

**Application of non-invasive blood tests
for liver fibrosis
in primary or secondary care in the UK
*A Health-Economic Approach***

Prof William Rosenberg

UCL Institute for Liver and Digestive Health

**Belgian Liver Symposium
30th September 2022**

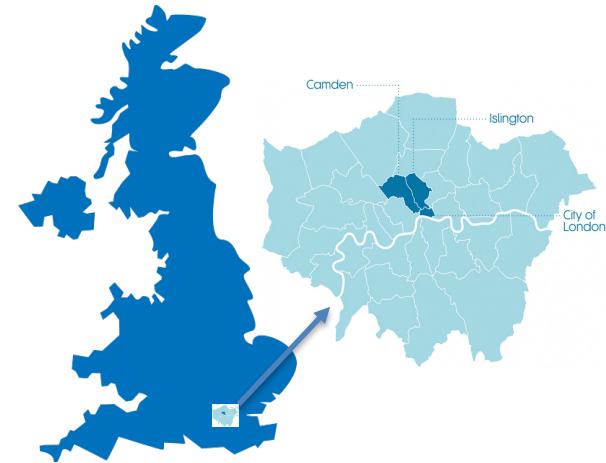
Overview

- Context – North London
- The need for better case selection
 - *An evidence based approach*
- Evaluation of a NAFLD pathway
- **Modelling the health-economic impact of using non-invasive tests in managing NAFLD**

The Camden and Islington Pathway

Population 430,000 Central London

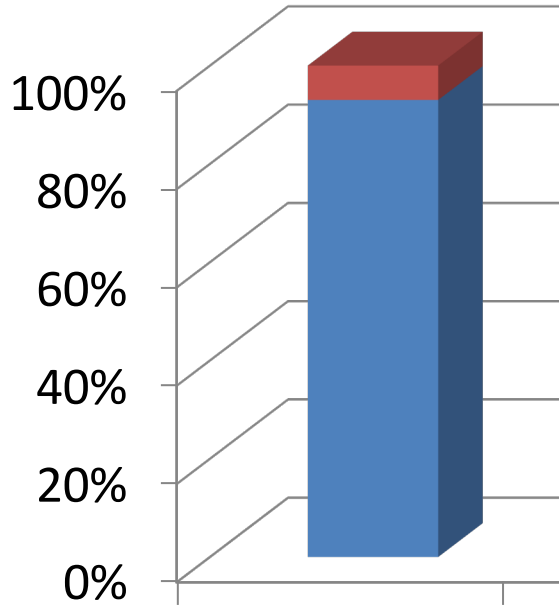
- Primary Care Engagement
- Multiple stakeholders
 - Primary Care Physicians
 - Liver specialists
 - Public Health
 - Commissioners
 - Laboratories
 - Patients and the public
- Pathway design and Test evaluation



Goals of the Pathway & Evaluation

- Improve detection of significant liver disease
 - >F2 fibrosis and cirrhosis – *refer to specialist*
- Limit secondary care referrals
 - Overall and <F3 – *maintain in Primary Care*
- Generate evidence of
 - Clinical effectiveness and Cost-effectiveness

