



INTERNATIONAL
NASH DAY



JUNE 10, 2022



World NASH Day



International NASH Day (2022)

အသည်းအဆီဖုံးရောဂါ

သိကောင်းစရာအချက်များနှင့် နောက်ဆုံးပေါ်ကုထုံးများ



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Dr. Aung Hlaing Bwa

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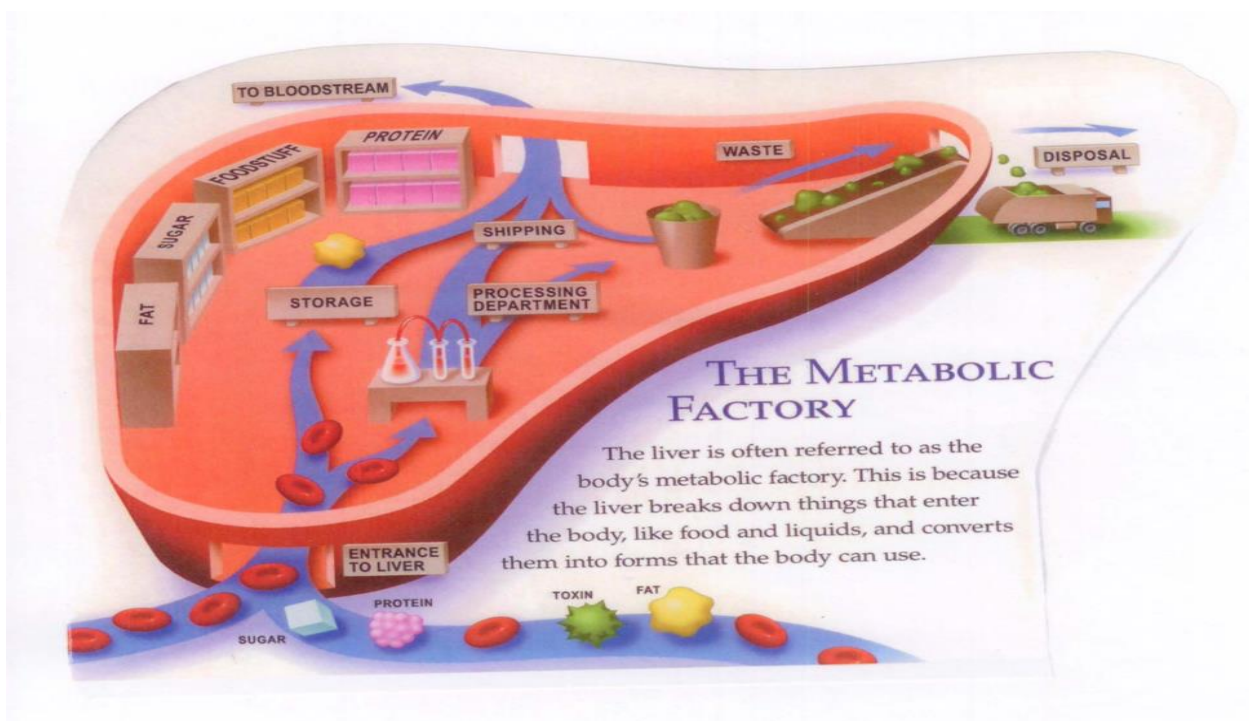
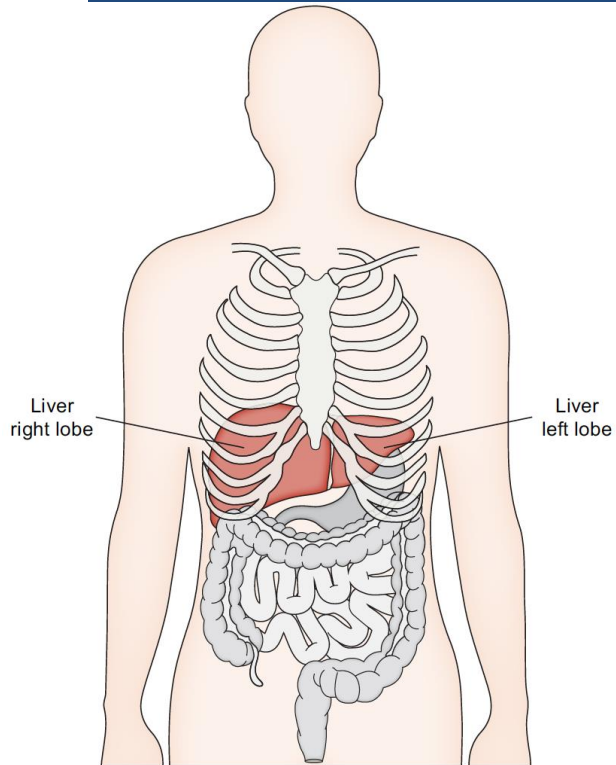


Facebook Live (Zifam Myanmar)

12-6-2022 (Sunday) | 3:00 PM

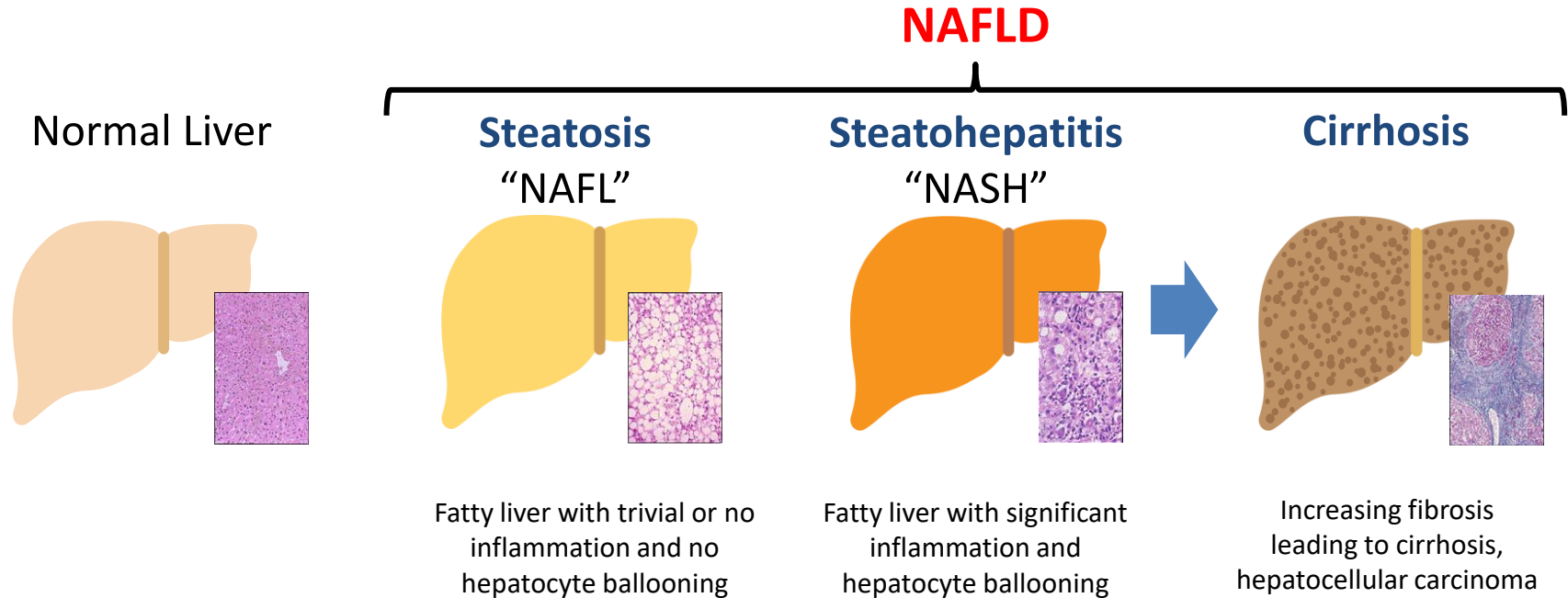


What kind of organ is the liver? Where is it located? What is its function?



အသည်းအကြောင်း

What is non-alcoholic fatty liver disease or NAFLD? What is the difference between NAFLD and non-alcoholic steatohepatitis (NASH)?



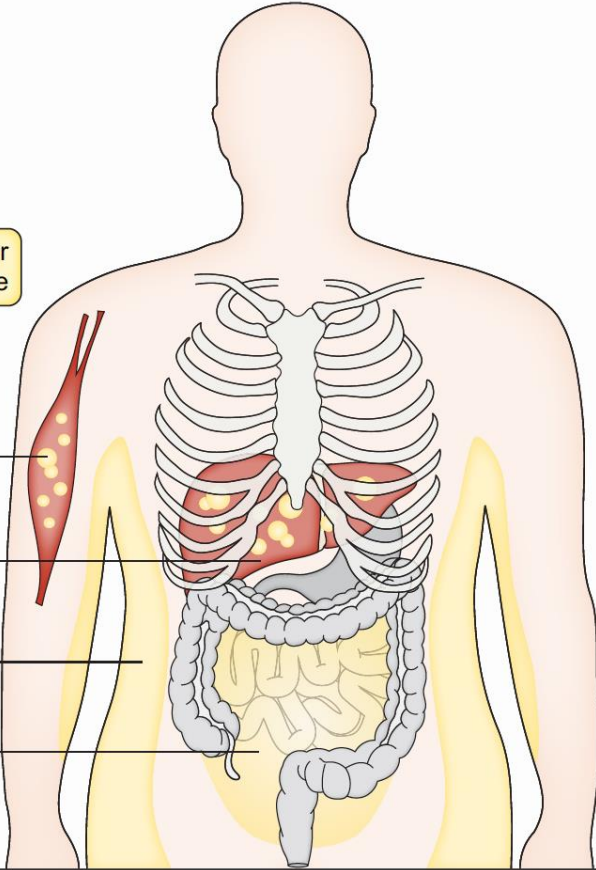
အသည်းအဆီဖုံးရောဂါဆိုတာဘာလဲ

The body harbours different types of fat or adipose tissue.

A

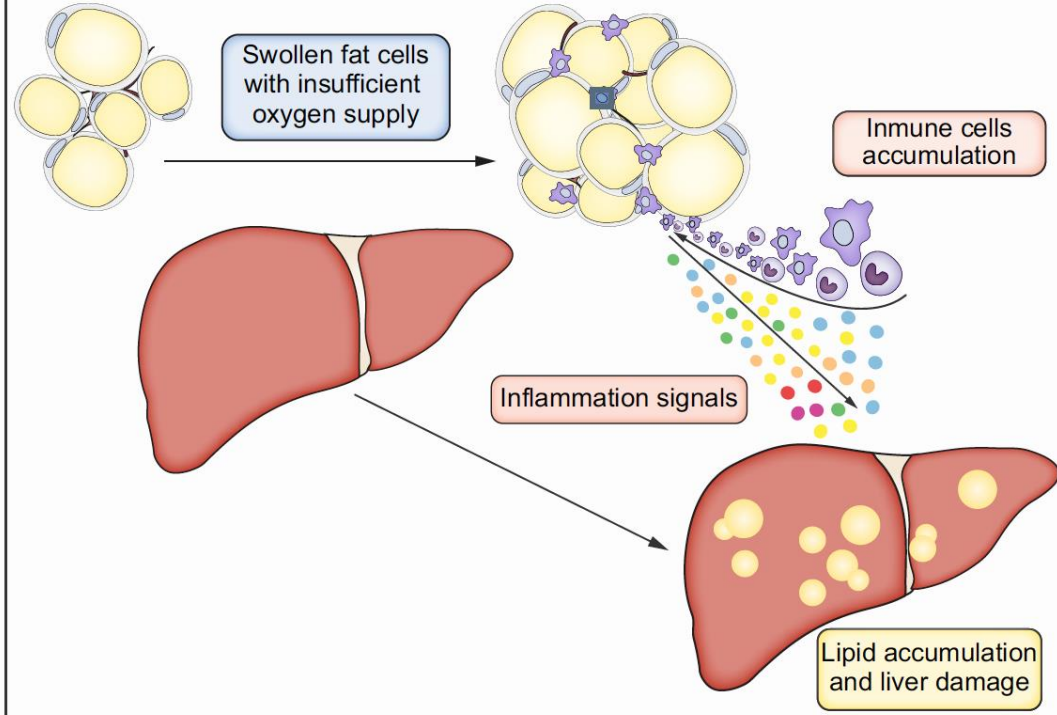
Types of fat or adipose tissue

- Inside the muscle
- Inside the liver
- Subcutaneous
- Intra-abdominal or visceral



B

ကိုယ်ထဲမှာရှိတဲ့ အဆီအမျိုးမျိုး

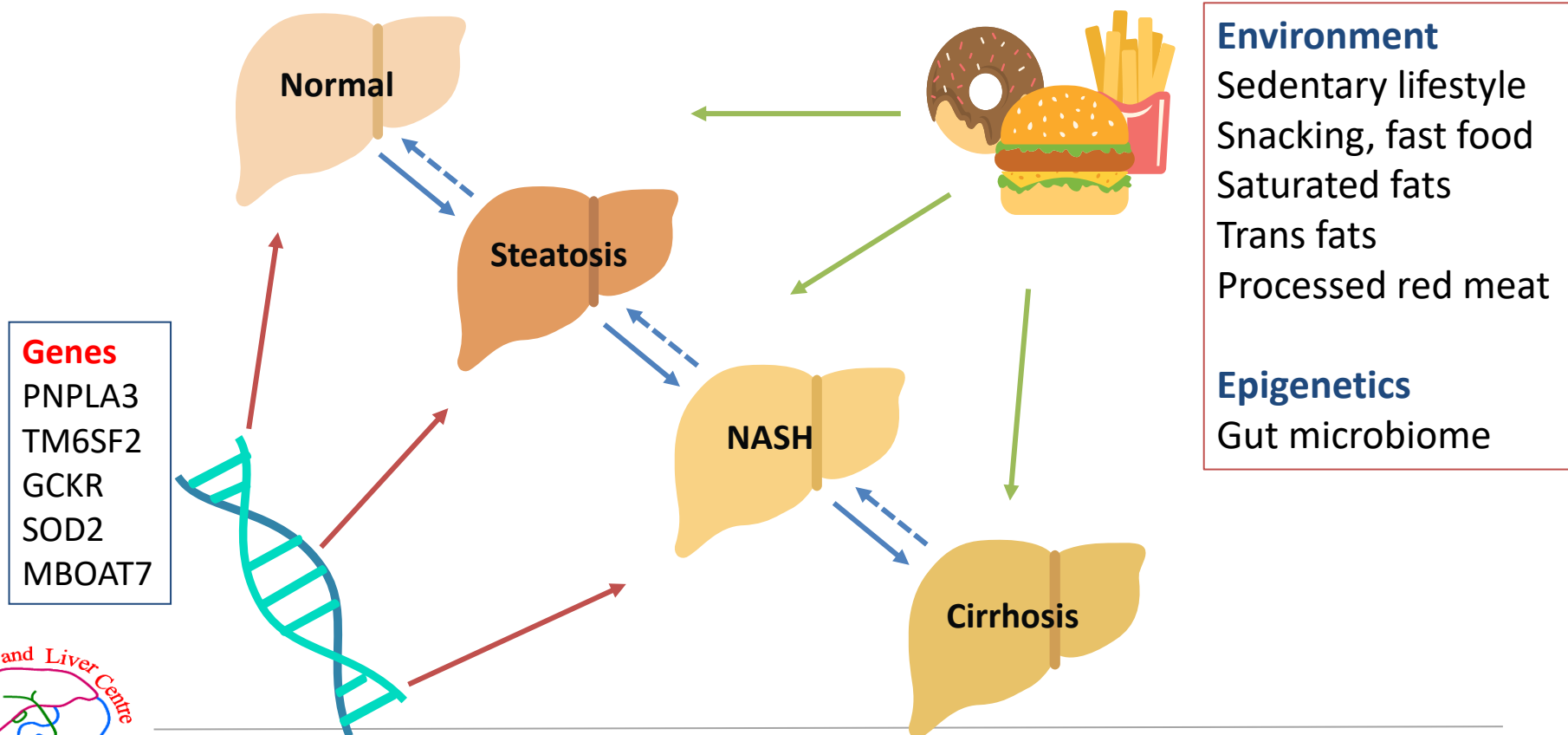


အသည်းအဆီဖုံးရောဂါဘာကြောင့်ဖြစ်တာလဲ

What is the cause of NAFLD/NASH? How do you get it?

