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Gastroenterological Society of Australia

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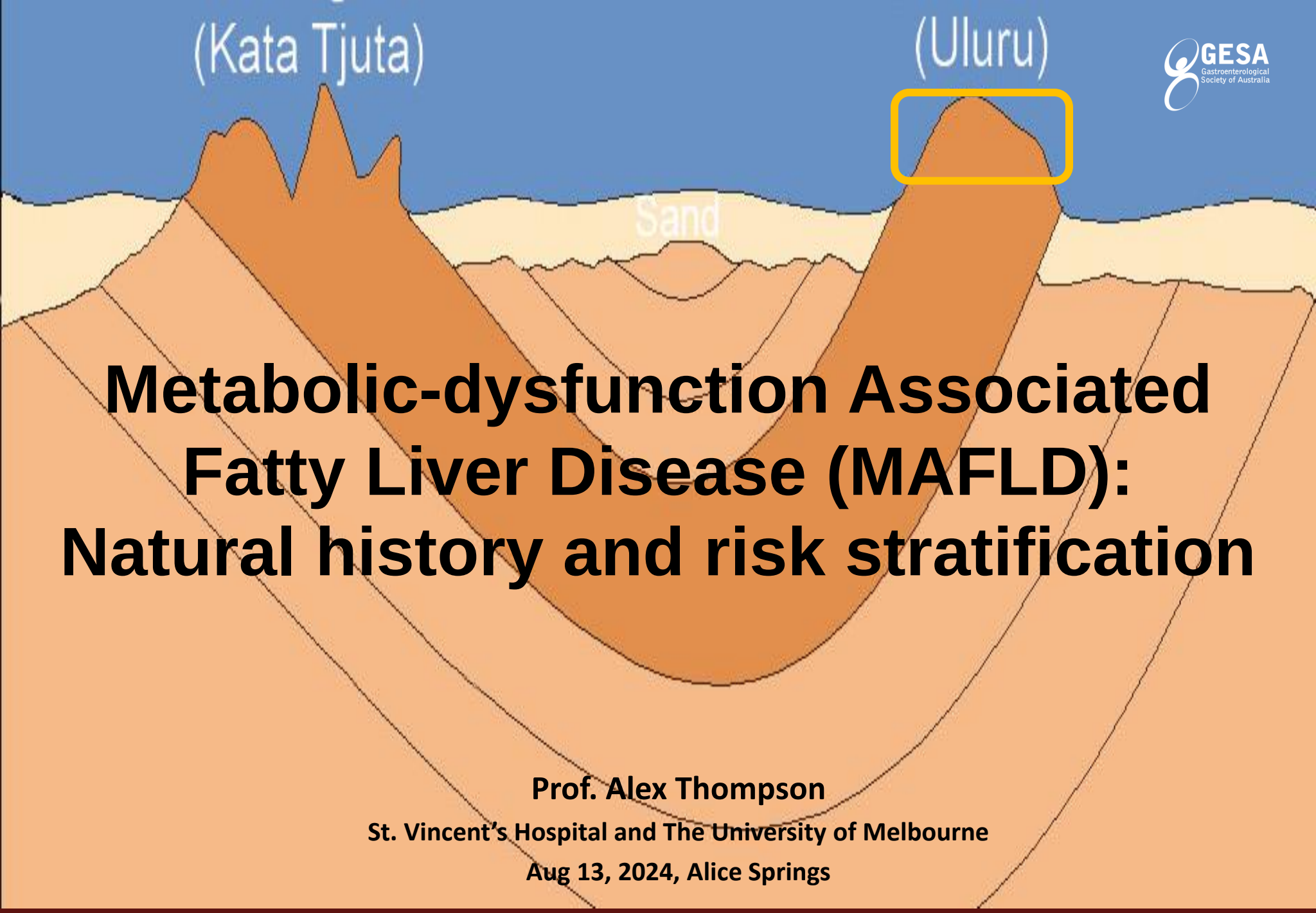
GUT CENTRE

