

# ABNORMAL LIVER FUNCTION TESTS

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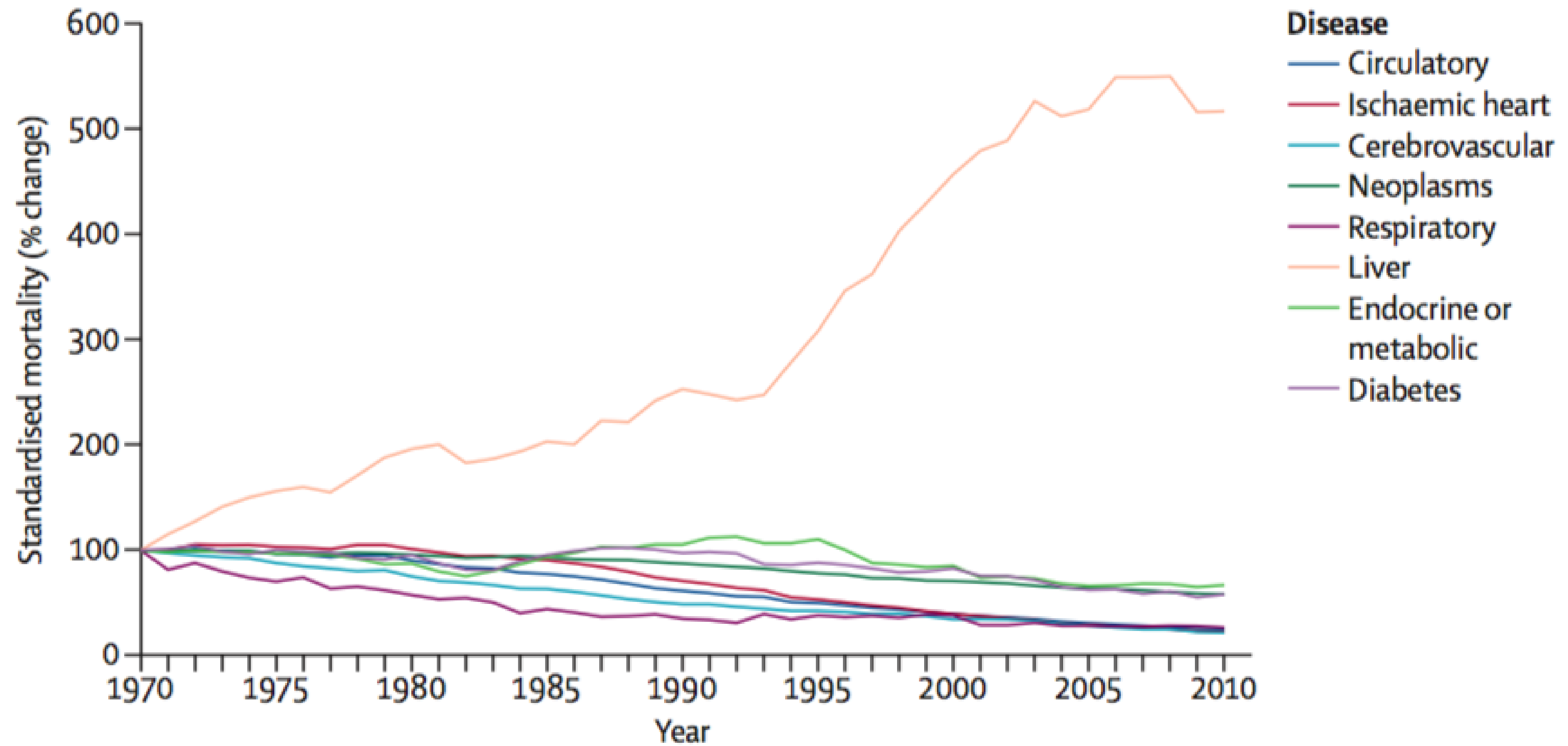
# INTRODUCTION

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- Liver function tests
- Cases
- Non invasive fibrosis measurement
- Questions

