Interventions to maintain a healthy Liver

66th NAMS Foundation Day

Subrat K Acharya

Pro-Chancellor KIIT University

Executive Director Gastroenterology, Fortis Escort Digestive & Liver diseases, New Delhi

Emeritus professor Gastroenterology , AIIMS

Why the Liver Matters

500+

Functions performed by the liver

1.5 kg

Average weight of an adult liver

75%

Liver can be removed and still regenerate

Core Liver Functions

Detoxification

Filters blood & neutralizes toxins, drugs, alcohol

Metabolism

Regulates glucose, fats & protein breakdown

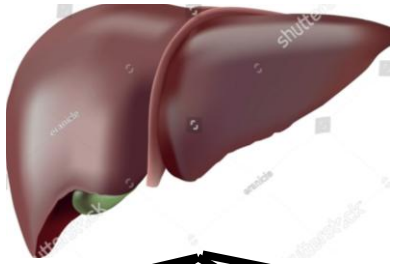
Bile Production

Produces bile for fat digestion & cholesterol excretion

Immune Defence

Kupffer cells remove bacteria & foreign particles

Liver Performs multiple Important Functions



Metabolic Function

Food Processing

Carbohydrate/Protein/ Fat

Synthetic Functions

Proteins : Albumin

Clotting Factors

Fat synthesis

Bile Acids Synthesis

Detoxification

Food processing byproducts

Ammonia disposal

Drugs/Anesthetic agents

Alcohol

Immune Function

Barrier between environment and body

Opsonic proteins

Complements

Resident macrophages

Global burden of liver disease: 2023 update

2 million deaths worldwide

1 out of 3 liver deaths among females

11th leading cause of death worldwide

15th leading cause of disability-associated life-years

Cost of liver disease in the United States (2016): $32.5 billion

Devarbhavi H et al J hepatology 2023. vol. 79 j 516–537

Aetiology of Liver Disorder

1. Alcohol
2. Obesity- MASLD (Metabolic dysfunction) – Increase Cardiometabolic risk)
3. Met- ALD (Obesity and small amount of alcohol)
4. Diabetes *de-novo*
5. Alcohol-Diabetes and Obesity
6. Drugs
7. CAMs
8. Hepatitis

- Acute Liver Injury
- Chronic Liver Injury
- Sequels of Chronic Liver injury : Cirrhosis , HCC, ACLF & Liver Failure

Whole spectrum are Preventable and one can keep the liver healthy

Alcohol

Alcohol –Global Burden(WHO 2024)

- Globally 43% consume Alcohol – AUD : 400 million(7 % world population)
- 2.6 million deaths : 2019 ; Increasing (20% increase from 2010)
- AUD (AUDIT)-WHO 10 point questionnaire(4 score each = 40 total)

  Risk of Liver disease increase by 260 times(35% develop liver disease ; Age 15 -44 yrs)

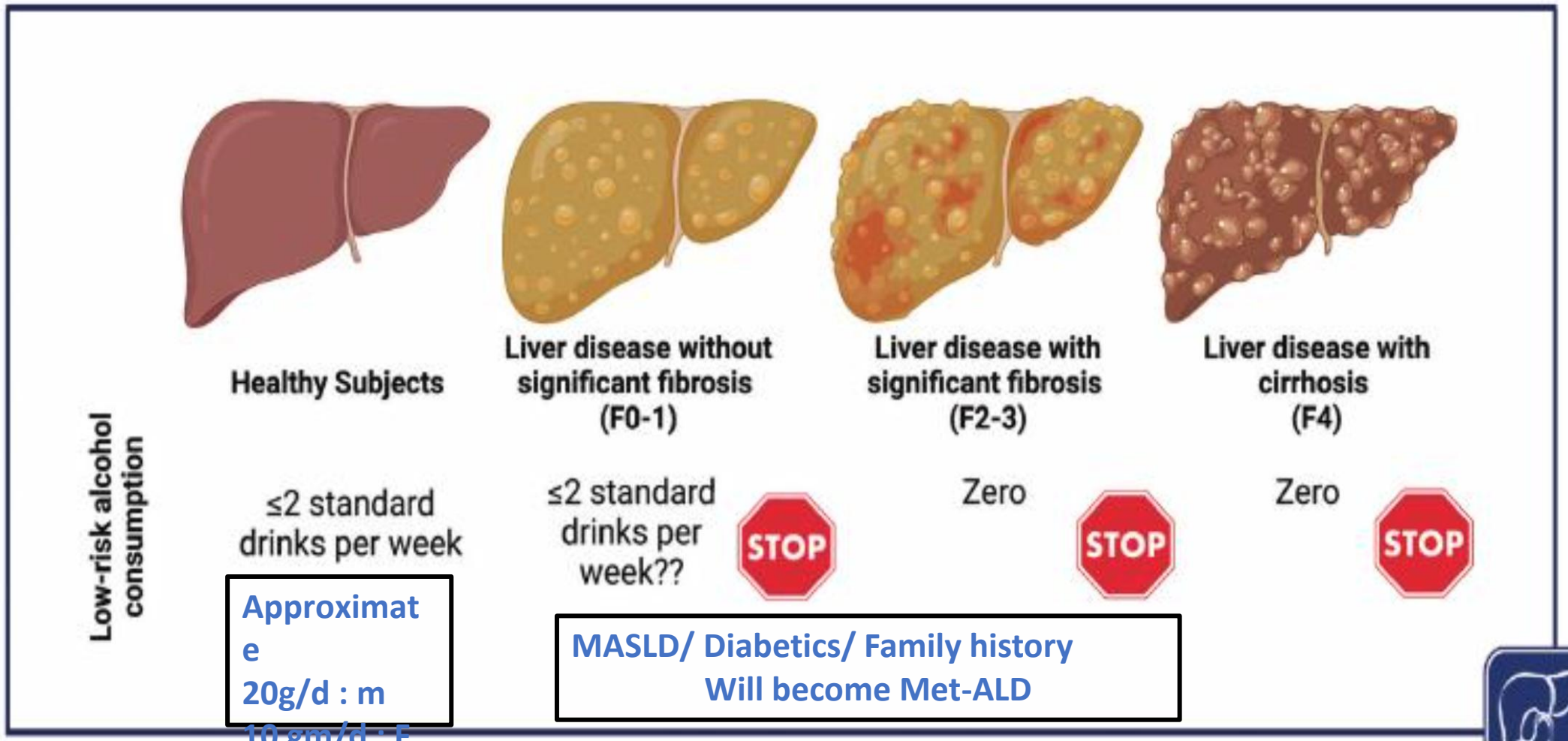
  CVS increase by 3.2 times

  Cancer increase by 5 times(2019; 4.4% Cancer deaths were attributed to alcohol)

- Aetiology of Cirrhosis : Changed to alcohol in 60%
- Potentiation (Synergistic effect) . T2DM , Obesity – Met-ALD ; Rapid progress

Semin Liver Dis 2024;44:69–78.