Pre-Pathway Unnecessary Referrals

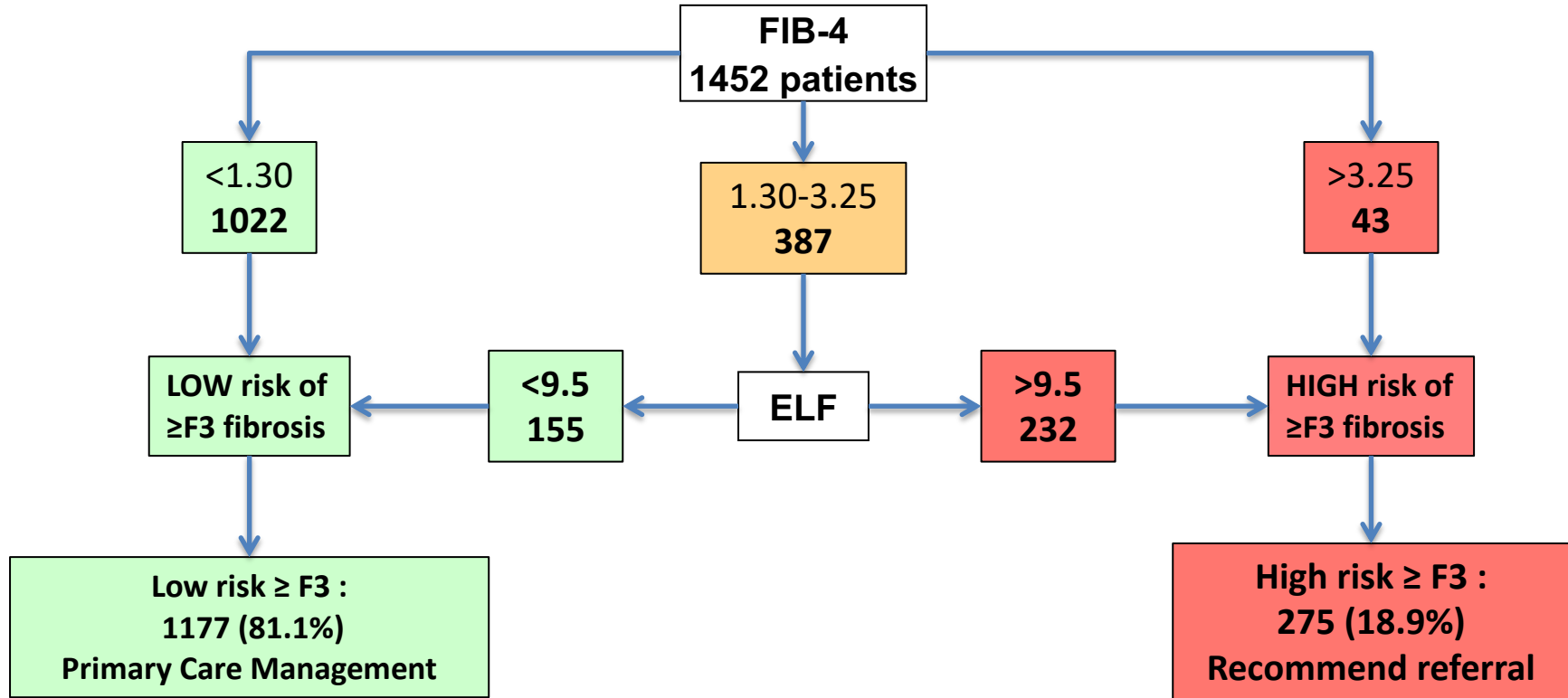


93% of referrals <F3

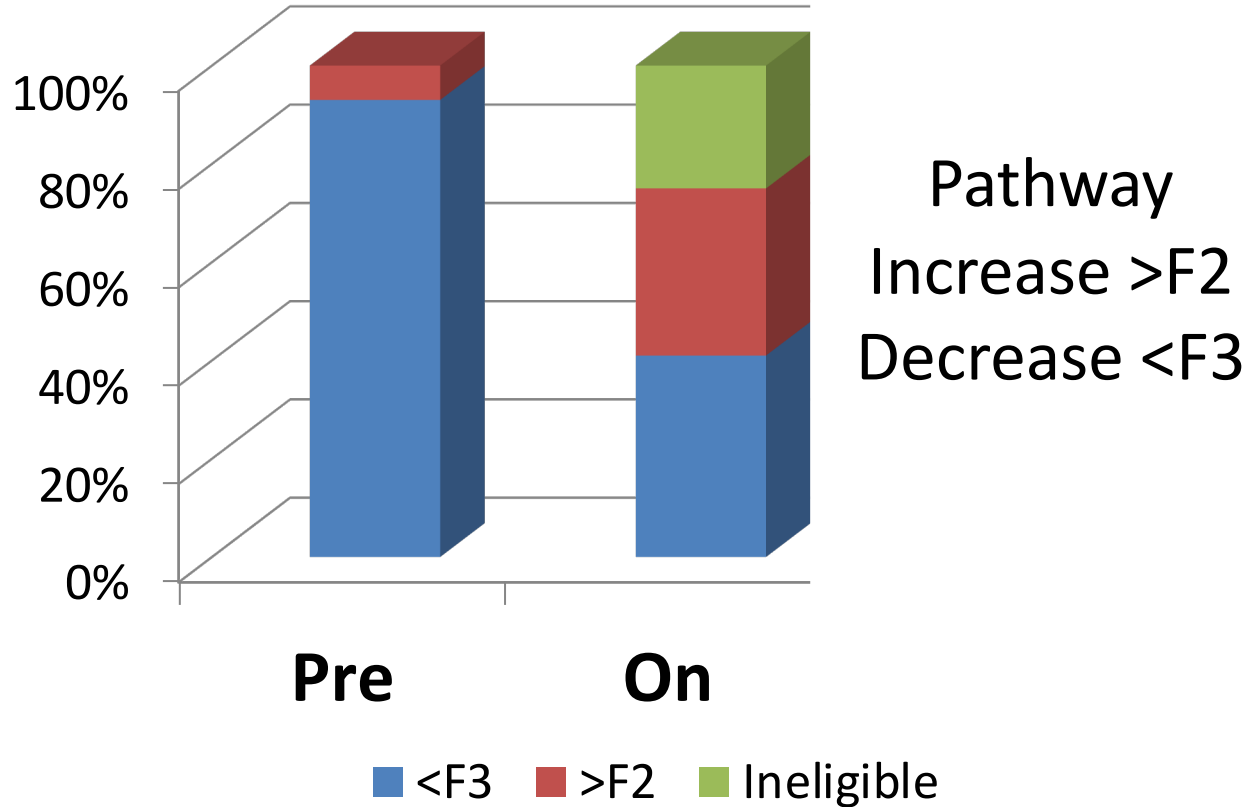
Pre