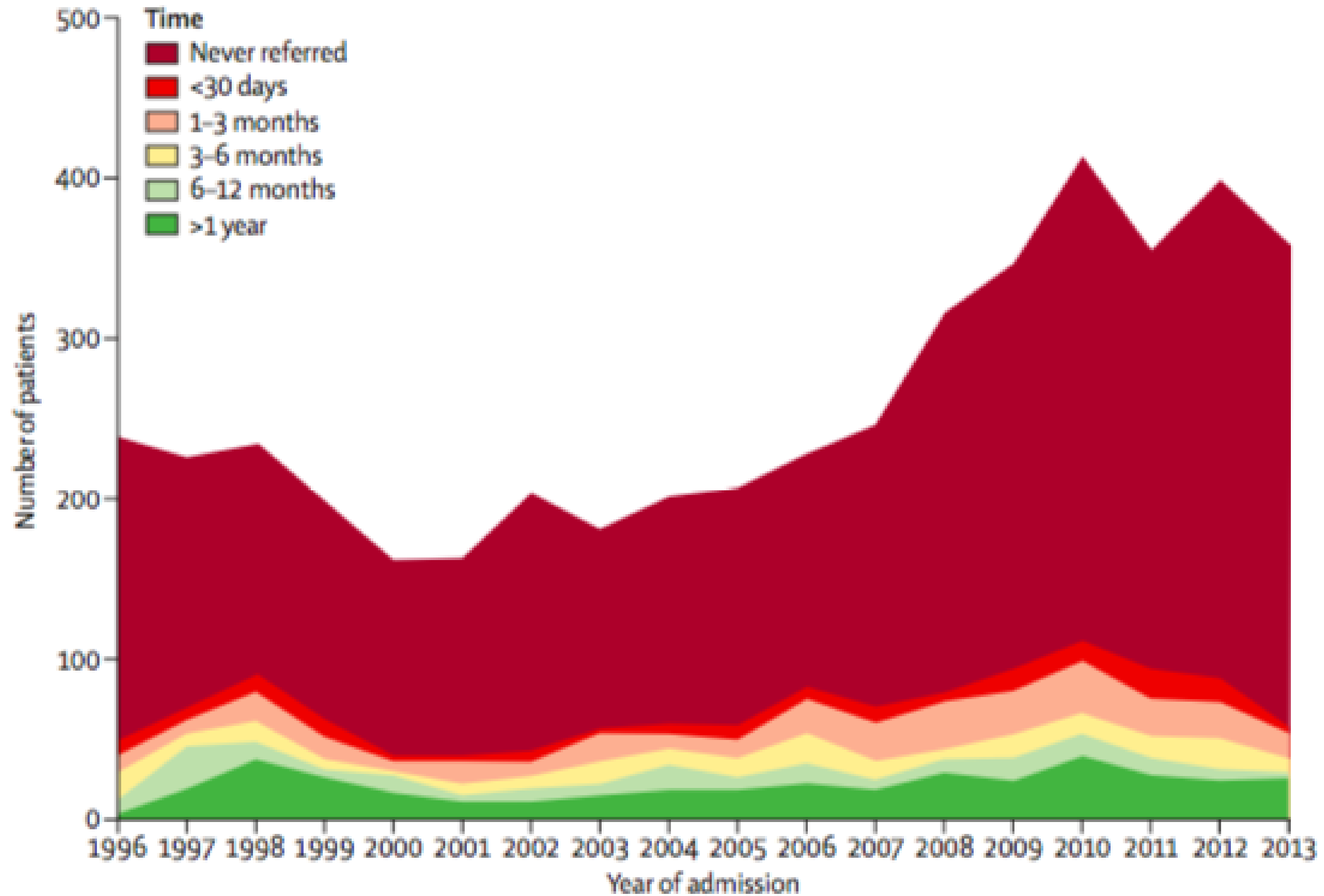
# UK MORTALITY RATE

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# TIME FROM REFERRAL TO FIRST HOSPITAL ADMISSION

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# TRUE OR FALSE ?

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- Can patients with normal LFTs have cirrhosis ?
- Can patients with normal ultrasound scans have cirrhosis ?
- Can patients with normal CT scans have cirrhosis ?

- LFTs are a blunt tool to diagnosis extent of liver disease
- Do not help differentiate those at risk of progressive fibrosis
- Who to refer ?
- Who to monitor ?
- When to retest ?

# MARKERS OF LIVER INJURY

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- Alanine transaminase
- Aspartate transaminase
- Gamma GT
- Alkaline phosphatase

# ALT

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- Intracellular enzyme in hepatocyte
- Transfers amino groups of alanine to ketoglutaric acid
- Predominantly liver
- Also smaller amounts in kidney and muscle
- Normal is F 19 IU/L and M 30 IU/L