13 - 16 August 2024
Alice Springs Hospital

The epicentre of gastrointestinal and liver education in Australia

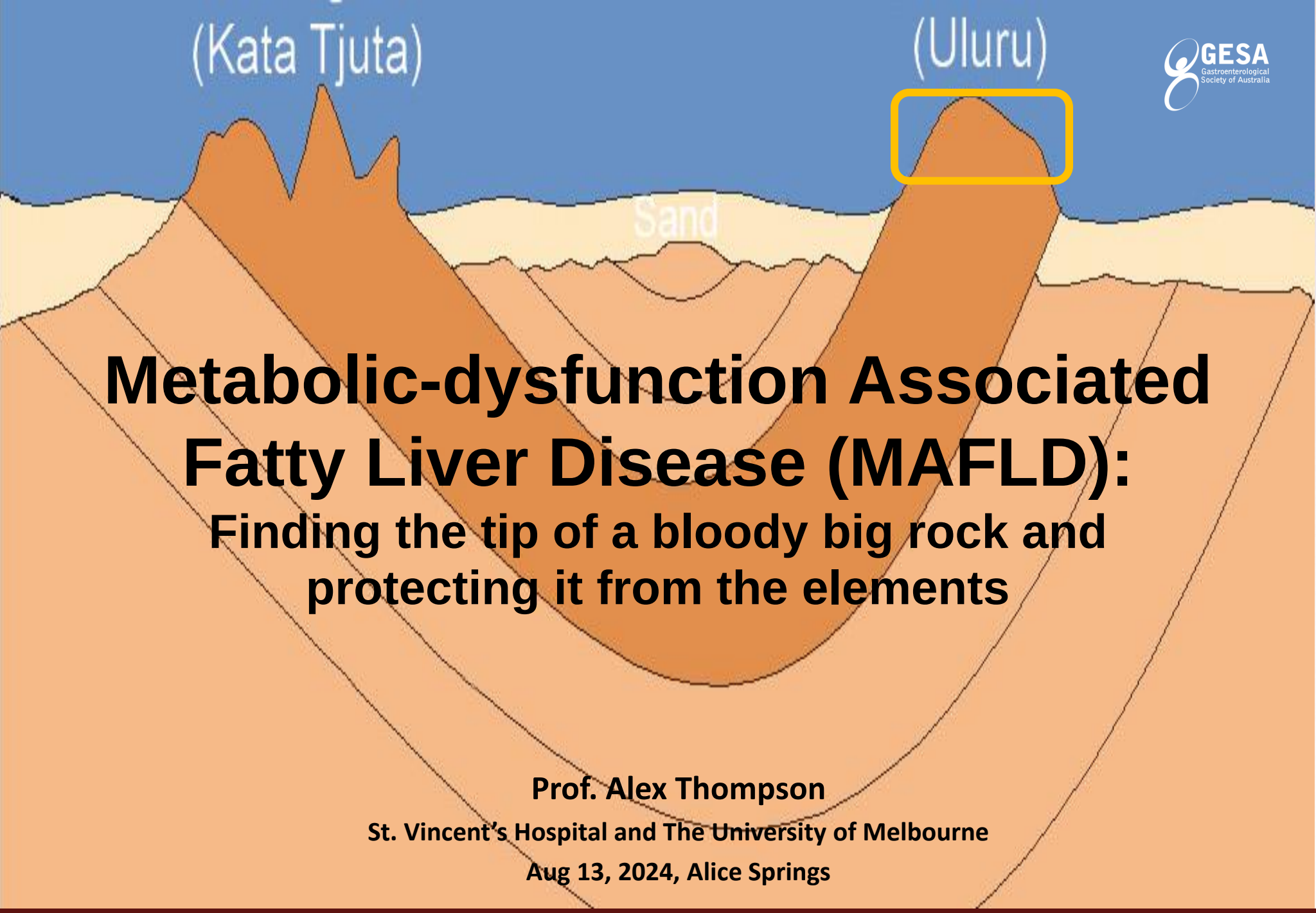


Metabolic-dysfunction Associated Fatty Liver Disease (MAFLD): Natural history and risk stratification

Prof. Alex Thompson

St. Vincent's Hospital and The University of Melbourne

Aug 13, 2024, Alice Springs



Metabolic-dysfunction Associated Fatty Liver Disease (MAFLD):

Finding the tip of a bloody big rock and protecting it from the elements

Prof. Alex Thompson

St. Vincent's Hospital and The University of Melbourne

Aug 13, 2024, Alice Springs

ACKNOWLEDGEMENT OF COUNTRY

- I begin today by acknowledging the Arrernte people, the traditional custodians of Mparntwe, the land on which we meet today, and pay my respects to their Elders past and present.
- I extend that respect to all Aboriginal and Torres Strait Islander peoples here today.

DISCLOSURES

- Consulting
  - Abbvie, Gilead Sciences, Assembly Biosciences, Roche Moelcular Systems
- Speaker
  - Roche Diagnostics, Roche, Abbvie, Gilead Sciences
- Research / grant support
  - Gilead Sciences, Abbvie, Roche Diagnostics

NAFLD: Diagnosis of Exclusion

- Non-alcoholic fatty liver disease (NAFLD) was a diagnosis of exclusion
  - Identified by raised liver enzymes (ALT)
  - Documentation of steatosis
  - Exclusion of other causes of liver disease
    - Alcohol
    - Viral hepatitis
    - Auto-immune liver diseases
    - Wilson's disease, hemochromatosis
    - Drugs – corticosteroids, methotrexate, anti-psychotics, valproate, amiodarone, tamoxifen

Recommendations for the assessment of metabolic dysfunction-associated fatty liver disease (MAFLD) in primary care: a consensus statement. GESA 2024

MAFLD: Diagnosis of INclusion

FATTY LIVER (hepatic steatosis on imaging / biomarkers / histology)	
+ one of:	Overweight/obesity
	Type 2 diabetes
	Two or more metabolic risk factors*

* Central obesity, HT, raised TG, low level HDL, pre-diabetes

Note – can co-exist with other causes of liver disease e.g. excessive alcohol consumption

