Fatty Liver Disease *for GPs*

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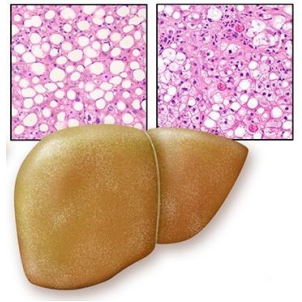
Royal Brisbane and Women's Hospital,

UQ Medical School & QIMR-Berghofer

GP Workshop – 25 March 2023

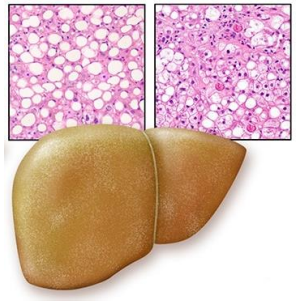
Disclosures

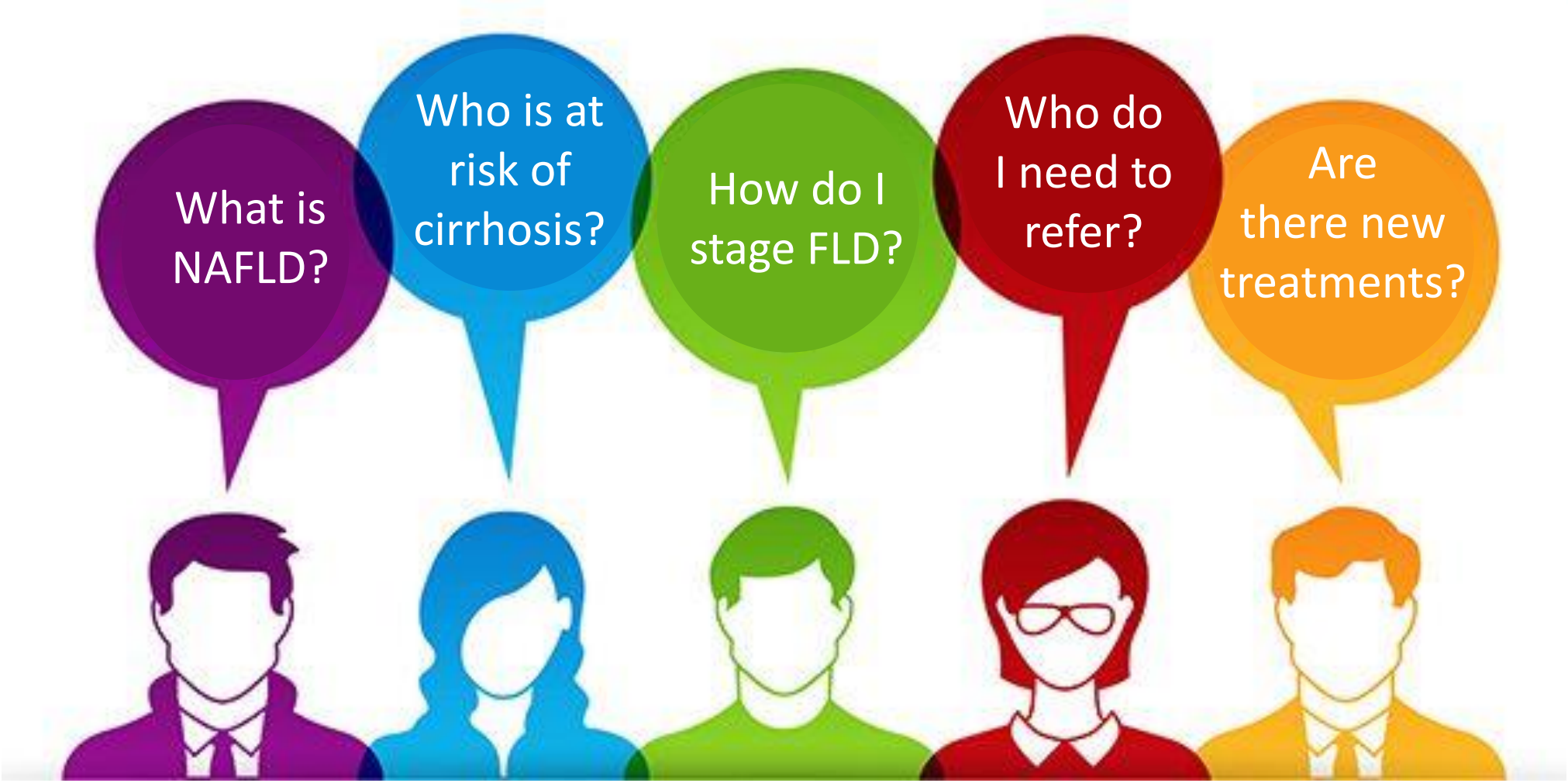


- Speaker's Honoraria, Advisory Board appearances
  - AbbVie, Bayer, BMS, Chiesi Australia, Eisai, MSD
- Principal Investigator for multi-centre NASH Trials
  - Gilead Sciences, Intercept Pharmaceuticals, Inventiva Pharma, Madrigal Pharmaceuticals, Tobira/Allergan
- Travel/conference subsidies and project grants
  - AbbVie, Bayer, BMS, Cromwell Property Trust, Gilead, Roche

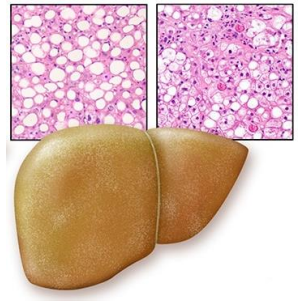
- My talk: Published data only
  Summarises current professional guidelines (AASLD, EASL)
  Reflects my own personal assessment of that literature

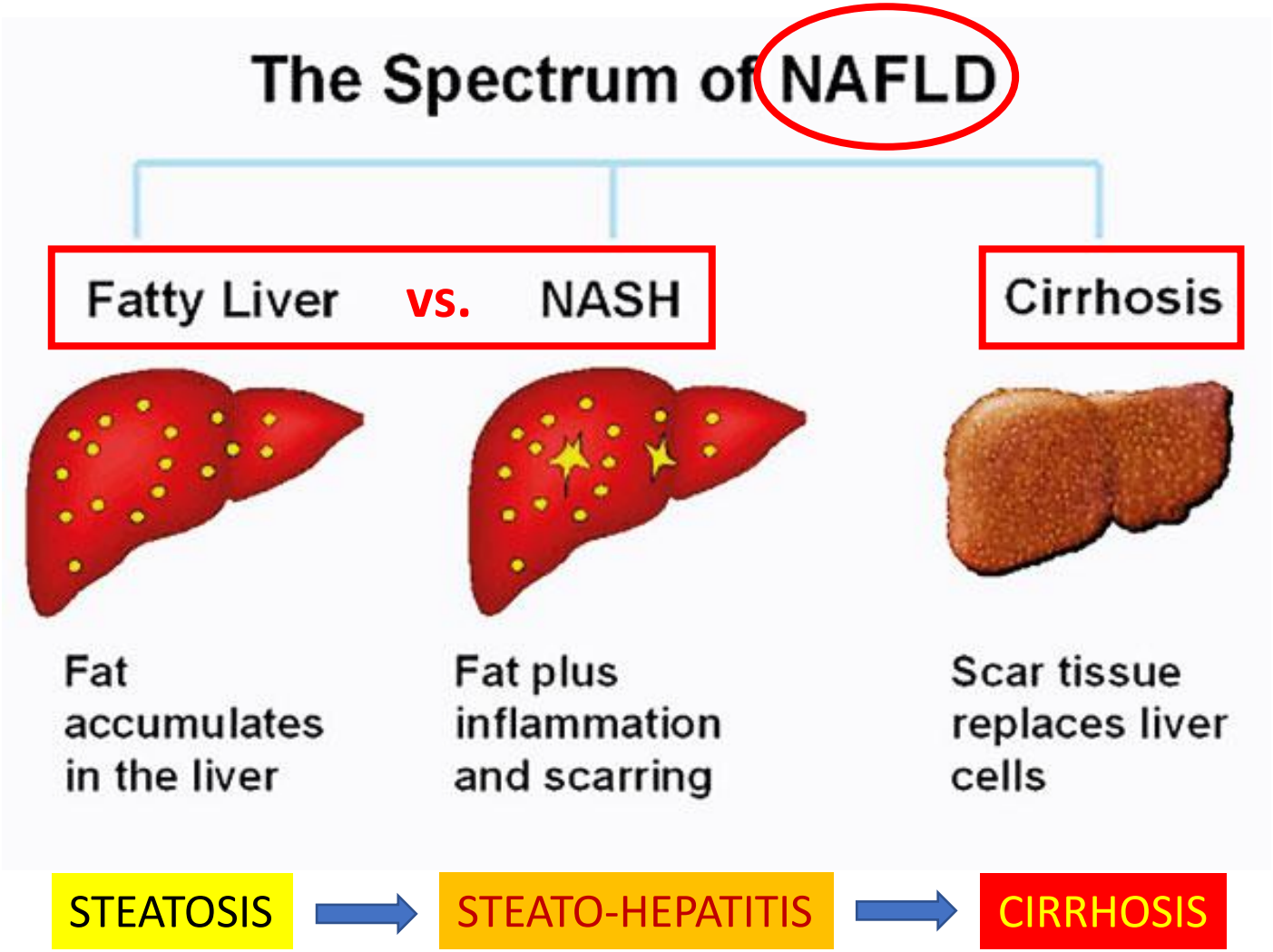
What Do You Need to Know?





