NHS
Blackburn with Darwen
Clinical Commissioning Group

NHS
East Lancashire Hospitals
NHS Trust

Overview of proposed Liver Pathway (NAFLD)

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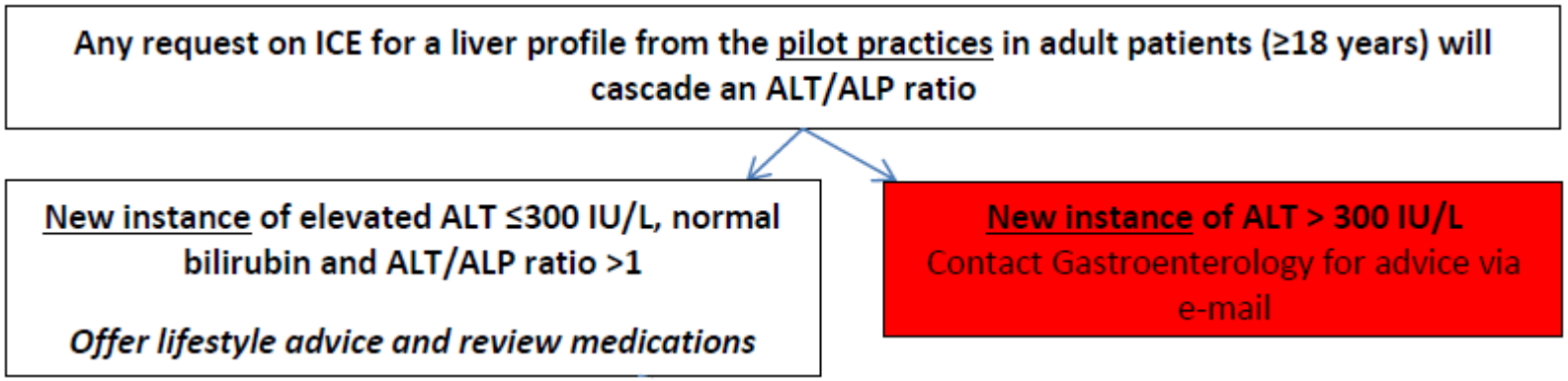
Stage 1

- All adult patients that have a liver profile requested from the pilot practices will automatically receive an ALT/ALP ratio with the other LFT results.



Stage 1 - Results

- Liver profile reported on ICE with ALT/ALP ratio

Sample N,18.0000500.K (BLOOD) Collected 19 Feb 2018 10:19 Received 19 Feb 2018 10:25

Liver profile				
Total Bilirubin		16	umol/L	0 - 21
ALT	*[HI]	65	IU/L	3 - 53
Alk. Phos		52	IU/L	30 - 130
Albumin		40	g/L	35 - 50
ALT:ALP Ratio				
ALT:ALP Ratio	*[HI]	1.3		0.0 - 1.0

Stage 1 - Results Interpretation

If ALT 100 – 300 IU/L OR ALT <100 IU/L with risks for the metabolic syndrome *[see Box A]*, repeat tests in 6 weeks.

Request on ICE: NAFLD Lifestyle Repeat *(LFT & GGT)*

If the ALT <100 IU/L and the patient has no risks for the metabolic syndrome *[see Box A]*, repeat tests in 3-6 months

Request on ICE: NAFLD Lifestyle Repeat *(LFT & GGT)*

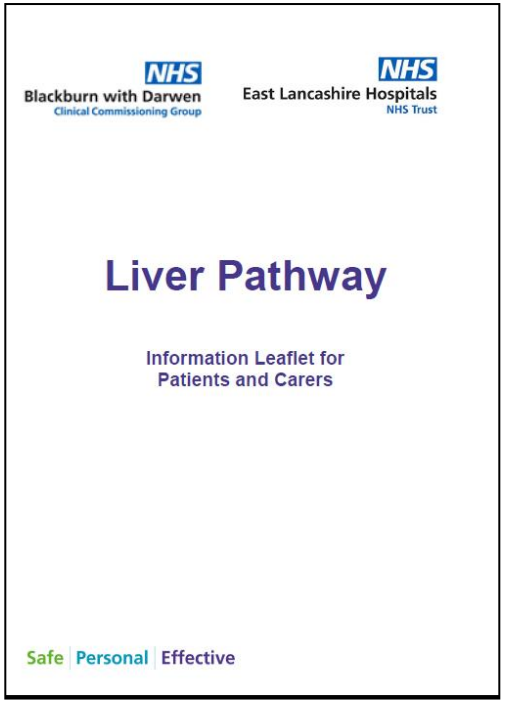
Box A: Metabolic Syndrome

The International Diabetes Federation (IDF) criteria to diagnose metabolic syndrome:

Metabolic syndrome may be diagnosed if the patient has a large waist circumference (≥94 cm in European men or ≥90 cm in South Asian men; ≥ 80 cm in European and South Asian women).