How much Alcohol is Safe ??



How much Alcohol is Safe

AUDIT: score 40

- Consumption
- Dependency
- Behavior/harm

0-7 : Low risk

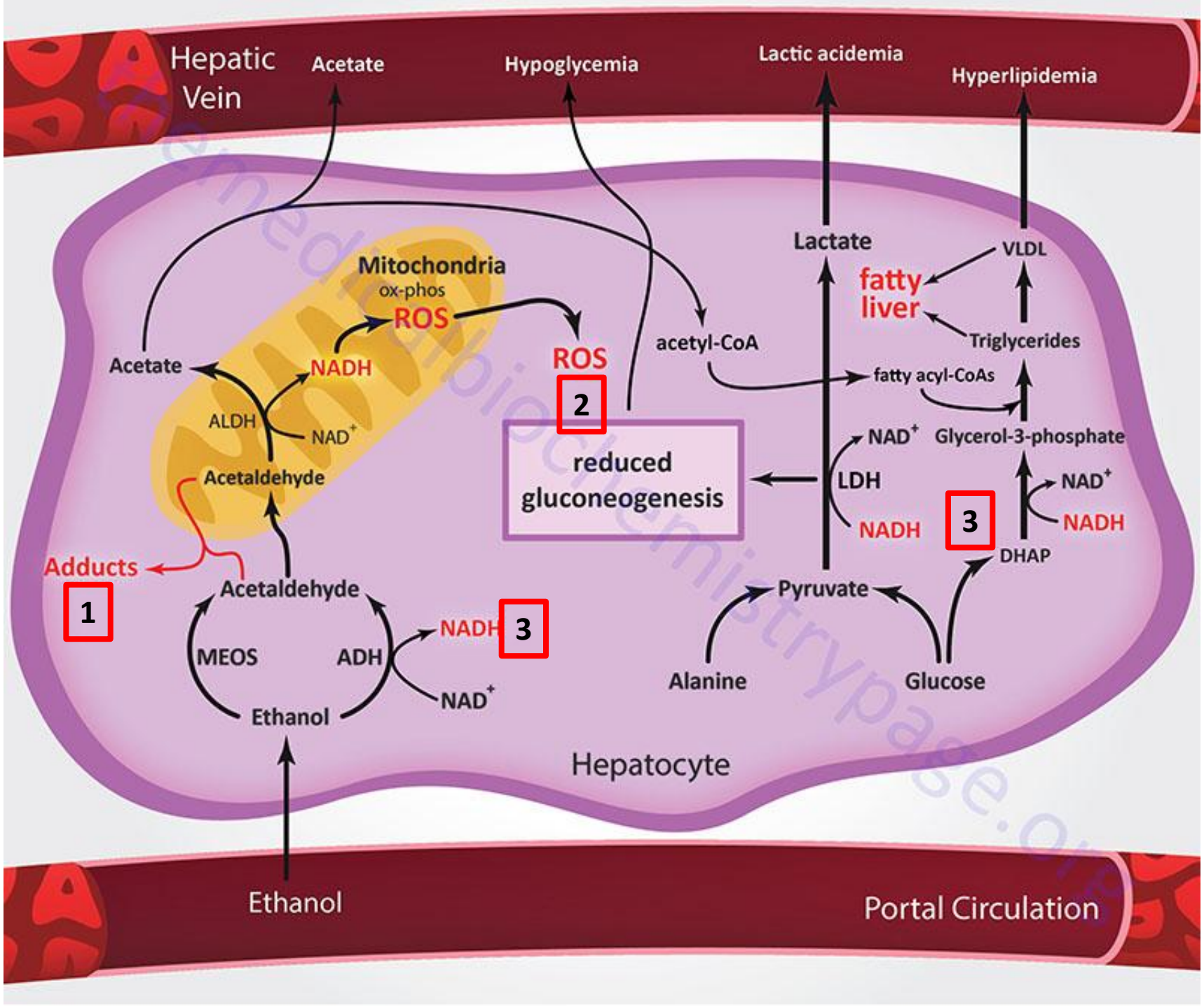
8-15: Hazardous

16-19: Treatment

20-40: Disease

Diagnosis	ALD	MetALD	MASLD
Alcohol amount (g/week)	>350 for women >420 for men	140-350 for women 210-420 for men	≤140 for women ≤210 for men
Alcohol Use Disorder (AUD) AUDIT	75-80%	5-12% or higher	No
Metabolic Dysfunction	Not required	At least one metabolic dysfunction	Metabolic dysfunction is the key disease driver
Spectrum	Steatosis Steatohepatitis Cirrhosis HCC Alcohol-associated hepatitis/ACLF	Steatosis Steatohepatitis Cirrhosis HCC ACLF	Steatosis Steatohepatitis Cirrhosis HCC ACLF

Alcohol induced
Metabolic alteration
Liver Damage



How much Alcohol is safe ????

World Health Organization

Deaths from excessive alcohol use :178,000/ Yr in developed/developing countries : about 500 die / day ????