What is NAFLD?

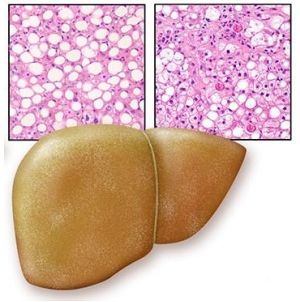




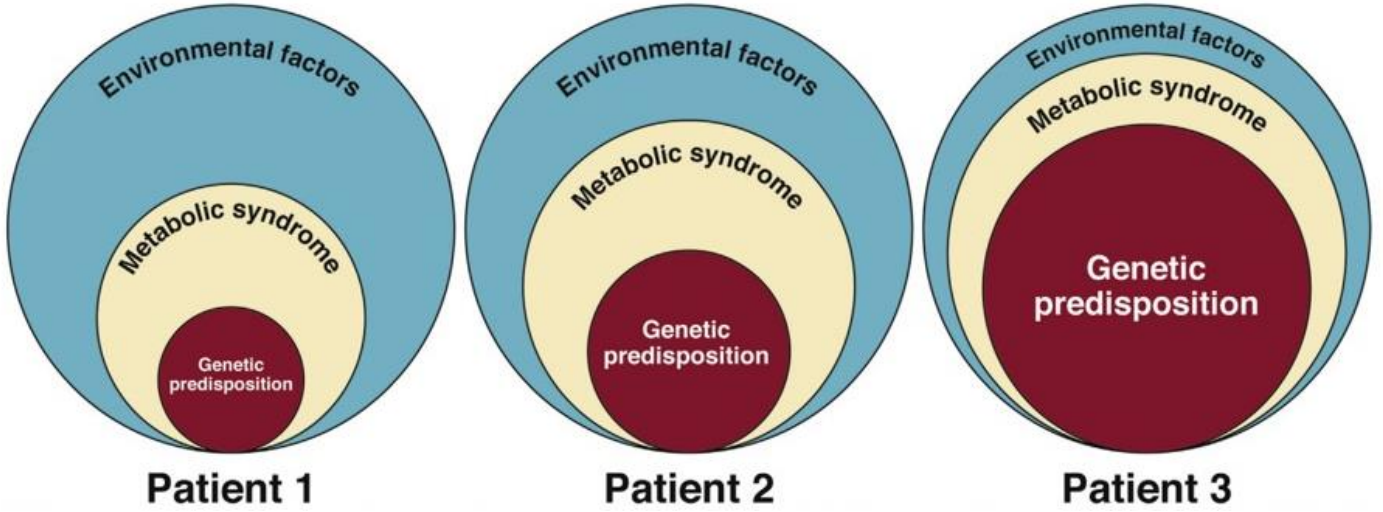
- Steatosis affecting ≥ 5% of hepatocytes
  - USS may not pick up < 30%
- No alternative cause for hepatic steatosis
  - < 20-30g alcohol per day
- Steatohepatitis = inflammation + ballooning
- Progressive fibrosis → nodule formation/cirrhosis

Adapted from www.nash24x7.com

What About “MAFLD”?

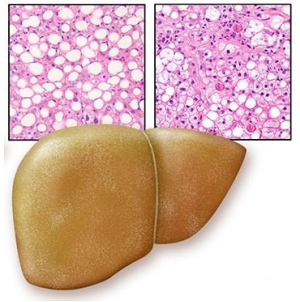


- Consensus amongst experts that the name should change:
  - Not a diagnosis of exclusion
  - Importance of metabolic dysfunction
  - Name should encompass heterogeneity of NAFLD
- Proposed “Metabolic-Associated Fatty Liver Disease” (MAFLD)
- Recognised that MAFLD <u>may co-exist</u> with other CLDs
  - Progressive disease may be due to both MAFLD and ARLD



Eslam et al. Gastroenterology 2020;158:1999–2014

Who is at Risk of NAFLD and NASH?



- Seen in association with obesity, T2 DM, hypertension, dyslipidaemia

- Prevalence (25-30%) increasing with obesity/metabolic disease

  Younossi et al. Hepatology 2016;64:73–84

  - Higher prevalence of NASH with DM (and duration of DM) + vice versa

    Mantovani et al. Diabetes Care 2018;41:372–82

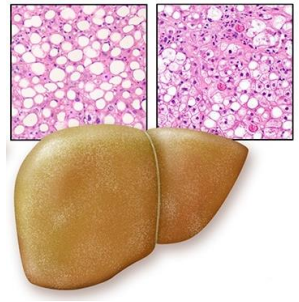
  - Presence of NAFLD/NASH = higher incidence of HT and dyslipidaemia
  - Statins are safe in NASH, use with caution in decompensated cirrhosis

    Abdallah et al. Ann Hepatol 2022;27:100738

- Prevalence of stage 2 (of 4) fibrosis had doubled from 2011 to 2021
  - NASH cirrhosis complications (HCC, death) to increase 2-3 fold by 2030

    Estes et al. Hepatology 2018;67:123– 33

How Quickly Does NAFLD/NASH Progress?



- Fatty Liver: progresses 1 stage of fibrosis per 14 yrs follow-up
- NASH: progresses 1 stage of fibrosis per 7 yrs follow-up

Singh et al. Clin Gastroenterol Hepatol 2015;13:643–54

- "Significant fibrosis" (F2 – F4) = "at risk" population
- "Advanced fibrosis" (F3 – F4) have approx. 3x all-cause mortality risk

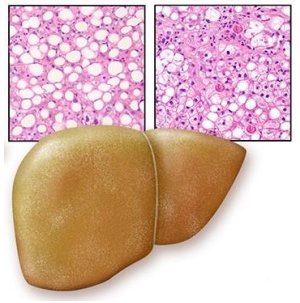
Sanyal et al. N Engl J Med 2021;385:1559–69

- Steatohepatitis is the major prerequisite of disease progression

  BUT fibrosis is the major determinant of poor outcomes

Hagstrom et al. J Hepatol 2017;67:1265–73

What is the Pathogenesis of NASH?

