



York Teaching Hospital
NHS Foundation Trust



Workshop: Liver BLOOD tests 11th April 2019

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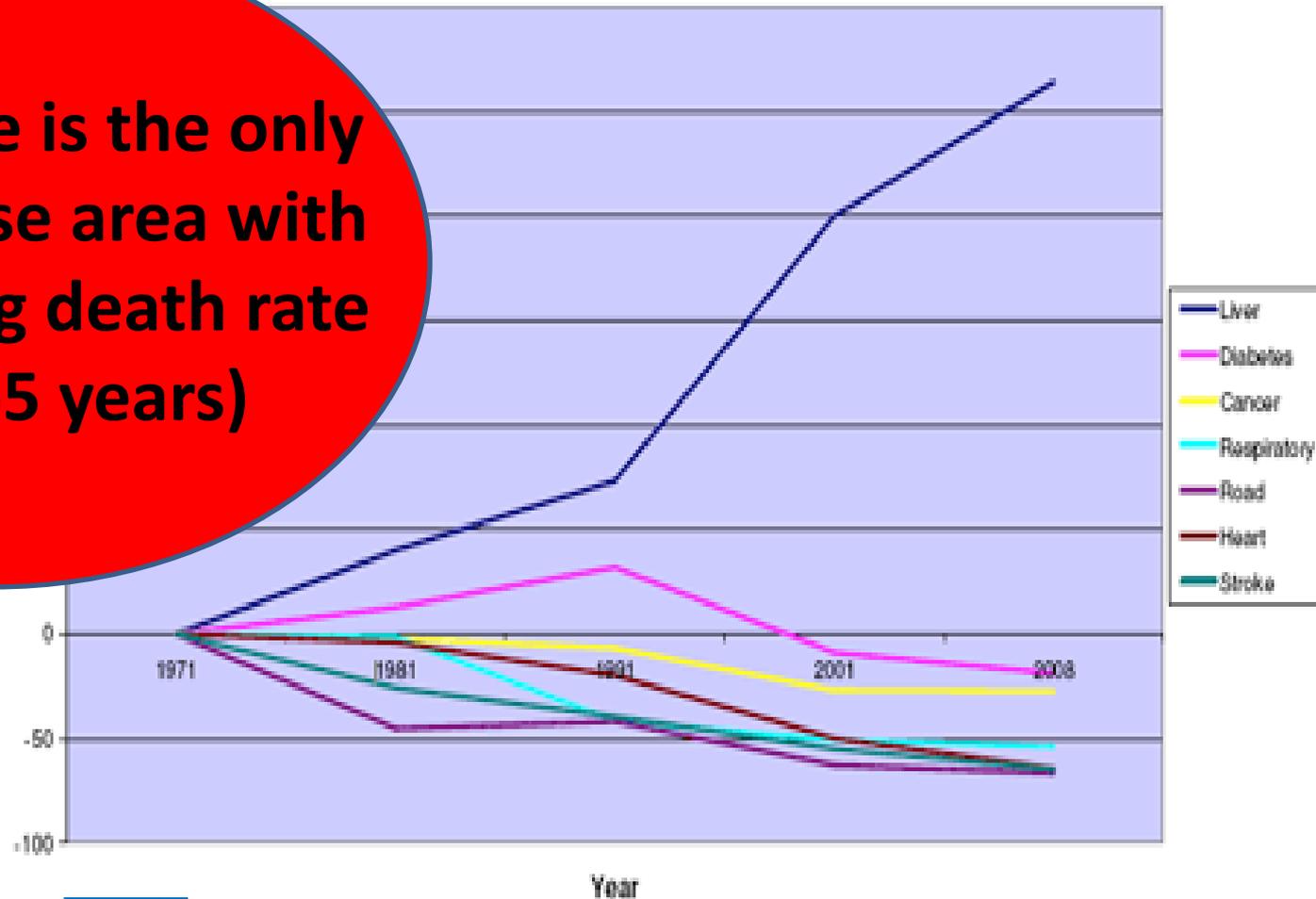
Aims

- 1) Causes of liver disease**
- 2) LFTs - poor marker of liver disease**
- 3) FibroScan – novel, non-invasive test**
- 4) Case Finding**