No level of alcohol consumption is safe for our health

Carcinogenic, Liver damage , Pancreatitis , Cardiomyopathy

Life Style & Obesity

Life Style & Obesity

MASLD :60 -70%

In India:

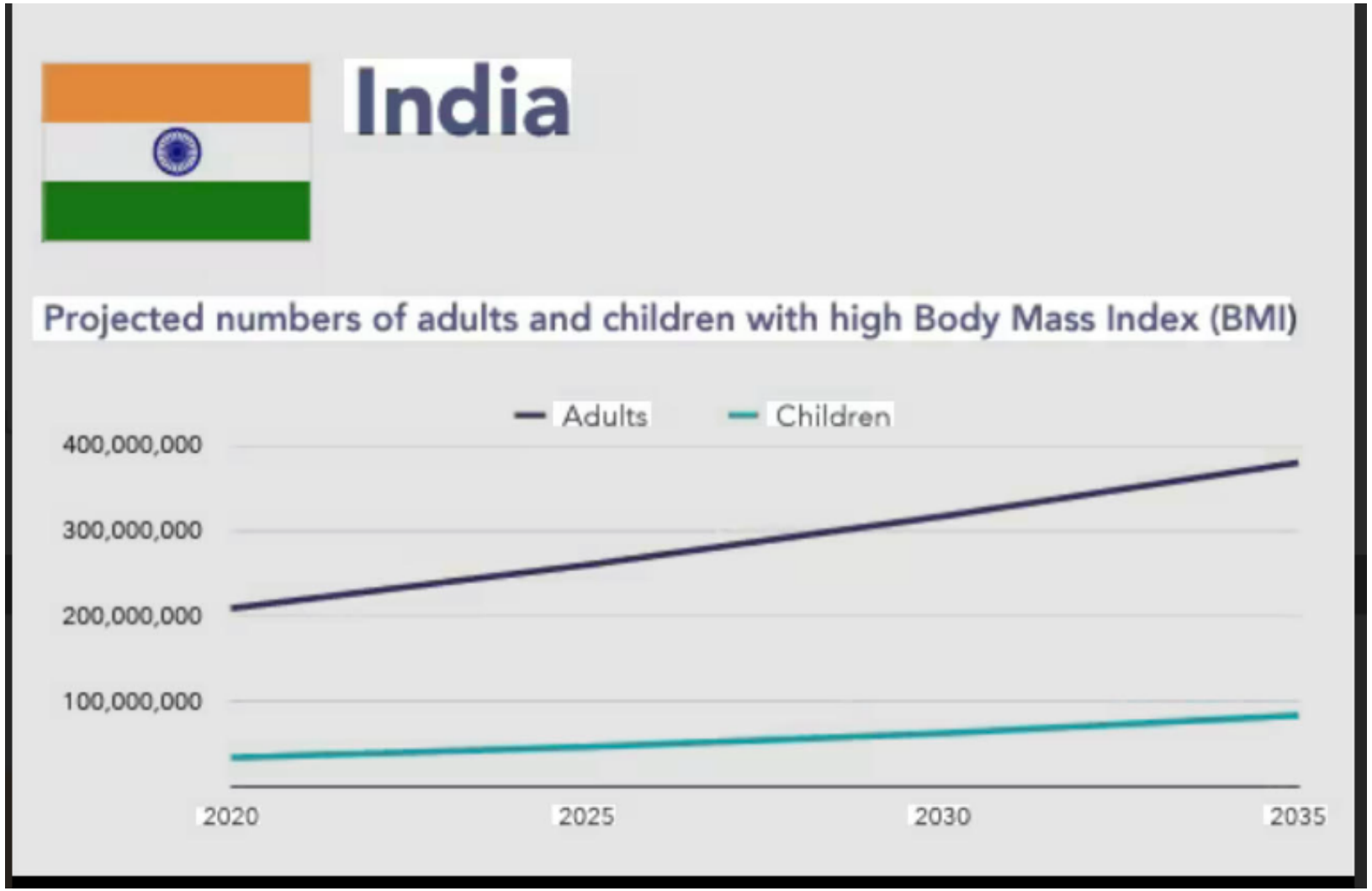
- 27 million Children < 16 yrs
- 254 million Adults Obese(BMI>25)
- 351 million abdominal Obesity
- 1 in 4 Cardivascular fitness

World Obesity Federation (WOF):

2030: 1.1 billion Obese adults .

2060: Global Medical > ₹1544 trillion

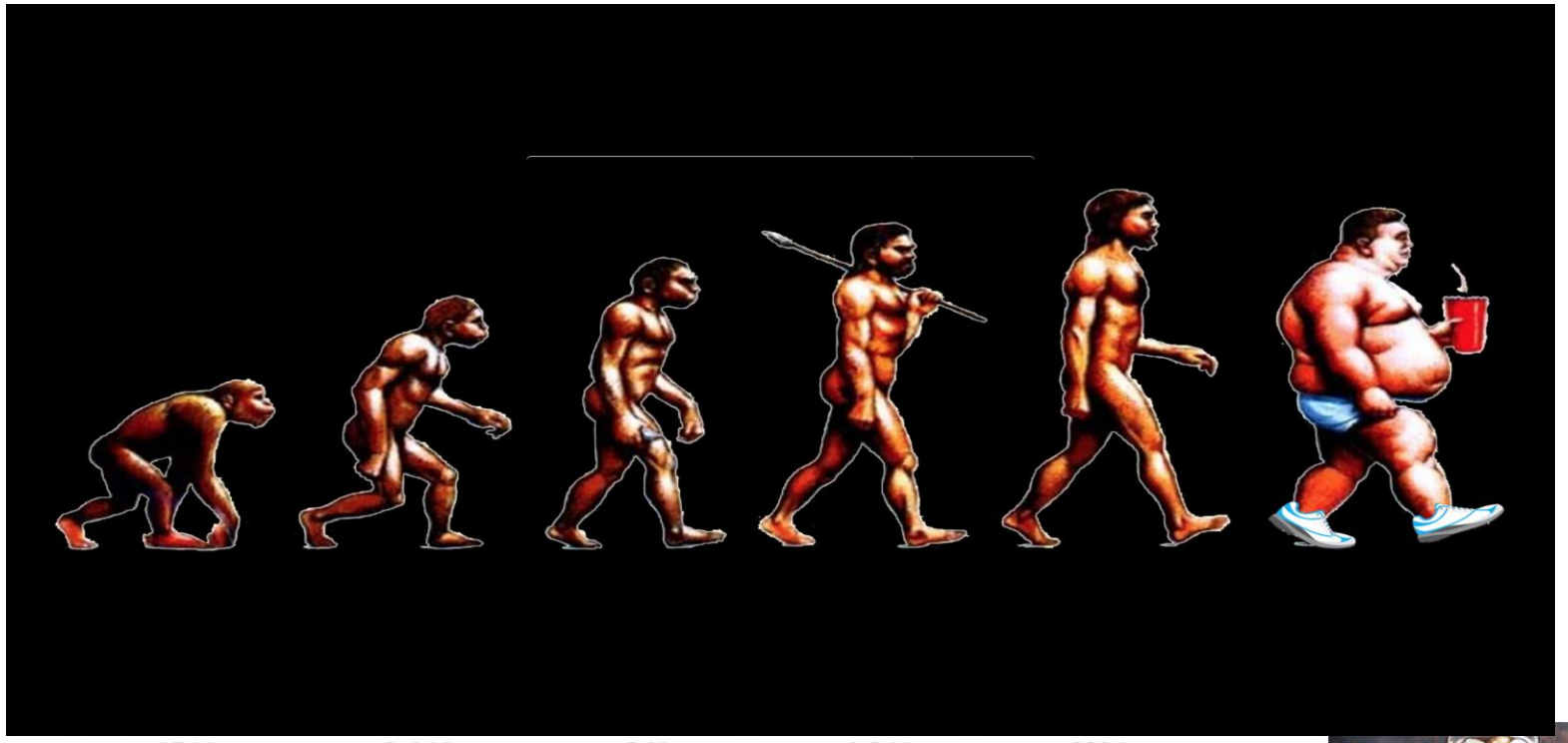
(converted on 2/1/2025 at 1$ to ₹ 85)