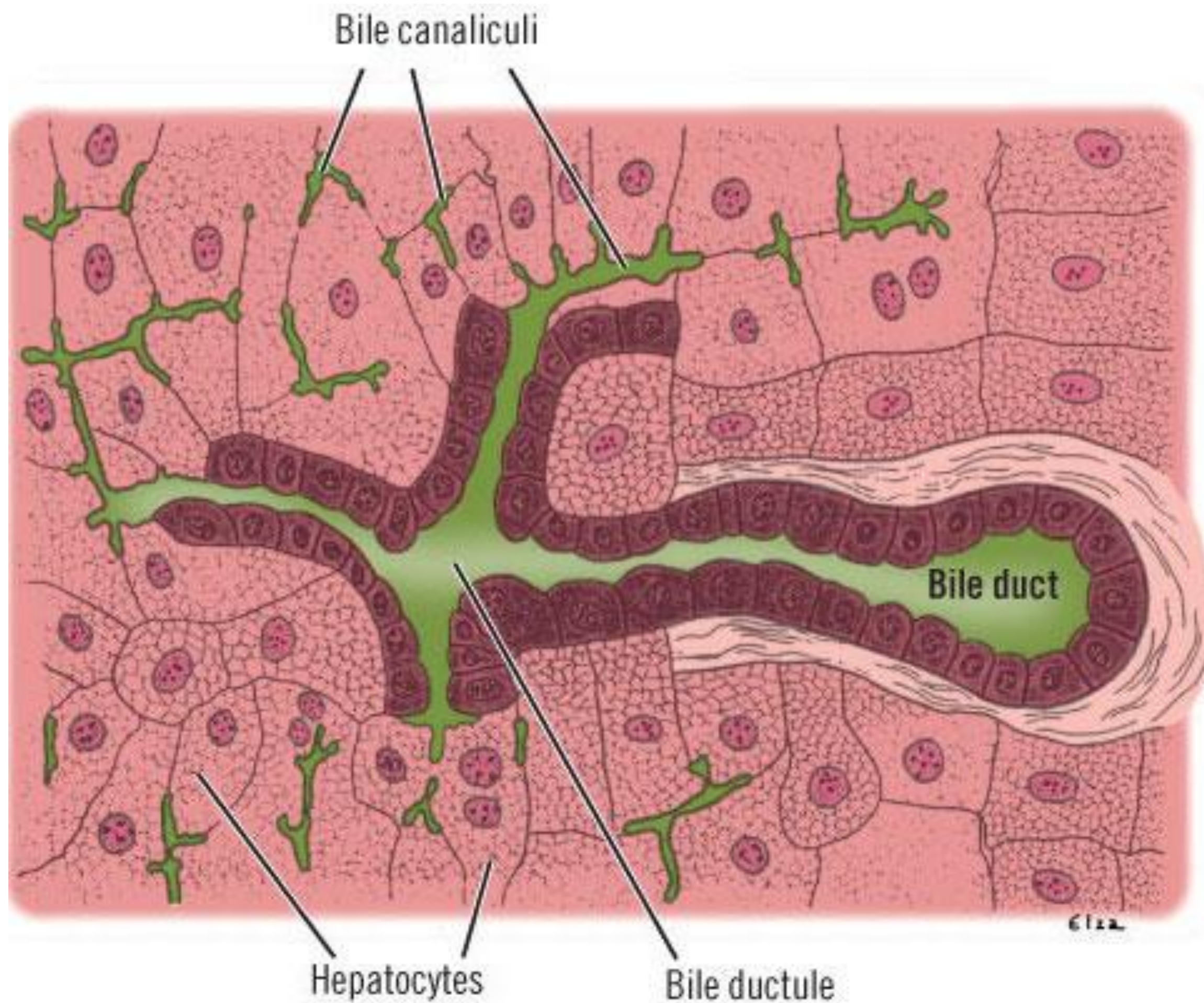
# AST

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- Intracellular enzyme in hepatocyte
  
- Transfers of amino groups of aspartate to ketoglutaric acid
  
- Found in:
  - liver
  - cardiac muscle and skeletal muscle
  - kidney
  - brain

# ALP

- Enzyme found on hepatocyte bile canaliculi
- Also bone, small bowel, kidney, placenta
- Increased in:
  - Children and > 50 years (bone)
  - Blood group O & B after meals (intestinal)





# GAMMA GT

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- Bile canaliculi enzyme
- Non specific regarding cause of LFT abnormality
- Useful if ALP is elevated

# MARKERS OF LIVER FUNCTION

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## ➤ Bilirubin

- unconjugated and conjugated fractions
- bilirubin also bound to albumin

## ➤ Albumin

- plasma protein
- half life 3 weeks

## ➤ Prothrombin time / INR

# PATTERNS OF LIVER INJURY

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- Hepatocellular
  - Hepatocyte damage
  - ALT/AST predominantly elevated
  
- Cholestatic
  - Predominantly ALP elevated
  
- Mixed
  - Both elevated

# CASE JG

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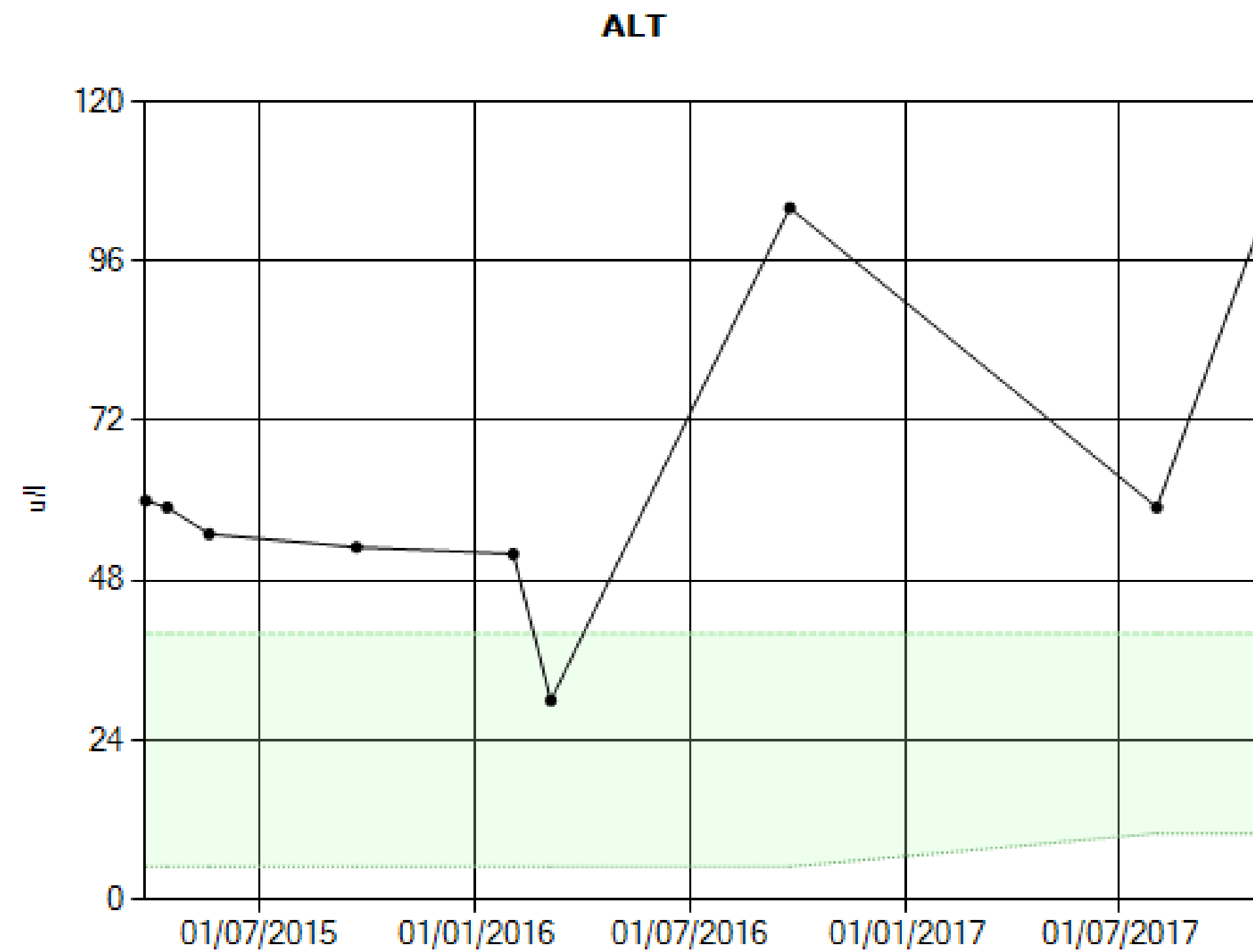
- 60 year old female
- No alcohol
  