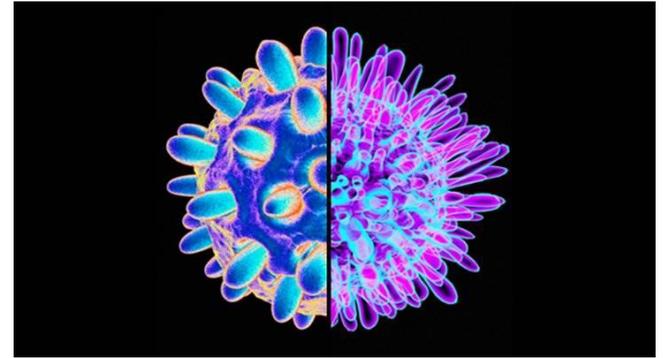
Liver Disease in the UK

Movements in mortality 1971-2008
Deaths per million of population

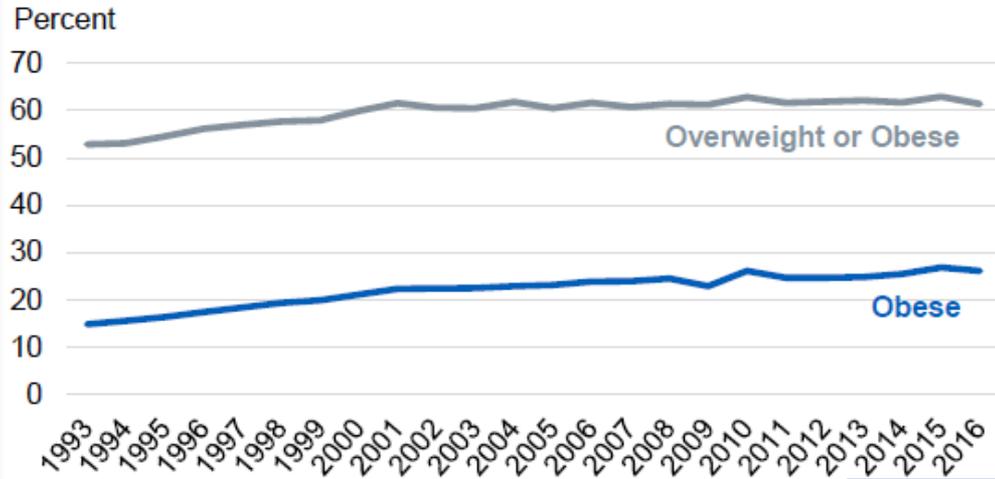
Liver disease is the only major disease area with an increasing death rate (under 65 years)



95% of liver disease in UK

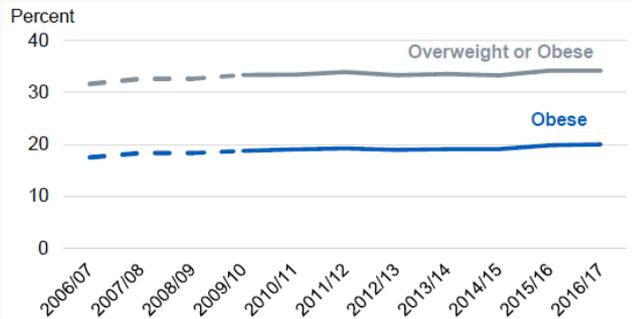


Prevalence of overweight and obese adults in England

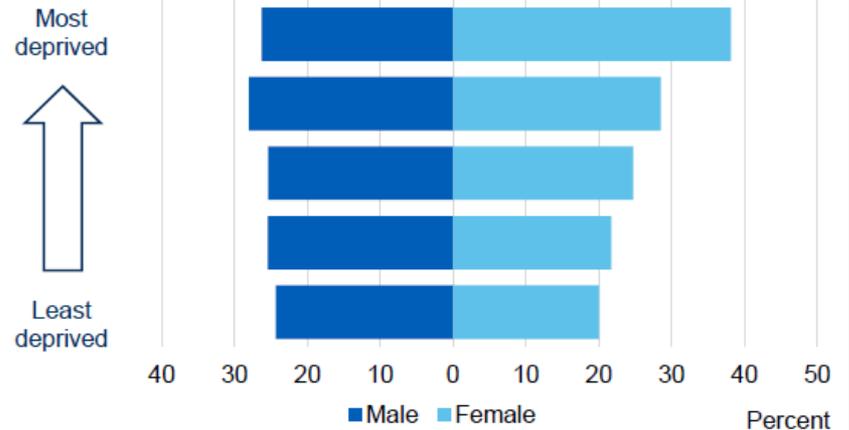


Prevalence of overweight and obese children (10-11 yrs)

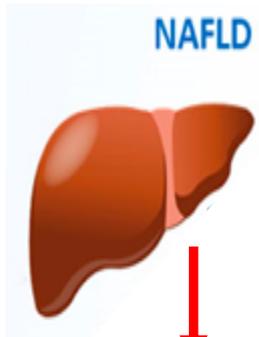
Year 6



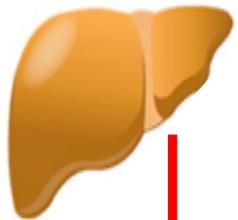
Obesity prevalence by sex and area deprivation



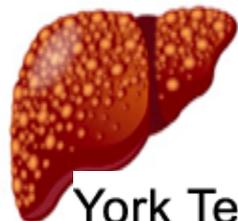
Liver disease in the 21st century



NASH



Cirrhosis



NAFLD
Global prevalence
24%

	UK cohort	
NAFLD	14,678,931	22%
NASH	905,022	1.3%
NASH fibrosis	352,273	0.5%
NASH cirrhosis	128,976	0.2%
HCC	1,684	0.003%

Alcohol

	Women	Men	
Hazardous	14 – 35 units/week	21 – 50 units/week	Increases risk of harm
Harmful	> 35 units/week	> 50 units/week	Causes medical / physical damage