Plus any two of the following:

- HDL-cholesterol <1.0 mmol/L (men), <1.3 mmol/L (women)
- Triglycerides ≥1.7 mmol/L
- Blood pressure ≥130/85 mmHg
- Fasting plasma glucose ≥5.6 mmol/L



Issue the patient information leaflet at this stage

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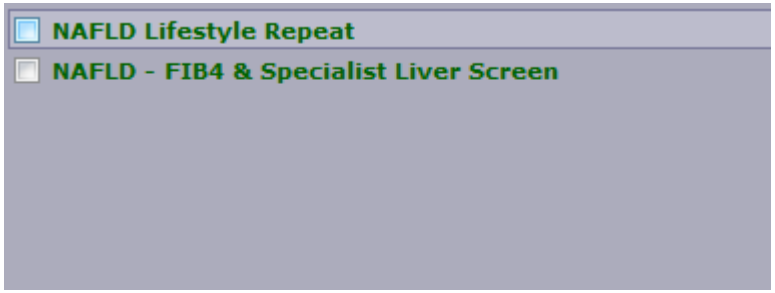
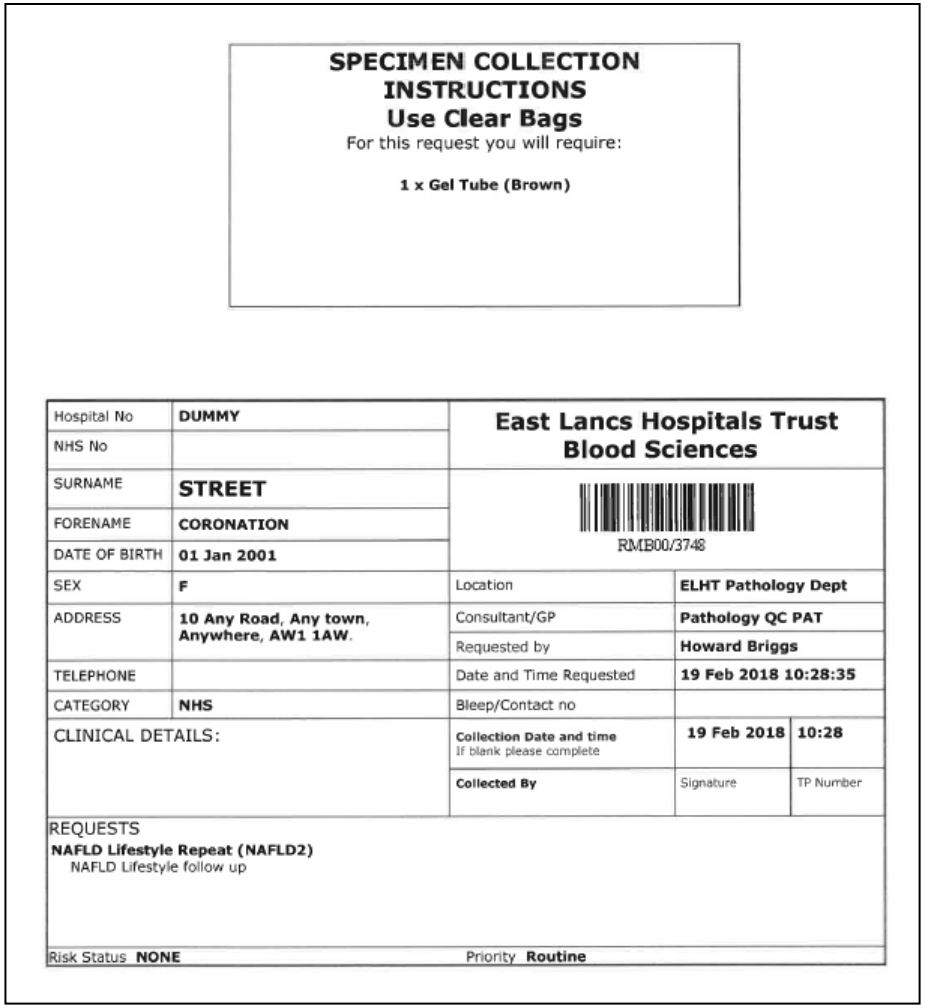
Stage 2 - Repeat tests