NAFLD as a Complex Disease Trait: Genetic and Environmental Modifiers

ရှုပ်ထွေးလှတဲ့ အသည်းအဆီဖုံးဖြစ်စဉ်တွေ



အသည်းအဆိပ်းရောဂါကို ပြောင်းလွှဲစေတဲ့ ဖြစ်ရပ်တွေ ဆိုင်ငန်များ သံ ဖြို

Comorbidities	Genetic	Microbiome products	Nutrition and behavior
<ul style="list-style-type: none"> • Obesity • Metabolic syndrome • Insulin resistance • Type 2 DM • Dyslipidemia • Hypertension • OSA • PCOS • Hypopituitarism • Low GH • Low testosterone • Thyroid disease • LAL-D • Iron overload • Psoriasis • Osteoporosis 	<ul style="list-style-type: none"> • PNPLA3 • TM6SF2 • A1AT Pi*Z • HSD17B13 • LYPLAL1 • GCKR • MBOAT • DNA methylation • Chromatin remodeling • Non-coding RNAs 	<ul style="list-style-type: none"> • ETOH • Lipopolysaccharide • Reactive oxygen species • Cholesterol oxidation products • Butyrate • Acetate • Phenylacetate • Secondary bile acids • Choline deficiency 	<ul style="list-style-type: none"> • Alcohol • Cholesterol • Fructose • Exercise • Coffee
<p>Black = association with evolving evidence Red = established association Green = protective Bold = drives NASH progression</p>			



အသည်းအဆီဖုံးရောဂါရဲ့ အကျိုးဆက်တွေ

What is the impact in terms of liver disease?

What will happen to me?



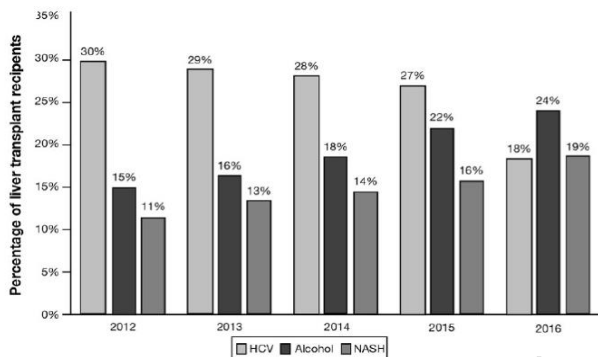
အသည်းအဆီဖုံးရောဂါက စီပိုးထက် ပိုဆိုး A changing landscape of liver transplantation: King HCV is dethroned, ALD and NAFLD take over!

Norah A. Terrault^{1,*}, Georges-Philippe Pageaux^{2,*}

¹Gastroenterology/Hepatology, University of California San Francisco, CA, USA; ²Hepatology and Liver Transplantation Unit, CHU Saint Eloi, Montpellier University, 34295 Montpellier, France

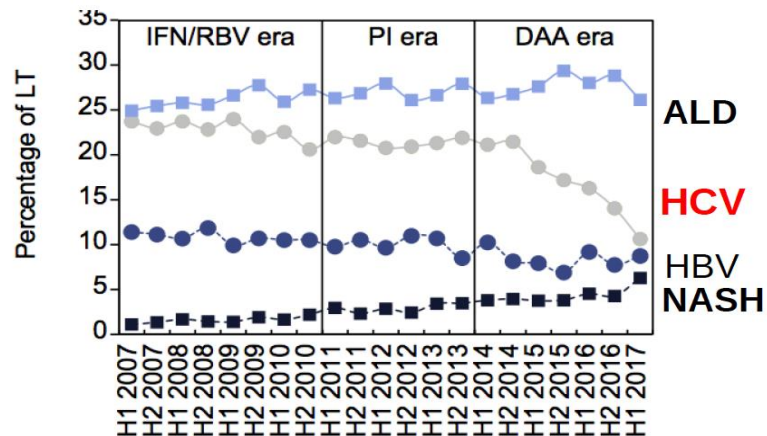
(See Articles pages 810–817 and pages 966–968)

UNITED STATES (UNOS) HCC excluded



HCV: 30→18%
ALD: 15→24%
NASH: 11→19%

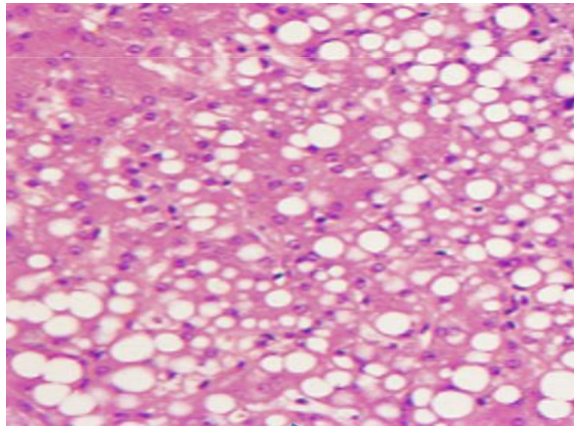
EUROPE (ELTR)



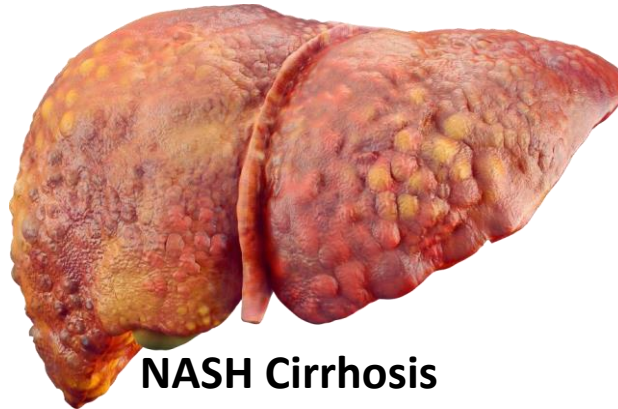
အသည်းအဆီဖုံး ဖြူ ကနေ အသည်းရောင် ဖြူ အဆင့် ရောက်သွားရင် ပိုပြီးအသည်းခြောက်လွယ်

Patients with NASH Progress to Cirrhosis at Much Higher Rate

Isolated Steatosis (NAFL)

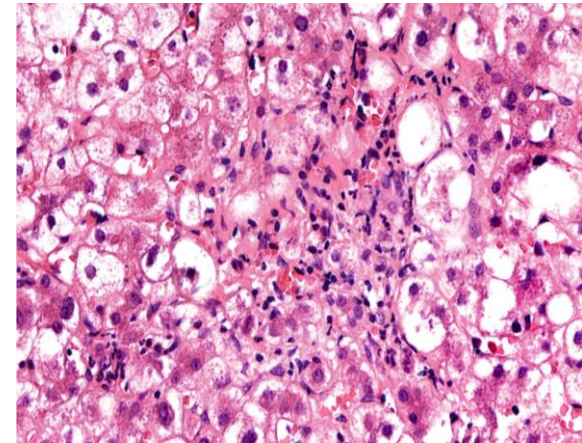


< 4%

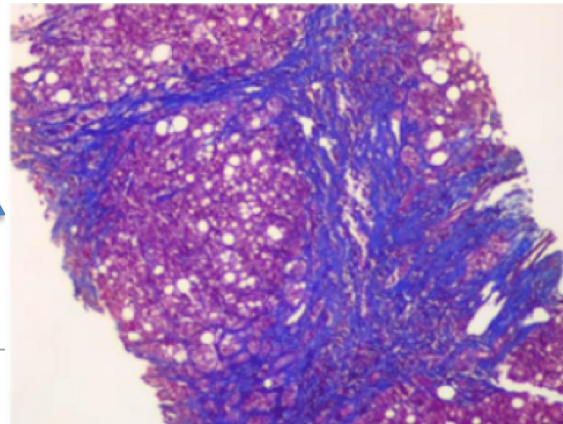


NASH Cirrhosis

NASH

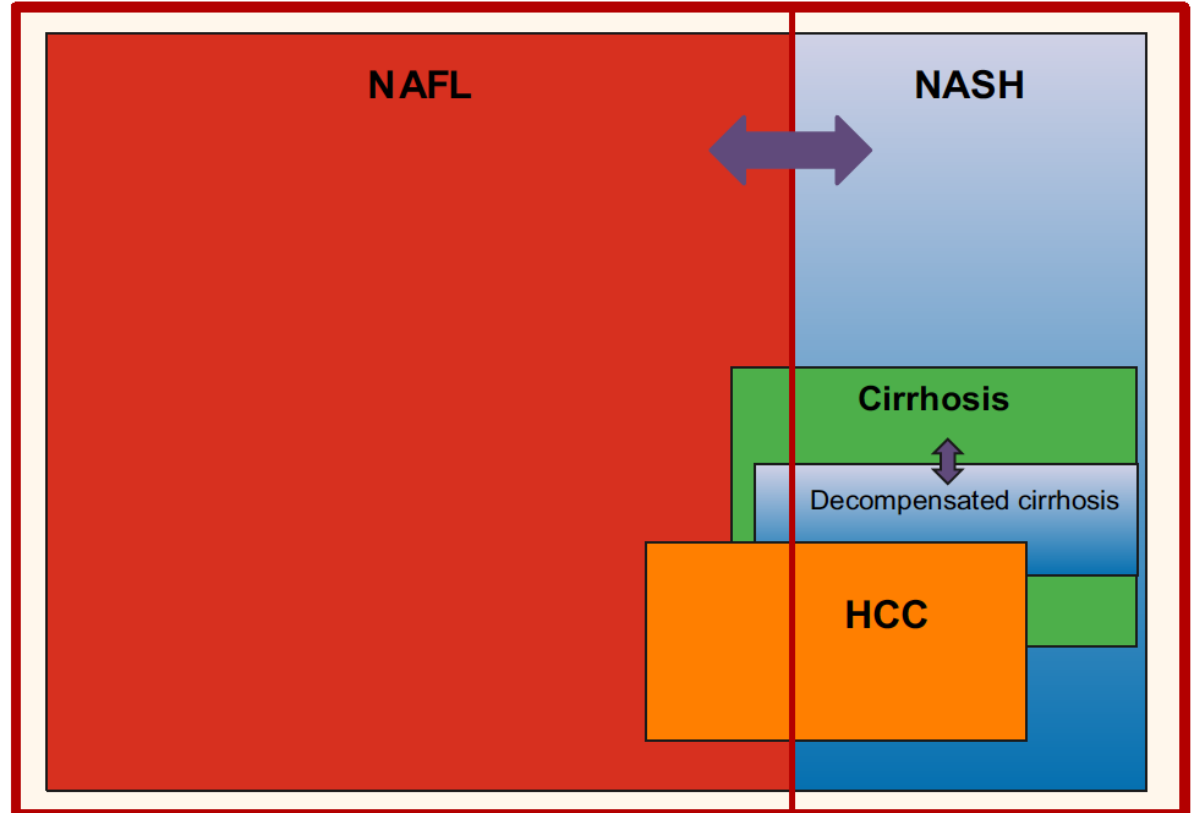


≈ 20%



The different subtypes of NAFLD and their relationships with the severe consequences of the disease.

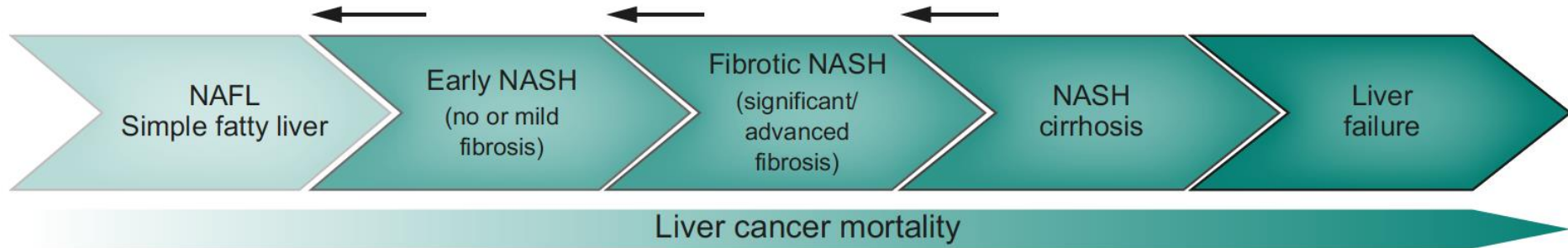
NAFLD



အသည်း အဆီဖုံးရောဂါ
အဆင့်ဆင့်နှင့် ဆိုးဝါးတဲ့
အကျိုးဆက်များ

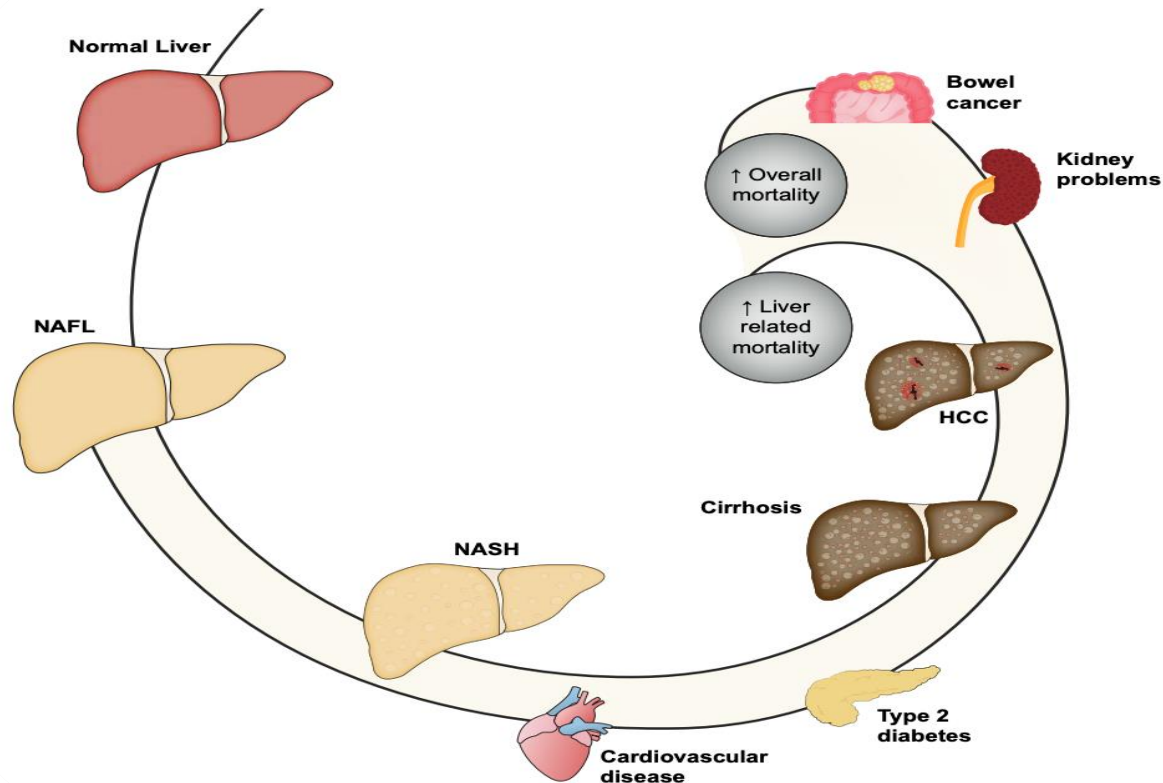
ရိုးရိုးအသည်းအဆီဖုံးကနေ ဆိုးဝါးတဲ့ အသည်းရောဂါတွေဖြစ်လာနိုင်