Alcohol-related hospital admissions



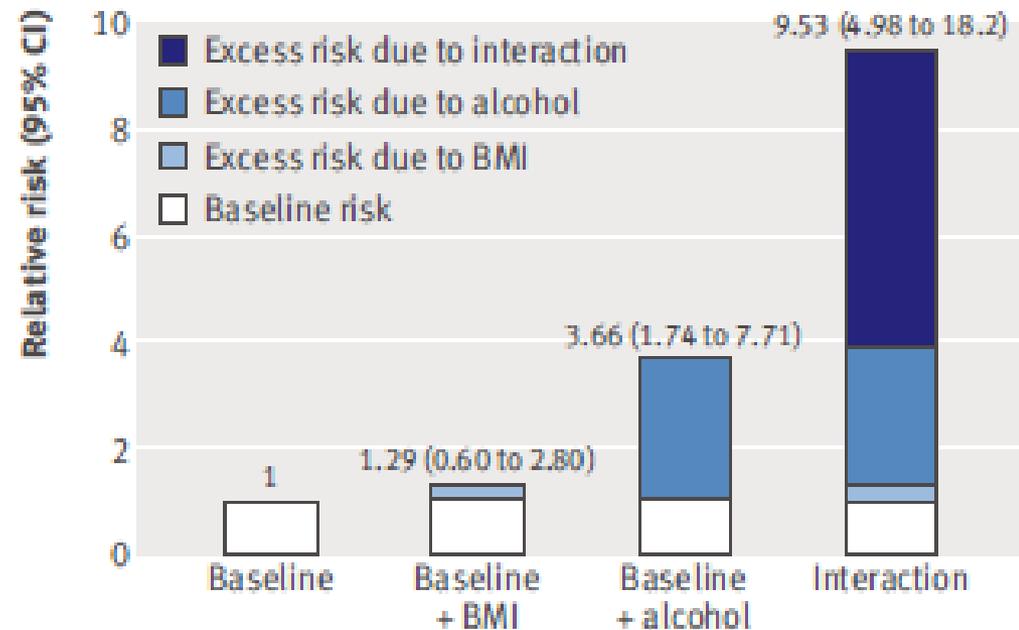
21%
adults (16+) drank
more than 14 units of
alcohol per week

28% of men, 14% of women

Effect of BMI and alcohol consumption on liver disease: analysis of data of two prospective cohort studies.

Hart CL, Morrison DS *et al*

- Prospective cohort study of 9559 men
- Follow-up 29 years
- 146 deaths liver disease (80 'main' cause)
- Alcohol intake: 0, 1-14 or ≥ 15 u/week
- Weight: under/normal < 25 , BMI 25-29, BMI ≥ 30



Relative risks of contributions of BMI and alcohol to liver disease mortality (adjusted for all risk factors).

Aims

- 1) **Causes of liver disease**
 - NAFLD
 - Alcohol
 - Hepatitis B / C
- 2) LFTs - poor marker of liver disease
- 3) FibroScan – novel, non-invasive test
- 4) Case Finding

Liver “function” tests (LFTs)

- Renowned for being poor markers of liver disease
- Liver blood tests are often normal in fibrosis and cirrhosis
- Equally often abnormal in the face of no fibrosis or cirrhosis
- Liver disease is not common in those with abnormal LFTs

BALLETS Study

11 GP practices (Brum and Lambeth)

Prospective study

No obvious or pre-existing liver disease

Significant liver disease prevalence ~ 5%

ALFIE Study

Tayside

15 year follow-up

No obvious signs of liver disease

95,977 patients

21.7% had one abnormal liver blood test

1.14% developed liver disease

A red oval with a blue border containing text.

**> 20% of
initial LFTs
are abnormal**

Aims

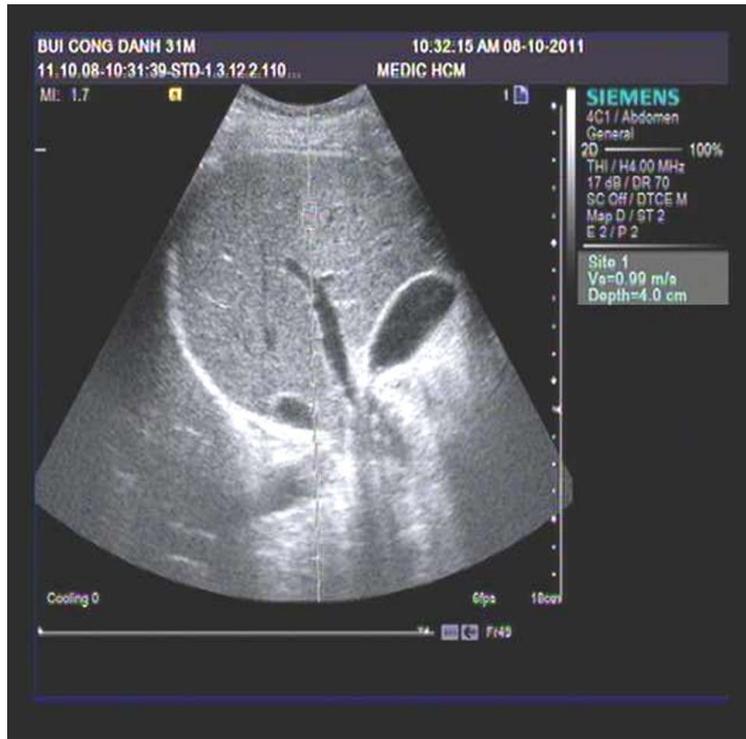
- 1) **Causes of liver disease**
 - NAFLD
 - Alcohol
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- 2) **LFTs - poor marker of liver disease**
- 3) **FibroScan – novel, non-invasive test**
- 4) **Case Finding**

Alternatives?