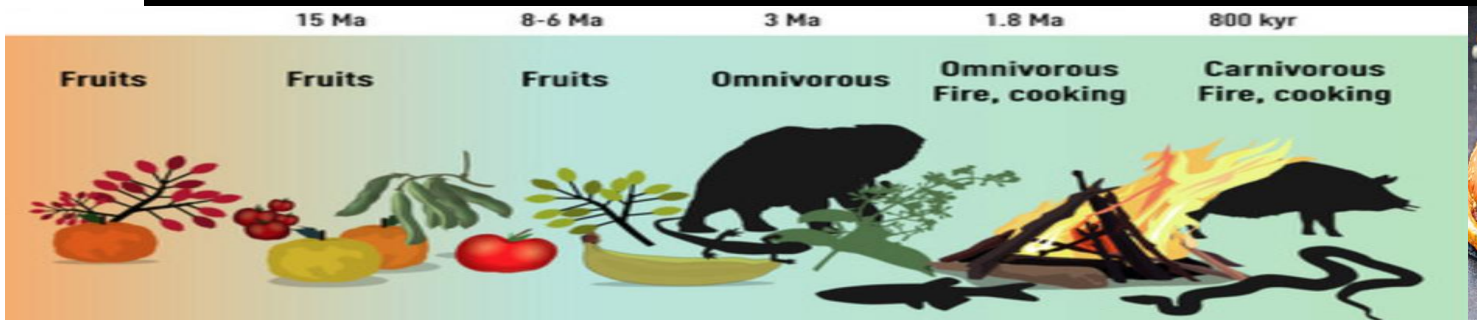


WHO. Obesity. https://www.who.int/health-topics/ obesity#tab=tab_2024

Life Style Change

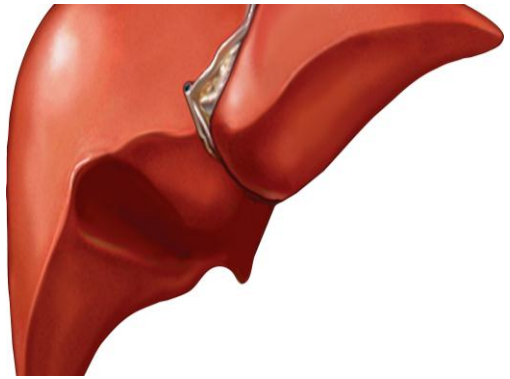
1. **Dietary excess**
2. **Refined Sugars**
3. **Food with high Glycemic index**
4. **Sedentary hobbits**
5. **Prolonged Sitting**
6. **Alcohol**
7. **Sleep**
8. **Mental health**
9. **Pollution**
10. **Genetic risks : Asians: SAT VS VAT**

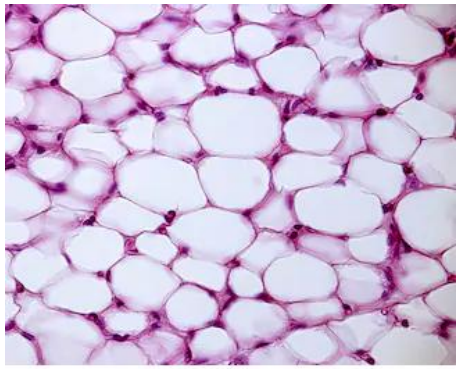




Review-Symposium
Evolutionary basis for the human diet: consequences for human health *P. Andrews R.J. Johnson*
First published:16 November 2019 https://doi.org/10.1111/joim.13011Citations: 2

Metabolic Switch : Fed state Vs Non-Fed State





Glucose burning-TCA

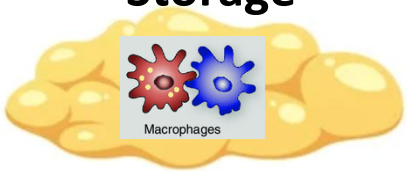
Fat burning
Ketones

FED State : Glucose is Energy

Non-FED State : Fat burning

Nutrient Excess – Decrease Energy Requirement
Energy Storage

Energy Storage



→ Inflammation

Excess Fat

↓

Asian: more Visceral Fat(Liver , heart , muscles , Vessels)