Non-alcoholic fatty liver disease can evolve from just a fatty liver to severe liver disease, over different stages of severity



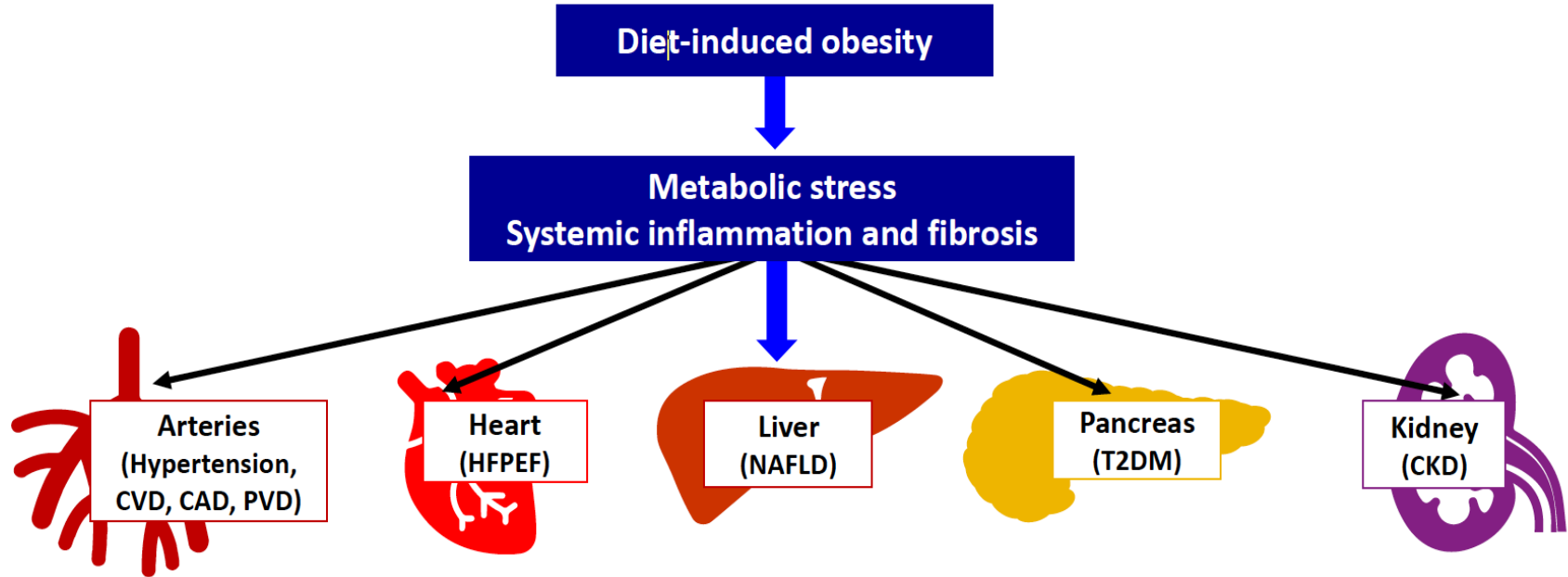
အသည်းအဆီဖုံးရောဂါက လူကျန်းမာရေးကို ဘယ်လို ထိခိုက်နိုင်တာလဲ

How does NAFLD affect general health?



အသည်းအဆီဖုံးဘယ်အဆင့်မှာ ပြဿနာတွေစပေါ်လာပြီလဲ

In which stage of NAFLD do problems occur?



အသည်းအဆီဖုံးကနေဘဝကို ဘယ်လိုထိခိုက်နိုင်တာလဲ

Impact of the NAFLD/NASH on health-related quality of life



Depression

Imaging

Blood Test

Diabetes

Obesity

Medication

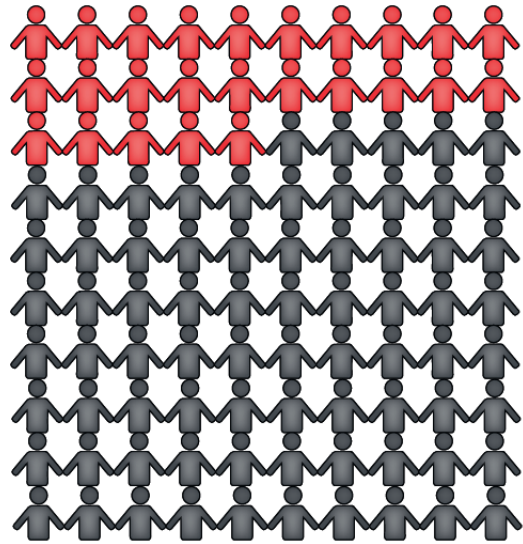
Alcohol

Hospital

Cost

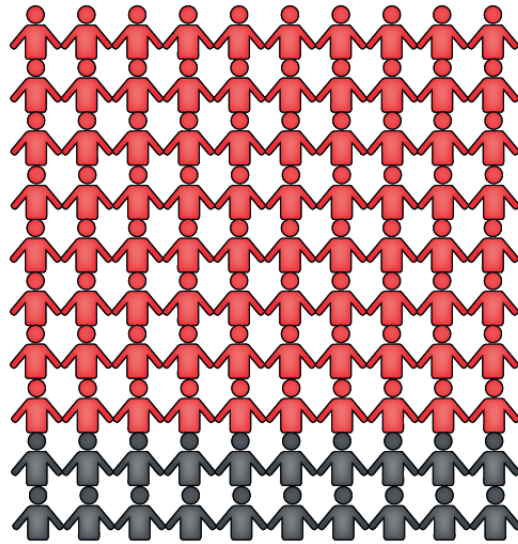
ဘယ်လိုလူတွေ အသည်းအဆီဖုံးရောဂါ ရနိုင်သလဲ

Who gets NAFLD/NASH?



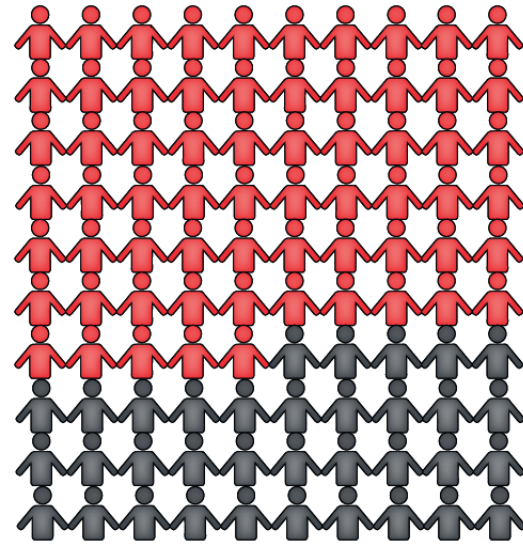
Community (25% NAFLD)

လူတန်းစားအားလုံး (၂၅%)



Obesity (80% NAFLD)

အလွန်တဲ့သူတွေ (၈၀%)

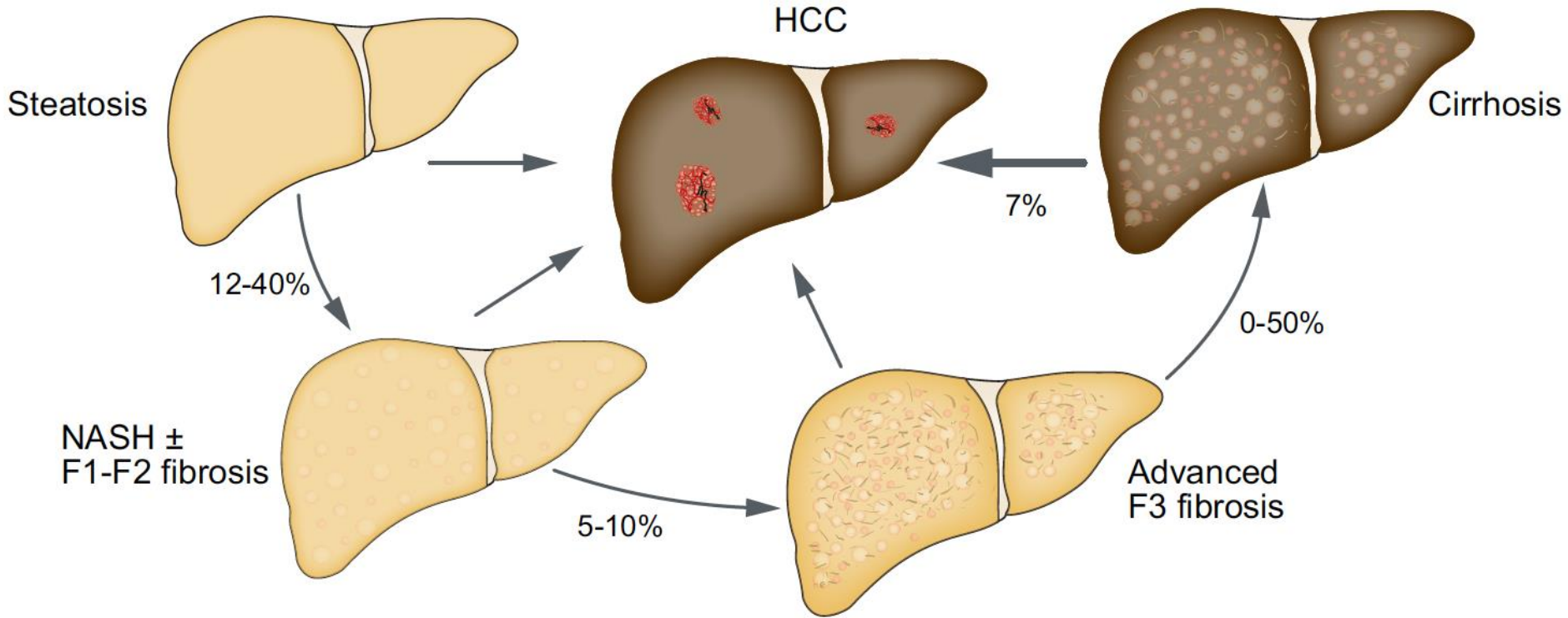


Type 2 diabetes (65% NAFLD)

ဆီးချိုရှိတဲ့သူ (၆၅%)

■ NAFLD
■ Non-NAFLD

အသည်းအဆီဖုံးရောဂါမှာ ဆိုးဝါးတဲ့ အကျိုးဆက်ရောဂါ ဖြစ်နိုင်ချေ How frequent are the complications?



ဘယ်လိုလူတွေကို အသည်းအဆီဖုံးရောဂါ ရှိ၊ မရှိ စစ်ဆေးနိုင်သလဲ Who should be screened?

အသည်းအဆီဖုံးဗြို့ရောဂါ ဖြစ်တဲ့ သူတွေရဲ့ ဘယ်လောက်များများ အသည်းရောင်မြဲအသည်းမာတာ ဖြစ်လဲ

Who Is at Risk for NASH and Advanced Hepatic Fibrosis?

Risk Factors for NAFLD^[1]

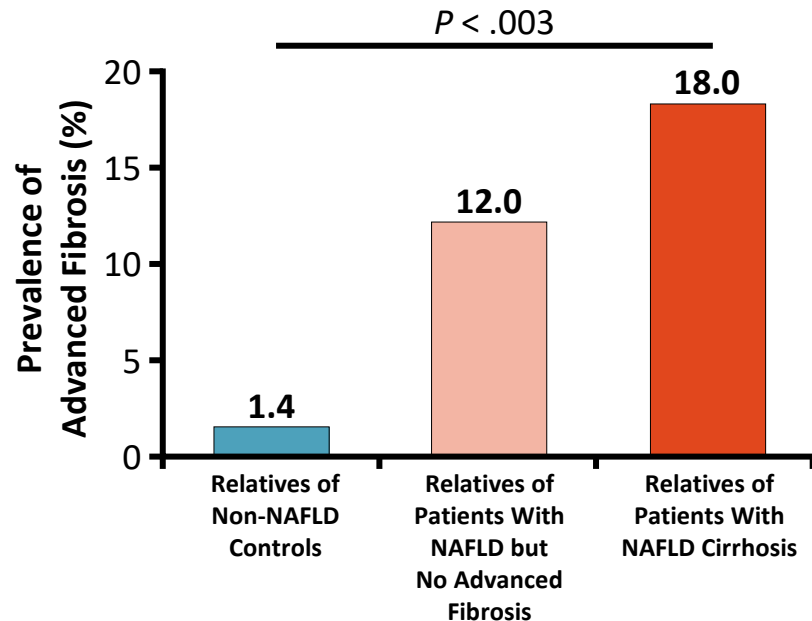
Type 2 diabetes

Obesity

Dyslipidemia

Metabolic syndrome

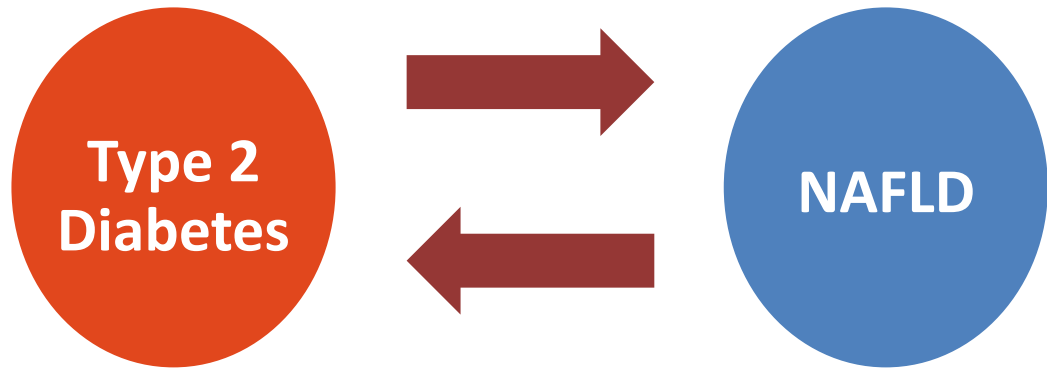
Polycystic ovary syndrome



- Risk of advanced fibrosis higher in first-degree relatives of patients with NAFLD cirrhosis^[2]