Liver Biopsy

- Not without risk
- Significant morbidity and mortality
 - “Serious bleeding 1 in 200”
 - “Bleeding mortality 1 in 2000”
- Perrault *et al.* reviewed 1000 patients
 - 5% hospitalised secondary to procedure

Non invasive assessment



Composite Scores

Score	Serological composite		Diagnostic accuracy	
			Sensitivity	Specificity
AST to platelet ratio index (APRI) ⁴⁸	AST	Platelet count	81%	55%
European Liver Fibrosis (ELF®) ⁵⁴	HA TIMP-I	PIIINP	91%	69%
Fibrometer® ⁴⁶	Platelet count Prothrombin index AST	HA Urea α-2macroglobulin	80%	84%
Fibrospect® ⁵⁵	HA α-2-macroglobulin	TIMP-II	71%	74%
Fibrotest® ⁵⁶	Age Gender αGT α-2-macroglobulin	Total bilirubin Haptoglobin Apolipoprotein-A	61%	80%
Forns Score ⁵⁷	Platelet count αGT	Age Cholesterol	30%	95%
HepaScore® ⁵⁸	αGT Age Gender	HA Total bilirubin A2- macroglobulin	70%	79%
For NAFLD only				
BARD score ⁵⁹	BMI AST / ALT ratio	T2DM	44%	70%
NAFLD Fibrosis Score (NFS) ⁶⁰	Age BMI IFG / Diabetes	AST / ALT ratio Platelet count Albumin	77%	70%
Fibrosis-4 (Fib-4) ⁵⁹	Age AST	Platelet count ALT	54%	88%

Transient Elastography

“Fibroscan”