- PMHx
  - T2DM
  - Obese with BMI 33
  
- DHx
  - Metformin
  - Simvastatin
  - Ramipril

# PREVIOUSLY...

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- Ultrasound in 2005
  - Fatty liver

- Blood tests



Units: U/L	
Collected ▲	Result
26 Mar 2015 11:10	*60
13 Apr 2015 13:25	*59
19 May 2015 09:25	*55
21 Sep 2015 11:02	*53
01 Feb 2016 12:20	*52
04 Mar 2016 15:36	30
23 Sep 2016 13:40	*104
01 Aug 2017 08:50	*59
02 Nov 2017 09:00	*104

# ROUTINE BLOOD TESTS

## FULL BLOOD COUNT

<b>Full Blood Count</b>		
<b>White Cell Count</b>	8.37 10 <sup>9</sup> /L	4.0 - 11.0
<b>Haemoglobin</b>	139g/L	120 - 150
<b>Platelets</b>	286 10 <sup>9</sup> /L	150 - 450

## ELECTROLYTES

<b>Sodium</b>	140mmol/L	133 - 146
<b>Potassium</b>	4.8mmol/L	3.5 - 5.3
<b>Creatinine</b>	55umol/L	45 - 84
<b>eGFR</b>	>90	mL/min



## LIVER FUNCTION TEST

<b>Total Bilirubin</b>		6umol/L	<21
<b>ALP</b>		80U/L	30 - 130
<b>ALT</b>	*	59U/L	10 - 40
<b>Albumin</b>		37g/L	35 - 50

# SO WHAT'S NEXT ?

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- Retest within a month?
- Retest at 1 year ?
- Stop statin and retest ?
- Liver screen - ultrasound and blood tests ?

# LIVER SCREEN

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- Ultrasound

*“Fatty liver and normal spleen.*

*Thin walled gall bladder with no stones seen”*

- Negative viral screen

- Negative autoimmune profile

- Referred to liver clinic

# IN LIVER CLINIC

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- Dx is Non-alcoholic fatty liver disease
- Fibroscan was 6 kPa
- Not consistent with advanced fibrosis
  
- Plan :
  - Target weight loss 10% over 6-12 months
  - Brisk exercise 5 days out of 7
  - Control BP / DM / cholesterol
  - Statins reduce fibrosis
  - 2-3 cups of coffee a day
  - Discharged to primary care and rescreen in 3 years

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➤ All patients with NAFLD require fibrosis screening

➤ Options are :

- AST/ALT ratio
- FIB 4
- Fibroscan
- ELF test

# AST/ALT RATIO

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- Simple test
- Not as sensitive as FIB4
- ratio  $> 1$  suggests significant fibrosis so should be referred for Fibroscan

# FIB-4

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$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = 0.76$$

- <1.3 then lifestyle modification, treat risk factors and retest in 3 years
- 1.3 - 3.25 further testing (Fibroscan or ELF test)
- >3.25 then refer to Hepatology

# ELF TEST

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- Will be accessible soon
- Blood test combining three fibrosis markers
  - Hyaluronic acid (HA)
  - Procollagen III amino terminal peptide (PIIINP)
  - Tissue inhibitor of metalloproteinase 1 (TIMP-1)
- Score < 9.5 then lifestyle modifications and rescreen in 3 years
- Score > 9.5 then Hepatology referral



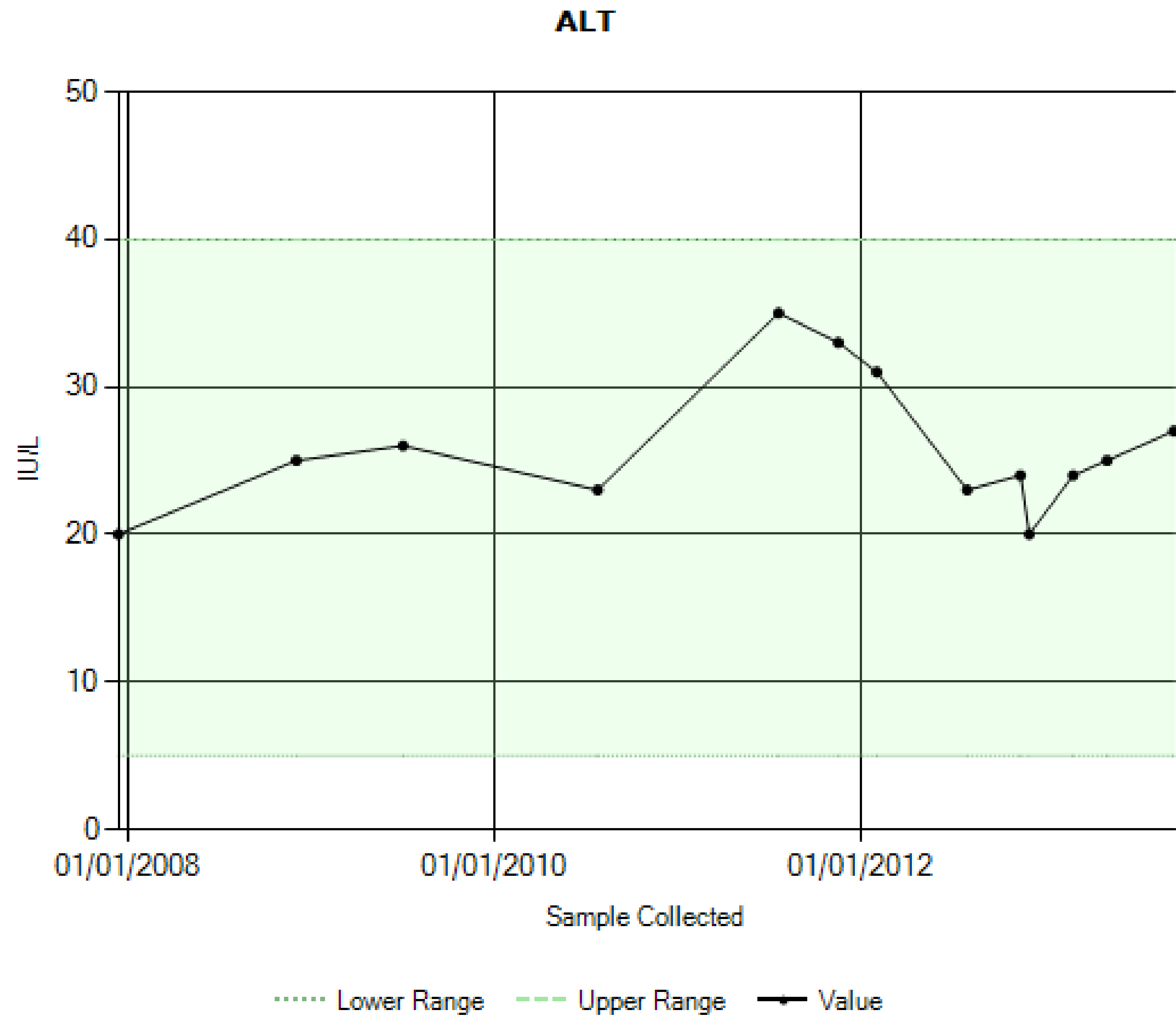
**FibroScan**<sup>®</sup>  
User tutorial - Practice for all