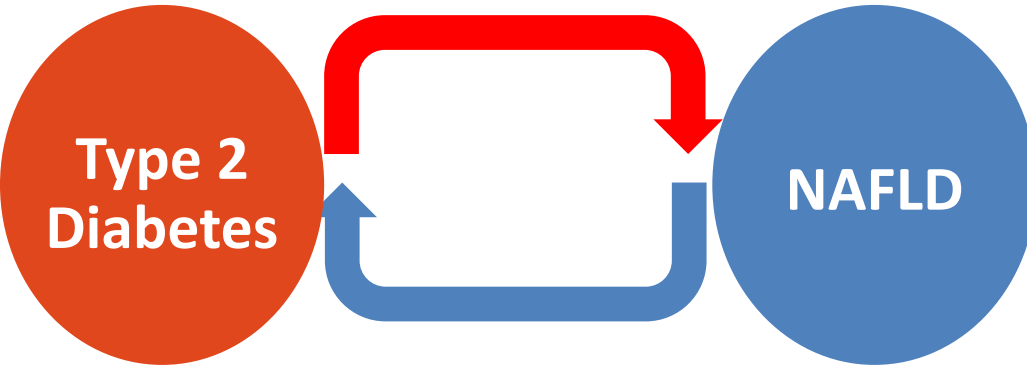
ဆီးချိုရောဂါနဲ့အသည်းအဆီဖုံးရောဂါ အပြန်အလှန် ဆက်စပ်ပုံ

Type 2 Diabetes and Fatty Liver Disease: “Bidirectional Association”



ဆီးချိုရောဂါနဲ့ အသည်းအဆီဖုံးနဲ့ နှလုံးရောဂါအဆက်အစပ်

The Liver and Cardiometabolic Risk Reduction in T2DM



Diabetes Promotes:

- ↑ Risk of Steatohepatitis
- ↑ Risk of Cirrhosis
- ↑ Hepatocellular Carcinoma

NAFLD Promotes:

Worse insulin resistance

- ↑ Risk of atherogenic dyslipidemia
- ↑ Risk of T2DM, ↑ difficult to manage
- ↑ Risk of CVD

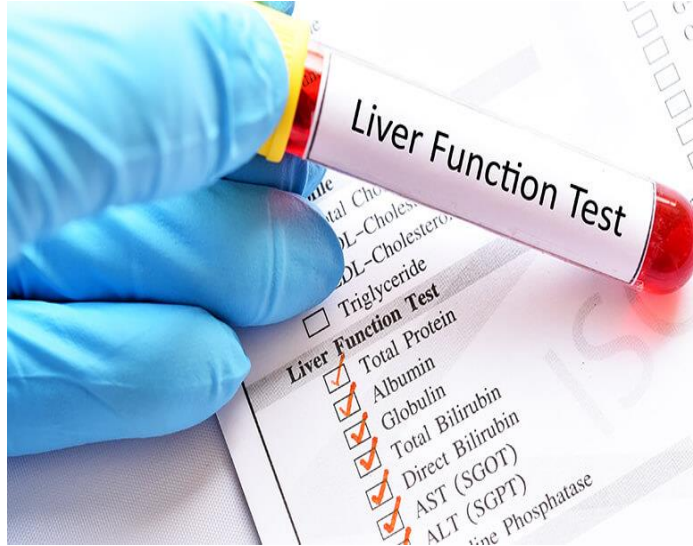
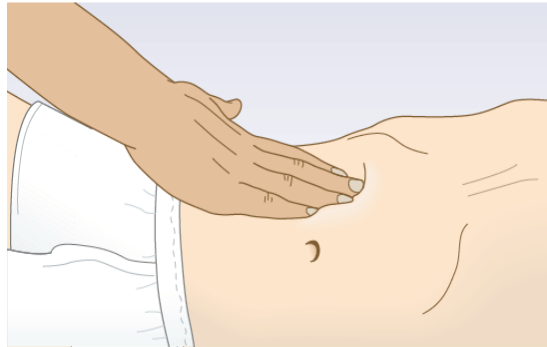
American Diabetes Association recommendation for NAFLD:

Recommendation 4.14

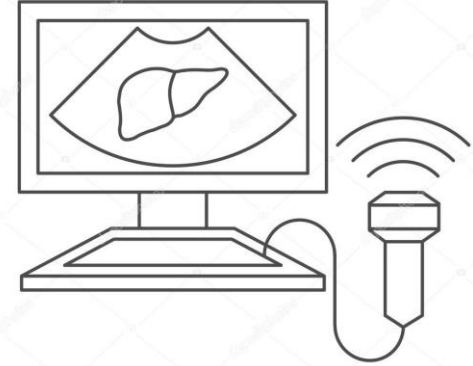
- Patients with T2DM or prediabetes and elevated liver enzymes (ALT) or fatty liver on ultrasound should be evaluated for presence of NASH and liver fibrosis.

အသည်းအဆီဖုံးရောဂါရှိ၊ မရှိ ဘယ်လိုစစ်မလဲ

How can screening be done?



ULTRASOUND OF THE LIVER



အလွန်၊ မလွန်စစ်တဲ့ BMI

BMI (Body Mass Index)

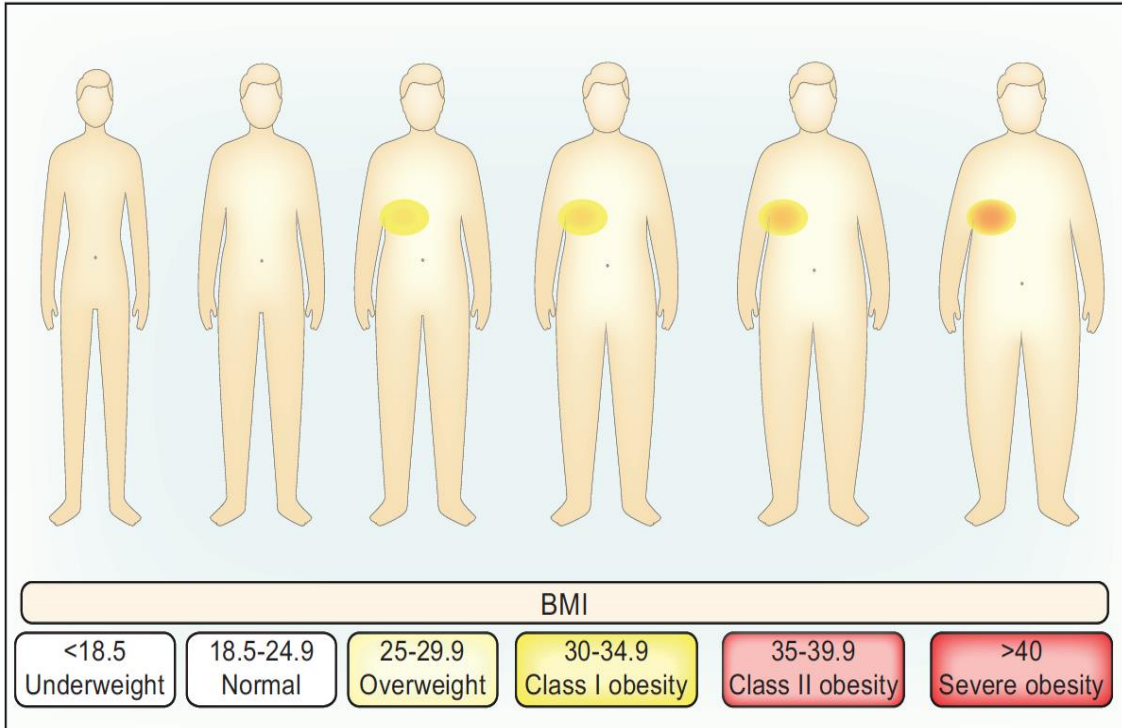


Table 2. International classification of adult underweight, overweight and obesity according to body mass index.⁷

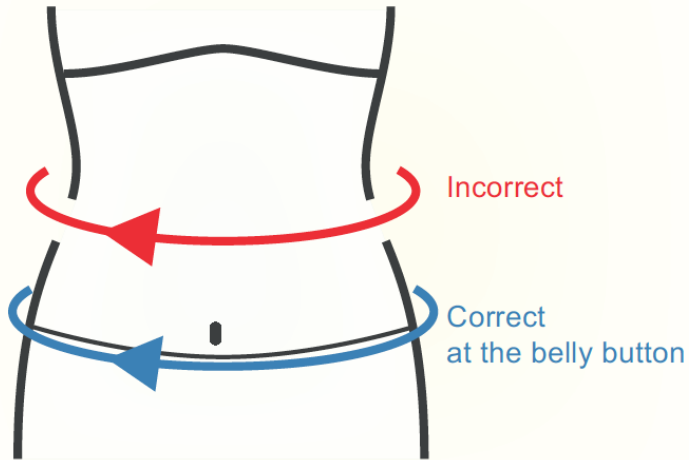
Classification	International	Asian [*]
Underweight	<18.5	<18.5
Normal range	18.5–24.9	18.5–22.9
Overweight	25.0–29.9	23.0–24.9
Obese class I	30.0–34.9	25.0–29.9
Obese class II	35.0–39.9	≥30.0
Obese class III	≥40.0	

* The classification for adult Asians was proposed by WHO in 2000. However, the WHO Expert Consultation recommended to keep the international classification for all populations in 2004 because of significant heterogeneity across Asian countries. That said, many studies from Asia still adopt the lower body mass index cut-offs according to the proposal in 2000.

ခါးဆုံဒီက အရေးကြီး

Waist Size Matters

Waist circumference measurement



Abdominal Obesity Measurement Guidelines

Organization	Measurement used	Definition of abdominal obesity
American Heart Association, National Heart, Lung and Blood Institute (10)	Waist circumference	Women: > 88 cm (35 inches), Men: > 102 cm (40 inches)
International Diabetes Federation (11)	Waist circumference	Women: > 80 cm (31.5 inches), Men: > 90 cm (35.5 inches) Different cut-points for different ethnic groups
World Health Organization (12)	Waist-to-hip ratio	Women: > 0.85, Men: > 0.9

ပိန်တုံ့လှူမှာလည်း အသည်းအဆီဖုံးရောဂါ ဖြစ်နိုင်

What About “Lean” NASH?

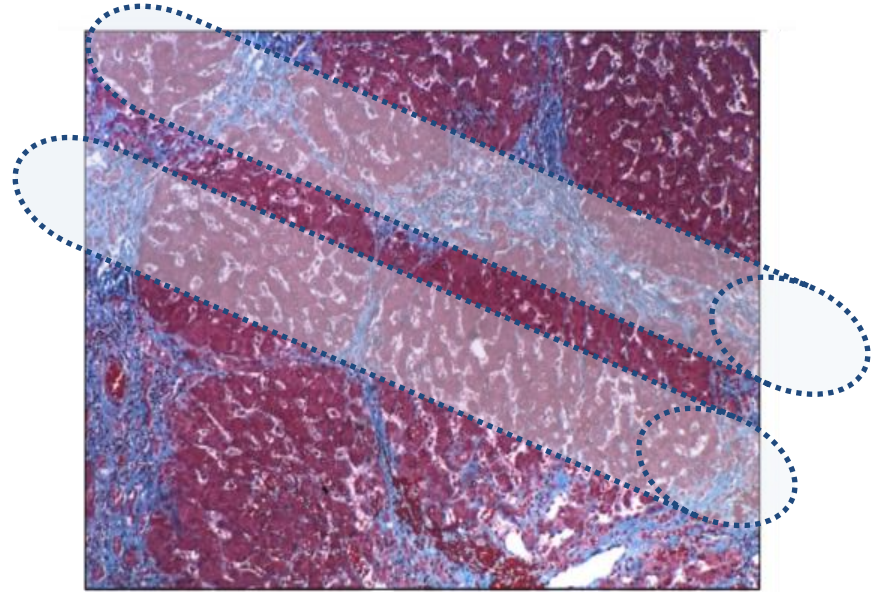
- Definitely occurs
 - Role of lifestyle modification?
 - Improvement in Asian individuals with BMI < 25 kg/m² [1]
 - Prevalence depends on definition of “lean”
 - BMI < 25 kg/m² but abdominal adiposity?[2]
 - BMI < 23 kg/m² in Asian individuals
- **PNPLA3 I148M** allele likely plays a major role in lean NAFLD^[3]

အသံ့အသားစ ယူမလား

Liver Biopsy: The Imperfect Gold Standard

- **Limitations**

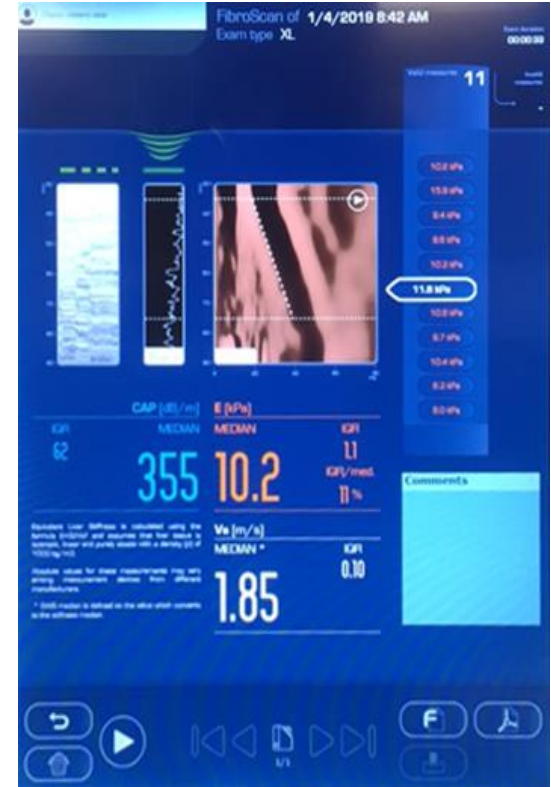
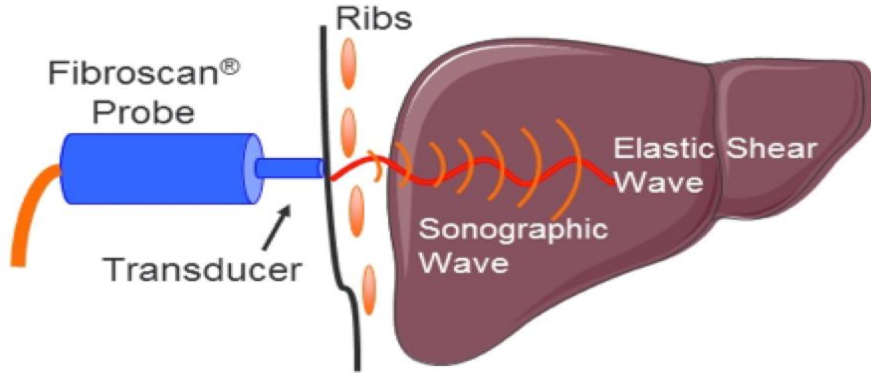
- Invasive
- Painful
- Expensive
- Morbidity/mortality
- Sampling variability
- Observer variability
- Expertise to perform
- Impractical for population screening



Sampling variability:
Same biopsy may give
2 different grades of liver
fibrosis

အသည်းအဆီဖုံးနှုန်းတိုင်းကရိယာဖိုင်ဖရိုစကင် (Fibroscan) Vibration-Controlled Transient Elastography

- Measures 1D velocity of low-frequency shear wave
- Directly related to tissue stiffness (fibrosis)
 - The stiffer the liver, the faster the shear wave propagates
- Quick, bedside test (~ 5 mins)
- Limited by obesity, food intake
operator experience



Sigrist. Theranostics 2017;7:1303.

အသည်းအဆီဖုံးနှုန်း၊ အသည်းခြောက်နှုန်းတွက်တဲ့ ဖော်မြူလာ NAFLD Fibrosis Score and FIB-4 Score: Online Calculators Easily Interpret Noninvasive Tests

- Based on age, platelet count, AST, ALT ± other lab values

10:48

NAFLD (Non-Alcoholic Fatty Liver Disease) Fibrosis Score

Estimates amount of scarring in the liver based on several laboratory tests.