■ <F3 ■ >F2

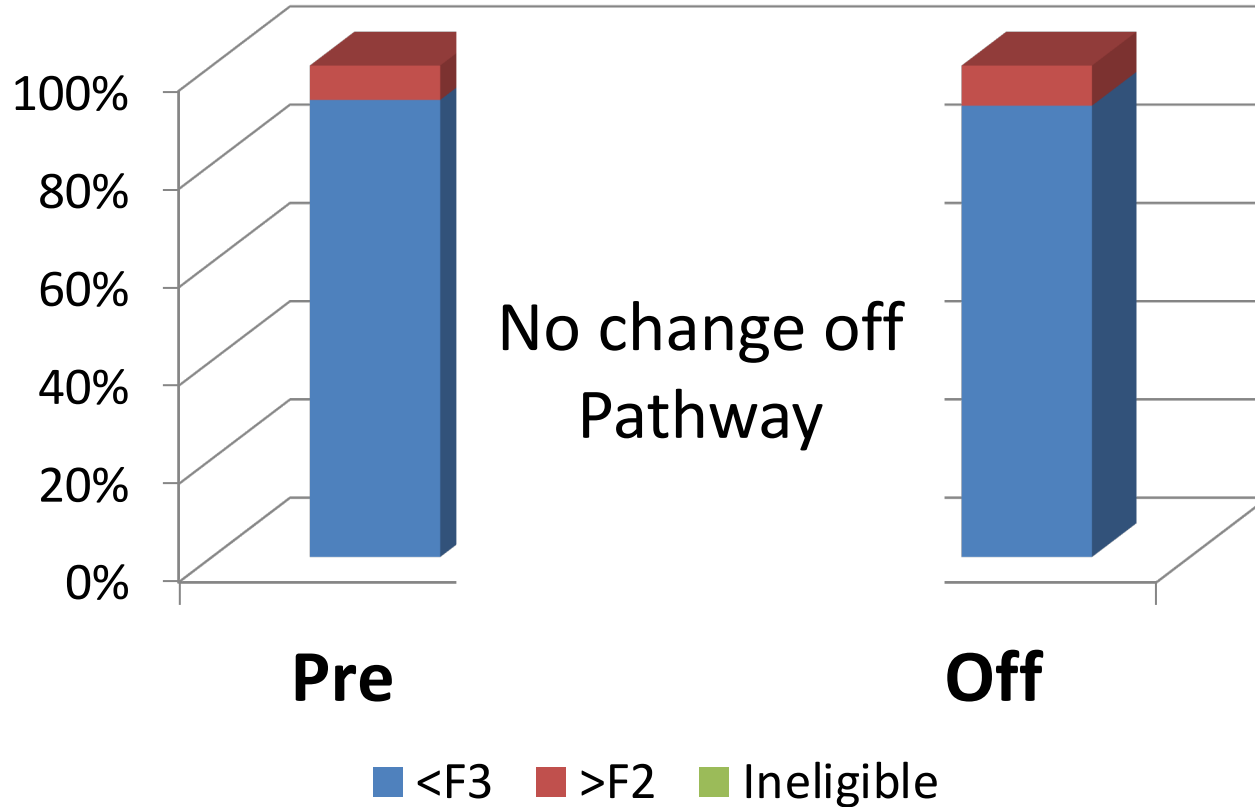
Primary Care Risk Stratification Using the Camden & Islington NAFLD Pathway 2014 - 2016