↓

Insulin Resistance

↓

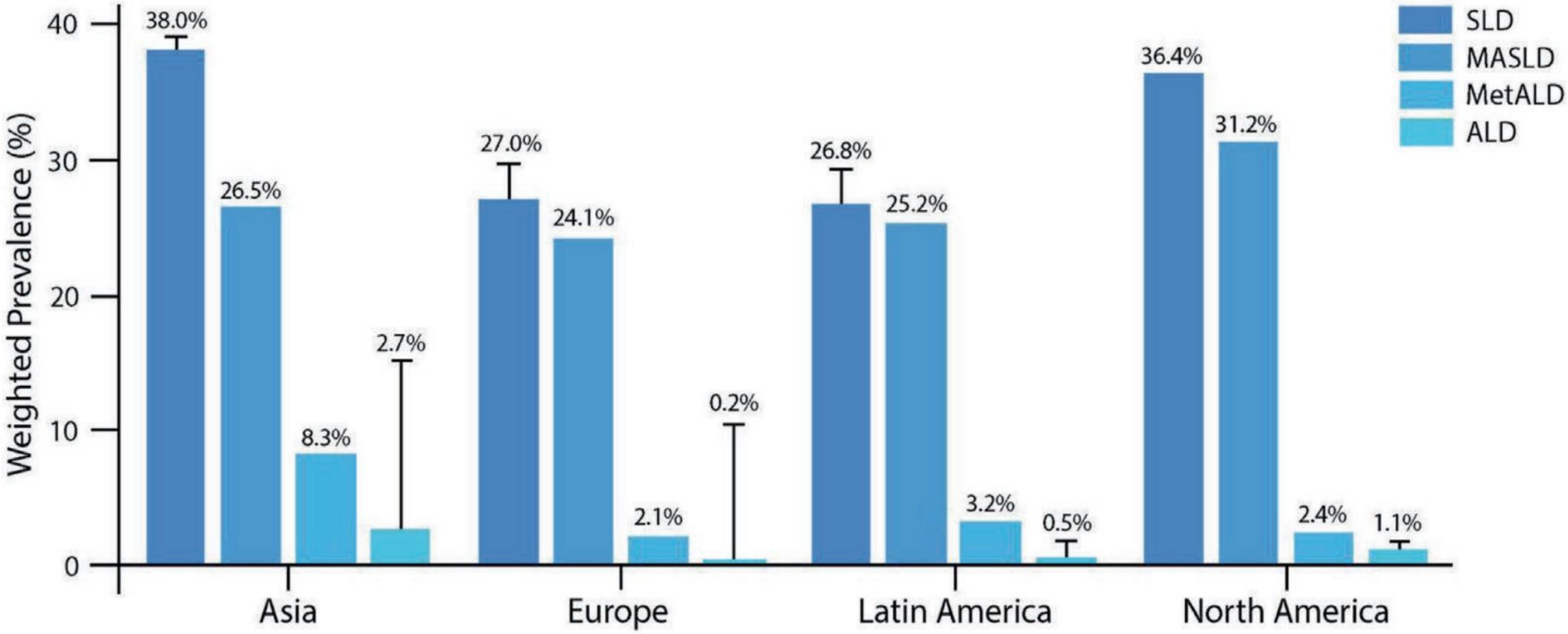
Diabetes / Fat in blood & vessels / heart disease / CVA

SAT VS VAT

Obesity(Public Health problem)

Low grade Inflammation – Adipose Tissue macrophages

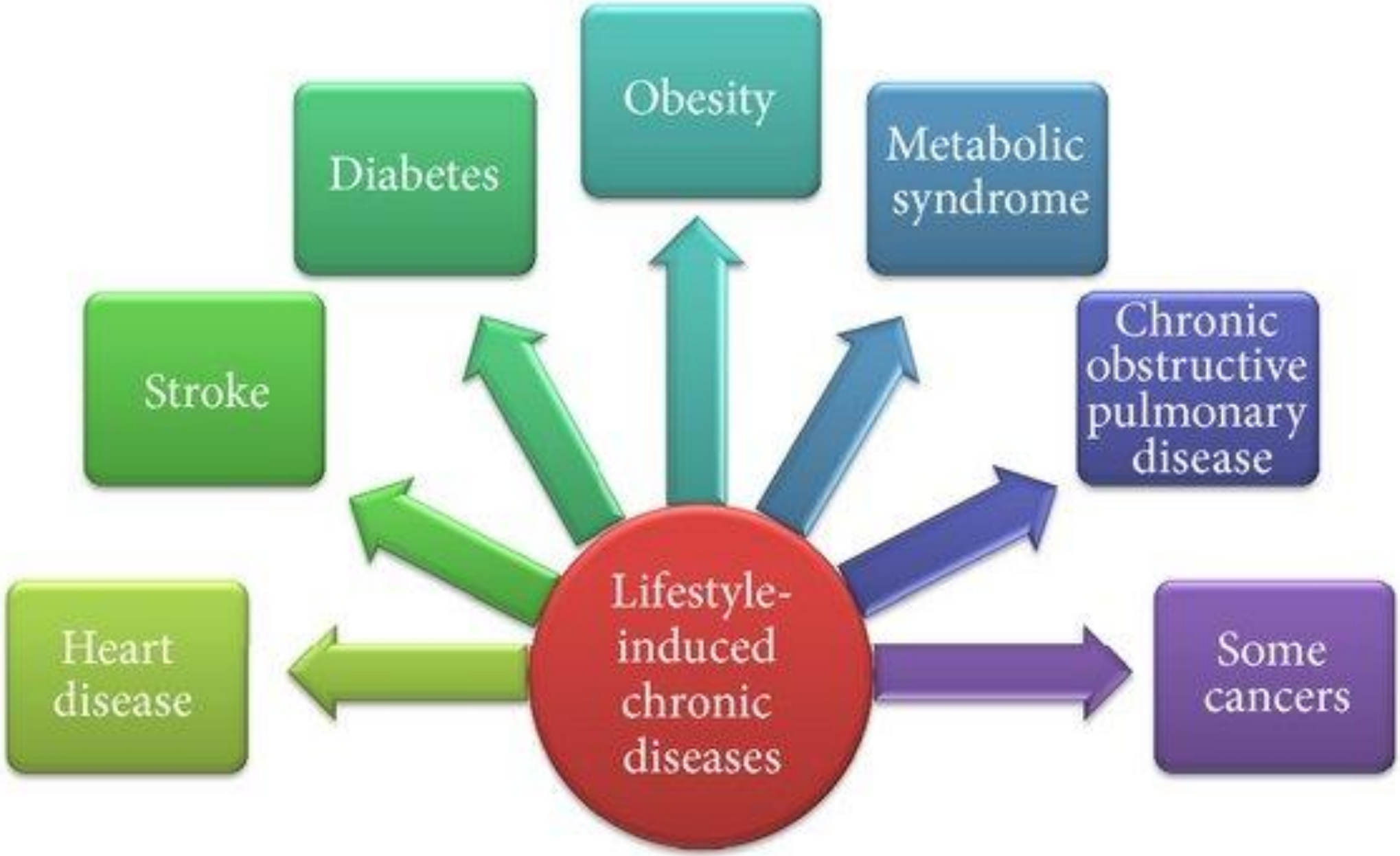
Regional Prevalence of SLD, MASLD, Met-ALD, ALD