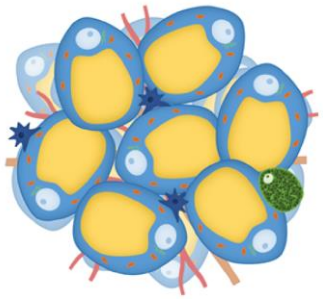


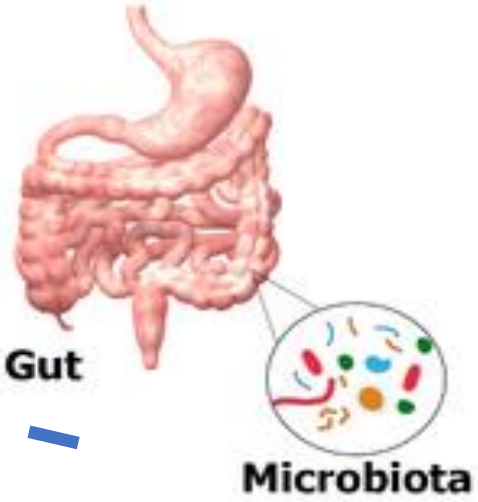
Hepatic Steatosis
+
Insulin Resistance
& "Lipotoxicity"

Lobular
Inflammation
+
Hepatocyte
Injury

Portal
Inflammation
+ Immune
Responses

Adipose Tissue
Dysfunction

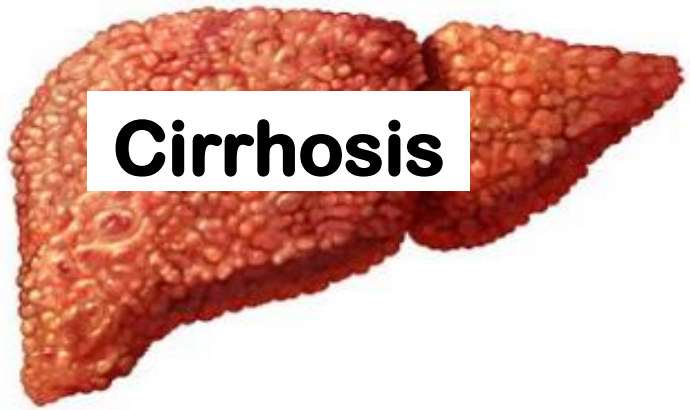




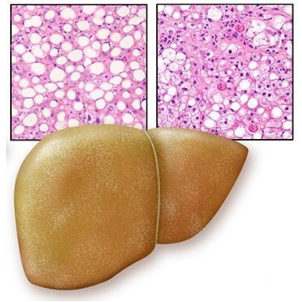
Stellate Cells

FIBROSIS

Cirrhosis



Question #1



- If I could reduce or limit one feature of NASH, it would be?
  - A. Hepatic steatosis
  - B. Lobular inflammation
  - C. Insulin resistance
  - D. Hepatic stellate cell activation
  - E. Obesity

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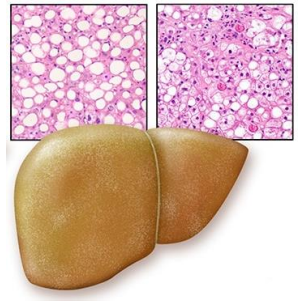

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  - A. Hepatic steatosis
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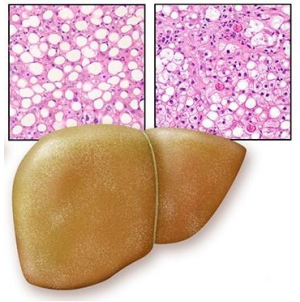
  - C. Insulin resistance
  - **D. Hepatic stellate cell activation**
  - E. Obesity

What Conditions are Associated with NAFLD?



- Obstructive Sleep Apnoea (OSA)
  - Studies suggest OSA is a risk factor for more advanced NASH histology
  - NAFLD patients who are obese should be screened for OSA

Rinella et al. AASLD Practice Guidelines in NAFLD. Hepatology 2023;DOI:10.1097

- Cardiovascular Disease (CVD)
  - Optimising management of CVD risk factors is critical to reducing CV events

Duell et al. Arterioscler Thromb Vasc Biol 2022;42:e168–85

- Chronic Kidney Disease (CKD)
  - NAFLD associated with 2-fold increase in CKD (met-analysis of 28,000 patients)

Musso et al. PLOS Med 2014;11:e1001680

  - See higher prevalence of CKD in NASH with advanced fibrosis

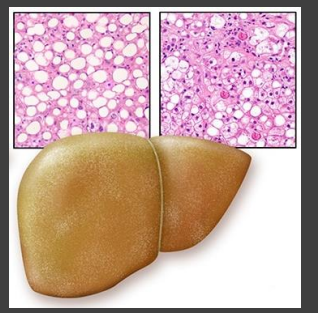
- For most of these conditions, extent to which NAFLD is *causative* is unclear

How do I Evaluate a Patient with NAFLD?

How Do I Evaluate a Patient with NAFLD?

- Screen for metabolic comorbidities
- Assess alcohol intake
- Physical exam (signs of CLD, portal HT)
- Exclude other CLD causes (CLD screen)
- *Consider secondary causes of steatohepatitis*

What Other Causes of FLD Should I Consider?



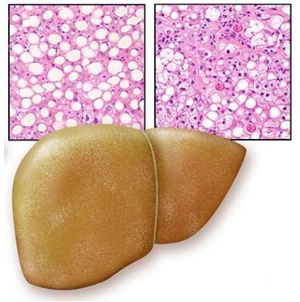
Consider drugs that can cause steatosis or exacerbate NAFLD:

- Amiodarone
- Methotrexate
- Corticosteroids
- 5-FU, irinotecan
- Tamoxifen
- Valproic acid

Consider rare causes of FLD:

- Hypobetalipoproteinaemia
- LAL deficiency
- Nutrient deficiency
  - e.g. carnitine, choline
- Wilson’s disease
- Coeliac disease
- Environmental toxins

What is Lean Fatty Liver Disease?



- NAFLD where BMI < 25 (< 23 in Asian population)
- Prevalence varies according to geography (up to 19% in Asia)

Ye et al. Lancet Gastroenterol Hepatol 2020;5:739–52

  - More likely to be of Hispanic or Asian ethnicity → impact of Western diet?

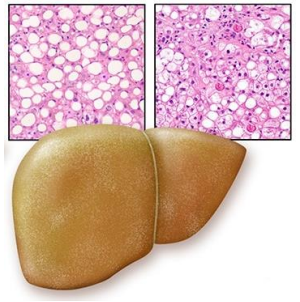
- Lean NAFLD: More IR, metabolic comorbidities, visceral adiposity
- Lean NAFLD: 40-50% have NASH, 30% have significant fibrosis (F2+)

Ye et al. Lancet Gastroenterol Hepatol 2020;5:739–52

- Lean NAFLD: Similar prevalence of CVD as obese population with NAFLD
  - Slightly higher risk of CV mortality (OR 1.50) vs. non-lean NAFLD

Bisaccia et al. Curr Probl Cardiol 2023;48(6):101643

Should I Screen Patients for NAFLD/NASH?