Requesting ‘NAFLD Lifestyle repeat’ on ICE automatically orders a liver profile and GGT

Stage 2 - ICE request form



SPECIMEN COLLECTION INSTRUCTIONS
Use Clear Bags
For this request you will require:

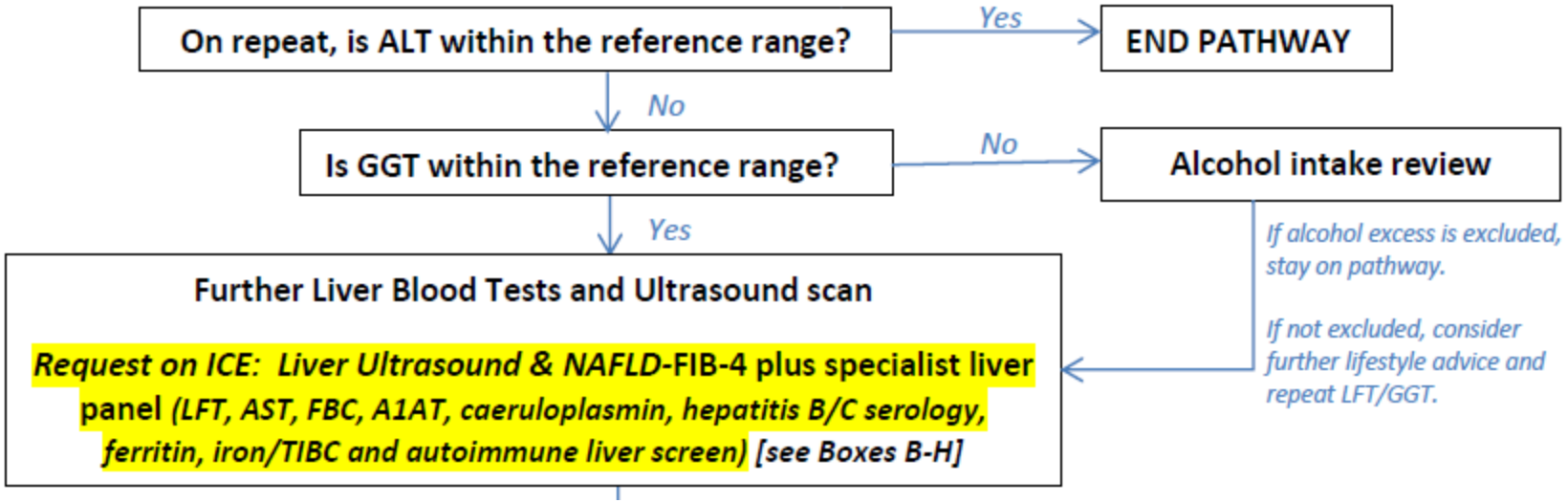
1 x Gel Tube (Brown)

Hospital No	**DUMMY**	**East Lancs Hospitals Trust Blood Sciences**		
NHS No				
SURNAME	**STREET**	RMB00/3748		
FORENAME	**CORONATION**			
DATE OF BIRTH	**01 Jan 2001**			
SEX	**F**	Location	**ELHT Pathology Dept**	
ADDRESS	**10 Any Road, Any town, Anywhere, AW1 1AW.**	Consultant/GP	**Pathology QC PAT**	
		Requested by	**Howard Briggs**	
TELEPHONE		Date and Time Requested	**19 Feb 2018 10:28:35**	
CATEGORY	**NHS**	Bleep/Contact no		
CLINICAL DETAILS:		**Collection Date and time** If blank please complete	**19 Feb 2018**	**10:28**
		Collected By	Signature	TP Number

REQUESTS
NAFLD Lifestyle Repeat (NAFLD2)
NAFLD Lifestyle follow up

Risk Status **NONE** Priority **Routine**

Stage 2 - Results Interpretation



Stage 3 - Request liver ultrasound and specialist biochemistry

Further Liver Blood Tests and Ultrasound scan

Request on ICE: Liver Ultrasound & NAFLD-FIB-4 plus specialist liver panel (LFT, AST, FBC, FIB-4 calculation, A1AT, caeruloplasmin, hepatitis B/C serology, ferritin, iron/TIBC and autoimmune liver screen) [see Boxes B-H]