Liver International, 2025; 45:e70017 PP:1-18
https://doi.org/10.1111/liv.70017

What Happens when Life-style changes results in

Obesity / Insulin Resistance / increase fat in blood


Obesity
Diabetes
Metabolic syndrome
Stroke
Chronic obstructive pulmonary disease
Heart disease
Lifestyle-induced chronic diseases
Some cancers

OBESITY

Symptoms of Obesity

Obesity Types
Obesity –I
Obesity II
(If any symptoms)

How do You Know that you are over weight or obese

And

Have high risk for Cardiometabolic risks

With

Fatty liver and its consequences

- **Anthropometry : BMI , WHR , Waist Circumference , Weight/height**
- **USG abdomen and specific tests (Non invasive tests –NITs)**
- **LFT**
- **T2DM- 70-80% have Fat in liver**
- **Alcohol ; Associated with weight gain : Both causes liver damage**
- **Family history : Genes**

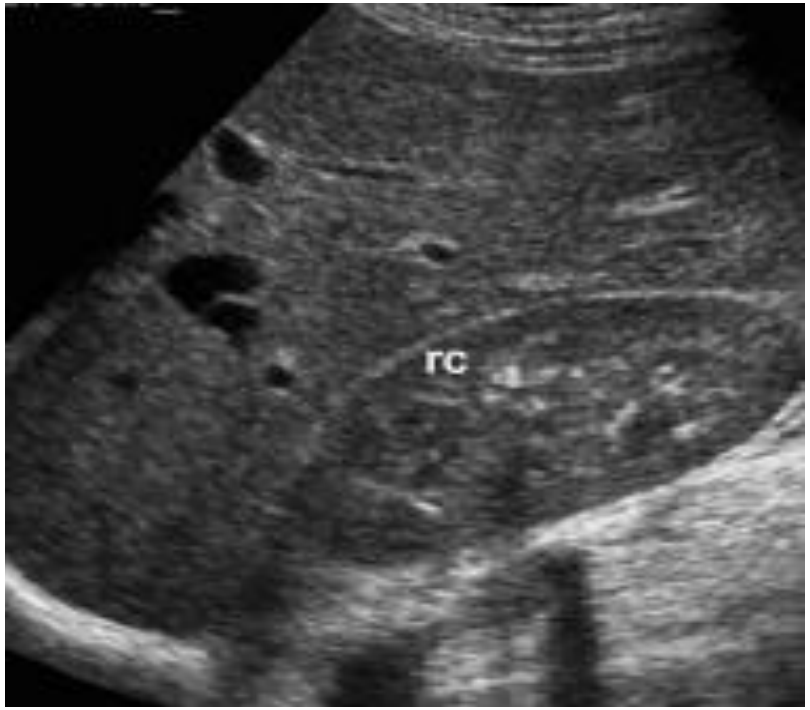
Cardio Metabolic Risk Factors

At least 1 out of 5:

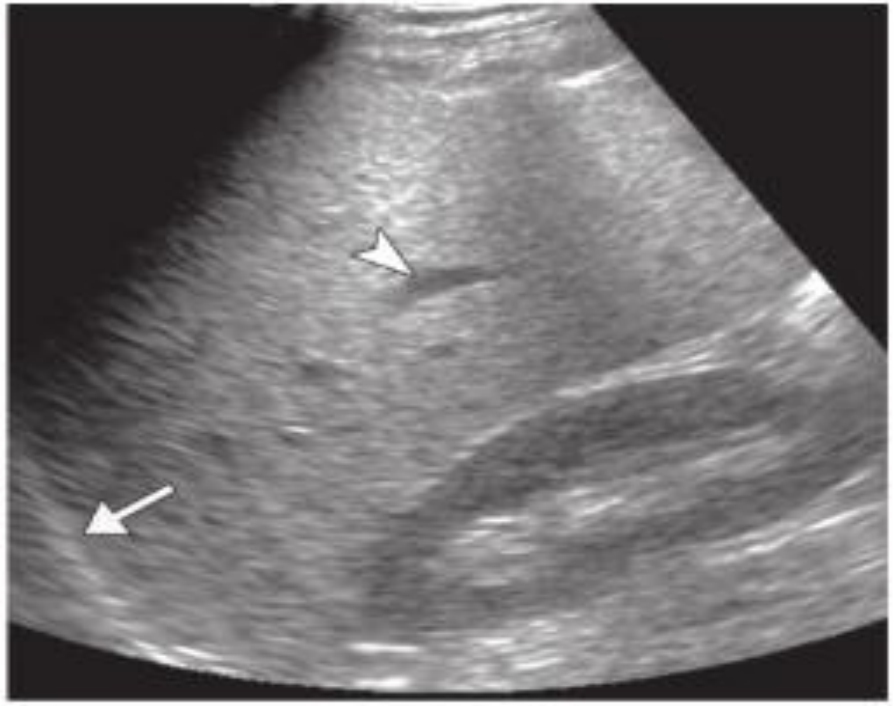
- ☐ BMI ≥25 kg/m² [23 Asia] **OR** WC >94 cm (M) 80 cm (F) **OR** ethnicity adjusted equivalent
- ☐ Fasting serum glucose ≥5.6 mmol/L [100 mg/dl] **OR** 2-hour post-load glucose levels ≥7.8 mmol/L [≥140 mg/dl] **OR** HbA1c ≥5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes
- ☐ Blood pressure ≥130/85 mmHg **OR** specific antihypertensive drug treatment
- ☐ Plasma triglycerides ≥1.70 mmol/L [150 mg/dl] **OR** lipid lowering treatment
- ☐ Plasma HDL-cholesterol ≤1.0 mmol/L [40 mg/dl] (M) and ≤1.3 mmol/L [50 mg/dl] (F) **OR**