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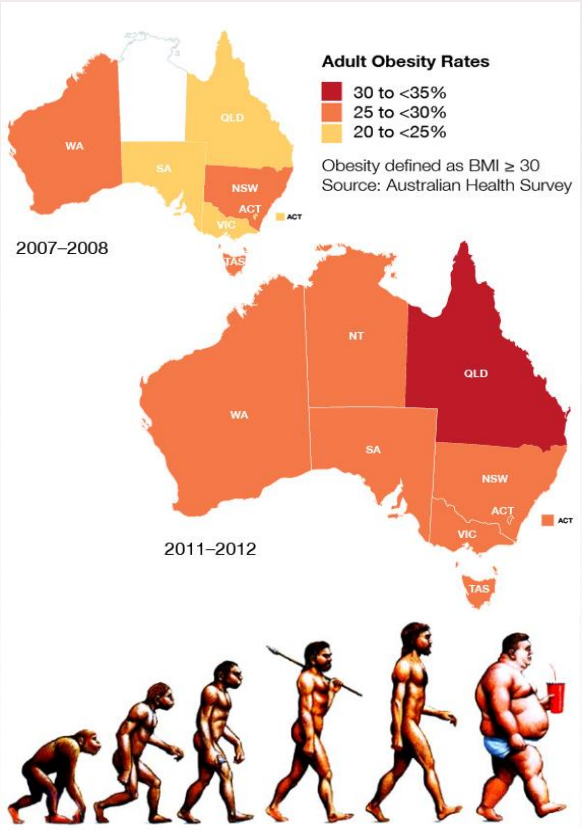
Epidemiology of MAFLD

- Estimated to affect 1 in 3 Australian adults[1,2,3]

- Increasingly common cause of:
  - Cirrhosis
  - Liver cancer (HCC)



1. Mahady SE, et a.. J Gastroenterol Hepatol 2018; 33 Suppl 1: 1-11. 2. Kemp W, et aJ. Gastroenterol Hepatol 2022; 37: 395-403. 3. Farrell AM, et al.Sci Rep 2022; 12: 1956

Epidemiology

Risk factor	Prevalence of MAFLD
Overweight	30%
Obese	55 – 75%
Type 2 DM	55 – 60%
Dyslipidaemia	55%
Hypertension	50%
Metabolic syndrome	70%

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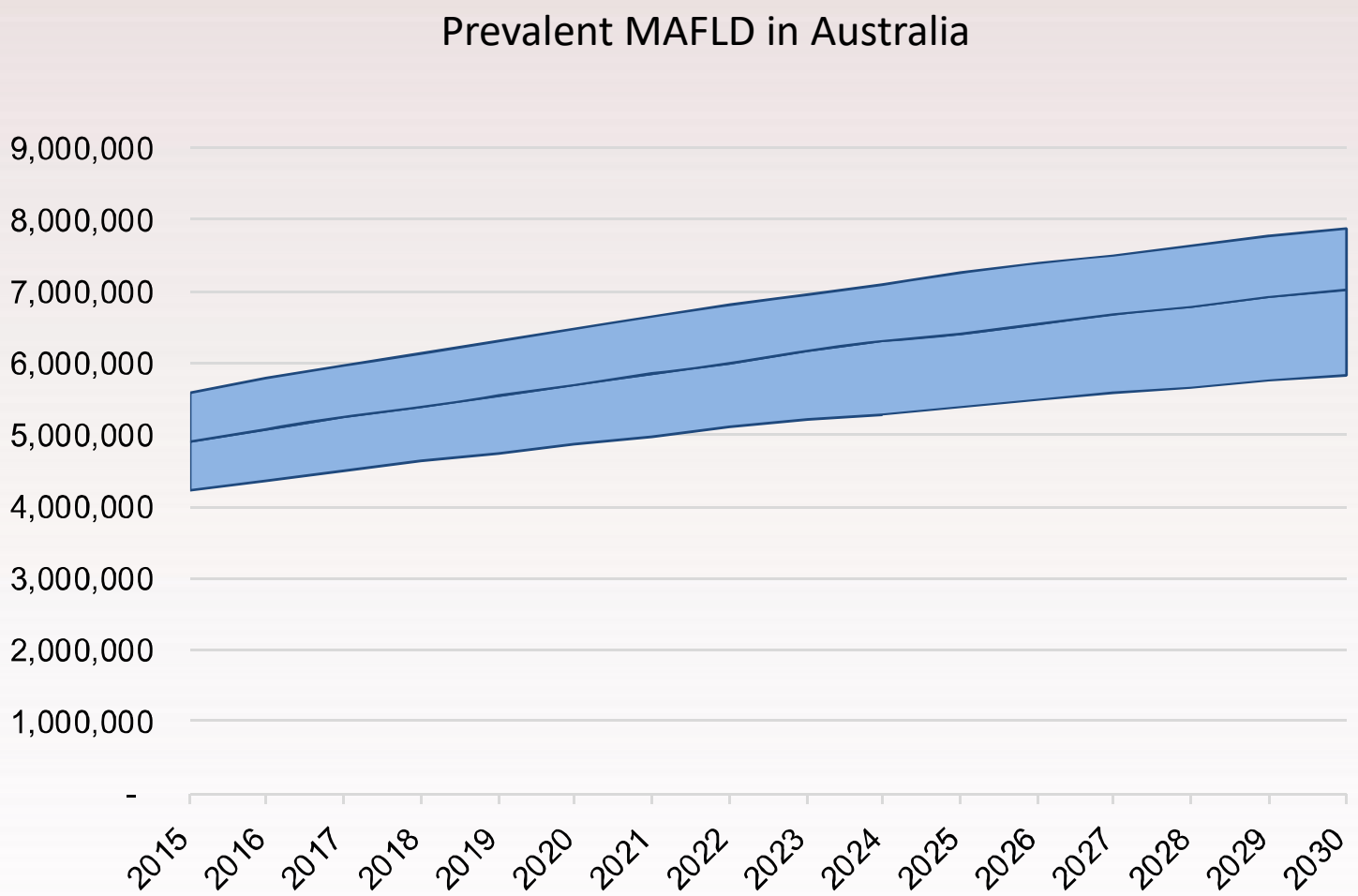
The rising tide of MAFLD