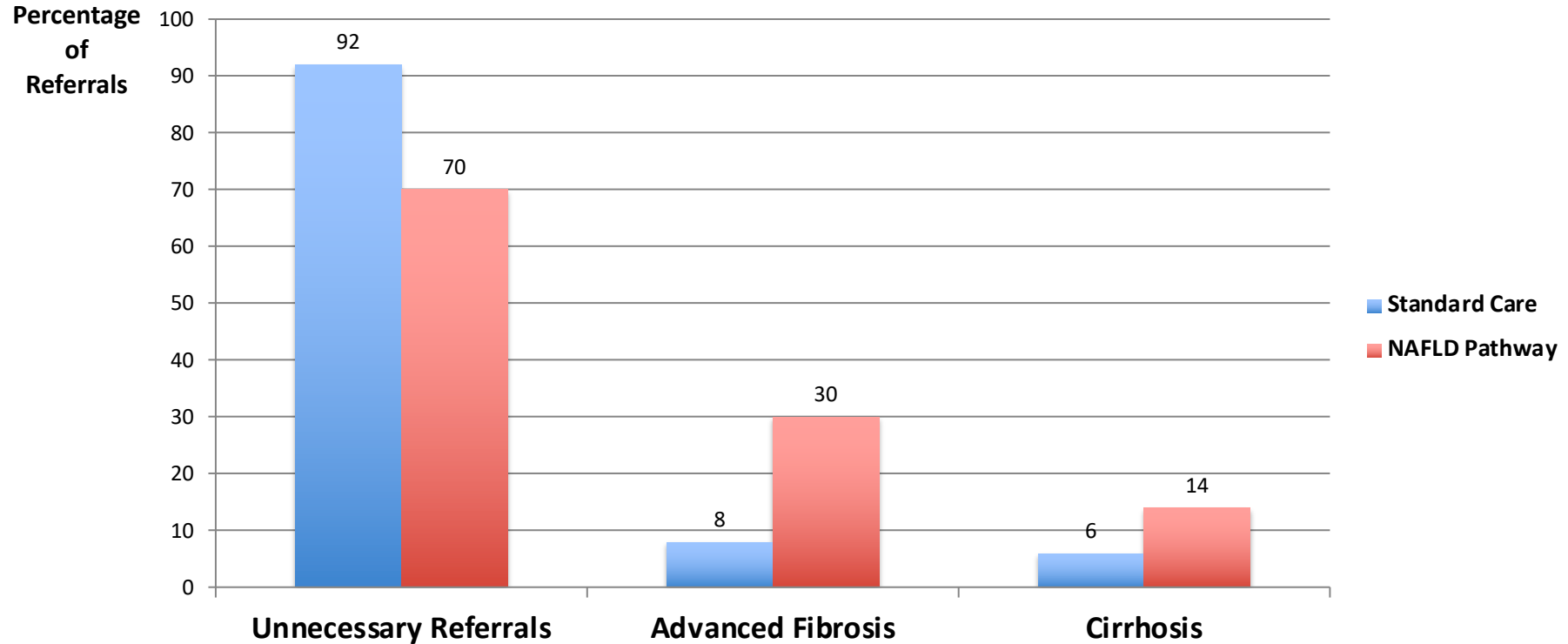
FIB4-ELF Stratification



FIB4-ELF Stratification



Evaluation of Patients Referred to Secondary Care From Camden and Islington 2014-2016



Impact of Higher Thresholds

	ELF \geq 9.8		ELF \geq 10.51	
Relative to ELF \geq 9.5	n	%	n	%
Referrals avoided	11	7.2	34	22.4
Missed Cases of F3/F4 fibrosis	3	6.7	10	22.2
Missed Cases of Cirrhosis	0		3	13.6