New tool for assessment

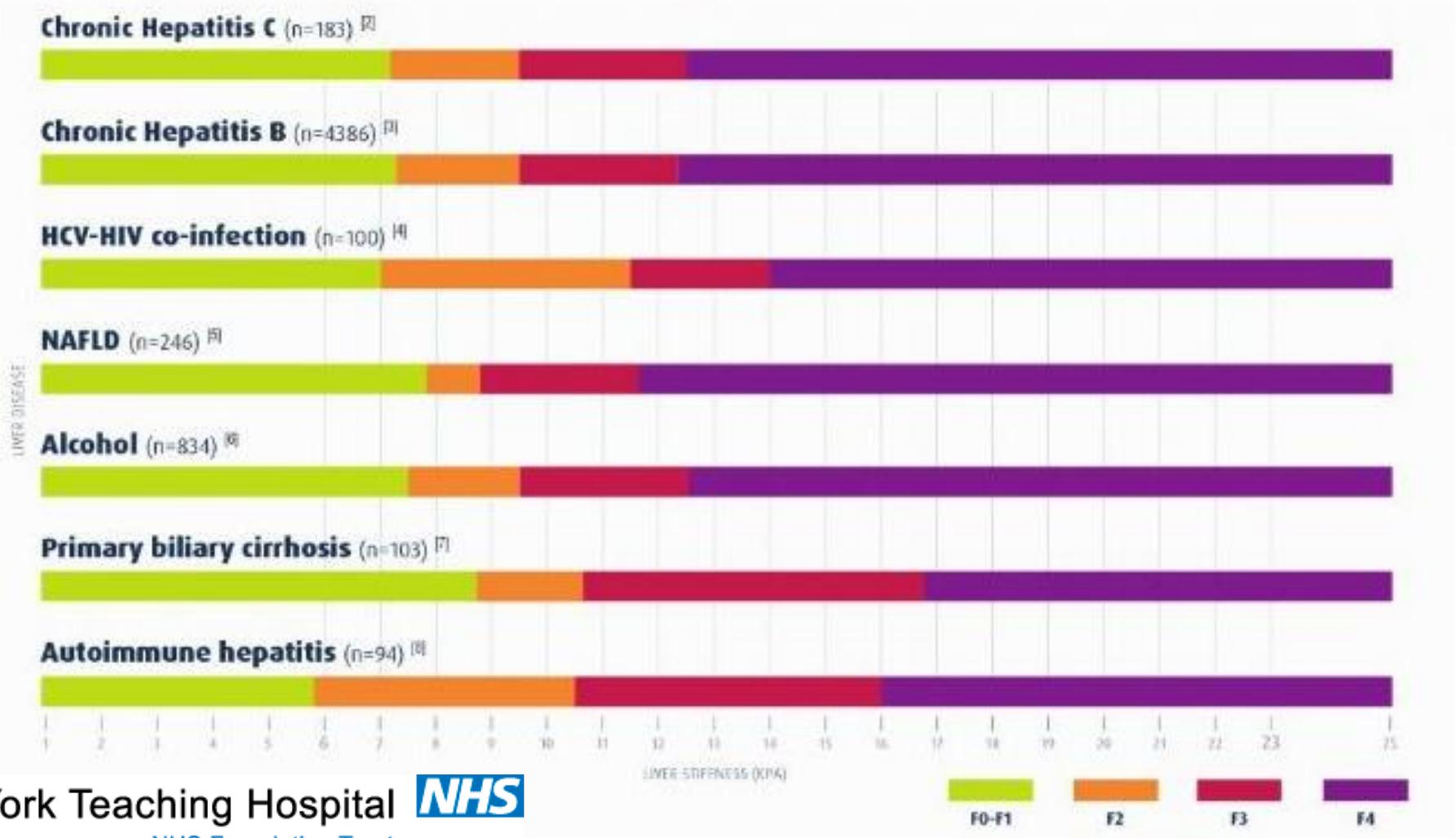
Quick

Non-invasive



	Sensitivity	Specificity
Fibrosis	83%	83%
Cirrhosis	98%	84%

Interpretation Guide



Why Transient Elastography?

CG165

Adults with chronic hepatitis B

Please refer to [recommendations](#)

EASL 2015

Recommendations

- Non-invasive tests should always be interpreted by specialists in liver disease, according to the clinical context, considering the results of other tests (biochemical, radiological and endoscopic) and taking into account the recommended quality criteria for each test and its possible pitfalls (A1)
- Serum biomarkers can be used in clinical practice due to their high applicability (>95%) and good inter-laboratory reproducibility. However, they should be preferably obtained in fasting patients (particularly those including hyaluronic acid) and following the manufacturer's recommendations for the patented tests (A1)
- TE is a fast, simple, safe and easy to learn procedure that is widely available. Its main limitation is the impossibility of obtaining results in case of ascites or morbid obesity and its limited applicability in case of obesity and limited operator experience (A1)
- TE should be performed by an experienced operator (>100 examinations) following a standardized protocol with the patient, fasting for at least 2 hours, in the supine position, right arm in full abduction, on the mid-

that there is an increased risk of cirrhosis in people who:

hepatitis B virus infection

hepatitis C virus infection

alcohol

obesity (BMI of 30 kg/m² or higher)

type 2 diabetes.

See the NICE guidelines on: [non-alcoholic fatty liver disease \(NAFLD\)](#), [alcohol-use disorders: diagnosis and management of physical complications](#), [alcohol-use disorders: prevention](#), [alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence](#), [diabetes in adults](#), [obesity](#) and [hepatitis B \(chronic\)](#).

Discuss with the person the accuracy, limitations and risks of the different tests for diagnosing cirrhosis.

Use transient elastography to diagnose cirrhosis for:

• People with hepatitis C virus infection

• People who drink over 50 units of alcohol per week and women who drink over 35 units of alcohol per week and have done so for several months

• People diagnosed with alcohol-related liver disease.

NG50

Aims

1) Causes of liver disease



- NAFLD
- Alcohol
- Hepatitis B / C

2) LFTs - poor marker of liver disease

3) FibroScan – novel, non-invasive test

FibroScan > 7 kPa = concerning?

4) Case Finding

Case finding

- 1) High risk of metabolic syndrome?
- 2) Hazardous alcohol use?
- 3) Have they ever injected drugs?

Case finding

1) High risk of metabolic syndrome?

Cholesterol

T2DM

BP

1.1 Assessment for NAFLD

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Identifying NAFLD in higher-risk groups

1.1.1 Be aware that non-alcoholic fatty liver disease (NAFLD) is more common in people who have:

- type 2 diabetes or
- metabolic syndrome.

1.1.2 Take an alcohol history to rule out

1.1.3 Do not use routine liver blood tests

What action should they take?

- GPs and practice nurses should offer testing for hepatitis B and C to adults and children at increased risk of infection, particularly migrants from medium- or high-prevalence countries and people who inject or have injected drugs (see [Whose health will benefit?](#)).
- GPs and practice nurses should offer testing for hepatitis B and C to people who are newly registered with the practice and belong to a group at increased risk of infection (see [Whose health will benefit?](#)).
- GPs and practice nurses should ask newly registered adults if they have ever injected drugs, including image and performance enhancement substances at their first consultation.
- GPs and practice nurses should offer hepatitis B testing and vaccination to men who have sex with men who are offered a test for HIV and have not previously tested positive for hepatitis B antibodies (see NICE guidance on [increasing the uptake of HIV testing among men who have sex with men](#)).
- GPs and practice nurses should offer hepatitis B vaccination to people who test negative for hepatitis B but remain at increased risk of infection (see the [Green book](#)).
- GPs and practice nurses should offer annual testing for hepatitis C to people who test negative for hepatitis C