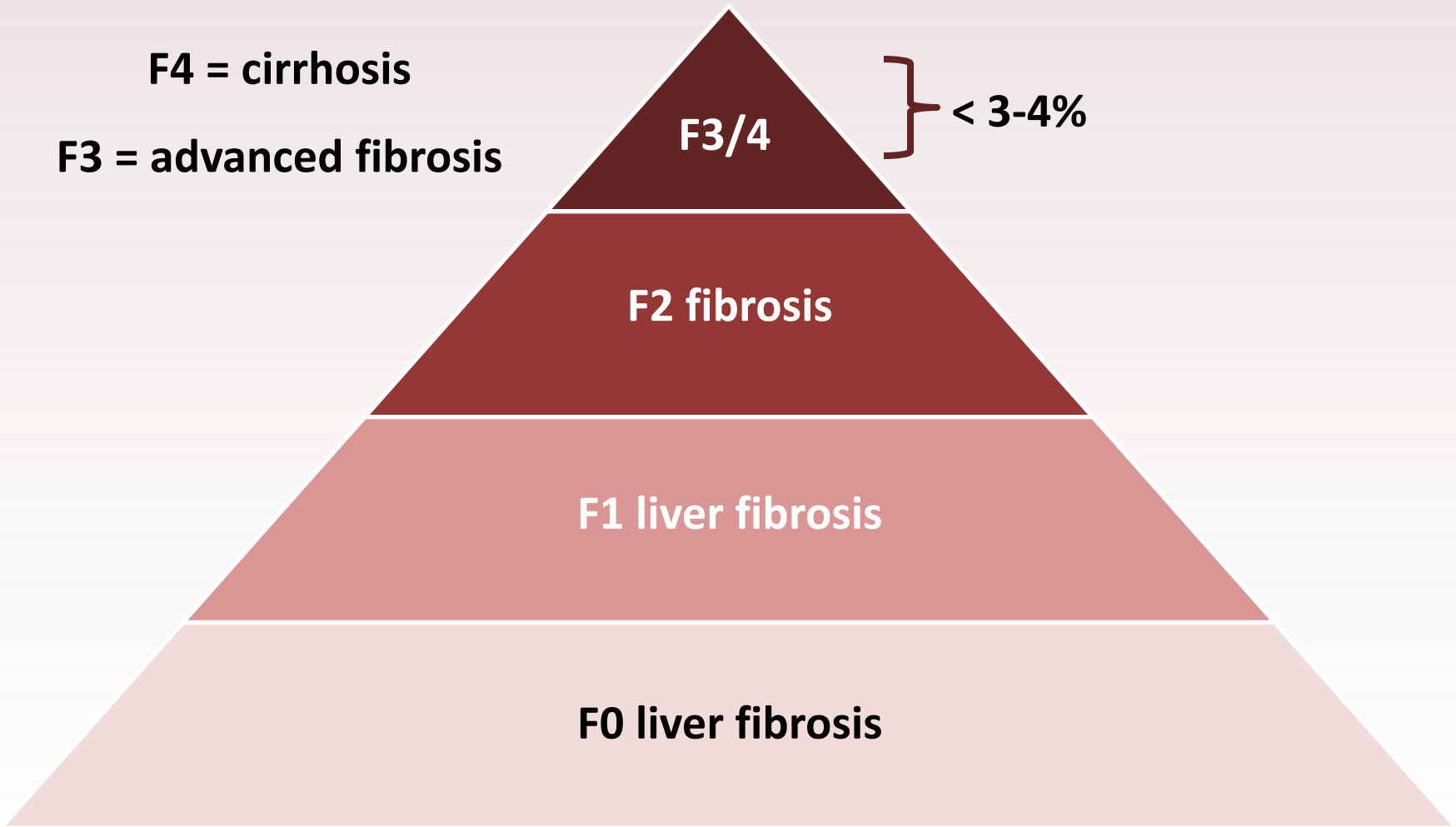


Adams L et al. JGH 2020

Most People w MAFLD do NOT have Advanced Liver Fibrosis or Cirrhosis

F4 = cirrhosis

F3 = advanced fibrosis



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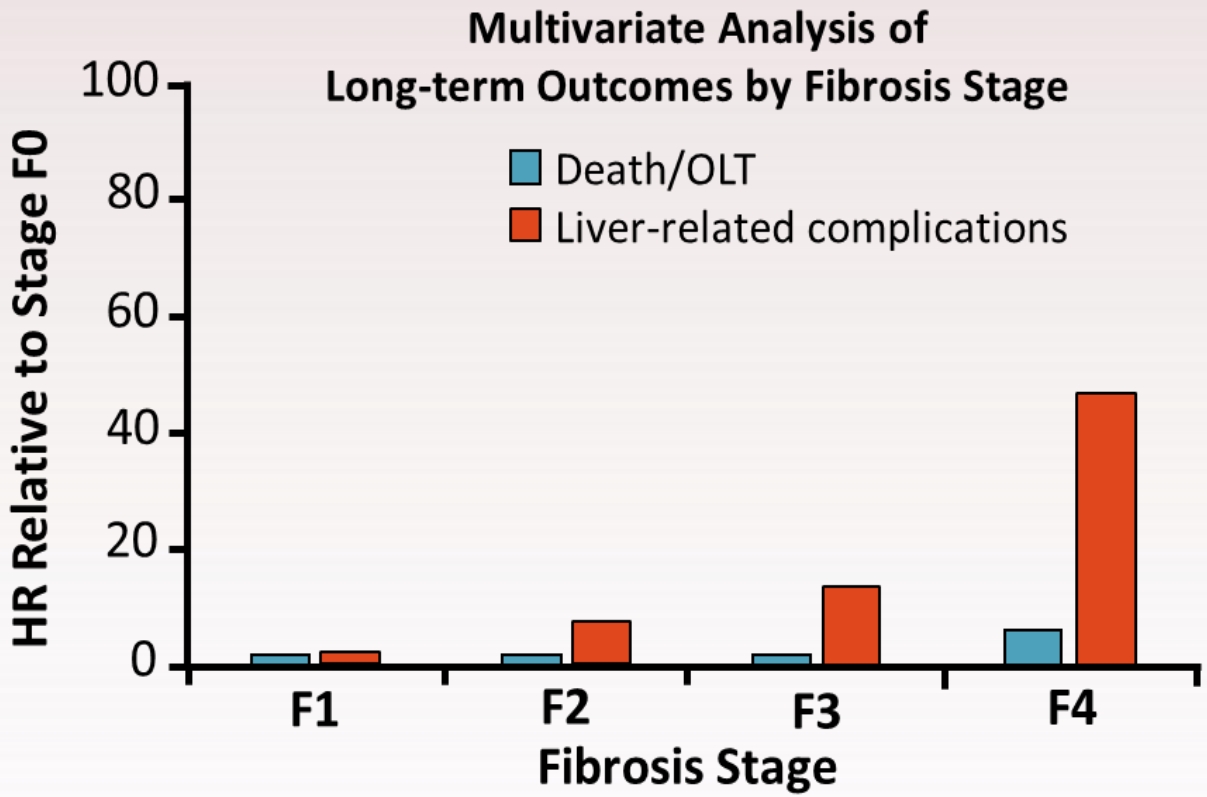