- Request liver ultrasound on ICE
- Request 'NAFLD- FIB4 and specialist liver screen' on ICE
  - This automatically requests LFT, AST, FBC, FIB-4, A1AT, ferritin, caeruloplasmin, hepatitis B/C serology, iron/transferrin saturation and autoimmune liver screen
  - Four request forms printed
  - A1AT and autoimmune liver screen referred to Immunology at Preston
  - Caeruloplasmin referred to Manchester Royal Infirmary
  - ***All results will be returned via ICE onto EMIS***

Stage 3 - Results Interpretation

Box B: Quick Reference Guide to interpret specialist liver panel test results
Patients stay on the liver pathway if the specialist liver panel test results meet **ALL** of the following criteria: • A1AT ≥1.10 g/L • Caeruloplasmin ≥200 mg/L • Negative Hepatitis B and C serology • Transferrin saturation <50% • Negative smooth muscle, mitochondrial (M2/non M2) and LKM antibodies **For any other results or for further information on each test, see boxes C-G.**

Stage 3 - Results Interpretation

Box C: Serum A1AT
Alpha-1-antitrypsin deficiency

Samples are referred for analysis at the Immunology Laboratory at the Royal Preston Hospital. Avoid sample collection if acute inter-current infection

Severe A1AT deficiency (0.6g/L) occurs with incidence 1:2000. Typical presentation includes COPD, emphysema and cirrhosis

Reference range (adults): 1.10 – 2.10g/L

- If the result is within the reference range or higher than the reference range, A1AT deficiency is excluded.
- If the A1AT is <1.00 g/L, the A1AT phenotyping will be performed.
- The 'Z' allele is most frequently associated with liver disease.
- PI*ZZ homozygotes occur in approximately 1 in 2,000-5,000 births in European populations.
- Patients with PI*ZZ should be referred to Hepatology.

Box D: Serum Caeruloplasmin
Wilson's disease

Samples are referred for analysis at the Biochemistry Laboratory at Manchester Royal Infirmary. Avoid sample collection if acute inter-current infection

Presentation of Wilson's Disease may be hepatic or neurological (clumsiness/ataxia).

Reference range (adults): 200-600 mg/L

- Further investigation is required if the serum caeruloplasmin <200 mg/L
- Collect a 24 hour urine sample for copper analysis (please contact Clinical Biochemists if further information is required on 01254 734153/735927)
- If 24 hr urine copper is increased, patients should be referred to Hepatology.

Stage 3 - Results Interpretation

Box E: Hepatitis B/C Serology
Samples are analysed at the Royal Blackburn Hospital. Any positive results are referred for confirmation. Patients with positive serology results should be referred to Hepatology.

Box F: Ferritin, Iron and Transferrin Saturation **Hereditary Haemochromatosis**
Samples are analysed at the Royal Blackburn Hospital. **Presentation of hereditary haemochromatosis includes abnormal LFT results (ALT), arthralgia/arthritis, late onset diabetes and bronze pigmentation.** **Causes of increased ferritin include chronic infection/inflammation, malignancy and haematological conditions** • If the transferrin saturation >50% and ferritin >500ug/L in males/ >350ug/L in females suggest repeat fasting sample for iron and TIBC (exclude alcohol excess) • If the above results are repeated on a fasting sample, send a sample for haemochromatosis (HFE) genotyping. • Patients that are homozygous for the C282Y variant should be referred to Hepatology.

Stage 3 - Results Interpretation

Test	Positive result
Reticulin (R1) antibodies	A positive result is not associated with liver disease.
Gastric parietal cell antibody	A positive result is not associated with liver disease.
Smooth muscle antibodies	The result is reported as either tubular (associated with type 1 autoimmune hepatitis) or vascular (commonly seen post viral infections).
Mitochondrial (M2) antibodies	Positive results are associated with primary biliary cirrhosis (or less commonly autoimmune hepatitis)
Mitochondrial (non M2 antibodies)	All patients with positive mitochondrial (non M2) antibodies should be referred to Hepatology.
LKM (Liver Kidney Microsome) Antibody	Mainly present in type 2 autoimmune hepatitis (80% prevalence)
Ribosomal antibody	A positive result is not associated with liver disease

Stage 3 - FIB-4

FIB-4= $\frac{\text{age (years) x AST (U/L)}}{\text{Platelet count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$