# ITS NOT ALWAYS ABOUT THE LFTS

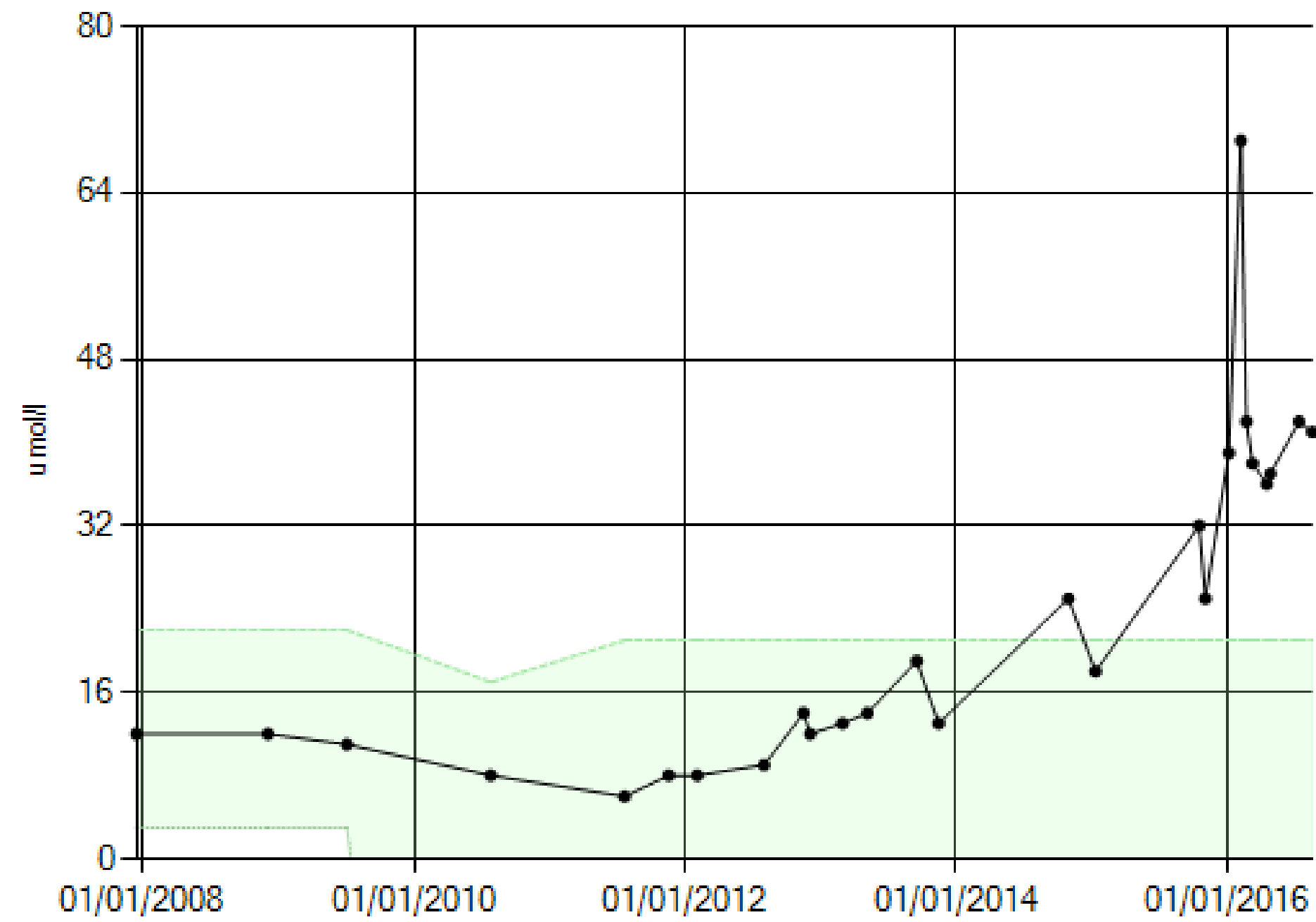
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- 51 year old female
- T2DM
- Obese BMI 36
- Fatty liver on ultrasound scan in 2014
- Osteoarthritis right knee - was for TKR in 2012 but not done due to thrombocytopenia
- Mother has NASH cirrhosis
- No alcohol
- Smokes 10 cigarettes per day