Risk of Liver Morbidity / Mortality Depends on Liver Fibrosis Stage



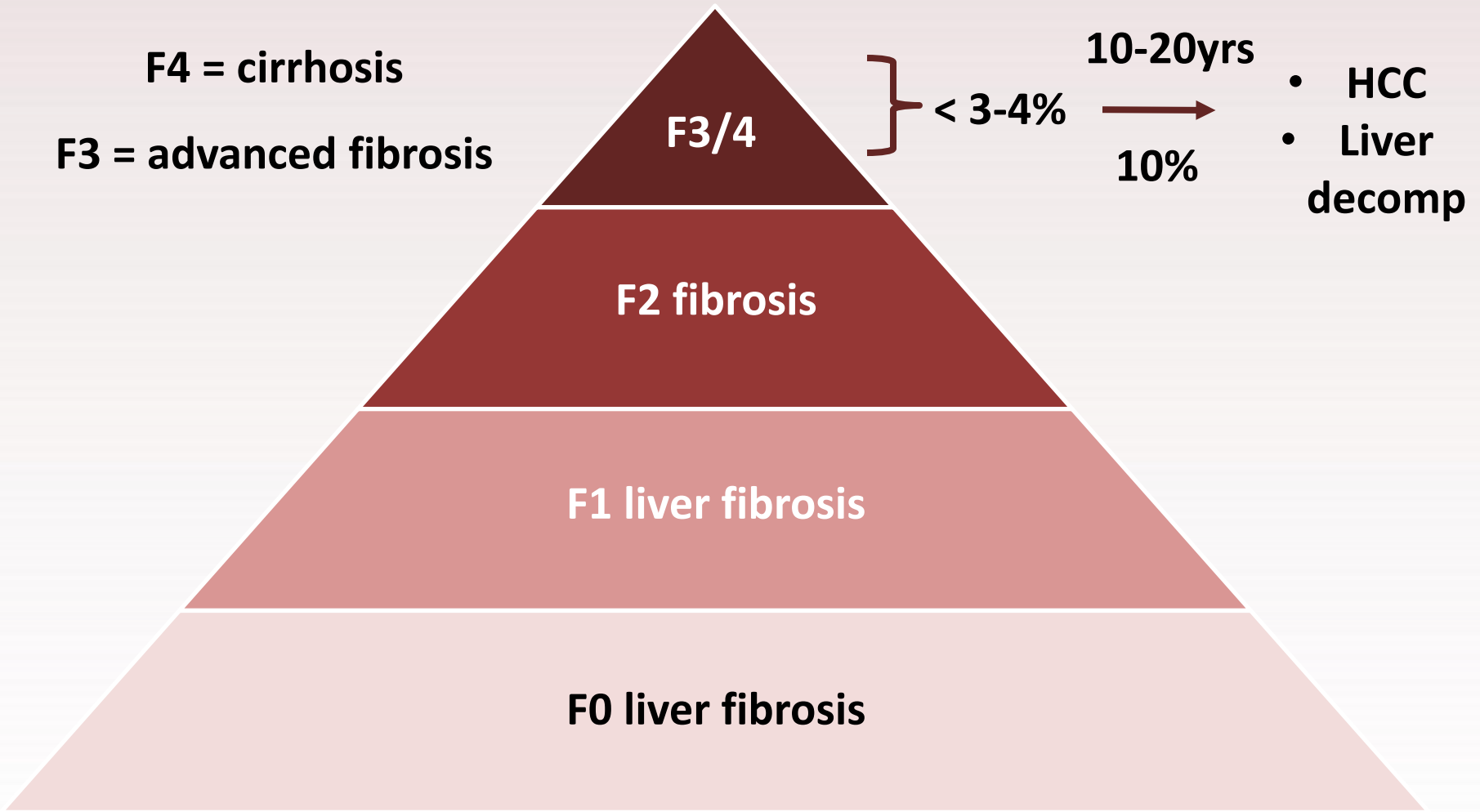
Only fibrosis stage was associated with overall mortality, OLT, and liver-related events.
Presence of MASH, NAS (or any of its components) had no independent prognostic effect.