Favorite ★

When to Use	Pearls/Pitfalls	Why Use
Age		years
BMI	Norm: 20 - 25	kg/m ²
Impaired fasting glucose/diabetes	No 0 Yes +1	
AST	Norm: 1 - 40	U/L
ALT	Norm: 1 - 35	U/L
Platelet count	Norm: 150 - 350	× 10 ⁹ /L ↕
Albumin	Norm: 35 - 55	g/L ↕

10:48

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

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

Favorite ★

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	years
AST Aspartate aminotransferase	Norm: 1 - 40	U/L
Platelet count	Norm: 150 - 350	× 10 ⁹ /L ↕
ALT Alanine aminotransferase	Norm: 1 - 35	U/L
Platelet count	Norm: 150 - 350	× 10 ⁹ /L ↕
Albumin	Norm: 35 - 55	g/L ↕

Noninvasive Tests Exclude or Determine Advanced Hepatic Fibrosis

အသုံးအဆုံးရောဂါမှာ အသုံးမာ မမာအလွယ်တကူတွက်နိုင်တဲ့ FIB-4 ဖစ်ဖိုးစကိုး

- FIB-4 recognized by AASLD as useful in identifying patients with a higher likelihood of F3 or F3-F4^[1]

Cutoff Scores for Measurement of Advanced Hepatic Fibrosis^[2,3]

FIB-4: ≤ 1.3
NFS: < -1.455

FIB-4: ≥ 2.67
NFS: > 0.675



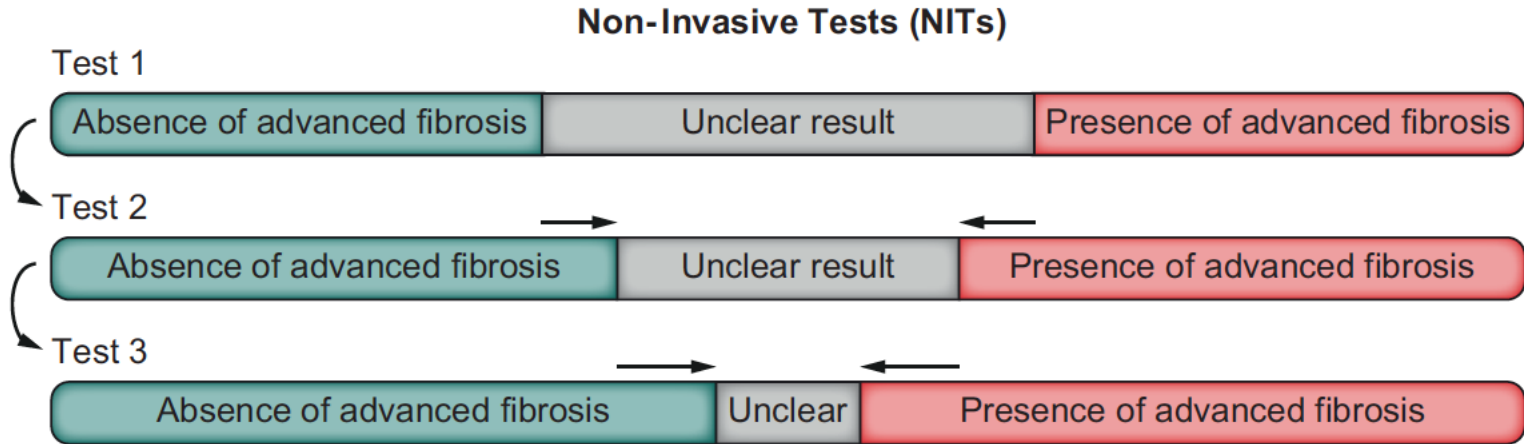
Absence of advanced fibrosis

Indeterminate

Presence of advanced fibrosis

Different tests & Different strategies

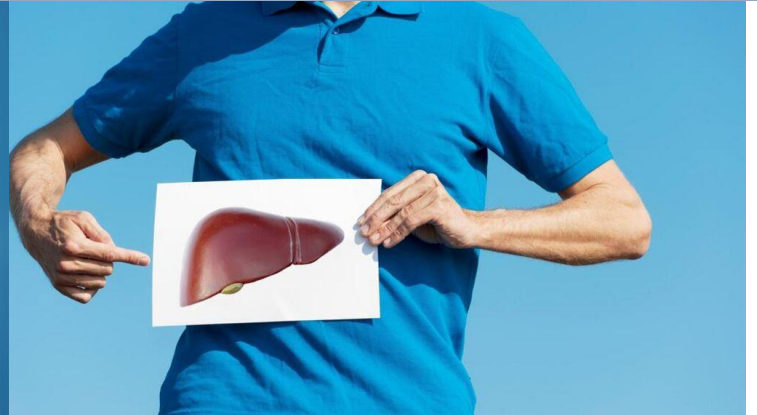
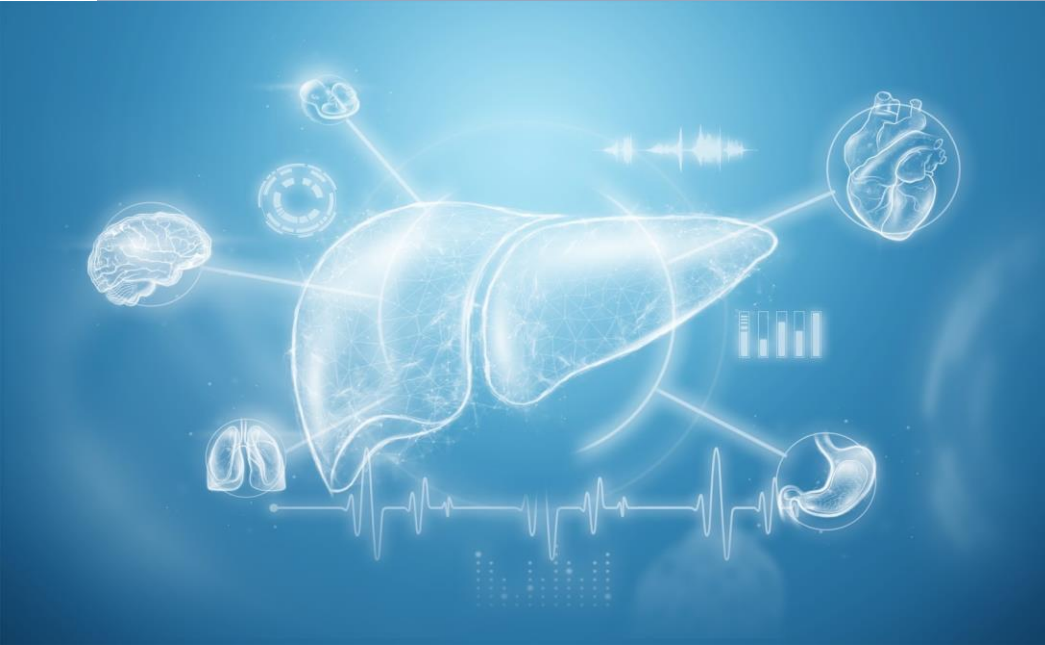
အသည်းမာလားတွက်မဲ့နည်းစနစ်တွေ



အသည်းမာ မမာစစ်တာတွေကို ဘယ်လောက်တစ်ခါ ပြန်စစ်မလဲ

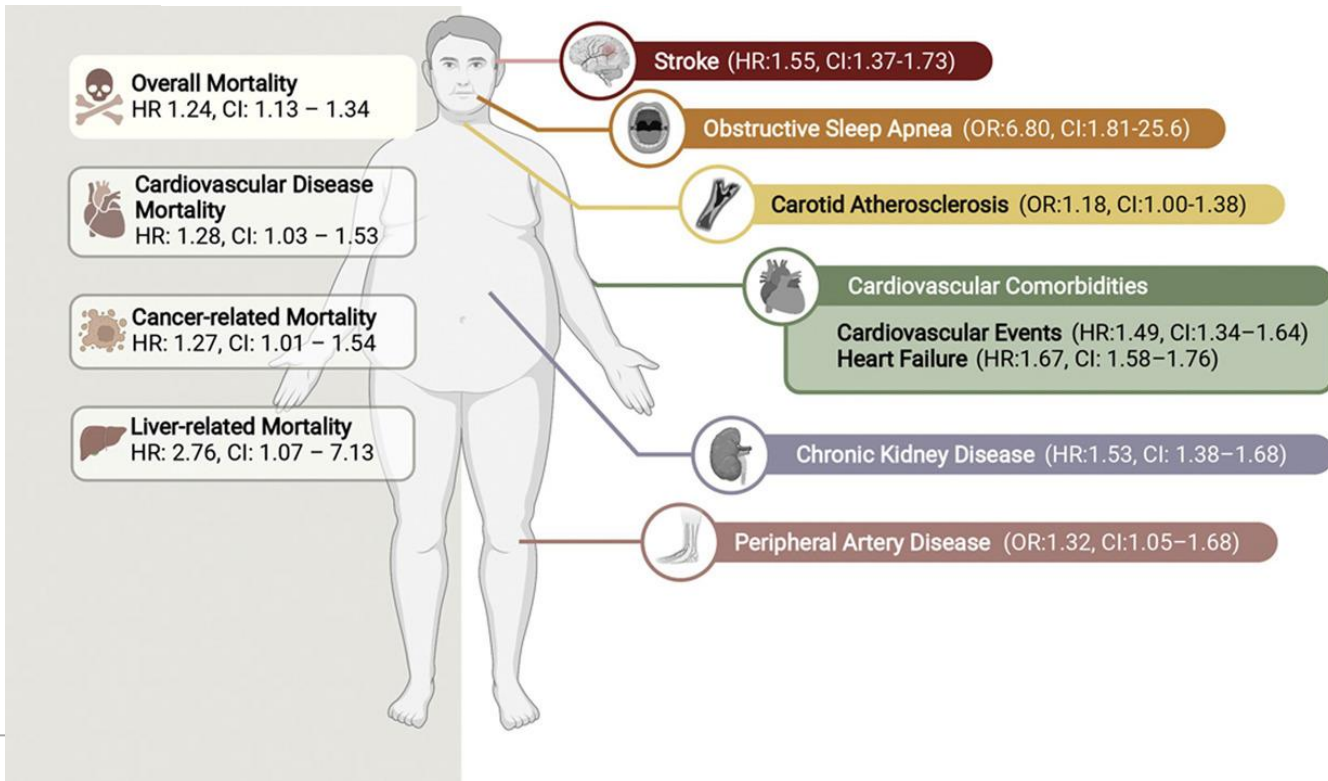
Should tests be repeated over time?

ရောဂါလက္ခဏာတွေ What are the symptoms?

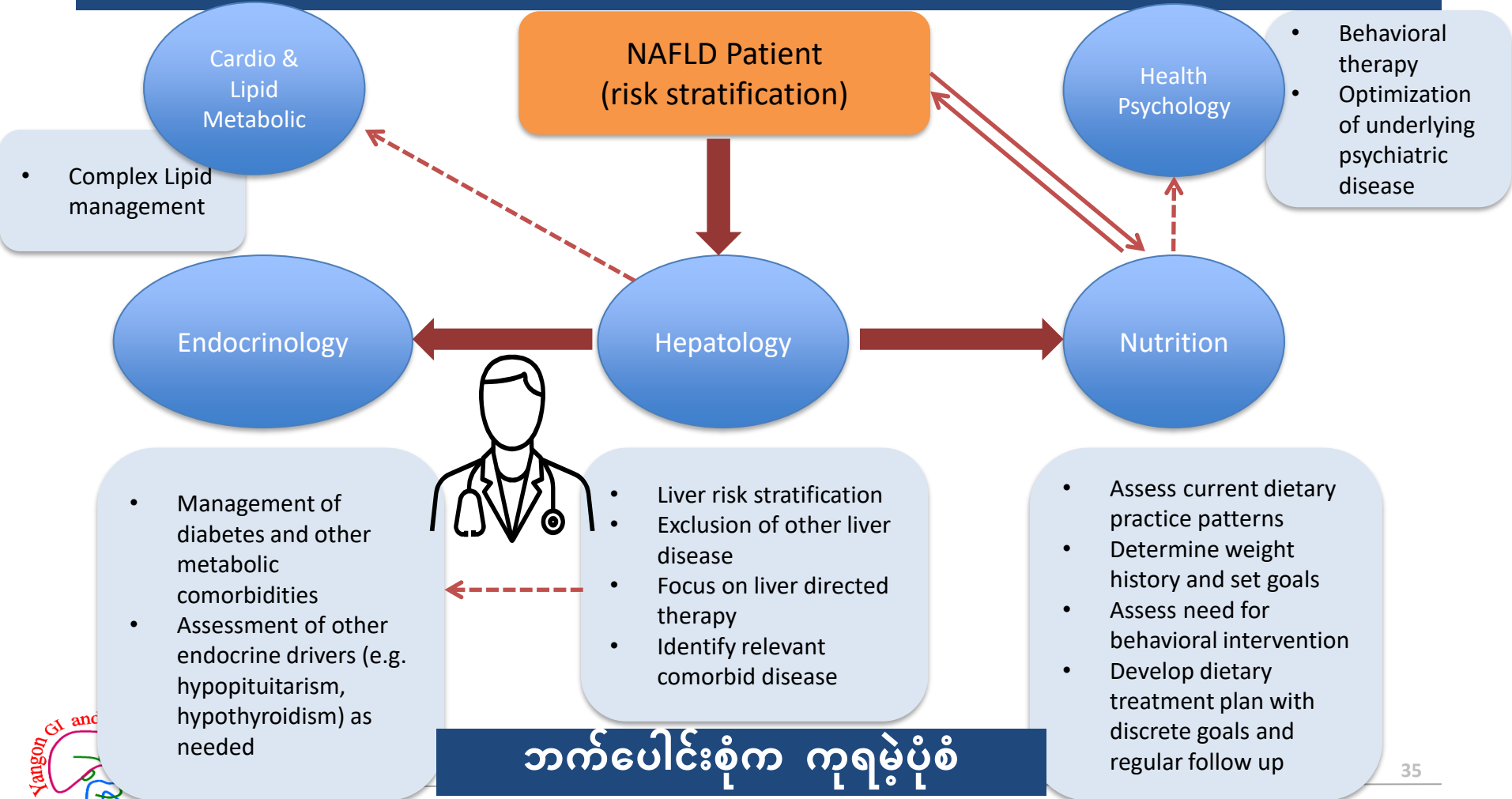


အသည်းအဆီဖုံးရောဂါသည်တိုင်းကို ကုမလား Should All NAFLD/NASH be treated?