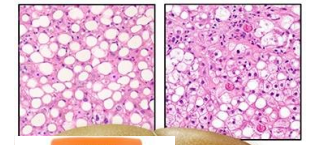
- Patients are largely asymptomatic or have vague symptoms (e.g. fatigue)

- Targeted screening is recommended:
  - Type 2 DM
  - Obesity with metabolic comorbidities
  - Family history of NASH cirrhosis (12-fold higher risk of advanced fibrosis)

Caussy et al. J Clin Invest 2017;127:2697–704

- Identifying candidates for intervention: NASH with F2+ fibrosis:
  - Referral to Hepatology services for further stratification (biopsy?)
  - More aggressive management, enrolment in clinical trials?
  - Diagnosis of cirrhosis → surveillance for HCC and cirrhosis complications

What Does Eating & Drinking in NAFLD Look Like?



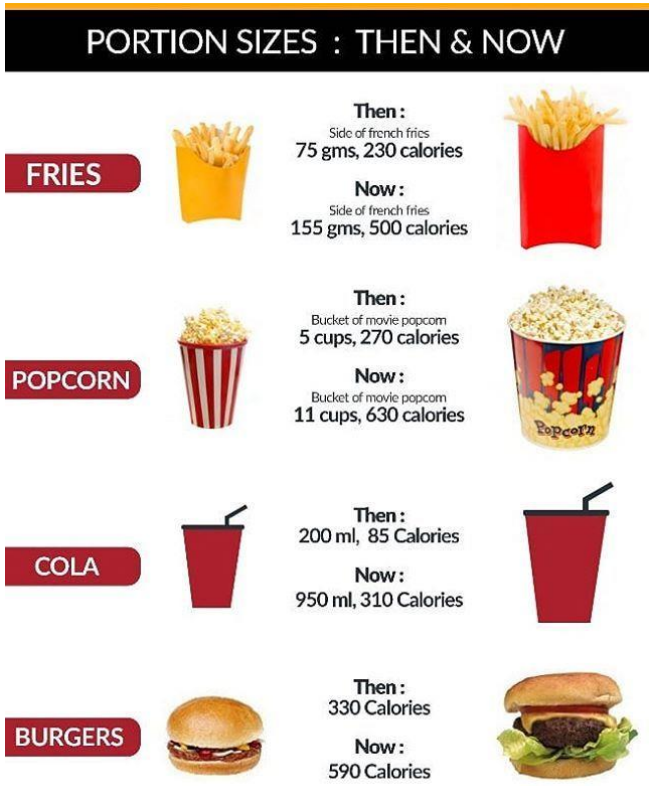
- Studies of diet and MAFLD:
  - Over-feeding is a consistent issue
  - Soft drinks: 1 can/day increases risk of NAFLD by 50%

    Abdelmalek et al. Hepatology 2010;51(6):1961-71
  - Lower satiety with soft drinks vs. solid form fructose
    - Reduced fibre intake in MAFLD (fibre increases satiety)
  - Artificially-sweetened beverages are still a problem
    - Can induce obesity, increase risk of DM

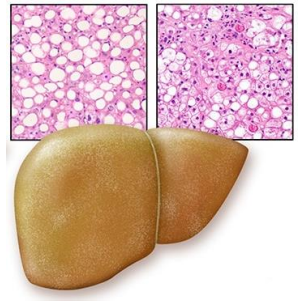
      Muraki et al. BMJ 2013 Aug 28;347:f5001
    - Increased mortality (esp. CV) with sweetened drinks

      Anderson et al. BMC Med 2020;18(1):97
- Fructose promotes SIBO
  - High prevalence in NASH (up to 40%)
  - Activation of inflammatory CKs
  - Role of intestinal dysbiosis in NAFLD remains unclear

    Gudan et al. Nutrients 2022 Dec 9;14(24):5261

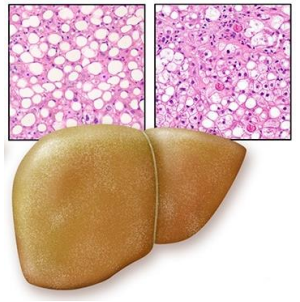


Question #2



- Martha is a 48 year old woman who is new to your practice
- She has a history of:
  - Mild obesity (BMI 32)
  - GORD (on daily PPI)
  - Hypertension
  - DVT (2020 – 6 months of rivaroxaban)
- Her fasting bloods are as follows:
  - Cr 85, eGFR (87), Glucose 5.2, ALT 115, AST 62
  - Hb 140, WCC 6.2, Plts 275
  - Chol 5.2, HDL 1.1, TG 2.3
- Her ultrasound shows evidence of “severe steatosis”
- She does not drink alcohol

Question #2



- Which of the following approaches is best in Martha's case?

A. Referral to RBWH Hepatology for specialist opinion regarding fatty liver

B. Commence a statin and re-test fasting lipids in 4 weeks

C. Lifestyle advice (dietary changes, exercise) to achieve weight loss

D. Referral for liver biopsy

E. Referral for non-invasive fibrosis assessment (eg. ARFI, Shearwave, FibroScan)

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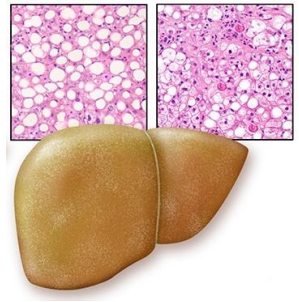

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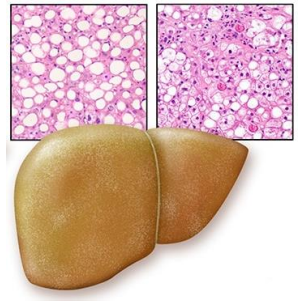
How do I Risk Stratify NASH as a GP?

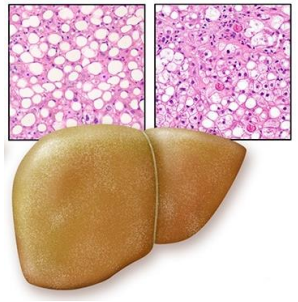


- Primary Objective is to identify patients who are low risk
- Use of FIB-4 Score < 1.3: Excludes advanced fibrosis with high NPV
- If moderate or high risk (FIB-4 ≥ 1.3):
  - Access to non-invasive liver stiffness measurement?
  - Referral for blood tests that stratify risk of fibrosis (e.g. ELF test)
- If still consistent with intermediate or high risk of fibrosis:
  - Referral to Hepatology services for specialty evaluation

If High FIB-4 (>2.67) then can refer immediately as high risk of cirrhosis

- Basic blood tests can give an indication of advanced fibrosis
  - AST ≥ ALT is a red flag for advanced fibrosis/cirrhosis
  - Low platelets (< 180) is another red flag (esp. if falling over time)
- FIB-4 Score uses these parameters + age $(Age \times AST) \div (Plts \times \sqrt{ALT})$
  - Remember that normal transaminases do not exclude advanced fibrosis

Staging Algorithm for GPs



FIB-4 ≥ 1.3 ?

No

Reassess periodically:

- FIB-4 every 1-2 years if T2 DM/IR or ≥ 2 metab risk factors
- FIB-4 every 2-3 years if no DM/IR and < 2 metab risk factors

Yes

FIB-4 > 2.67 ?
Consider referral

Secondary risk assessment:

Risk level	VCTE	ELF
Low	<8.0	<7.7
Intermed.	8-12	7.7-9.8
High	>12	>9.8

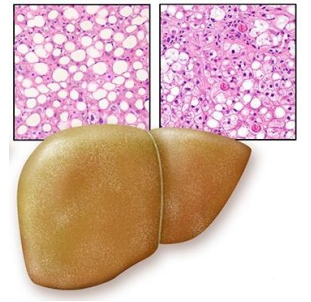
Specialist Hepatology Referral

All patients:

- CV risk factor reduction
- Preferential use of meds with potential NAFLD benefit
- Lifestyle modification: weight reduction, diet, exercise

Adapted from Rinella et al. AASLD Practice Guidelines in NAFLD. Hepatology 2023;DOI:10.1097

When Should a Patient with NAFLD be Biopsied?