Angulo. Gastroenterology. 2015;149:389.

Clinical Priority #1: Identifying F3/4 Fibrosis

F4 = cirrhosis

F3 = advanced fibrosis



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Clinical Priority #1: Identifying F3/4 Fibrosis

Need to identify at-risk people BEFORE liver morbidity occurs

Assessment for Advanced Liver Fibrosis using Non-invasive Tests in Primary Care

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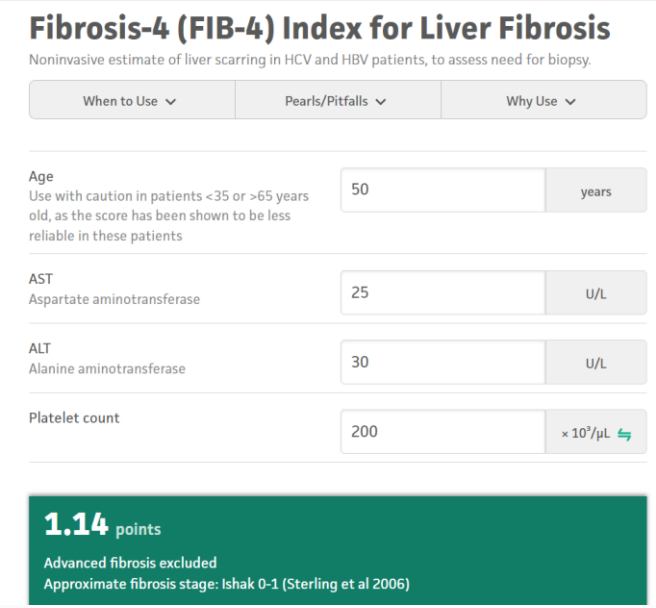
Step 1: Blood biomarker (FIB-4)

- https://www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis



Fibrosis-4 (FIB-4) Index for Liver Fibrosis

Noninvasive estimate of liver scarring in HCV and HBV patients, to assess need for biopsy.

When to Use | Pearls/Pitfalls | Why Use

Age Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients	50	years
AST Aspartate aminotransferase	25	U/L
ALT Alanine aminotransferase	30	U/L
Platelet count	200	× 10^3/μL