FIB-4 auto-comments added by the laboratory:

<1.30: Review patient and repeat LFTs in 1 year

1.30-3.25: Please request the Enhanced Liver Fibrosis (ELF) test

>3.25: Refer to Hepatology for further assessment

Stage 3 - FIB-4 Example

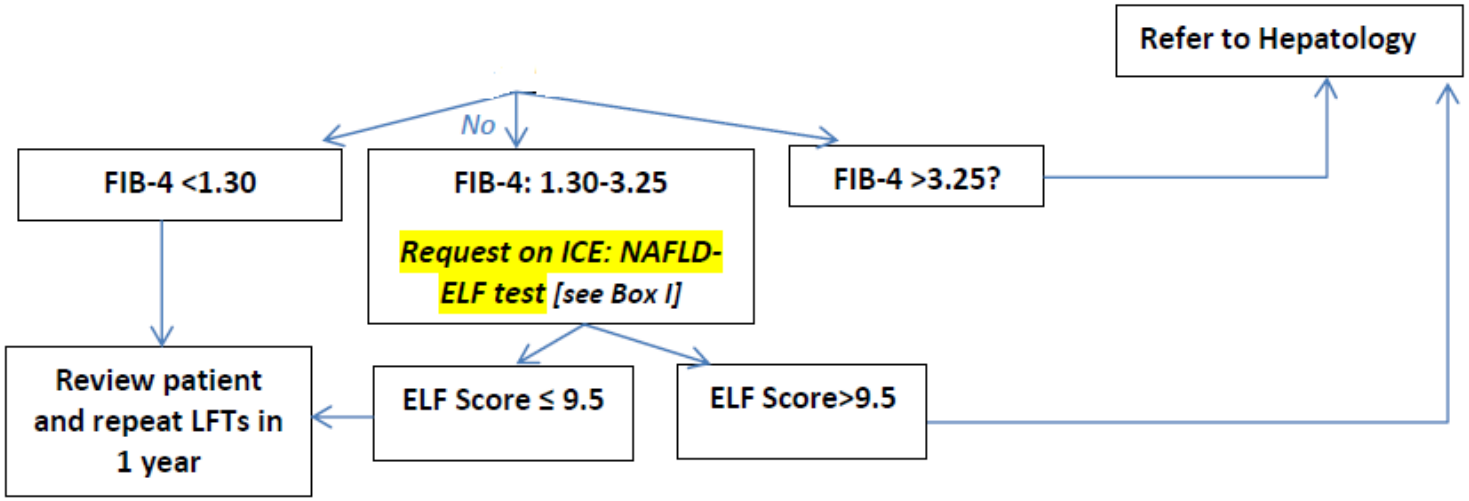
Sample N,18.0000510.N (BLOOD) Collected 19 Feb 2018 13:03 Received 19 Feb 2018 13:04

Liver profile					
	Total Bilirubin		9	umol/L	0 - 21
	ALT	*[HI]	75	IU/L	3 - 53
	Alk. Phos		87	IU/L	30 - 130
	Albumin		42	g/L	35 - 50
Iron					
	Iron		9.6	umol/L	9.0 - 32.0
TIBC (inc. iron)					
	TIBC		80.0	umol/L	45.0 - 80.0
	TIBC Saturation	*[LO]	12.0	%	20.0 - 55.0
Full Blood Count					
	HB	*[LO]	129	g/l	130 - 180
	WBC		5.6	10^9/L	4.0 - 11.0
	Plts		372	10^9/L	150 - 450
	RBC	*[LO]	3.98	10^{12}/L	4.50 - 6.50
	PCV	*[LO]	0.395		0.400 - 0.500
	MCV		99.1	FL	76.0 - 100.0
	MCH	*[HI]	32.3	pg	27.0 - 32.0
	MCHC		326.0	g/l	310.0 - 360.0
	RDW		14.1		10.0 - 15.7
	Neutrophils		3.8	10^9/L	2.0 - 7.5
	Lymphocytes	*[LO]	1.2	10^9/L	1.5 - 4.0
	Monocytes		0.4	10^9/L	0.2 - 0.8
	Eosinophils		0.0	10^9/L	0.0 - 0.4
	Basophils		0.0	10^9/L	0.0 - 0.1
	LUC		0.1	10^9/L	0.0 - 0.4
AST					
	AST	*[HI]	89	IU/L	14 - 59
FIB-4					
	FIB-4	*[HI]	1.52		0.00 - 1.29