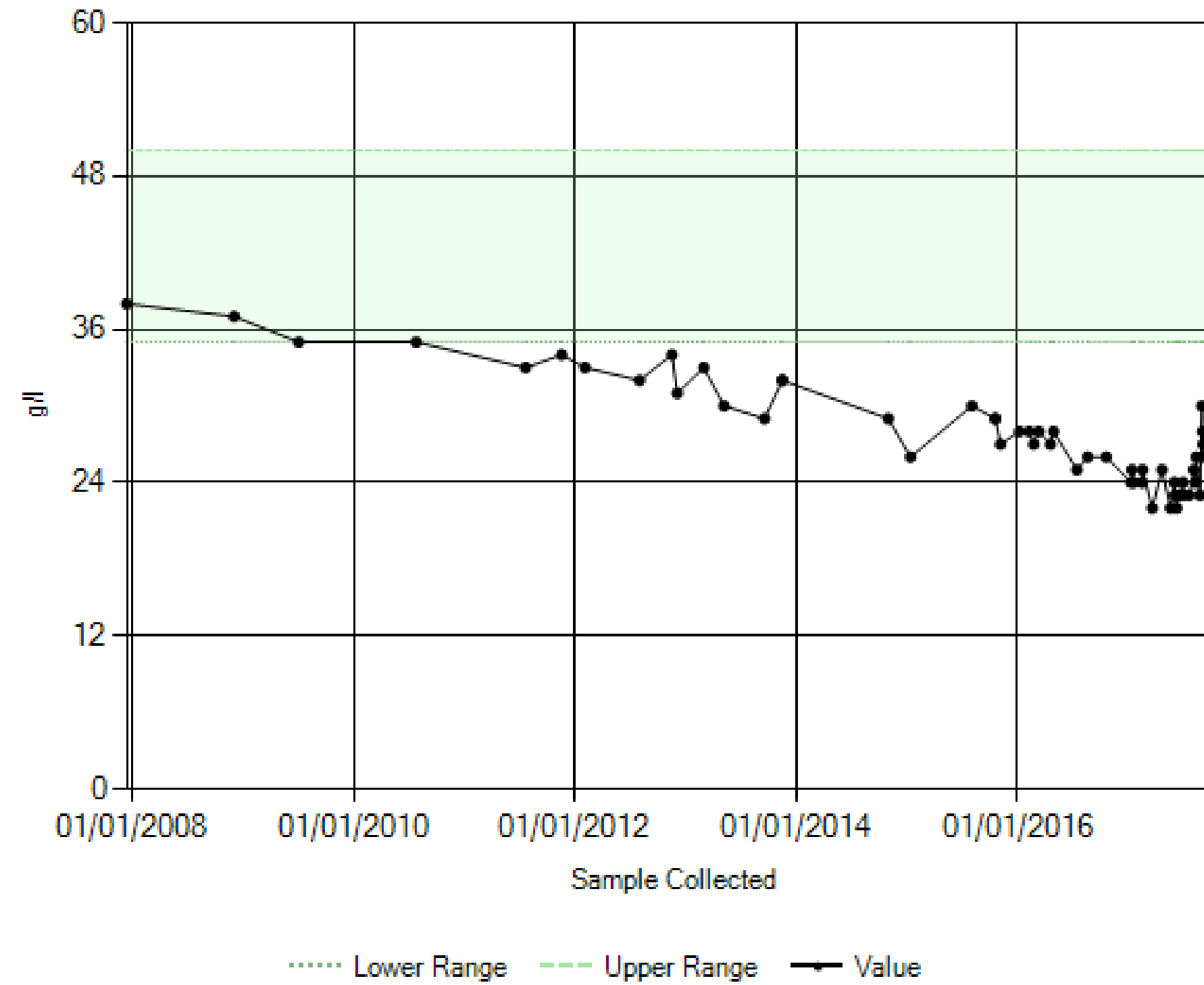


Units: IU/L	
Collected ▲	Result
13 Dec 2007 09:30	20
02 Dec 2008 10:45	25
03 Jul 2009 10:10	26
26 Jul 2010 10:10	23
22 Jul 2011 10:30	35
18 Nov 2011 09:12	33
03 Feb 2012 09:40	31
01 Aug 2012 11:46	23
16 Nov 2012 00:00	24
03 Dec 2012 12:00	20
01 Mar 2013 00:00	24
07 May 2013 11:00	25
17 Sep 2013 10:15	27