USG

Normal Liver



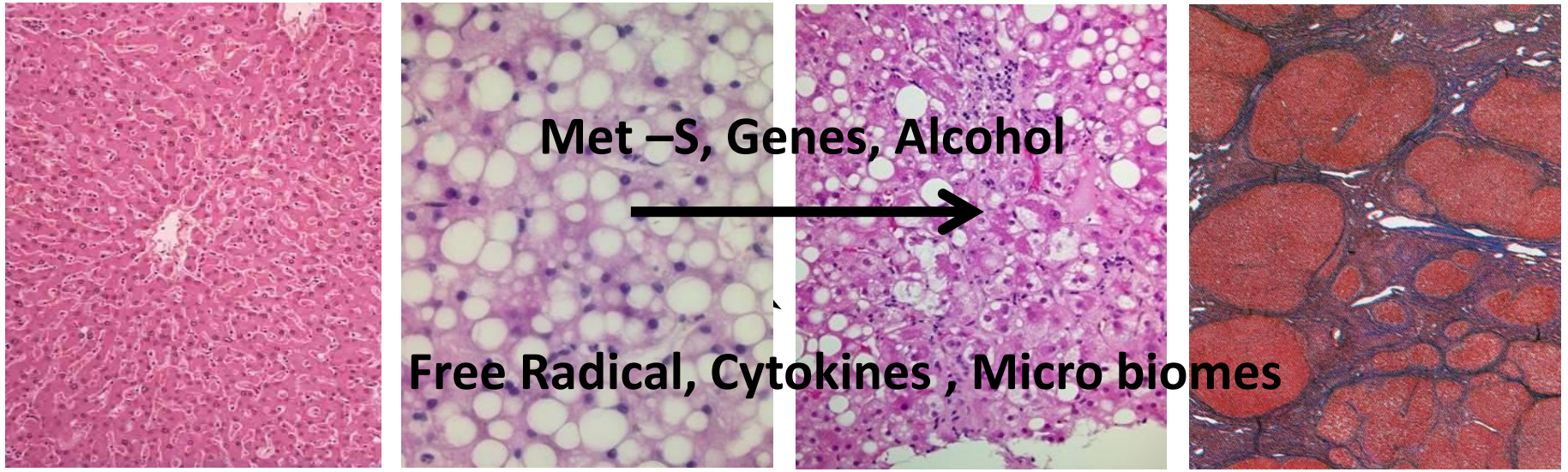
Fatty Liver



- **Echo: Liver >Renal Cortex**
- **Image of vessels & diaphragm: Poor**

Spectrum of MAFLD

Fat in Liver due to Obesity/T2DM/ Risk factor is a warning for multisystemic disease



Normal

Steatosis (MAFL)

Steatohepatitis (MASH)

Fibrosis/ cirrhosis

Liver Related mortality X
CVA Related mortality +
Cancers +
MET-S +

Liver Related mortality ++
CVA /Cancers +
All Cause mortality ++

Prevalence

Gastroenterology May 2025

Group	Value
Global NAFLD prevalence (2016–2019)	38% **India : Adults 38% Children :35%**
Highest global NAFLD prevalence	Middle East and North Africa (42.6%)
Prevalence of lean MASLD in general population	5%-7%
Prevalence of lean NAFLD within the NAFLD population	20% in the western and eastern hemispheres ~ 40% (nonobese) in eastern hemisphere

Prevalence of Progressive MASH

F1–F2 prevalence in general population	7%–8%
F3–F4 prevalence in general population	1%–2%
Incidence of NAFLD	48.89–50.09 per 1000 person-years

Mortality Rates

All-cause mortality	12.61–7.1 per 1000 person-years
Cardiac-specific mortality	4.2–5.5 per 1000 person-years
Extrahepatic cancer mortality	2.8–4.2 per 1000 person-years
Liver-specific mortality	0.92–1.75 per 1000 person-years

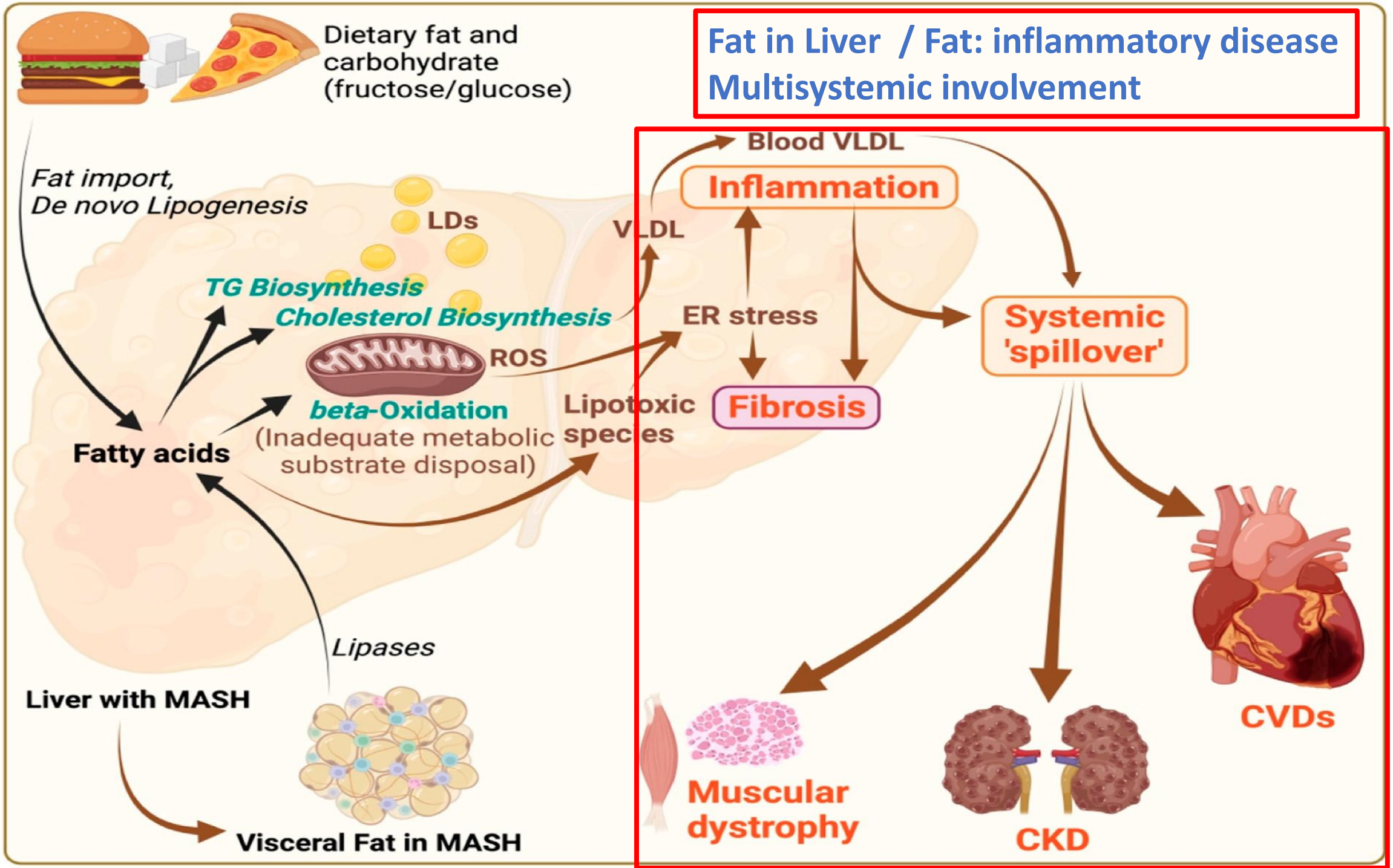
Global Statistic Included Indian Data INASL :JCEH2023