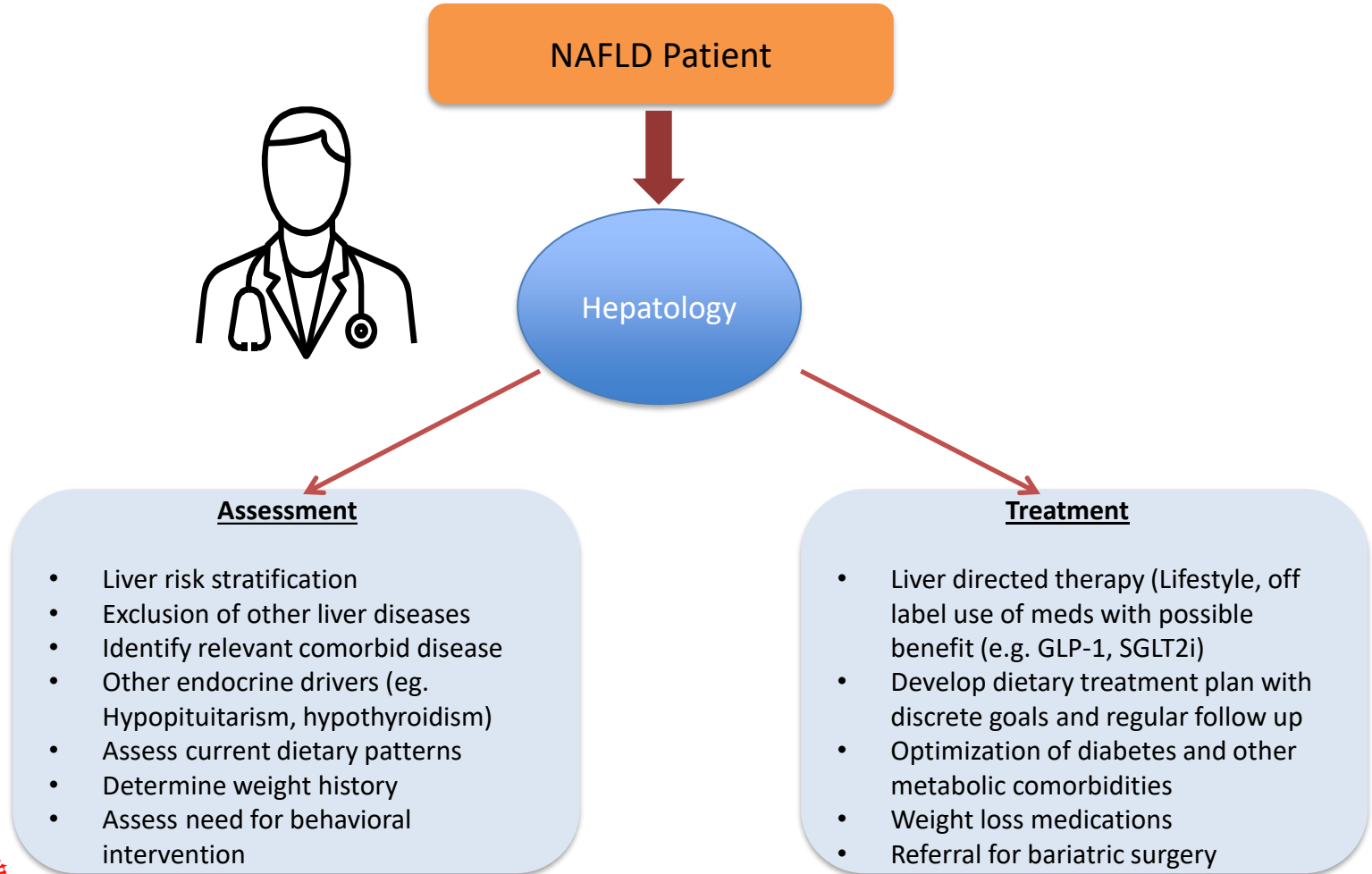
F0 (no fibrosis) F1 F2 F3 F4 (= cirrhosis)
Least severe → Most severe



Optimal Multidisciplinary Model (NAFLD/NASH Board)



အသည်းအဆီဖုံးရောဂါ လူနာတစ်ယောက်ကို တွေ့ရင်ဘာတွေဆက်လုပ်ရမှာလဲ



Risk Stratification of Patients with NAFLD

Clinical Assessment for NASH ± Advanced Fibrosis

Low Suspicion ?

- No MetS features
- BMI <30
- NFS <-1.455
- Normal ALT
- No Family h/o
- FIB4 < 1.3

Treat as low-risk:
Monitor for new risk factors

Intermediate to High Suspicion?

- MetS
- T2DM
- Dyslipidemia
- Hypertension
- NFS > 0.676
- Normal ALT
- Family h/o
- Persistently ↑ ALT
- Age > 50
- FIB4 > 2.67

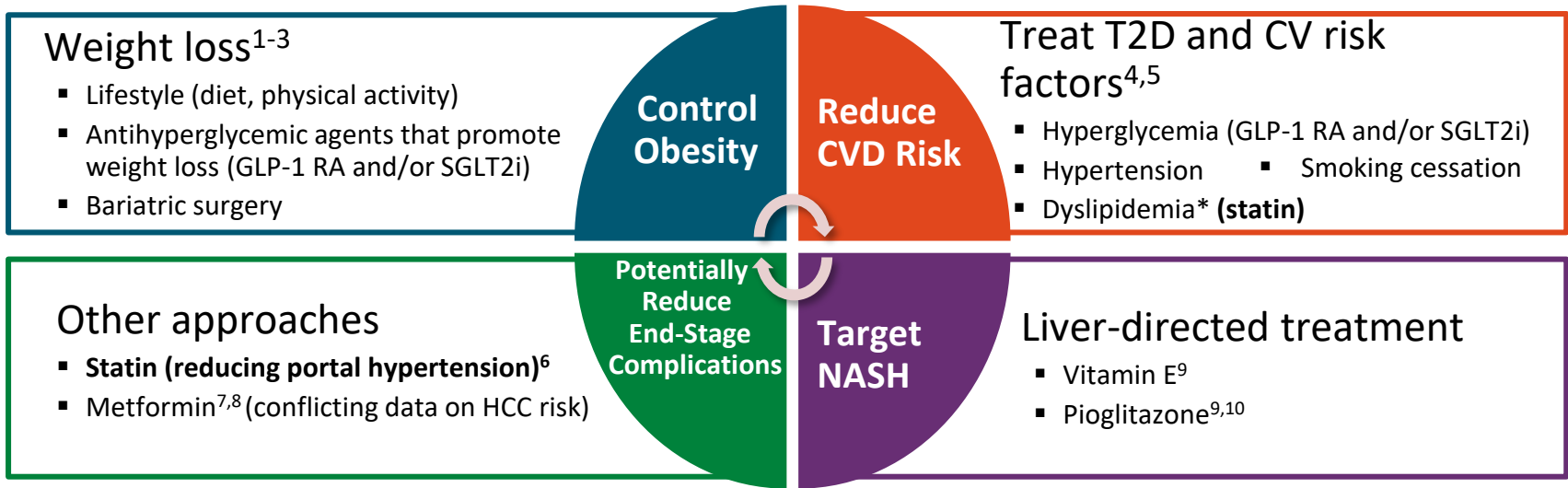
Assessment of Liver Stiffness



အသည်းအဆီဖုံးရောဂါဟာ
ဘယ်လောက်အန္တရာယ်ရှိလဲဆိုတာ
စစ်ဆေးနည်း

Approaches for Currently Available Treatments

ကုသဖို့နည်းလမ်းတွေ



*NAFLD does not increase statin risk of drug-induced liver injury.¹¹

In patients with advanced liver disease, choose or dose drugs appropriately.

Weight reduction

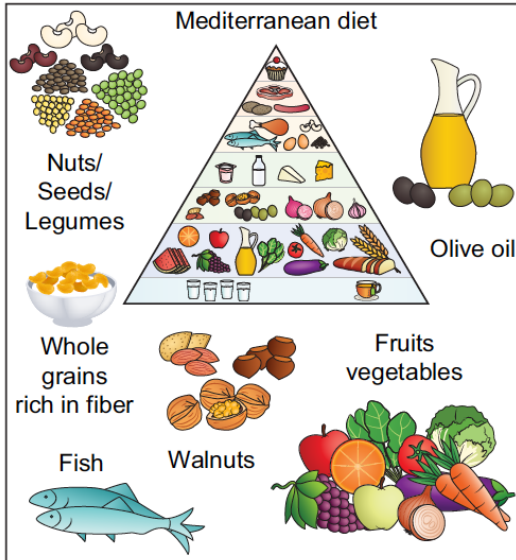
- The more severe the liver disease is, the higher the goals are in terms of weight loss
- Healthy diet with caloric restriction tailored for your preferences

- 3-5% reduction of weight even within the normal BMI range (especially if recent weight gain occurred or if abdominal obesity is present)

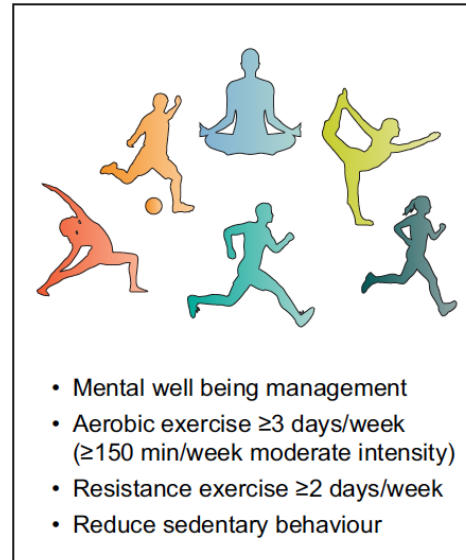
နေထိုင်စားသောက်မှုတွေပြုပြင်

Lifestyle advice for ALL patients with NAFLD

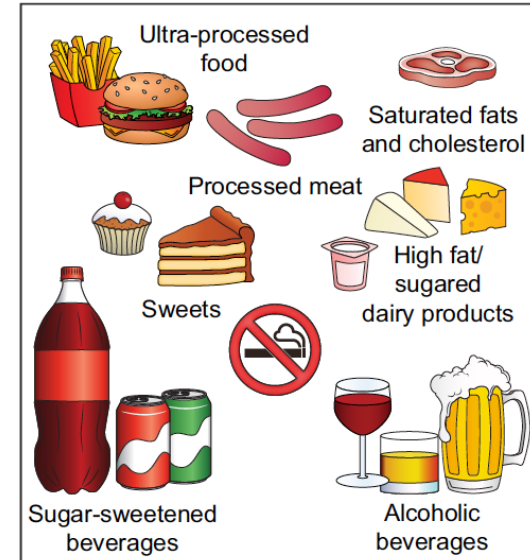
Recommended foods



Recommended activity



Non-recommended foods/ Minimize consumption

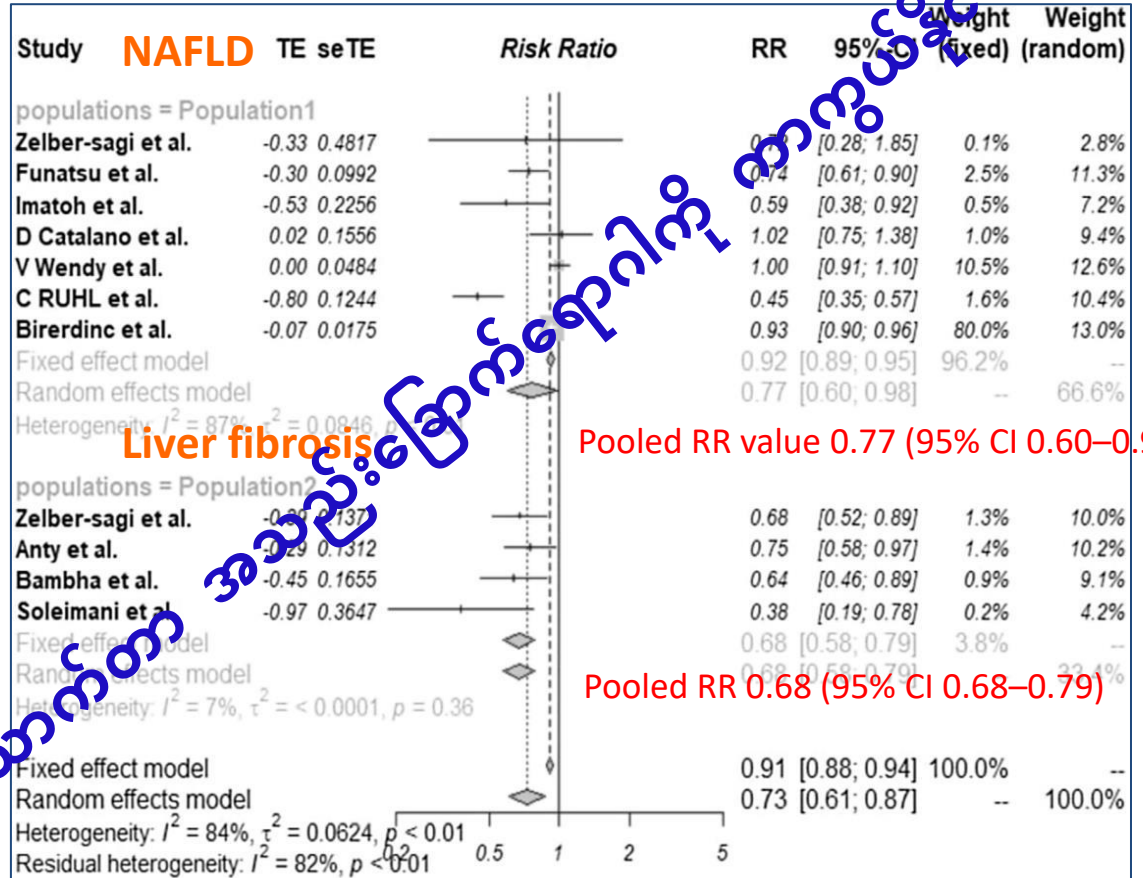


- Reduce added sugar (e.g. by reducing sweets, processed foods, sugared dairy products, etc.)
- Avoid sugar-sweetened beverages
- Reduce saturated fat and cholesterol (e.g. by eating low fat meat and low fat dairy products)

- Increase n-3 fatty acids found in fish, and walnuts; utilize olive oil over other oils more often
- Minimize “fast food” and ultra-processed food
- Home-cooked meals are preferable
- Try to follow the Mediterranean dietary pattern

Meta-analyses of coffee consumption impact on NAFLD and liver fibrosis

- 11 studies, varying designs



Liver fibrosis

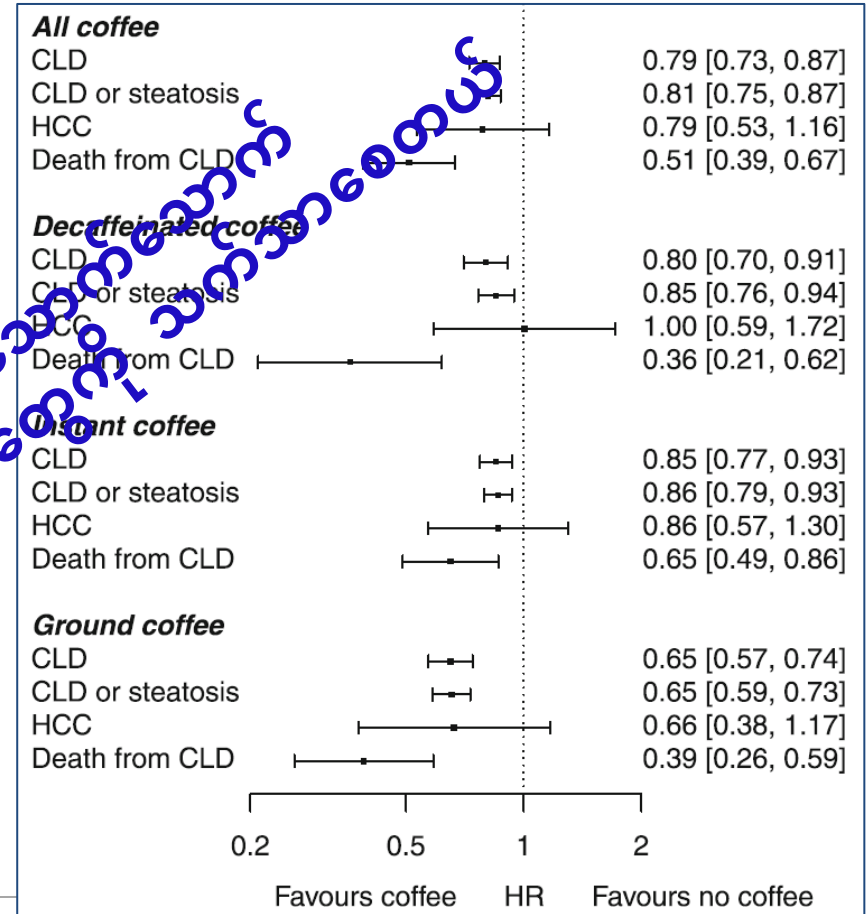
Pooled RR value 0.77 (95% CI 0.60–0.98)