Please request the Enhanced Liver Fibrosis (ELF) test

Stage 4 - Enhanced Liver Fibrosis (ELF) Test

- The ELF test is a biochemical measurement of the presence and extent of liver fibrosis
- Three biochemical markers measured and used to calculate an ELF score
  - PIIINP (amino terminal pro-peptide of type III collagen)
  - TIMP-1 (tissue inhibitor of matrix metalloproteinase 1)
  - Hyaluronic acid



Stage 4 - ELF test

- Request ‘NAFLD-ELF’ on ICE
- Samples will be referred to Biochemistry Laboratory at Leeds for analysis
- Samples will only be referred to Leeds for the ELF test if the FIB-4 is 1.30-3.25 and all other liver screen blood tests show no abnormalities that require Hepatology Referral

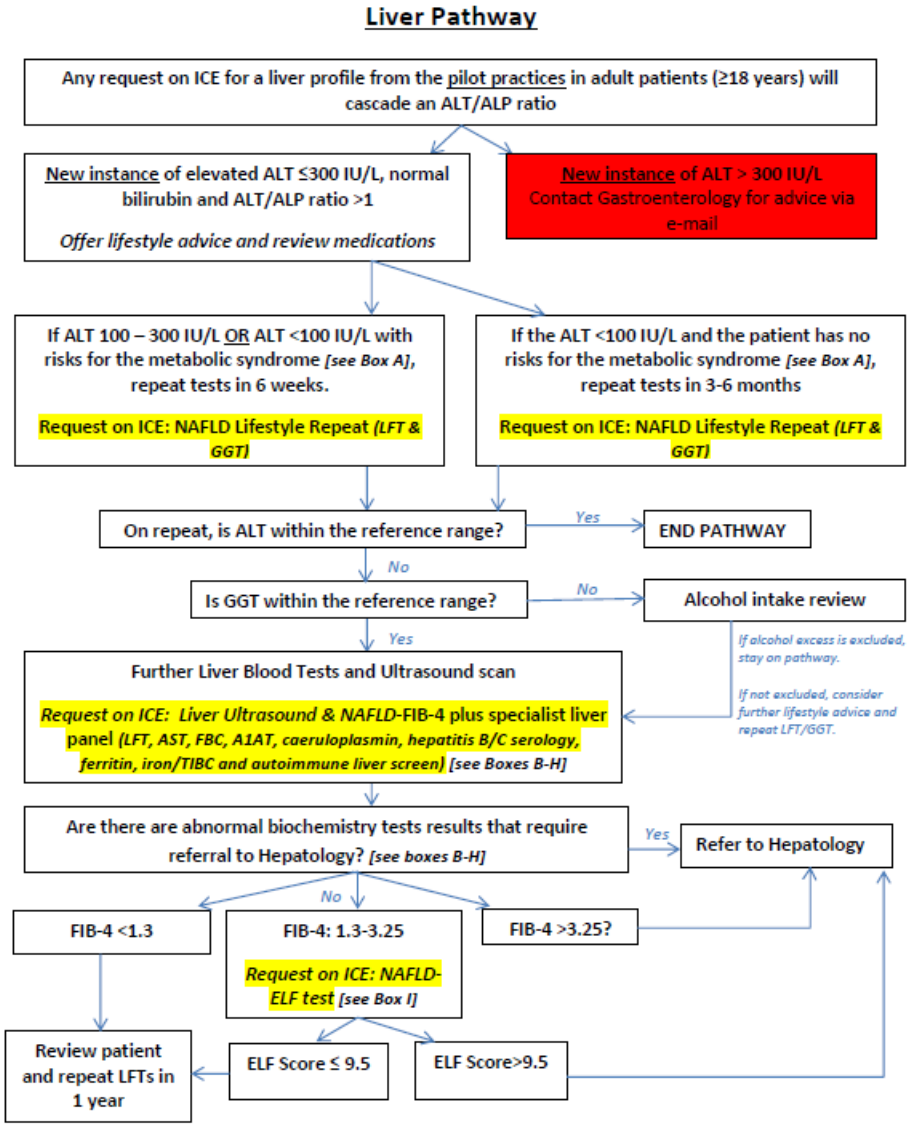
Liver Pathway

Stage 1
LFT

Stage 2
LFT/GGT

Stage 3
U/S and specialist liver tests

Stage 4
ELF test



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