Key Findings from North London

- 3,012 patients screened
- Use of ELF increased detection of advanced fibrosis in NAFLD
- 5x increase in detection of advanced fibrosis ($\geq F3$)
- **81% reduction in unnecessary referrals (F0-2)**

Implications of Better Cirrhosis Detection

- 108% increase in detection of cirrhosis/5 yrs
- 35% increase in detection of early v late HCC
 - *If introduce surveillance for cirrhotics*
- 26% decrease in variceal bleeding
 - *If survey and treat varices*

MODELLING PATHWAYS OF CARE

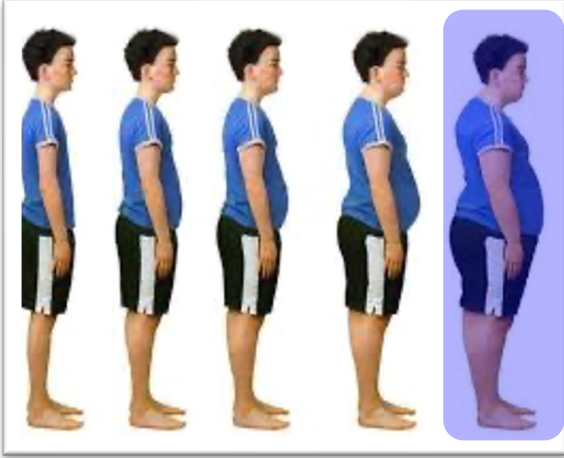
Probabilistic modelling to predict the impact of introducing non-invasive tests

Srivastava, A., Jong, S., Gola, A., Gailer, R., Morgan, S., Sennet, K., Pizzo, E., O'Beirne, J., Tsochatzis, E., Parkes, J. and Rosenberg, W.

Cost-Comparison Analysis of FIB4, ELF and Fibroscan in Community Pathways for Non-Alcoholic Fatty Liver Disease

BMC Gastroenterology. doi:10.1186/s12876-019-1039-4; 2019

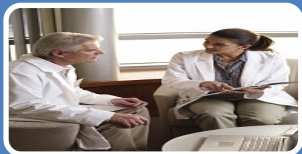
The Theoretical cohort



A hypothetical cohort of 1000 patients with NAFLD were simulated within the model

Local clinical audit
estimated SOC
sensitivity and
specificity of
0.35 and 0.70





Strategy 1 Standard of care (SOC)

- physicians clinical judgement



Strategy 2 SOC plus FIB-4 and ELF test

- FIB-4 initial screen



Strategy 3 SOC plus FIB-4 and TE

- FIB-4 initial screen



Strategy 4: SOC plus ELF

- ELF test for all



Strategy 5: SOC plus TE

- TE for all

The model was populated from literature, national UK data and expert opinion

A 5-year time horizon was applied

Who wants What?

- The Primary Care Physician
- The Specialist and the Patient
- The Commissioner

The Primary Care Physician

- *None of my obese patients have liver symptoms so they can't be ill*
- *I can advise most patients about dieting and exercise but I can't manage liver disease*
- *I only want to refer the patients that need to go to the hospital*
- *I don't know which patients to refer and which to monitor in the community*

Referrals to hospital: Use of ELF alone reduces referral of mild disease to hospital



**67%
reduction
of \leq F2
fibrosis
referrals**

*<F2 disease
93 referrals vs
278 referrals*

*Overall referrals
153 referrals vs
304 referrals*

*Per 1000 NAFLD
patients*

Optimisation of referrals: Use of FIB-4/ELF reduces referral of mild disease to hospital



**82%
reduction
of
referrals***

**49 v 278
≤F2 fibrosis**

**105 v 304
Referrals**
*Per 1000 NAFLD
Patients*

Liver Biopsy £642.75

*≤F2 fibrosis

The Liver Specialist

- Liver disease is an increasing cause of death in the community
- I want to find as many people with liver disease as possible
- I will measure my success by an increase in the number of cases of cirrhosis diagnosed
 - Reduced cases of variceal bleeding
 - Fewer cases of bleeding varices
 - Earlier diagnoses of liver cancer