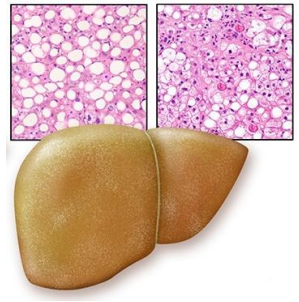


- Biopsy is the Gold Standard diagnostic test
  - Quality parameters: specimen length ≥ 15mm (preferably 20mm+)
    specimen contains ≥ 11 complete portal tracts
    specimen is not fragmented (continuous portal tracts)
  - Recommend 16GA cutting needle obtaining core biopsy specimen

- Generally indicated where there is diagnostic uncertainty:
  - Discordant non-invasive test results (ie. conflicting F-stages or unexpected imaging)
  - Accurate staging required for other treatment (e.g. chemotherapy, surgery, etc)
  - Aetiology of CLD (or the primary cause) remains unclear
  - Persistent unexplained elevation of LFTs (usually > 6 months)

- Hazards of liver biopsy: Severe pain (1 in 4)
  Significant bleeding (1 in 500-1,000)

How is NAFLD Graded and Staged?



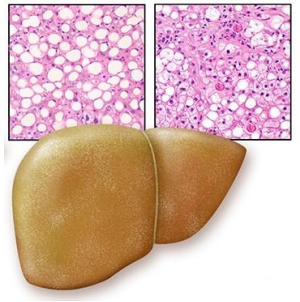
- Typically graded according to parameters of steatohepatitis:
  - Steatosis (< 5% → 5-33% → 34-66% → > 66%)
  - Inflammation (none → 1 focus per HPF → 2-4 foci per HPF → > 4 foci per HPF)
  - Ballooning (none → few → many)

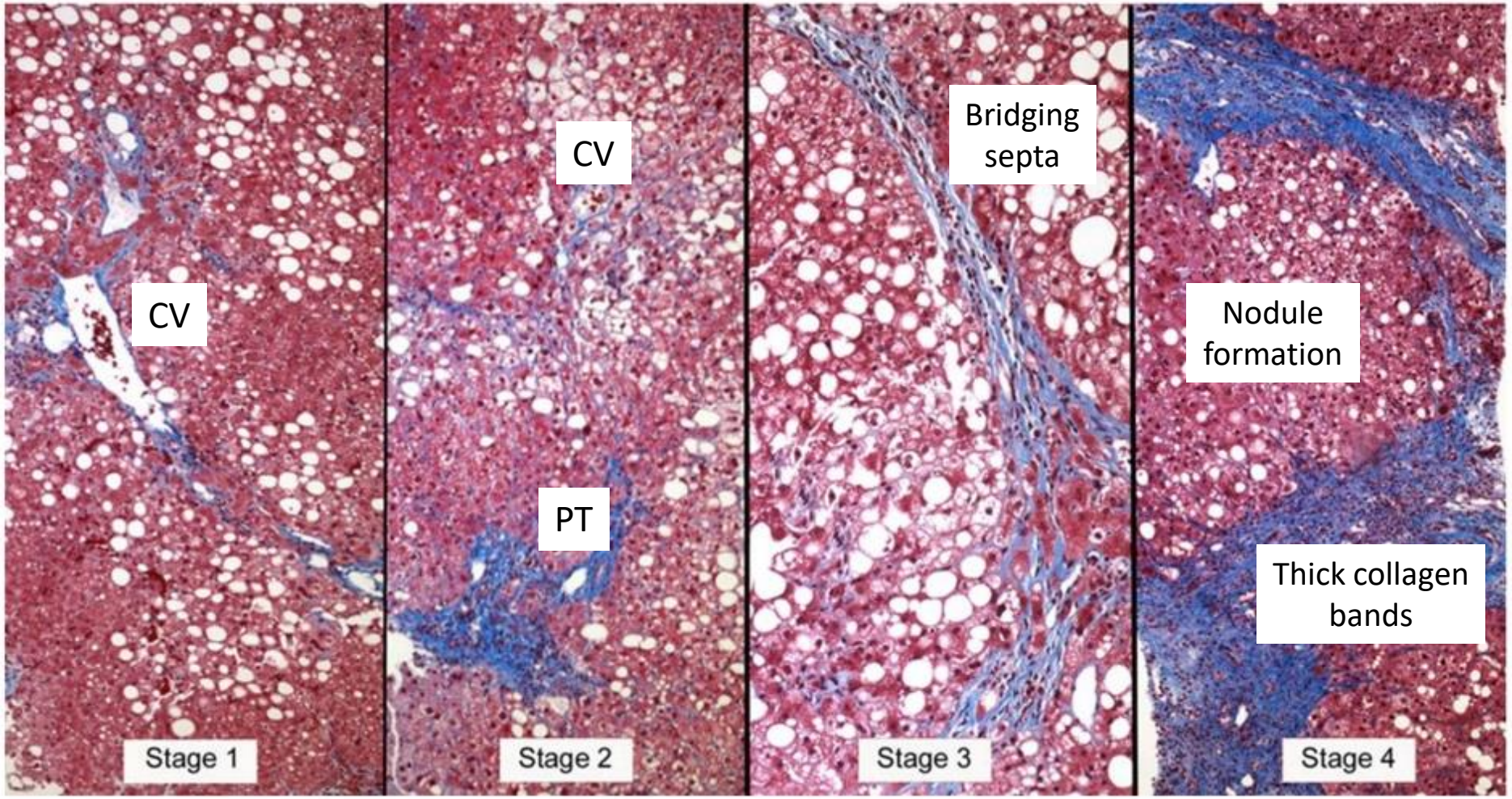
Kleiner et al. Hepatology 2005;41:1313–21

- NAFLD Activity Score (NAS): used in clinical trials and research
  - 0-3 = not NASH 4 = borderline NASH 5-8 = definite NASH
  - Common endpoints include: ≥ 2 point improvement in NAS
    ≥ 1 stage improvement in F-stage w/o NAS increase

- Fibrosis stage is the key clinical parameter
  - Major determinant of liver-related outcomes (eg. cirrhosis, HCC, mortality)

NASH CRN (Brunt) Stages of Fibrosis





Younossi et al. Hepatology 2018;68:349-360

How Do I Treat NAFLD?

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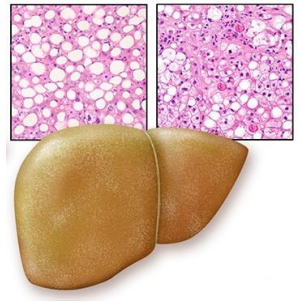
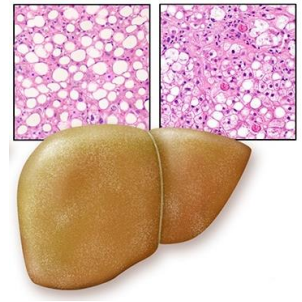


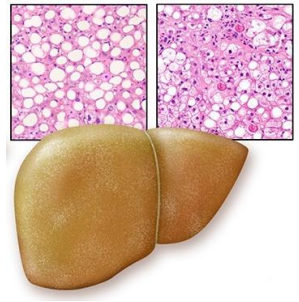
- Lifestyle modification
  - Weight loss
  - Dietary modification
  - Exercise
- Bariatric surgery
- Currently available medications
- Emerging medications
- Venesection

Question #3



- There is reliable evidence that all of the following treatments can improve NASH histology except:
  - A. GLP-1-receptor agonists (e.g. semaglutide, liraglutide)
  - B. Weight loss (diet and exercise)
  - C. Vitamin E
  - D. Venesection
  - E. Bariatric surgery

Question #3



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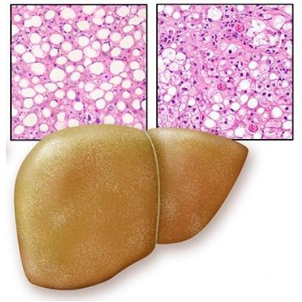
  - B. Weight loss (diet and exercise)
  - C. Vitamin E
  - **D. Venesection**
  - E. Bariatric surgery

How do I Assess Response to Treatment?



