;114:98-106.
N17.0		Acute renal failure with tubular necrosis	
K76.7		Hepatorenal syndrome	
N18		Chronic kidney disease	
N19		Unspecified kidney failure	
R94.4		Abnormal results of kidney function studies	

APPENDIX A: LIST OF CLD & NON CLD CONDITIONS REPORTED AT UKB INTERVIEW

The 725 UKB participants included in this study reported 241 distinct medical conditions when asked, at their UKB interview, to reported all serious medical conditions that have been diagnosed by a doctor. We categorised these conditions into CLD diagnoses and non-CLD diagnoses; as follows:

CONDITIONS INDICATING A DIAGNOSIS OF CLD:

alcoholic liver disease / alcoholic cirrhosis; bile duct obstruction/ascending cholangitis; haemochromatosis; hepatitis; hepatitis c; infective/viral hepatitis; liver failure/cirrhosis; liver/biliary/pancreas problem; non-infective hepatitis; oesophageal varices; primary biliary cirrhosis; sclerosing cholangitis

CONDITIONS THAT DO NOT INDICATE A DIAGNOSIS OF CLD:

abdominal hernia; alcohol dependency; allergy or anaphylactic reaction to drug; allergy or anaphylactic reaction to food; anaemia; angina; ankylosing spondylitis; anxiety/panic attacks; aortic aneurysm; aortic dissection; aortic stenosis; aortic valve disease; appendicitis; arthritis (nos); asthma; atrial fibrillation; back pain; back problem; bell's palsy/facial nerve palsy; benign / essential tremor; benign breast lump; bladder problem (not cancer); blistering/desquamating skin disorder; bone disorder; bph / benign prostatic hypertrophy; brain haemorrhage; breast cysts; breast disease (not cancer); bronchiectasis; bronchitis; cardiomyopathy; carpal tunnel syndrome; cataract; cellulitis; cervical spondylosis; cholecystitis; cholelithiasis/gall stones; chronic fatigue syndrome; chronic obstructive airways disease/copd; chronic sinusitis; chronic/degenerative neurological problem; clotting disorder/excessive bleeding; colitis/not crohns or ulcerative colitis; constipation; crohns disease; cushings syndrome; deep venous thrombosis (dvt); deliberate self-harm/suicide attempt; depression; diabetes; diabetic eye disease; diabetic neuropathy/ulcers; disc problem; diverticular disease/diverticulitis; dry eyes; duodenal ulcer; dupuytren's contracture; dysmenorrhoea / dysmenorrhea; dyspepsia / indigestion; ear/vestibular disorder; ectopic pregnancy; eczema/dermatitis; emphysema/chronic bronchitis; endometriosis; enlarged prostate; epilepsy; erectile dysfunction / impotence; essential hypertension; eye/eyelid problem; fibromyalgia; fibrosing alveolitis/unspecified alveolitis; fracture clavicle / collar bone; fracture fibula; fracture hand; fracture lower leg / ankle; fracture patella / knee; fracture pelvis; fracture rib; fracture shoulder / scapula; fracture skull / head;

fracture tibia; fracture toe; fracture upper arm / humerus / elbow; fracture vertebra / crush fracture / vertebral collapse; fracture wrist / colles fracture; gastric/stomach ulcers; gastritis/gastric erosions; gastro-oesophageal reflux (gord) / gastric reflux; giant cell/temporal arteritis; glaucoma; gout; gynaecological disorder (not cancer); haemorrhoids / piles; hayfever/allergic rhinitis; head injury; headaches (not migraine); heart arrhythmia; heart attack/myocardial infarction; heart failure/pulmonary odema; heart valve problem/heart murmur; heart/cardiac problem; helicobacter pylori; hepatitis a; hereditary/genetic haematological disorder; hiatus hernia; high cholesterol; hiv/aids; hypertension; hyperthyroidism/thyrotoxicosis; hypertrophic cardiomyopathy (hcm / hocm); hypothyroidism/myxoedema; infectious mononucleosis / glandular fever / epstein barr virus (ebv); inflammatory bowel disease; inguinal hernia; insomnia; iritis; iron deficiency anaemia; irregular heart beat; irritable bowel syndrome; jaundice (unknown cause); joint disorder; joint pain; kidney stone/ureter stone/bladder stone; leg claudication/ intermittent claudication; lichen planus; low platelets/platelet disorder; lymphoedema; malabsorption/coeliac disease; mania/bipolar disorder/manic depression; meniere's disease; meningitis; menorrhagia (unknown cause); migraine; mitral valve disease; multiple sclerosis; muscle or soft tissue injuries; muscle/soft tissue problem; myasthenia gravis; myositis/myopathy; nasal polyps; nasal/sinus disorder; nervous breakdown; obsessive compulsive disorder (ocd); oesophageal disorder; oesophagitis/barretts oesophagus; opioid dependency; optic neuritis; osteoarthritis; osteomyelitis; osteoporosis; other abdominal problem; other demyelinating disease (not multiple sclerosis); other joint disorder; other neurological problem; other renal/kidney problem; other respiratory problems; ovarian cyst or cysts; paget's disease; pancreatitis; parkinsons disease; pericardial problem; peripheral neuropathy; peripheral vascular disease; peritonitis; pernicious anaemia; pleurisy; pneumonia; pneumothorax; polio / poliomyelitis; polycystic kidney; polycystic ovaries/polycystic ovarian syndrome; polycythaemia vera; polymyalgia rheumatica; prolapsed disc/slipped disc; prostate problem (not cancer); prostatitis; psoriasis; psoriatic arthropathy; psychological/psychiatric problem; pulmonary embolism +/- dvt; pyelonephritis; raynaud's phenomenon/disease; rectal or colon adenoma/polyps; renal failure requiring dialysis; renal/kidney failure; retinal artery/vein occlusion; retinal detachment; rheumatic fever; rheumatoid arthritis; rosacea; sarcoidosis; scarlet fever / scarlatina; schizophrenia; sciatica; sjogren's syndrome/sicca syndrome; sleep apnoea; soft tissue inflammation; spinal injury; spine arthritis/spondylitis; spontaneous pneumothorax/recurrent pneumothorax; stomach disorder; stroke; subarachnoid haemorrhage; subdural haemorrhage/haematoma; svt / supraventricular tachycardia; systemic lupus erythematosus/sle; tennis elbow / lateral epicondylitis; testicular problems (not cancer); thalassaemia; throat or larynx disorder; thyroid problem (not cancer); thyroiditis; tinnitus / tinitis; tonsillitis; transient ischaemic attack (tia); tuberculosis (tb); type 1 diabetes; type 2 diabetes; ulcerative colitis; unclassifiable; ureteric obstruction/hydronephrosis; urinary frequency / incontinence; urinary tract infection/kidney infection; uterine fibroids; uterine polyps; vaginal prolapse/uterine prolapse; venous thromboembolic disease; wegners granulomatosis; whooping cough / pertussis