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Non invasive assessment



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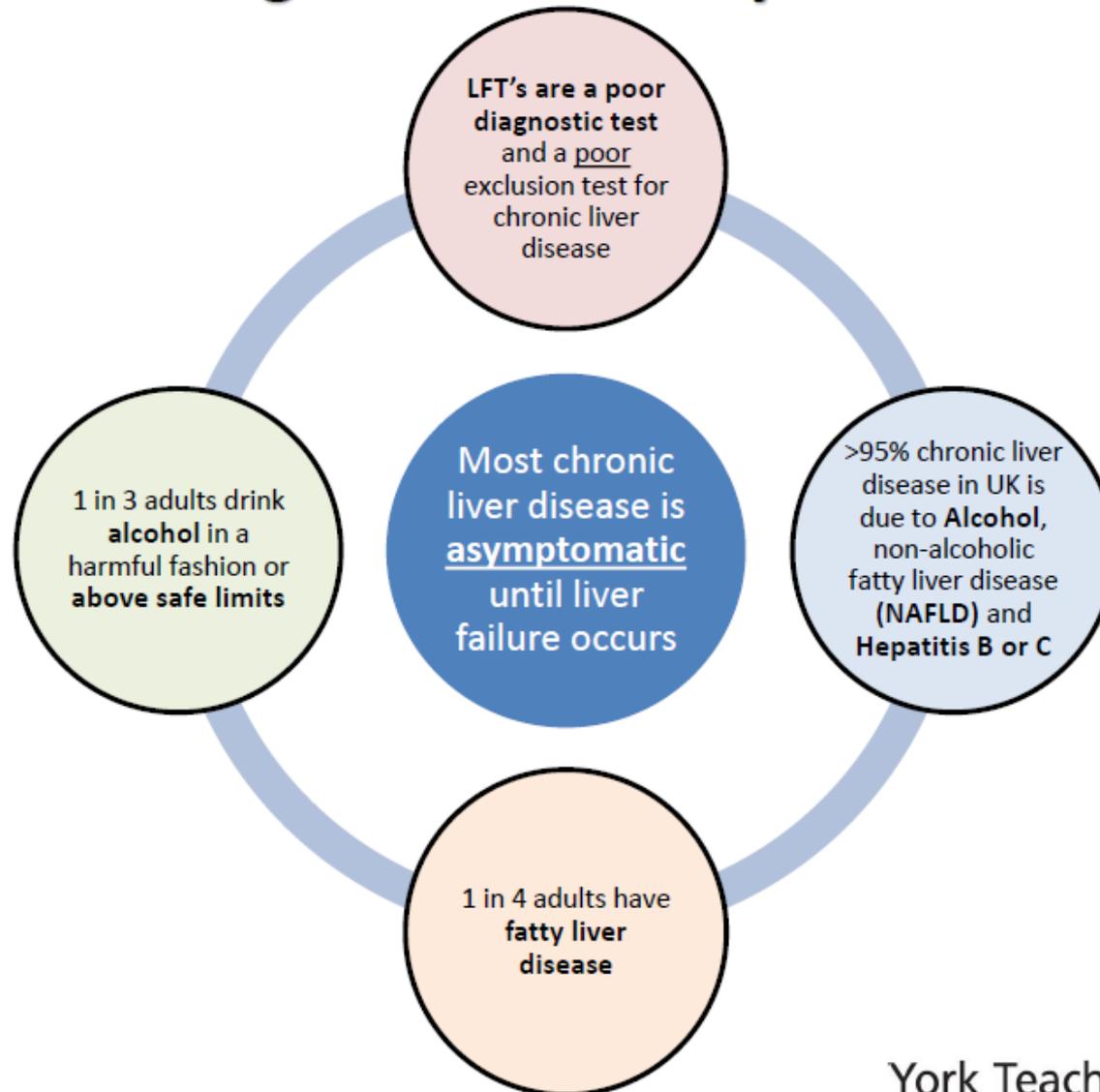
3) FibroScan – novel, non-invasive test

FibroScan > 7 kPa = concerning?

4) Case Finding

- 1) Metabolic syndrome?
- 2) Hazardous alcohol?
- 3) Ever injected drugs?

Liver Disease and Liver Function Tests: A guide for Primary Care



Isolated ↑ Bilirubin

Conjugated/
Unconjugated
Bili

Unconjugated
↑ Bilirubin

Conjugated
↑ Bilirubin

Retic. count &
Haptoglobins

Abnormal

Normal

Refer
Haematology

Gilbert's
[British Liver Trust](#)

Isolated ↑ALP <1000

Normal

GGT

Raised

?Bone origin
Check Vit D

ALP < 2xULN
No Symptoms

ALP > 2xULN
OR weight loss /
biliary pain

Repeat 3
months

Normal

Abnormal

Repeat at
12 months

Ultrasound &
NLS ** blood panel

ALT < 200

or

Combined ↑ALT & ↑ALP

Drug history, risk factors for viral
hepatitis, family history, co-
morbidities

[AUDIT-C](#)

>4

≤4

Alcohol
Misuse*

- Advise abstinence & weight loss
- Repeat in 1 month
- Screen for HBV/HCV

Abnormal

Normal / Improving

Ultrasound & NLS ***
blood panel (via ICE)

[NAFLD
score](#) **

POSITIVE

NEGATIVE

REFER HEPATOLOGY: Call (01904 725622, 0900h – 1700h) Or Fax Referral (01904 725401)

* See Management of Alcohol Misuse pathway

** See Management of NAFLD pathway

*** NLS = Non-Invasive Liver Screen

Alcohol use disorders identification test consumption (AUDIT C)

This alcohol harm assessment tool consists of the consumption questions from the full alcohol use disorders identification test (AUDIT).