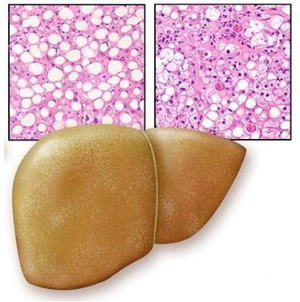
- Histological response:
  - Repeat liver biopsy = gold standard, not practical in real world
- Surrogate markers of histological response: thresholds to be validated
  - Improved ALT correlates with clinical outcomes

    Loomba et al. Gastroenterology 2019;156:88–95
  - FIB-4, ELF, liver stiffness: correlate with improvements in fibrosis

    Rinella et al. J Hepatol 2022;76:536–48
  - Imaging: ≥ 30% reduction in MRI-PDFF associated with resolution of NASH

    Tamaki et al. Gut 2022;71:983-90
  - Other markers of disease: improved insulin resistance (IR), obesity, dyslipidaemia
- Liver-related outcomes: cirrhosis, PHT, ascites, varices, HCC
  - Clinically defined endpoints where patient's prognosis changes

Question #4



- Regarding my personal approach to lifestyle modification for NAFLD:
  - A. I think it is a useful intervention for all forms of fatty liver disease
  - B. I think it may help treat steatosis but will not reverse NASH
  - C. I think it may help steatohepatitis but will not reverse fibrosis
  - D. It is effective but has no role in patients with a normal BMI
  - E. I never recommend it as weight loss is rarely sustained

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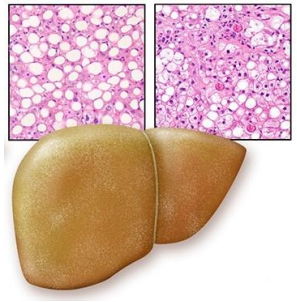

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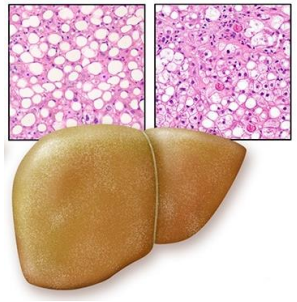

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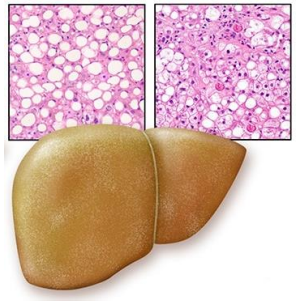
How Effective is Weight Loss in NAFLD?



- Amount of weight loss correlates with response:
  - 5% = improvement in steatosis
  - 7% = improvement in steatohepatitis
  - 10% = improvement in fibrosis

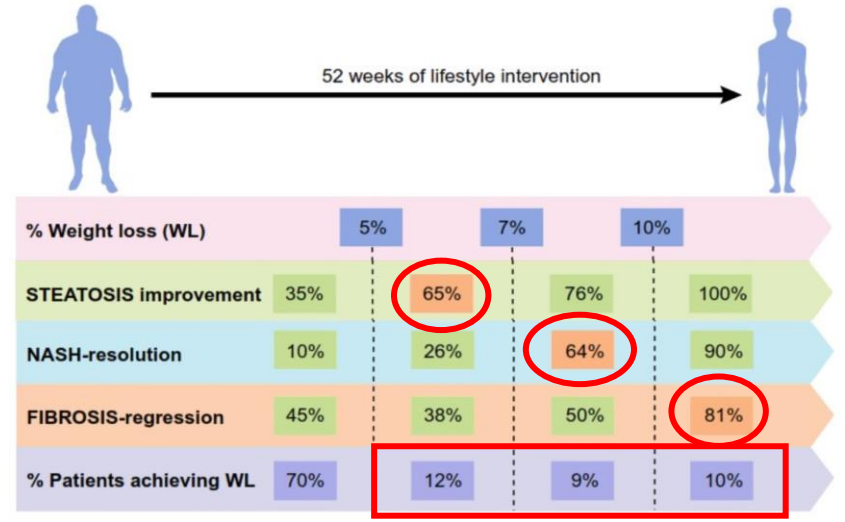
Long et al. Gastroenterology 2022;163:764-74

- Sustained weight loss <u>is</u> difficult
  - ≤ 10% achieve significant weight loss at 1 year
  - < 25% <u>of these</u> maintain weight loss at 5 years

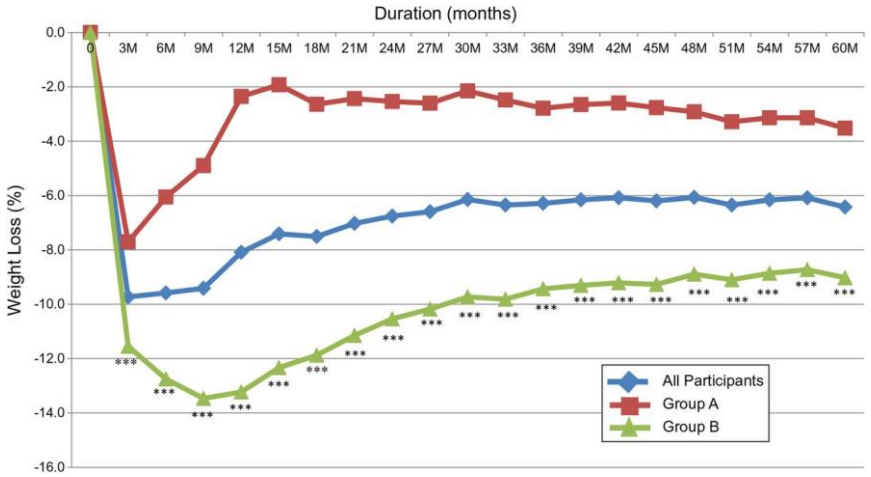
Malespin et al. Clin Gastroenterol Hepatol 2022;20:2393-5

- Optimal model of care still to be defined
  - Reduced calories → Reduced metabolic rate
  - Psychological barriers to engagement
  - MDT approach probably best (incl. psychology)

Stewart et al. Liver Int 2015;35:936-43

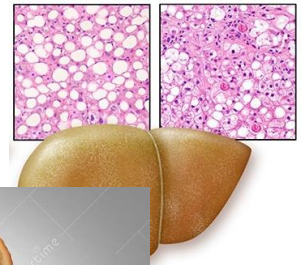


Adapted from www.foodasprevention.com/liverpatient



Hamdy et al. BMJ Open Diabetes Res Care. 2017;5(1):e000259.

What Diet Should I Recommend?