Pooled RR 0.68 (95% CI 0.68–0.79)

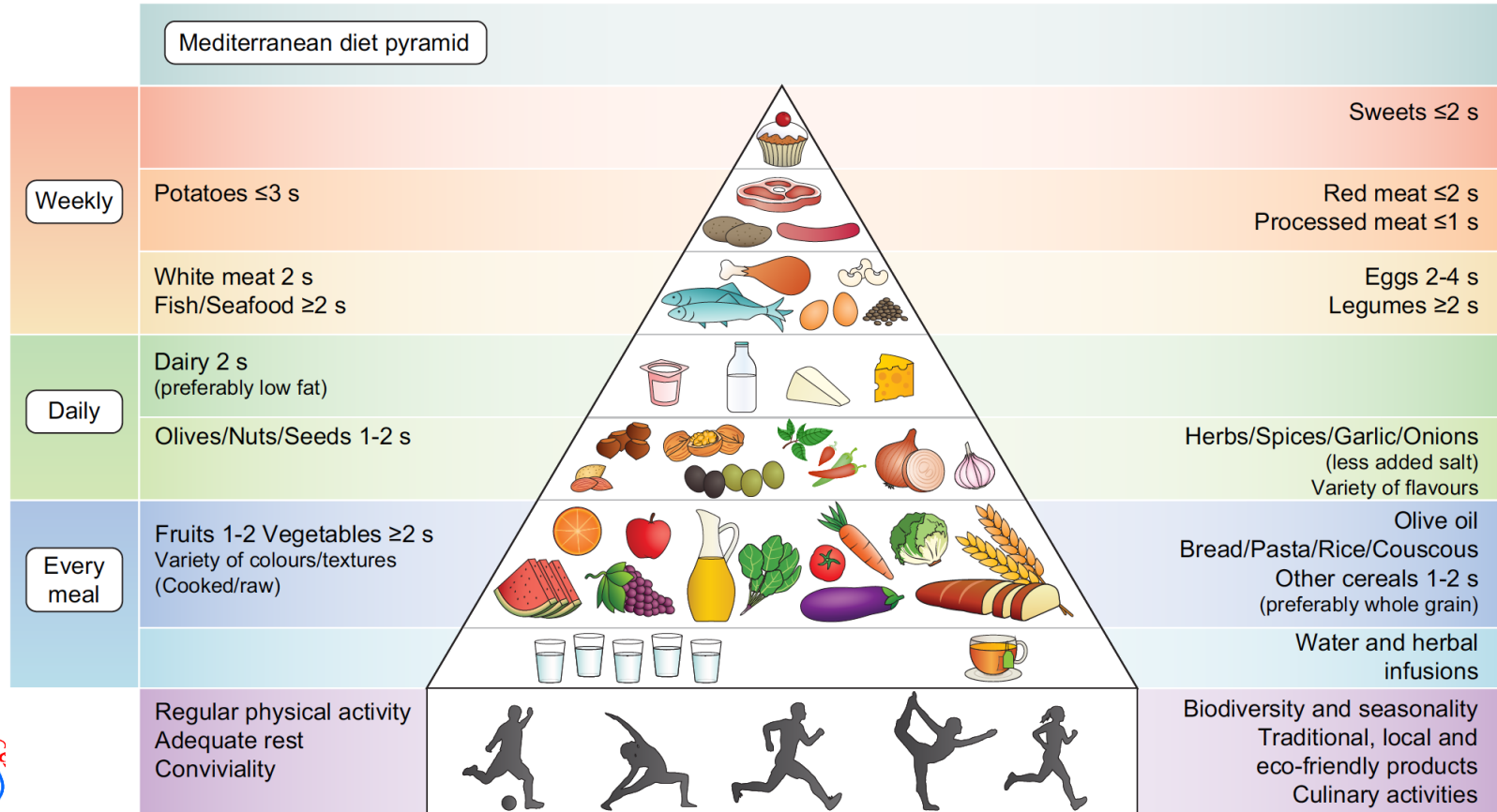
All coffee types decrease the risk of adverse clinical outcomes in chronic liver disease

- 494,585 UK Biobank participants
- Linkage to hospital, death and cancer records
- Adjusted HRs: age, sex, deprivation, smoking status, diabetes, ethnicity, alcohol

အားလုံးသုံးဆောင်မှုသည် ကျန်းမာရေးအကျိုးကျေးဇူးများကို ဖြစ်စေသည်။

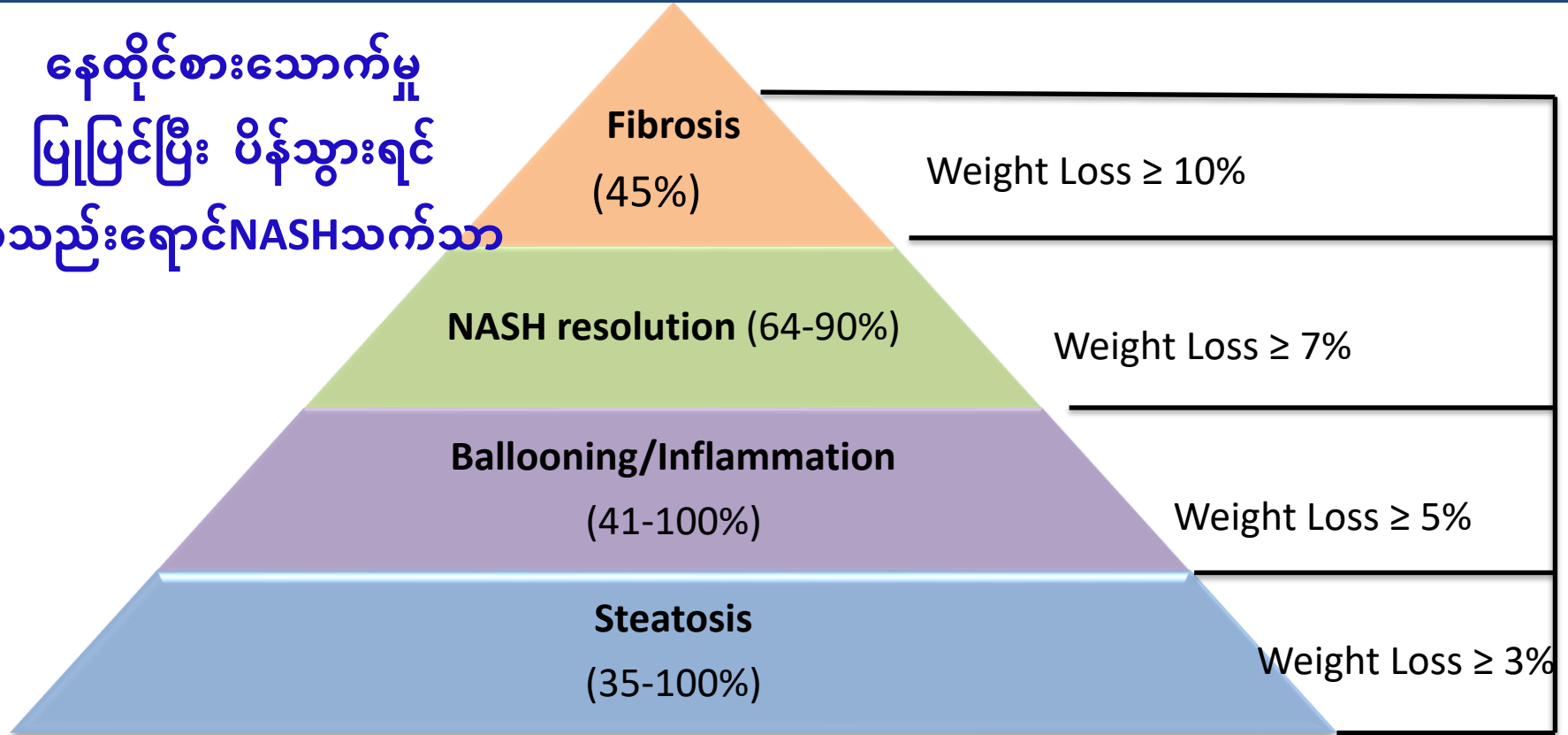


Mediterranean Diet Pyramid



Weight Loss Through Life-style Modification Reduces NASH

နေထိုင်စားသောက်မှု
ပြုပြင်ပြီး ပိန်သွားရင်
အသည်းရောင် NASH သက်သာ



Alternatives Anti-Obesity Approaches

ပိန်အောင်လုပ်တဲ့နည်းတွေ

FDA Approved Anti-Obesity Drug

Bariatric Endoscopy

Bariatric Surgery



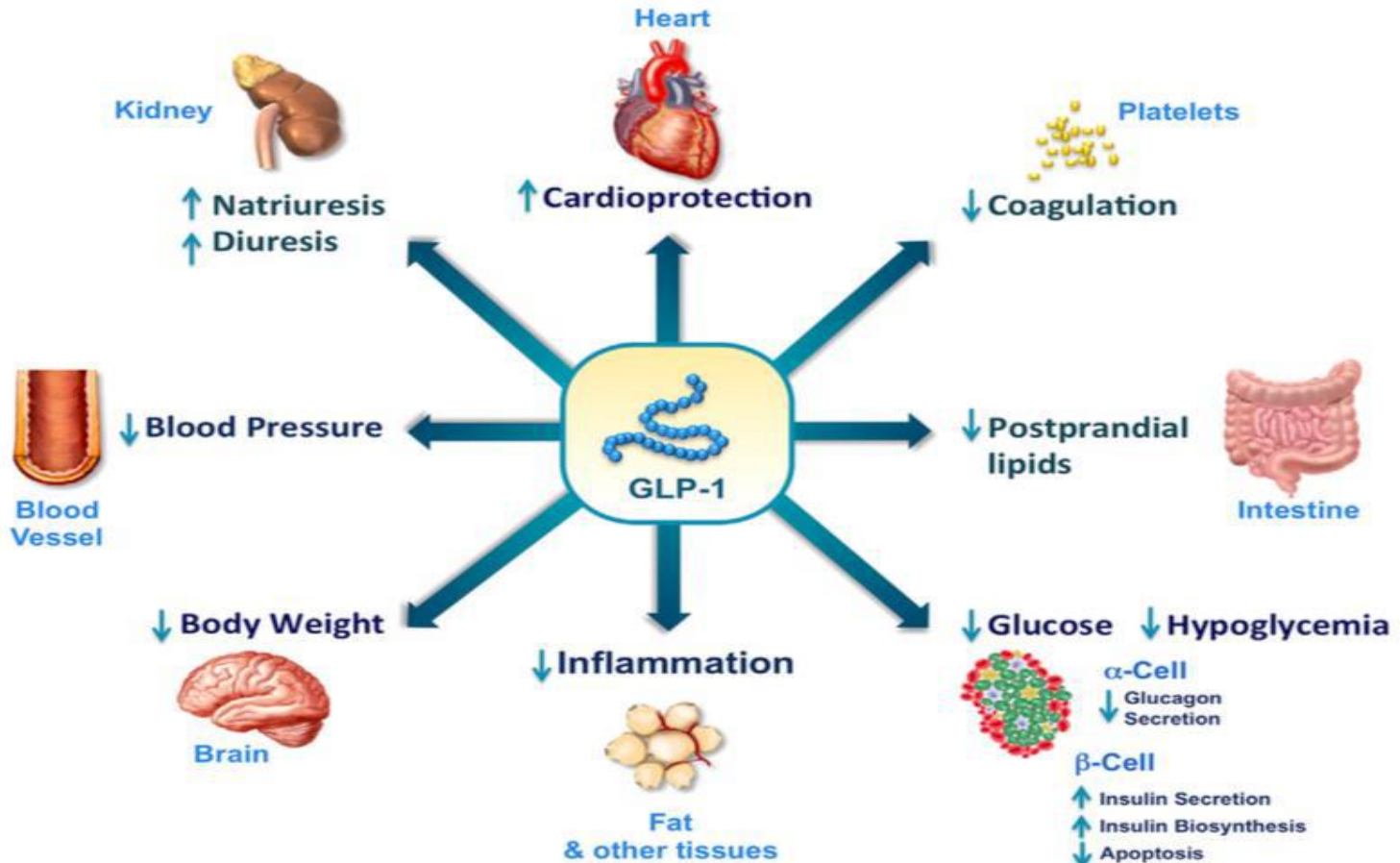
Pharmacotherapy Targeting Weight Loss and Insulin Resistance (Off Label)

Mechanism of Action	Compound	Weight Loss	Trial in NASH/NAFLD	Outcome
GLP-1 RA	Exenatide	+	Phase 2b	Improvement of hepatic steatosis by US
	Laraglutide	<div style="border: 1px solid red; padding: 5px; text-align: center;"> + <u>Approved for Obesity</u> </div>	L Trial	Resolution of NASH without worsening fibrosis
	Semaglutide	<div style="border: 1px solid red; padding: 5px; text-align: center;"> +++ <u>Approved for Obesity and DM</u> </div>	Phase 2b	Resolution of NASH without worsening fibrosis
SGLT2	Canagliflozen	++	Multiple studies	Improvement in liver TG by 1H-MRS; improvement in steatosis biomarkers
	Empagliflozin	+	Multiple studies	Improvement in liver fat by MRI-PDFF Improvement in CAP and liver stiffness by TE