### Bilirubin



### Albumin

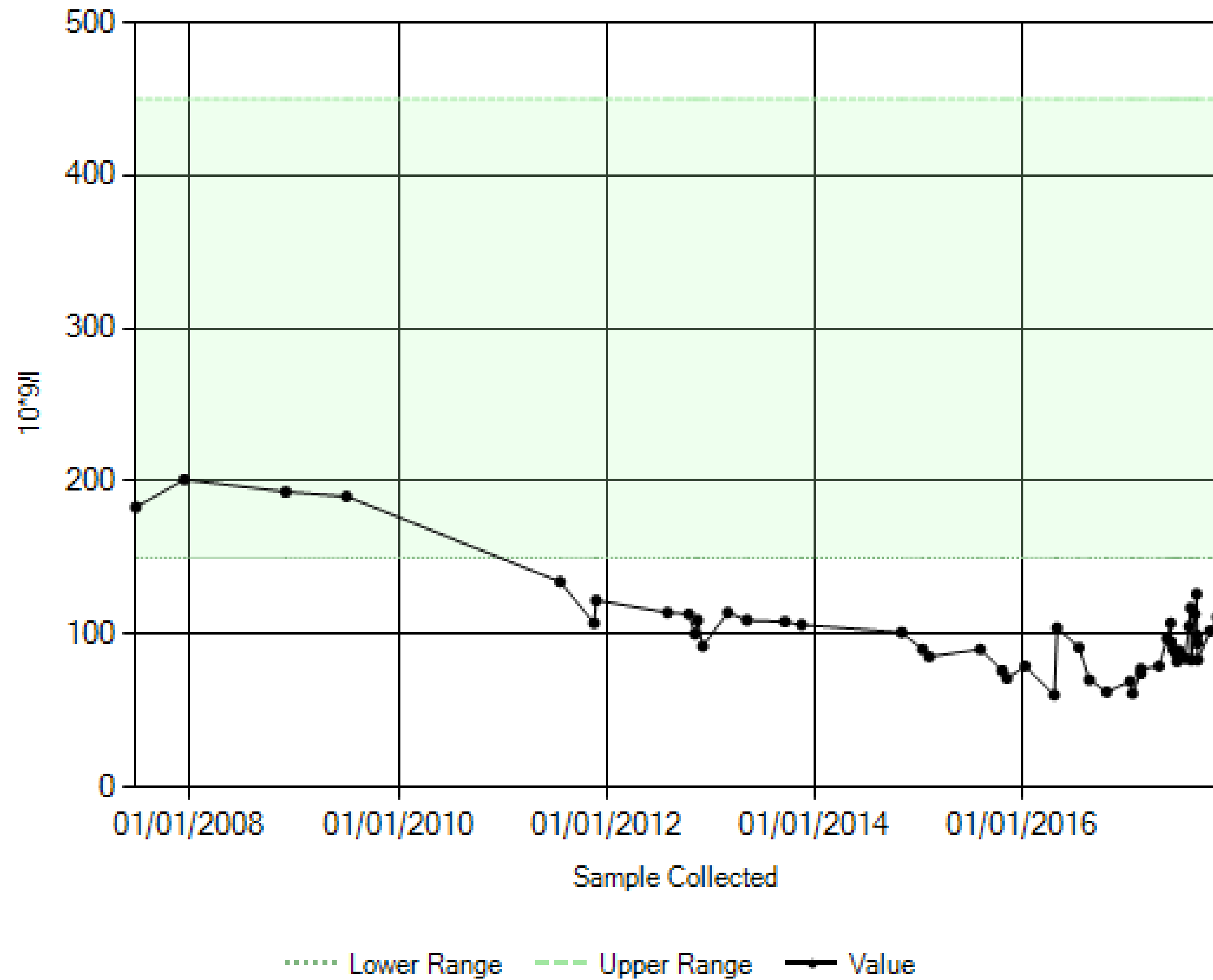


Reference range: (35 - 50)

Units: g/L

Collected ▲	Result
13 Dec 2007 09:30	38
02 Dec 2008 10:45	37
03 Jul 2009 10:10	35
26 Jul 2010 10:10	35
22 Jul 2011 10:30	*33
18 Nov 2011 09:12	*34
03 Feb 2012 09:40	*33
01 Aug 2012 11:46	*32
16 Nov 2012 00:00	*34
03 Dec 2012 12:00	*31
01 Mar 2013 00:00	*33
07 May 2013 11:00	*30

### Platelets



Reference range:  
(150 - 450)

Units: 10<sup>9</sup>/L

Collected ▲	Result
26 Jun 2007 00:00	183
13 Dec 2007 09:30	201
02 Dec 2008 10:45	193
03 Jul 2009 10:10	190
22 Jul 2011 10:30	*134
18 Nov 2011 09:12	*107
25 Nov 2011 09:15	*122
01 Aug 2012 11:46	*114
15 Oct 2012 10:20	*113
06 Nov 2012 11:45	*100
16 Nov 2012 00:00	*109
03 Dec 2012 12:00	*92

# IN LIVER CLINIC

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- Referred in June 2016 when became jaundiced
- USS showed cirrhosis with splenomegaly, trace of ascites
- Decompensated with gross ascites February 2017
- Liver transplant assessment November 2017

# IN HINDSIGHT

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- Probably cirrhotic with impaired function in 2012
  - albumin 33
- Also low platelets likely due to portal hypertension
- Despite - ALT within normal limits and normal ultrasound in 2014

## SO WHAT TO DO...ABOUT INCIDENTAL ABNORMAL LFTS

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➤ Ask about :

- Alcohol
- Drugs including over the counter or herbal remedies
- Family hx of liver disease

➤ Are they :

- Obese
- Family history of high BP / Cholesterol / Diabetes

➤ Check the liver screen



# LFTS

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- ALT elevated
  - Alcohol (not above 5 x ULN)
  - Viral (HBV / HCV / HIV / EBV / HEV)
  - New medications
  - NAFLD/Haemochromatosis/A1AT/Coeliac
  - Autoimmune hepatitis
  - Liver lesion
  - USS and liver screen

# LFTS

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- ALP
  - Is it biliary – USS
  - PBC/PSC/new medications/NAFLD
- Gamma GT
  - Non specific – can be biliary or hepatic causes
- If isolated bilirubin rise only – check conjugated/unconjugated  
Gilberts / haemolysis

# ULTRASOUND

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➤ Looking for:

- Fatty liver (reliable if  $>20\%$  steatosis or BMI  $< 40$ )
- signs of cirrhosis
- signs of portal hypertension
- liver lesions

# AUTOIMMUNE PROFILE AND IMMUNOGLOBULINS

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## ➤ Autoimmune Hepatitis

- ALT elevated
- anti smooth muscle, Anti nuclear antibody
- High IgG

## ➤ Primary Biliary Cholangitis

- ALP elevated
- Anti-mitochondrial antibody
- High IgM

## ➤ Primary Sclerosing Cholangitis

- ALP elevated
- Radiological diagnosis on MRCP

# METABOLIC

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- Ferritin +/- iron studies
- Alpha 1 antitrypsin
- Caeruloplasmin if < 45 years old
- TTG
- Lipid profile / HbA1c

# VIRAL

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- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis E - If acute and  $> 5 \times \text{ULN}$  OR on immunosuppression
- EBV - if acute and  $> 5 \times \text{ULN}$

## LIVER SCREEN AND USS IS NORMAL/FATTY LIVER

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➤ Do they have risk factors for NAFLD ?