- Obesity = excess calories & saturated fats
  refined carbs

- Many approaches: comparable efficacy
  - Low-carb vs low-fat diets
  - Unsaturated vs Saturated fat diets
  - Intermittent fasting vs Mediterranean diets
  - Different intensities of calorie restriction

Pugliese et al. Eur J Clin Invest 2022;52:e13659

- Mediterranean diet: improves CV health

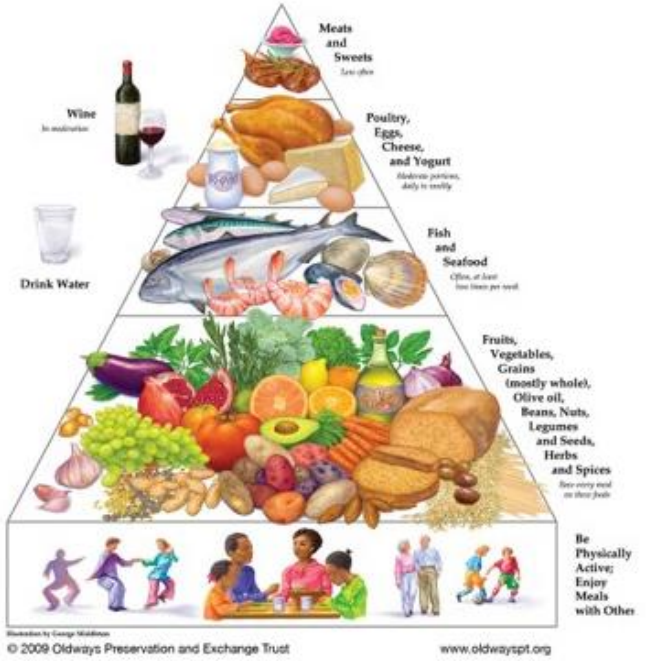
Kouvari et al. Clin Nutr 2021;40:3314-24

- Coffee beneficial?
  - ≥ 3 cups per day, independent of caffeine

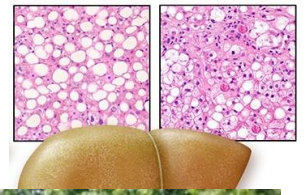
Chen et al. Clin Nutr 2019;38:2552-7

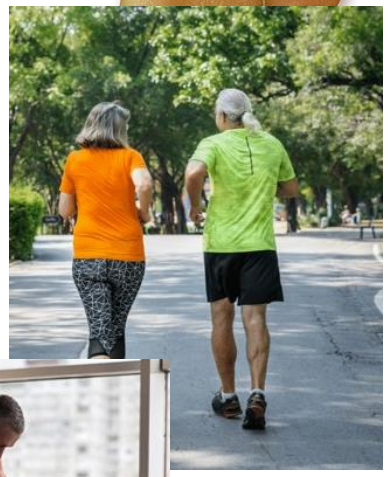
- Cirrhosis: ↑ protein, ↓ calories judiciously

Mediterranean Diet Pyramid



How Important is Exercise to Response?





- Exercise = Liver and CV benefits independent of weight loss

- How much is enough?
  - Regular exercise: ≥ 5 times per week, total of ≥ 150 mins per week
  - Increased exercise: doing ≥ 60 mins more per week than usual
  - Higher intensity: ↑vigorous exercise = ↓ severity of NASH

Semmler et al. Liver Int 2021;41:2249–2268

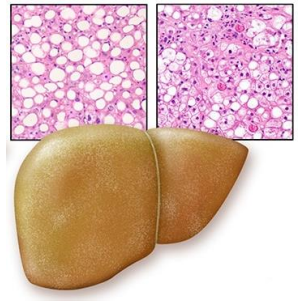
Kistler KD. Am J Gastroenterol 2011;106:460-8

- Encourage patients to exercise <u>as much as possible</u>
  - Type + intensity + duration tailored to individual's ability

- Combining diet + exercise consistently reduces steatosis

Franco et al. Nutrients 2021;13:66

Should I Recommend Bariatric Surgery?



- Usual criteria for bariatric surgery: BMI ≥ 40
  BMI ≥ 35 with comorbidities
  - NASH being increasingly accepted as an important comorbidity
- Can resolve NASH and improve fibrosis in up to 30% of patients
  - See improvements in IR and all-cause morbidity and mortality

Wiggins et al. PLOS Med 2020;17:e1003206

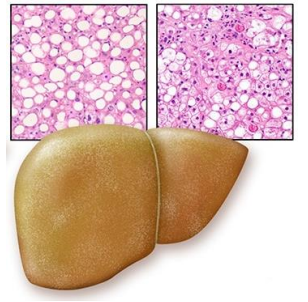
- Long-term follow-up data: maintenance of response at 5 yrs
  - Treatment failure associated with failure to achieve substantial weight loss

Lassailly et al. Gastroenterology 2015;149:379-88

- Malabsorptive procedures generally more effective than restrictive surgery
- Cirrhosis: limited data on safety and efficacy
  - Safe in selected patients: no decompensation or clinically significant PHT

Jirapinyo et al. Clin Gastroenterol Hepatol 2022;20:511-24

What Medical Treatment is Currently Available?



- Vitamin E: 800mg/d improves histology vs. placebo over 2 years (PIVENS)
  - ALT reduction associated with response

Sanyal et al. N Engl J Med 2010;362:1675–85; Hoofnagle et al. APT 2013;38:134–43

  - Retrospective study (n=236): ↓ decompensation and ↑ Tx-free survival

Vilar-Gomez et al. Hepatology 2020;71:495-509

- Pioglitazone: Improves NAS and IR with trend towards improved fibrosis

Cusi et al. Ann Intern Med 2016;165:305–15

  - Concerns re: weight gain, osteoporosis, bladder cancer, worsening CCF

- Metformin: Extensively studied but does not improve NASH histology
- Natural therapies: (e.g. *Silymarin* – milk thistle)
  - Well tolerated but evidence of efficacy in NAFLD remains inconclusive
  - No evidence of improvement of NASH histology, some improvement in non-invasive scores?

Wah et al. Clin Gastroenterol Hepatol 2017;15:1940–9

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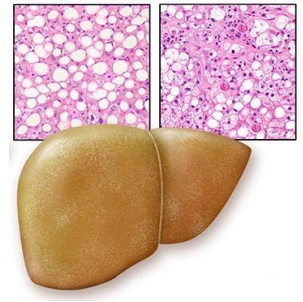


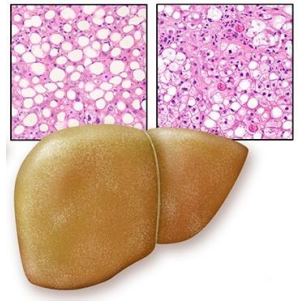
- GLP-1-receptor agonists: Approved for T2 DM and used in obesity
  - Liraglutide: improved steatosis, resolved NASH and reversed fibrosis
  - Semaglutide: dose-dependent reversal of NASH, trend towards improved fibrosis
  - Tirzepatide (GLP-1/GIP): significant reductions in ALT and liver fat, no NASH studies

Muzurovic et al. J Cardiovasc Pharmacol Ther 2022;27:10742484221126371

- SGLT-2 inhibitors: Approved for T2 DM, induce weight loss (2-3% BW)
  - Improve hepatic steatosis but small sample sizes and lack of histological outcomes

- DPP-4 inhibitors: not efficacious in the treatment of NAFLD
- Glycaemic control: no evidence that glycaemic control itself impacts NASH

What Medical Treatments are on the Horizon?