Cirrhosis detection: Improved with FIB-4 + ELF



108%
increased
cirrhosis
detection
over 5 years

10.9 cases
v
5.2 cases

*Per 1000 NAFLD
patients*

Cirrhosis detection: ELF improves results further



**123% increase
in cirrhosis
detection
over 5 years**



11.8 cases
v
5.2 cases
Per 1000 NAFLD patients



Cirrhosis detection: Fibroscan alone detected most cases of cirrhosis



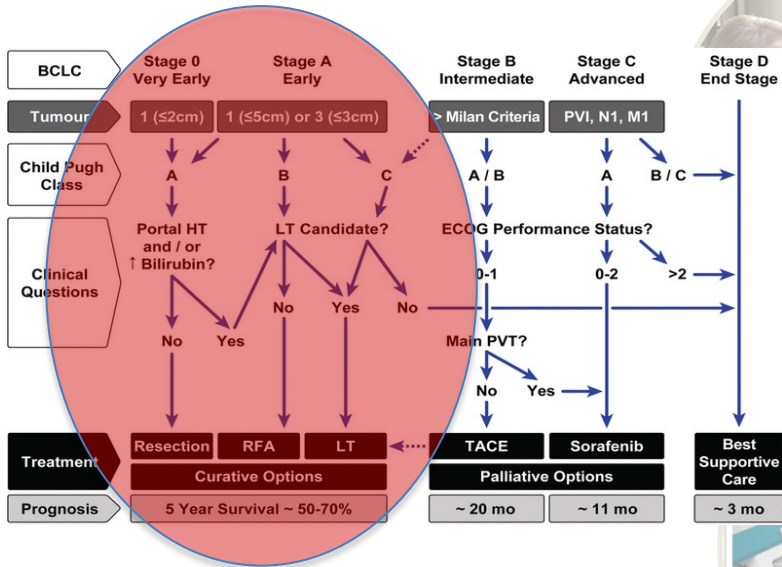
134%
increase in
cirrhosis
detection
over 5 years