- Obese
- T2DM
- Triglycerides > 1.7
- HDL > 1 mmol/L
- Hypertension

➤ Do they drink too much alcohol?

- Brief intervention NNT = 8-12
- Consider referral to alcohol services

# FIBROSIS SCREENING

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## ➤ Non invasive fibrosis testing

- AST/ALT ratio > 1
- FIB-4 (Fibrosis-4)
- Fibroscan
- ELF test



# WHO TO REFER

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➤ Who to refer:

- Those with positive findings on the liver screen
- Those at risk of liver disease elevated bilirubin, low albumin or low platelets
- those with elevated ALP (check GGT or isoenzymes)
- those with ALT > 3 x ULN 3 months
- ALT > 5 x ULN (do liver screen and refer)
- NAFLD/Alcohol patients with abnormal FIB4 - for Fibroscan

# FIBROSIS SCREENING

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- High risk patients for fibrosis screening:
  - NAFLD
  - Harmful or hazardous alcohol consumption

Questions	Scoring system					Your score
	0	1	2	3	4	
How often do you have a drink containing alcohol?	Never	Monthly or less	2 - 4 times per month	2 - 3 times per week	4+ times per week	
How many units of alcohol do you drink on a typical day when you are drinking?	0 - 2	3 - 4	5 - 6	7 - 9	10+	
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	

# MANAGEMENT

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## ➤ NAFLD patients :

- Target weight loss 10% over 6-12 months
- Brisk exercise 5 days out of 7
- Control BP / DM / cholesterol
- Statins reduce fibrosis
- 2-3 cups of coffee a day
- If no advanced fibrosis then rescreen in 3 years

## ➤ Alcohol:

- reduction in alcohol consumption
- Cirrhosis - no alcohol

# IN SUMMARY

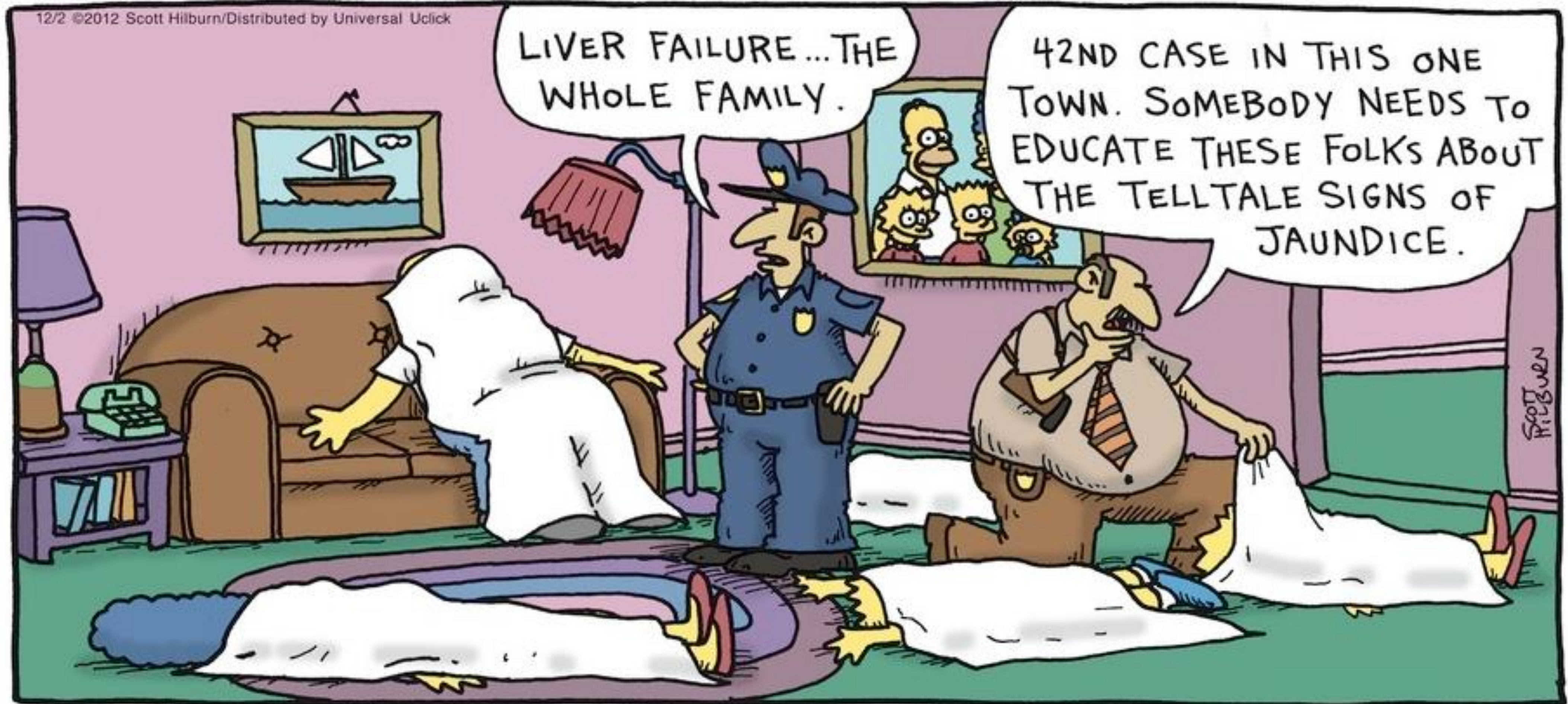
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- LFTs are not the whole story
- Can screen for fibrosis with FIB4 or refer for Fibroscan in alcohol/NAFLD patients
- Refer those with ALT > 5 x ULN to hepatology
- Refer those with NAFLD/ alcohol risk factors and high bilirubin / low albumin / low platelets to hepatology
- ELF testing will sooner be available
- There will be a NAFLD algorithm as part of the ELF test roll out



# THE ARGYLE SWEATER

BY SCOTT HILBURN



THE END