- Obeticholic acid: FXR agonist (↓ *de novo* lipogenesis and bile acid synthesis)
  - REGENERATE Ph3 Study: 931 patients with NASH and F2-3 on biopsy, 2 doses vs placebo
  - 22.4% showed ≥ 1 stage improvement in fibrosis (vs. 9.6% with placebo)
  - Major adverse effects were pruritus and biliary events (incl. gallstone disease)

  REGENERATE Press Release 7 July 2022 (available at https://ir.interceptpharma.com/news-releases)

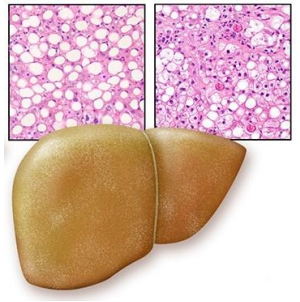
- Resmetirom: thyroid hormone receptor-β agonist (↓ lipotoxicity, ↑ fat metabolism)
  - MAESTRO Ph3 Study: 966 patients with NASH and F2-3 on biopsy, 2 doses vs placebo
  - 24-26% showed ≥ 1 stage improvement in fibrosis (vs. 14% with placebo)
  - 26-30% showed ≥ 2 point improvement in NAS (vs. 10% with placebo)
  - Well tolerated with mildly increased rates of diarrhoea and nausea with Resmetirom

  MAESTRO Press Release 19 Dec 2022 (available at https://ir.madrigalpharma.com/news-releases)

- Lanifibranor: Pan-PPAR agonist (improves insulin sensitivity, reduces fibrosis)
  - NATIVE Ph2b Study: 247 patients with NASH and F1-3 on biopsy, 76% with F2-3 (Ph3 study underway)
  - 49% (vs. 22%) showed ≥ 1 stage improvement in fibrosis without worsening of NASH
  - 55% (vs. 33%) showed improvement in NASH activity without worsening of fibrosis
  - 35% (vs. 9%) showed resolution of NASH and ≥ 1 stage improvement in fibrosis

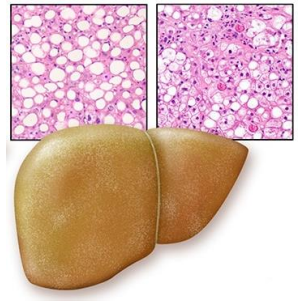
  Francque et al. N Engl J Med 2021; 385:1547-1558

My Take on Emerging Therapies?

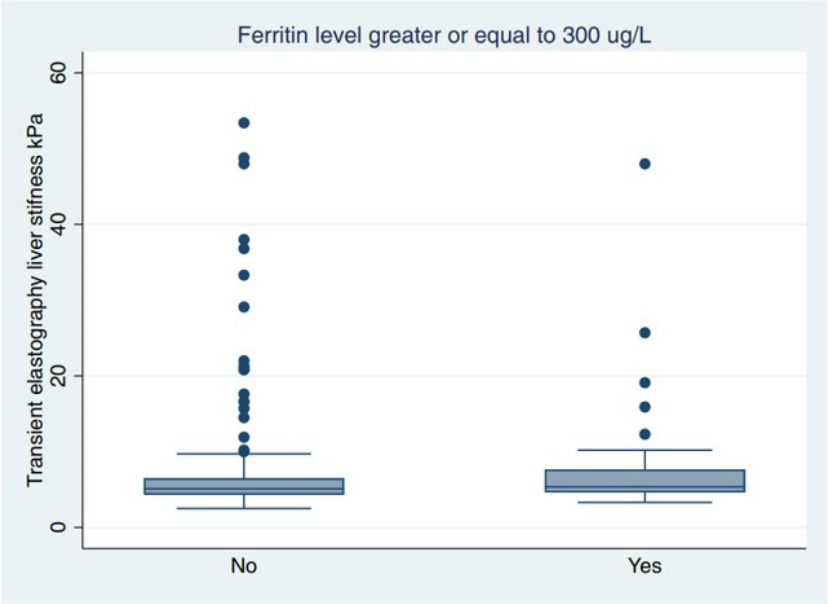


- Multiple targets being studied
  - NASH is heterogeneous → combination/tailored regimens?
- Generally targeting F2-3 (esp. F3)
  - Likely to be hard to show reversal of fibrosis in F4
  - Treatment of F0-1 very unlikely to be cost-effective
- Generally show promising results:
  - Improved/resolved NASH without worsening fibrosis
  - Improved fibrosis without worsening of NASH
- All trials tend to have high placebo responses
  - NASH is a variable disease, progresses and regresses
  - Effect of intervention not as great in absolute terms
- Biomarkers of response are still imperfect

Should I Offer Venesection?



- Dysmetabolic hyperferritinaemia (DHF): raised ferritin without iron overload
  - Caused by the metabolic syndrome and commonly seen in NAFLD
  - Ferritin may be high (can be > 1000) but transferrin saturation is usually normal
- Level of ferritin does not correlate with degree of fibrosis
  - Similar liver stiffness if Ferr > 300 or < 300
- Systematic review of venesection in DHF:
  - No impact on IR, AST in dysmetabolic HF
  - Minimal improvement in ALT (range 2-11)
- Systematic review of venesection in NAFLD:
  - No impact on IR, insulin levels, ALT or AST
  - No effect on liver inflammation or fibrosis



Trasolini et al. Can Liver J 2022;5(2):152-159

Murali et al. Hepatol Res 2018;48:E30-E41

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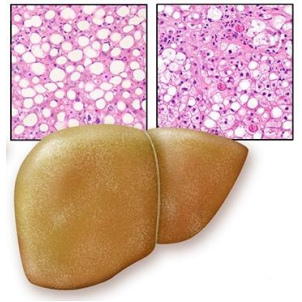

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  - No impact on IR, insulin level, ALT or AST in DHF
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- Systematic review of venesection in NAFLD:
  - No impact on IR, insulin level, ALT or AST
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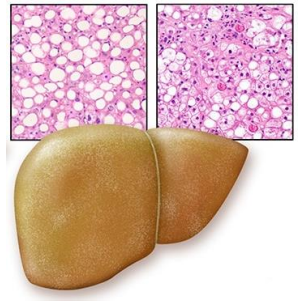
Venesection only indicated if hyperferritinaemia reflects true iron overload

Trasolini et al. Can Liver J 2022;5(2):152-159

Murali et al. Hepatol Res 2018;48:E30-E41

Take Home Messages & Discussion

Take Home Messages



- NAFLD is a highly prevalent disease
  - CV and metabolic consequences = “bread and butter” for GPs
- Serious consequences if progressive disease
  - Cirrhosis-related complications, decompensation, HCC
- Work-up of NAFLD is simple (Clinical Assessment + Bloods + USS + FIB-4 Score)
  - Majority of cases will have “benign” NAFLD (F0-1 → no need to refer, manage co-morbidities)
  - Some patients will have “significant” NAFLD (F2+) → need further intervention
- Lifestyle modification is effective for all forms of NAFLD
  - Target “obesity” diet + significant weight loss (5%, 7%, 10%)
  - Assess response to treatment using basic blood tests and improvements in cardiac risk profile
- Currently-available drugs <u>are</u> effective in NAFLD
  - Use these medications to manage co-existing CV risk factors
- New therapies are emerging but not here yet + unlikely to be widely available?

Thank you

Key References: This presentation has borrowed heavily from the most recent (2023) professional guidelines

- Rinella et al. AASLD Practice Guidance on the Clinical Assessment and Management of Nonalcoholic Fatty Liver Disease. Hepatology 2023. DOI:10.1097/HEP.0000000000000323.
- EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol 2016;64:1388-1402.
- Bahirwani and Griffin. The diagnosis and management of nonalcoholic fatty liver disease: A patient-friendly summary of the 2018 AASLD guidelines. Clinical Liver Disease 2022;19:222-226.
- Francque et al. Non-alcoholic fatty liver disease: A patient guideline. JHEP Reports 2021;3:100322.