12.2 cases
v
5.2 cases
Per 1000 NAFLD patients

*5% failure rate

Detection of Cureable HCC



SOC



NIT

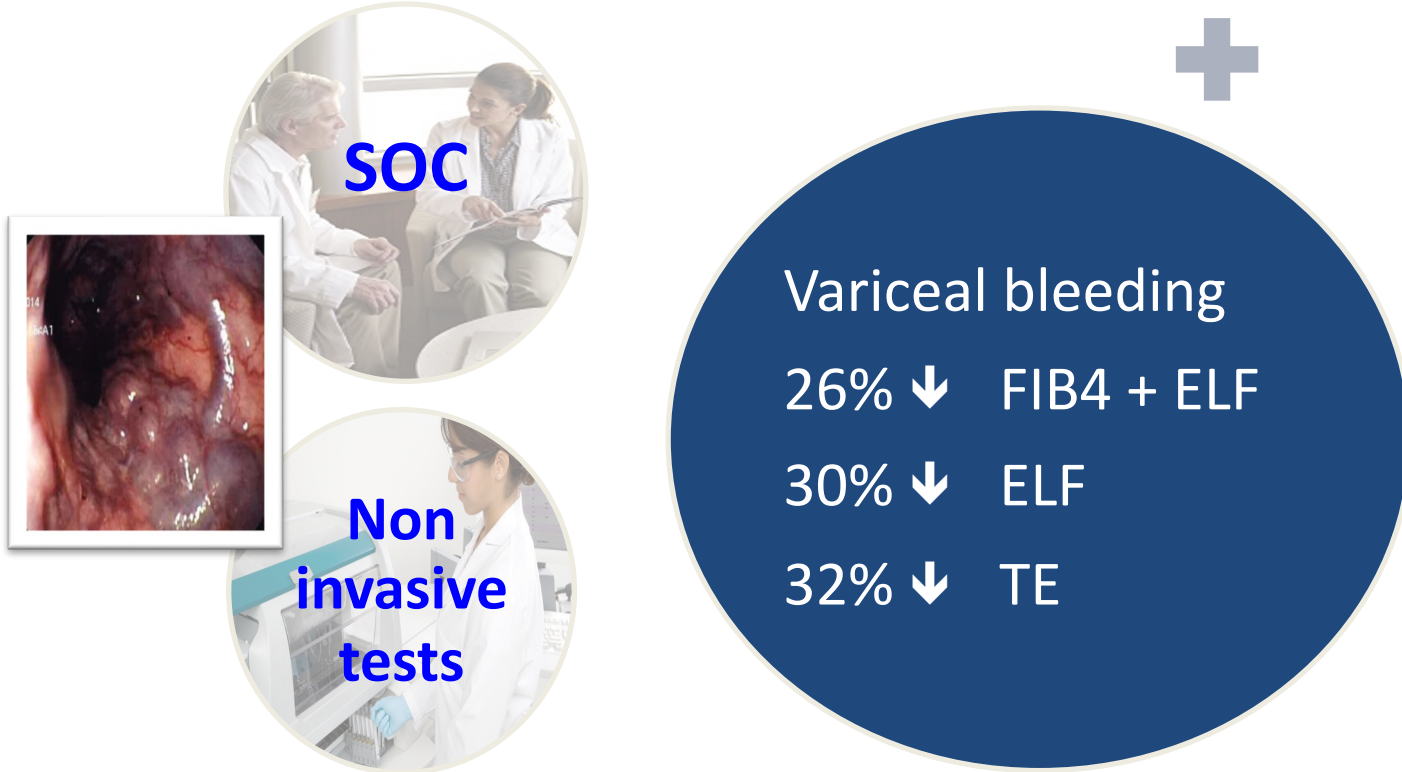
Stage 0/A HCC

35% ↑ FIB4/ELF

37% ↑ ELF

40% ↑ TE

Emergency variceal bleeding: life threatening event



The Commissioner

- Liver disease matters to me but I have to manage the whole healthcare economy
- I know that we are inefficient at finding cases of liver disease
- I want to find more cases of cirrhosis earlier so that I can improve well-being in my community and reduce the amount I am spending on end stage liver disease
- But I can't spend more money doing so
- Success for me will be measured in costs as well as outcomes

FIB-4 + ELF is cost effective



£170,000 saved
15% budget saving

SOC = £239.2K/ cirrhotic

NIT = £99.0K/ cirrhotic

58.6% reduction

Fibroscan alone is more costly than FIB4 + ELF



£20,000 increase in spending

1% budget increase

239.2K/ cirrhotic

104.6K/ cirrhotic

56.6% reduction

Recommendation

- NAFLD - Use FIB4 and ELF to stratify cases in primary care or ELF alone
- Progressed to adopt ELF alone for ArLD

IMPACT FOR A CITY

Cost savings : From Model to City

Greater Manchester Population of 2,500,000

SCENARIO	SOC	SOC + ELF	ELF v SOC
	Standard care	Standard Care plus ELF	Savings
Cirrhosis management costs over 5 years	£6,050,000	£2,525,000	£3,525,000

Prof Michael Arthur

Prof Julie Parkes

Mr Scott Harris

- **ELF Collaborators**

- **Wellcome Trust**

- **MRC**

- **Siemens/Bayer**

- Ellen Sampson
- Andrew Beard
- Daria Snack
- Bertrand Plouffe
- Paul Dhillon
- Hans Ijpelaar
- Jean Charles Clouet
- Matt Gee
- Omar Qurashi
- Louise Loughran

- **iQur Limited**

- Richard Cross
- Wiktoria Jonasson
- Raakesh Modi

- **NIHR**

- **NIH**

Prof Massimo Pinzani, Dr Manolis Tsochatzis,

Dr Sudeep Tanwar, Dr Paul Trembling, Dr Ankur Srivastava

Prof Alison Rodger, Dr Paul Trembling, Dr James Day,

Dr Simcha Jong, Dr Anna Gola, Dr Preya Patel, Dr Freya Rhodes

- **Queens Medical Centre Nottingham:** Prof Steve Ryder, Prof Guru Aithal, Dr Neil Guha

- **University of Newcastle Upon Tyne:** Prof Christopher Day

- **CDCP Atlanta USA:** Dr Beth Bell

- **UCSF:** Prof Marion Peters, Dr Norah Terrault

- **UTSW Dallas USA:** Marlyn Mayo

- **Bambino Gesu Childrens Hospital, Rome:** Dr. Valerio Nobili

- **University of Milan, Italy:** Pr. Pietro Lampertico

- **Oslo:** Prof Tom Karlsen, Dr M. Vesterhus

- **Camden and Islington:** Dr Karen Sennett, Dr Sarah Morgan

- **University of Brisbane:** Prof Elizabeth Powell