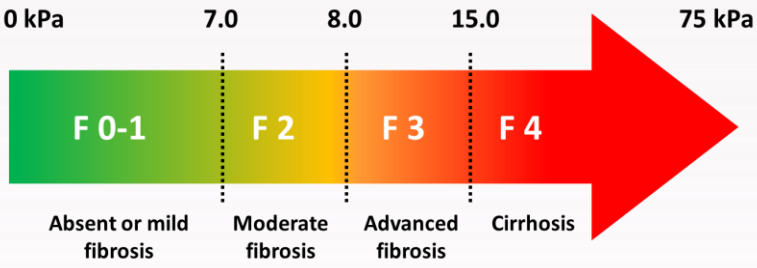
1.14 points

Advanced fibrosis excluded

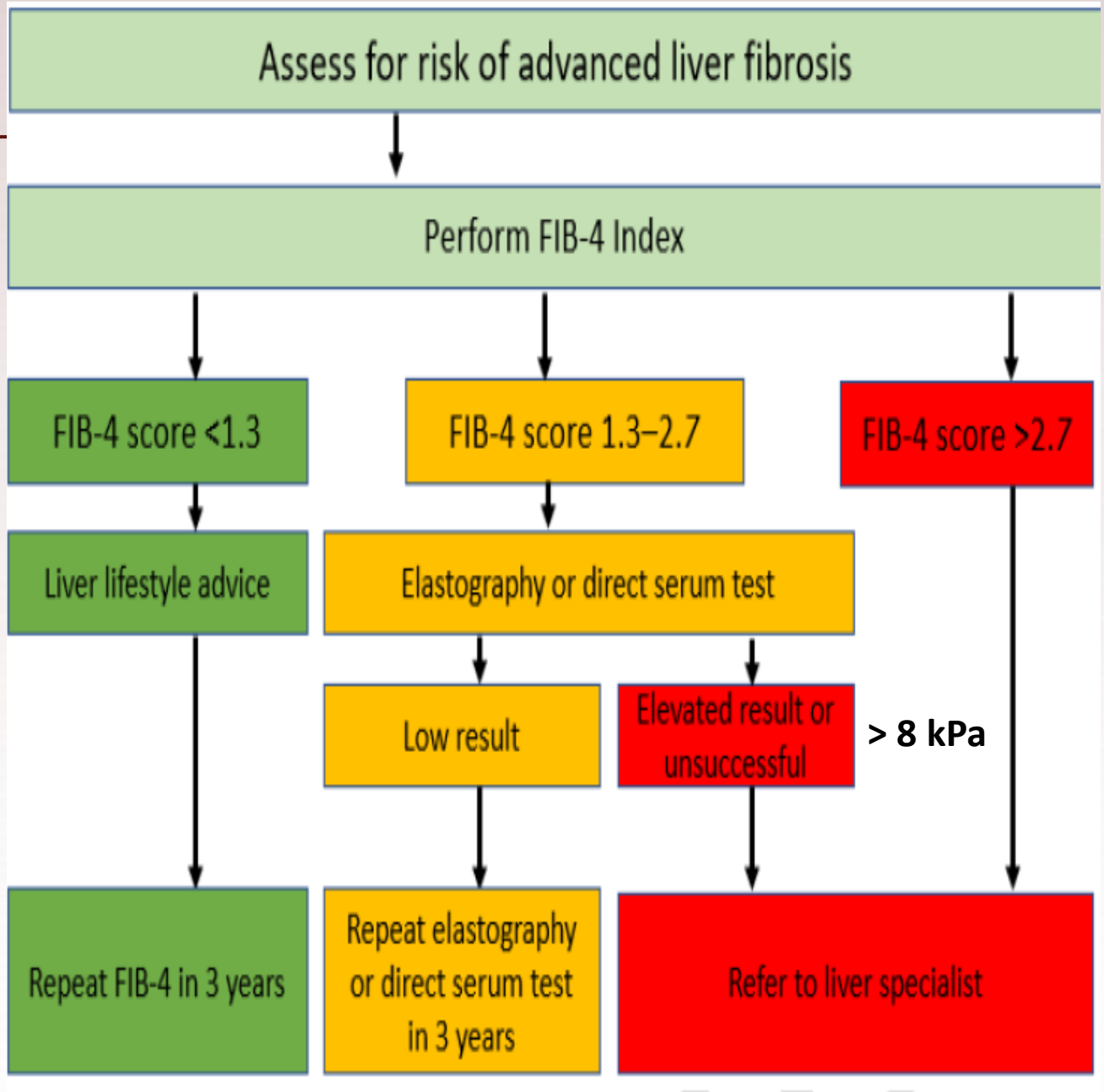
Approximate fibrosis stage: Ishak 0-1 (Sterling et al 2006)

FIB-4 < 1.3:
NPV for advanced fibrosis = 95-97%

± Step 2: Liver stiffness measurement (Elastography, e.g. Fibroscan™)



LSM < 8kPa:
NPV for advanced fibrosis = 98-99%



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Cardiovascular Disease is the Most Common Cause of Mortality in People with MAFLD