Questions	Scoring system					Your score
	0	1	2	3	4	
How often do you have a drink containing alcohol?	Never	Monthly or less	2 to 4 times per month	2 to 3 times per week	4 or more times per week	
How many units of alcohol do you drink on a typical day when you are drinking?	0 to 2	3 to 4	5 to 6	7 to 9	10 or more	
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	

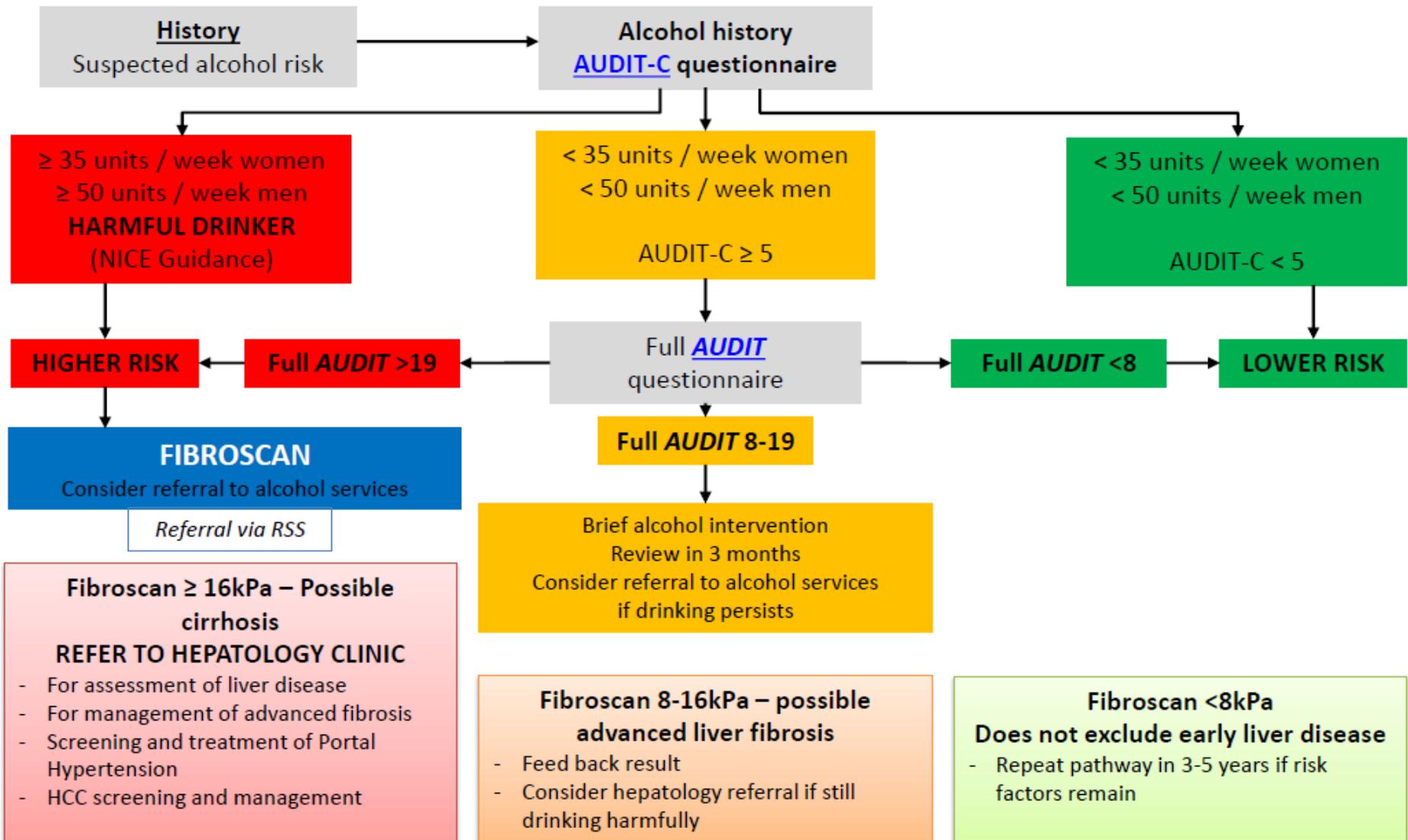
AUDIT C score	
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Scoring:

- A total of 5 or more is a positive screen

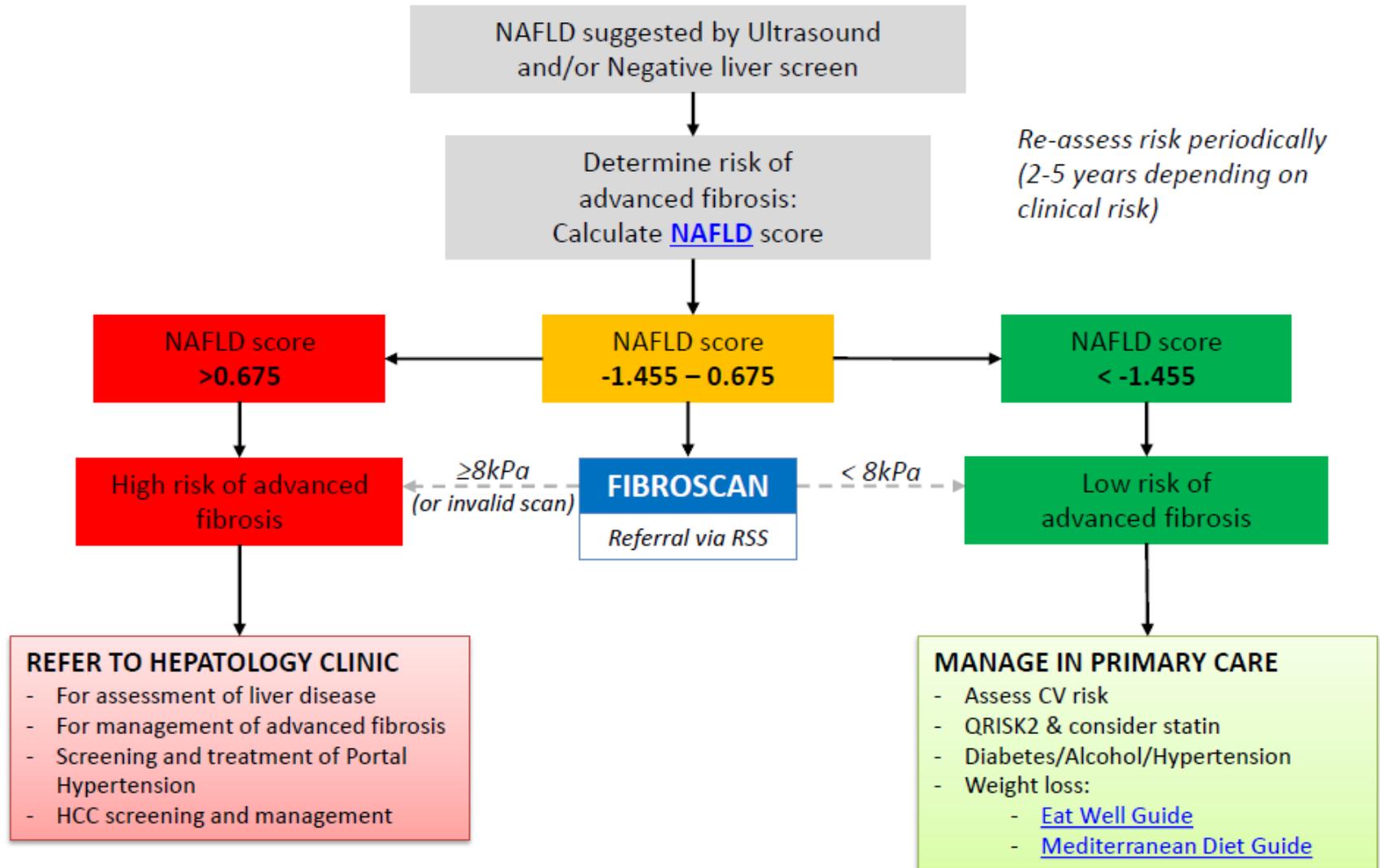
Management of Alcohol Misuse

Ref: Newsome PN, et al. *Gut* 2018; 67:6-19



Management of NAFLD

Ref: Newsome PN, et al. Gut 2018; 67:6-19



In conclusion

Liver blood tests are poor markers of liver disease

Liver disease; silent yet highly prevalent ~ 24% have NAFLD

Case finding:

- Alcohol
- Metabolic syndrome (high BMI)
- Viral hepatitis

If yes → Refer for FibroScan +/- hepatology opinion

A sign of things to come....?

Article
TextArticle
infoCitation
Tools

Share



Responses

Article
metrics

Alerts

Liver
Research

Development and validation of diagnostic triage criteria for liver disease from a minimum data set enabling the 'intelligent LFT' pathway for the automated assessment of deranged liver enzymes

FREE

Michael Hugh Miller¹, Andrew Fraser², Gillian Leggett², Alastair MacGilchrist³, George Gibson⁴, James Orr⁴, Ewan H Forrest⁴, Ellie Dow⁵, William Bartlett⁵, Christopher Weatherburn⁵, Axel Laurell¹, Kirsty Grant¹, Kathryn Scott⁶, Ronald Neville⁵, John F Dillon¹

[Author affiliations](#)

Abstract

Background Liver function tests (LFTs) are commonly abnormal; most patients with 'incidental' abnormal LFTs are not investigated appropriately and for those who are, current care pathways are geared to find an explanation for the abnormality by a lengthy process of investigation and exclusion, with costs to the patient and to the health service.

Objective To validate an intelligent automatable analysis tool (iLFT) for abnormal liver enzymes, which diagnoses common liver conditions, provides fibrosis stage and recommends management

Design A retrospective case note review from three tertiary referral liver centres, with application of the iLFT algorithm and comparison with the clinician's final opinion as gold standard.

Results The iLFT algorithm in 91.3% of cases would have correctly recommended referral or management in primary care. In the majority of the rest of the cases, iLFT failed safe and recommended referral even when the final clinical diagnosis could have been managed in primary care. Diagnostic accuracy was achieved in 82.4% of cases, consistent with the fail-safe design of the algorithm. Two cases would have remained in primary care as per the algorithm outcome, however on clinical review had features of advanced fibrosis.

Conclusion iLFT analysis of abnormal liver enzymes offers a safe and robust method of risk stratifying patients to the most



PDF



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