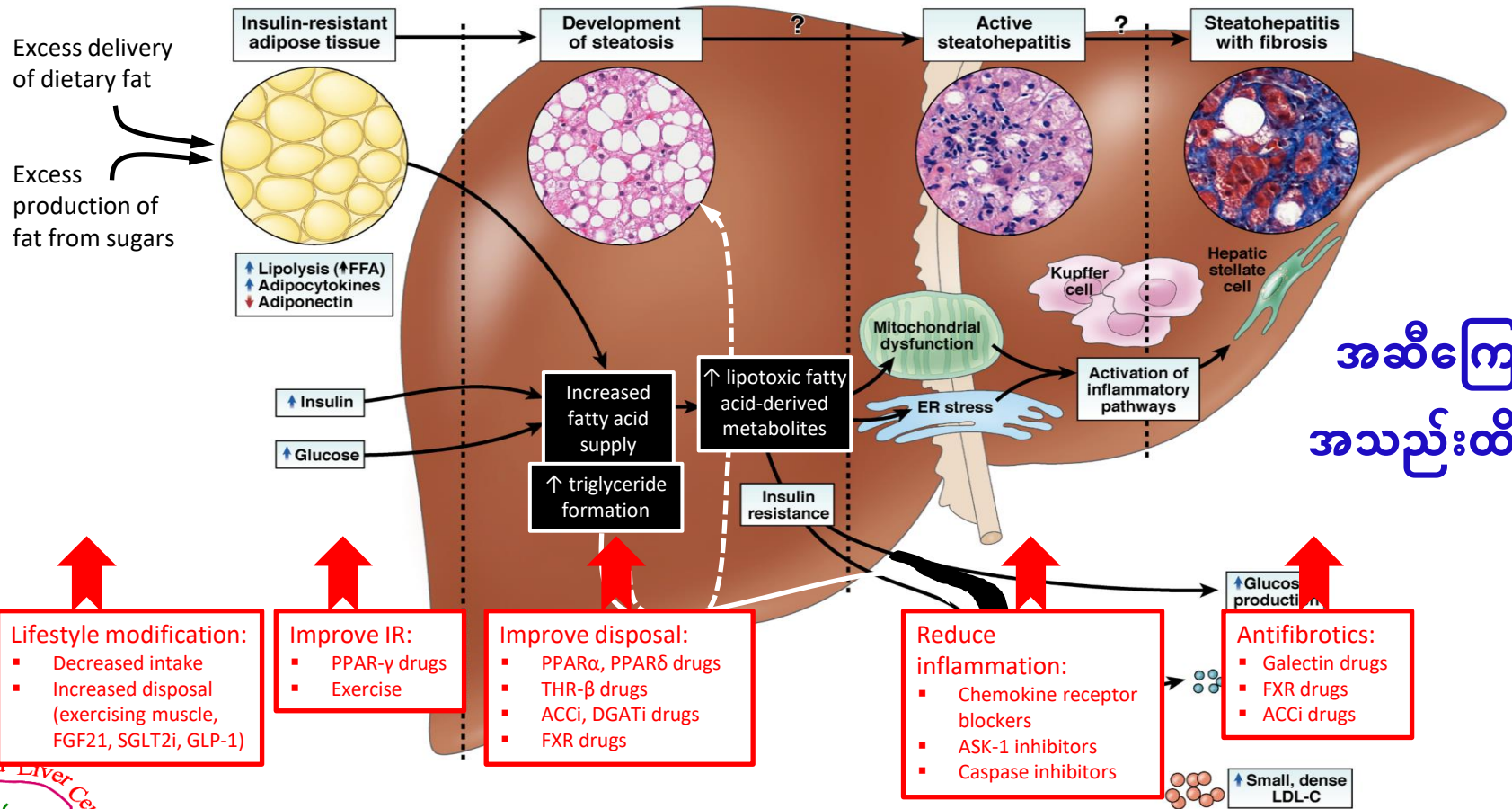
Shao. Diabetes/Metabolism Research Reviews. 2014;30:521. 2. Armstrong. Lancet. 2016;387:679-690. 3. Newsome. NEJM. 2021;384:1113. 4. Cusi. Diabetes Obes Metab. 2019;21:812. 5. Kuchay. Diabetes Care. 2018;41:1801. 6. Taheri. Advanc Ther. 2020;37:4697.

Systemic effects of GLP1-RA

ပိန်ဆေးထိုးဆေး GLP1-RAရဲ့ အကျိုးသက်ရောက်မှုတွေ



From Stressed Adipocytes to Hepatic Lipotoxicity, Inflammation, and Cirrhosis



အဆီကြောင့်
အသည်းထိခိုက်

Pharmacologic Therapy for NASH

No FDA approved drugs for NASH

Available Therapies for Off-Label Use



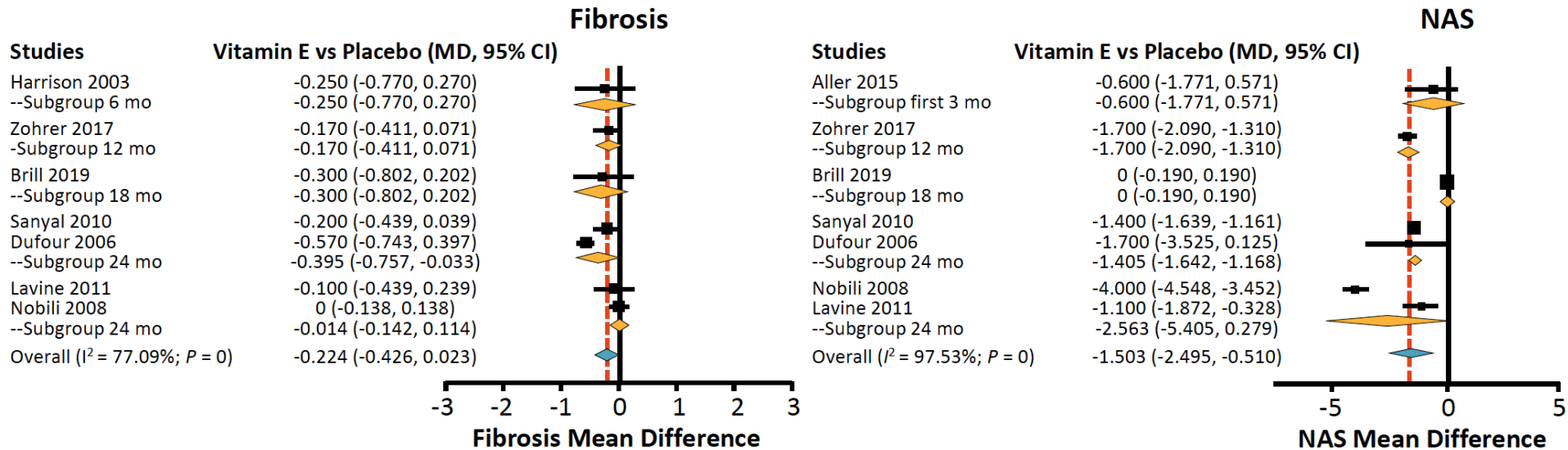
အသည်းအဆီဖုံး အသည်းရောင်ကုတဲ့ဆေးတွေ

Vitamin E ဗီတာမင်အီးဟာ အသည်းအဆီဖုံး ရောဂါသည်တွေမှာ

- အသည်းရောင်တာ
 - အသည်းမာတာ
- } ကိုကာကွယ်

Vitamin E Reduces NAS and Fibrosis in NAFLD

- Meta-analysis of N = 1317 patients with NAFLD in 15 RCTs
- Study limitations: variations in definition of NAFLD; moderately small sample sizes

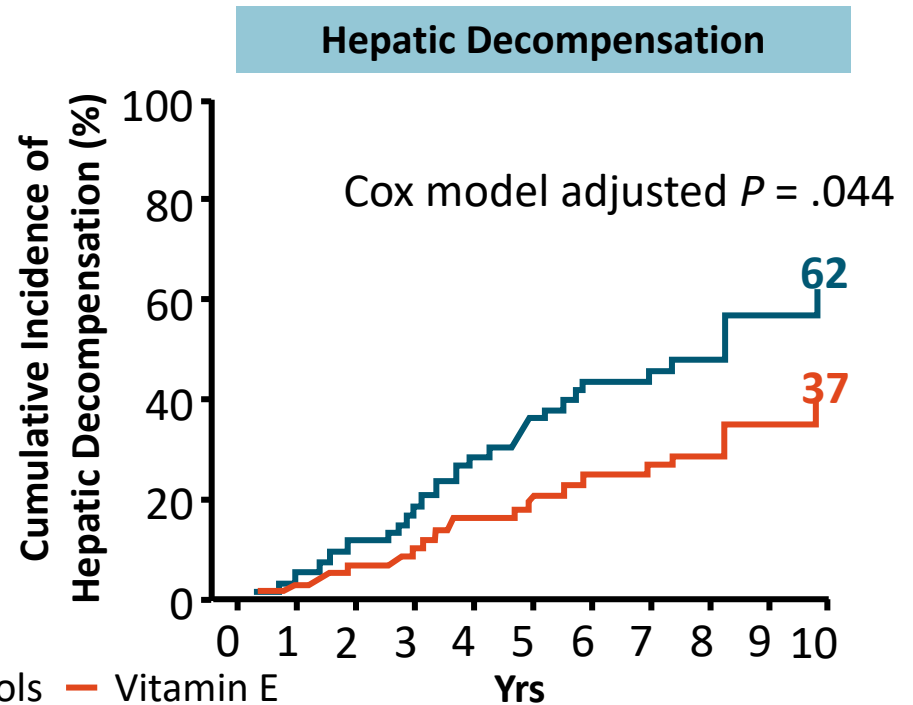
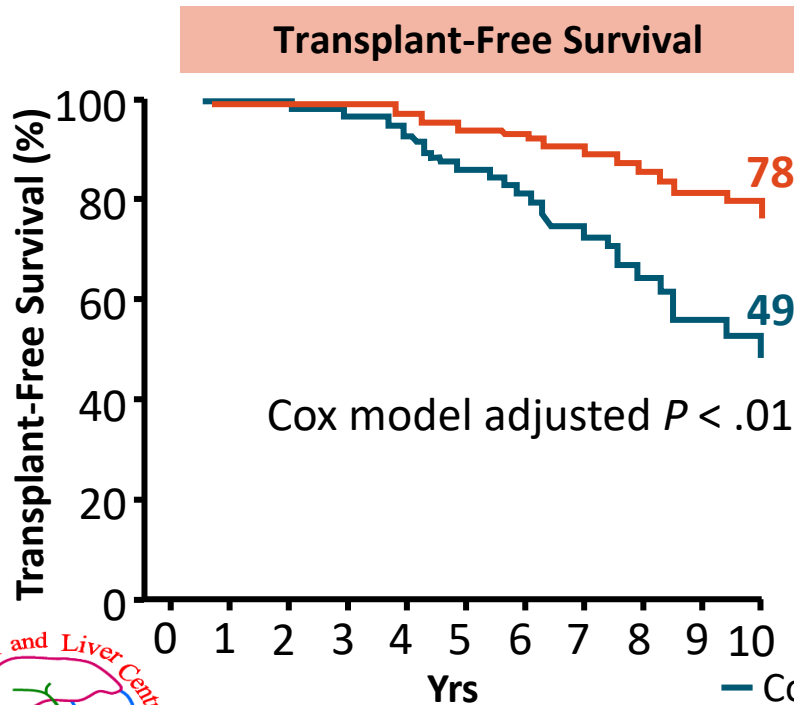


- Most promising patient for vitamin E treatment: an obese patient aged 15-50 yr, baseline AST >50 IU/L, daily intake of 400-800 IU vitamin E, liability to lose 5-10 kg

အသည်းအဆီဖုံး အသည်းရောင်ရောဂါသည်တွေမှာ
Vitamin E ဟာ ရောဂါပိုဆိုးမသွားအောင် အသည်းအစား
မထိုးရအောင်ကာကွယ်

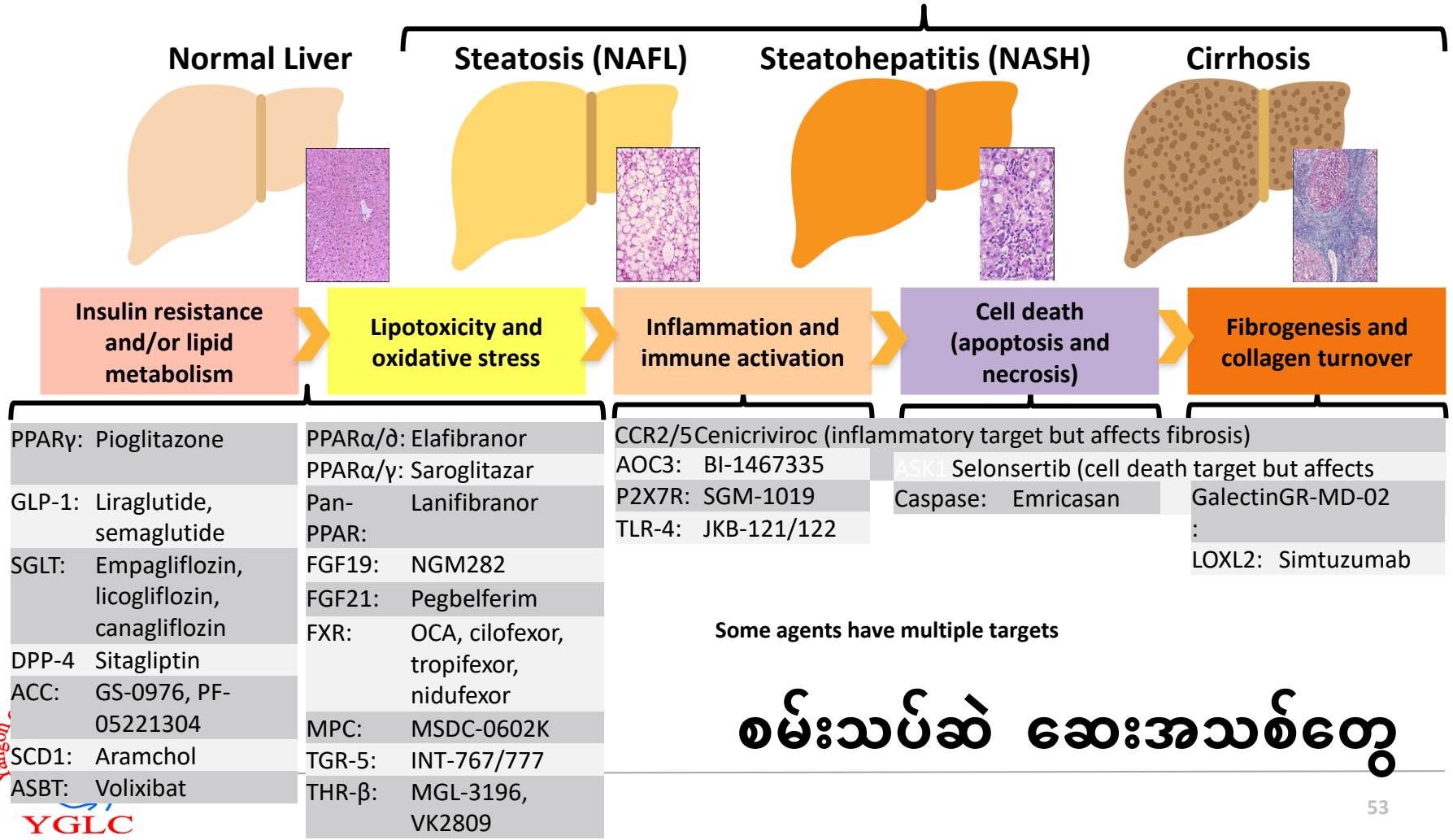
Vitamin E Improves Transplant-Free Survival and Hepatic Decompensation in NASH

- Single-center study of patients with biopsy-proven NASH and bridging fibrosis or cirrhosis (N = 236) followed for median 5.62 yr



Examples of NASH Treatments in Phase II or III Investigations

NAFLD



စမ်းသပ်ဆဲ ဆေးအသစ်တွေ

Yangon

- အသည်းအဆီဖုံး ရောဂါကို ကမ္ဘာ့နိုင်ငံအသီးသီးက ဘယ်လိုမြင်ကြသလဲ။
- ကာကွယ်ကုစားဖို့ ဘယ်လိုပြင်ဆင်ထားသလဲ။
- လူမသိ သူမသိ တိတ်တခိုး အသည်းအဆီဖုံးရောဂါကို အလေးထား ဦးစားပေး ထိန်းသိမ်းဖို့ နိုင်ငံအသီးသီးက ဆောင်ရွက်ဖို့ အသင့်ဖြစ်နေပြီလား။

The Global NAFLD Policy Review and Preparedness Index: Are Countries Ready to Address this Silent Public Health Challenges?

NAFLD preparedness index scores for 102 countries

- About a third of countries (n = 32/102) scored zero on the preparedness index.
- No country had a national or sub-national strategy for NAFLD.
- NAFLD was **rarely mentioned** in the strategies of related conditions such as diabetes.
- **Only 32 countries had national NAFLD clinical guidelines.**
- **A comprehensive NAFLD public health response is lacking in all 102 countries.**