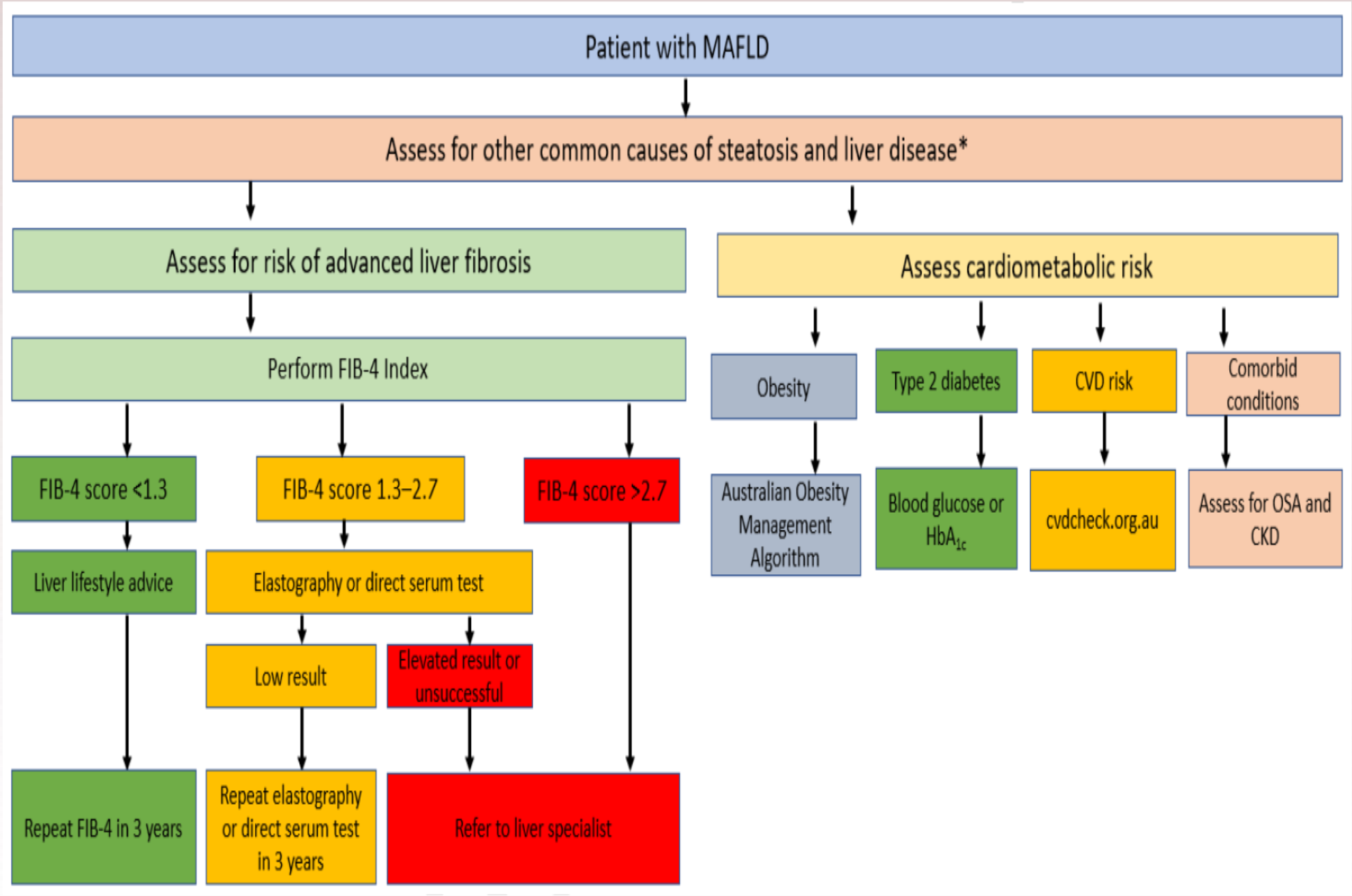
Outcome	Number
Death or OLT	(n = 193)
Cardiovascular disease	74 (38.3%)
Nonliver cancer	36 (18.7%)
Cirrhosis complications	15 (7.8%)
HCC	2 (1%)
Liver transplantation	1 (0.5%)
Infections	15 (7.8)
Other	35 (18.1%)
Spontaneous bacterial peritonitis	3 (11.5%)
Hepatocellular cancer	3 (11.5%)
Hepatopulmonary syndrome	2 (7.7%)
Hepatorenal syndrome	4 (15.4%)

MAFLD may confer increased CVD risk independently of established CV risk factors

Angulo. Gastroenterology. 2015;149:389.

Clinical Priority #2: Assessment for Comorbid Conditions

- **Obesity**
  - Aust Obesity Mx Algorithm
- **Type 2 diabetes**
  - Fasting glucose, HBA_1C
- **Cardiovascular risk factors**
  - Australian C/V risk chart (gender, smoker, DM, BP, lipids)
- **Obstructive Sleep Apnoea**
- **Chronic Kidney Disease**



Recommendations for the assessment of metabolic dysfunction-associated fatty liver disease (MAFLD) in primary care: a consensus statement. GESA 2024

Summary and Conclusion

- MAFLD is common – liver US is the first-line test
- MAFLD is a diagnosis of INclusion

FATTY LIVER (hepatic steatosis on imaging / biomarkers / histology)	
+ one of:	Overweight/obesity
	Type 2 diabetes
	Two or more metabolic risk factors*

* Central obesity, HT, raised TG, low level HDL, pre-diabetes

Summary and Conclusion

- **Advanced fibrosis** is uncommon BUT identifies patients at risk for liver-related morbidity and mortality
  - FIB-4 ± Fibroscan should be used to risk stratify patients
    - FIB-4 < 1.3 = low risk for advanced liver fibrosis
    - LSM < 8 kPa = low risk for advanced liver fibrosis
  - Low risk patients → primary care, reassess every 3 years
  - High risk patients → gastroenterologist / hepatologist

- **Cardiovascular disease** is the most common cause of death
  - MAFLD patients should be screened for cardio-metabolic RFs

Guidance documents

- Recommendations for the assessment of metabolic dysfunction-associated fatty liver disease (MAFLD) in primary care: a consensus statement, 2024