T2DM: **MAFLD /MASH:60% & 37%**

Obesity: **80% & 31%**

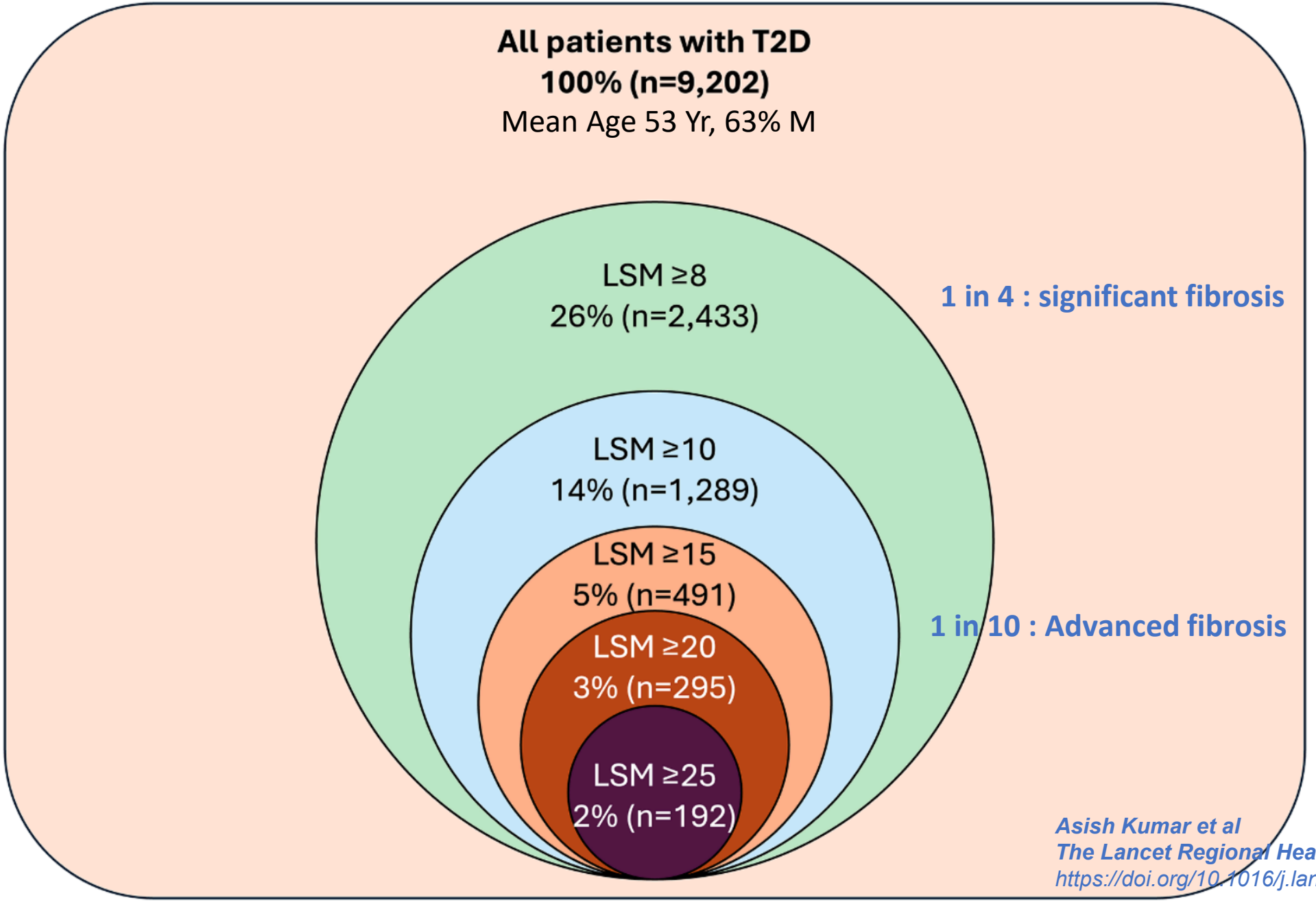
FU paired biopsy Study in F2 : *Hepatology. 2006;44:865–73*

In 14 yrs : 16% Regress, 40% stable, 40% progress, 5% Cirrhosis


Fat in Liver / Fat: inflammatory disease
Multisystemic involvement
Dietary fat and carbohydrate (fructose/glucose)
Fat import, De novo Lipogenesis
LDs
TG Biosynthesis
Cholesterol Biosynthesis
ROS
beta-Oxidation
(Inadequate metabolic substrate disposal)
Fatty acids
Lipotoxic species
Blood VLDL
VLDL
Inflammation
ER stress
Fibrosis
Systemic 'spillover'
Lipases
Liver with MASH
Visceral Fat in MASH
Muscular dystrophy
CKD
CVDs

Diabetes

Dia- Fib Study : Lancet April 2026



- **CAP: 65% steatosis.**

Independent predictor fibrosis :

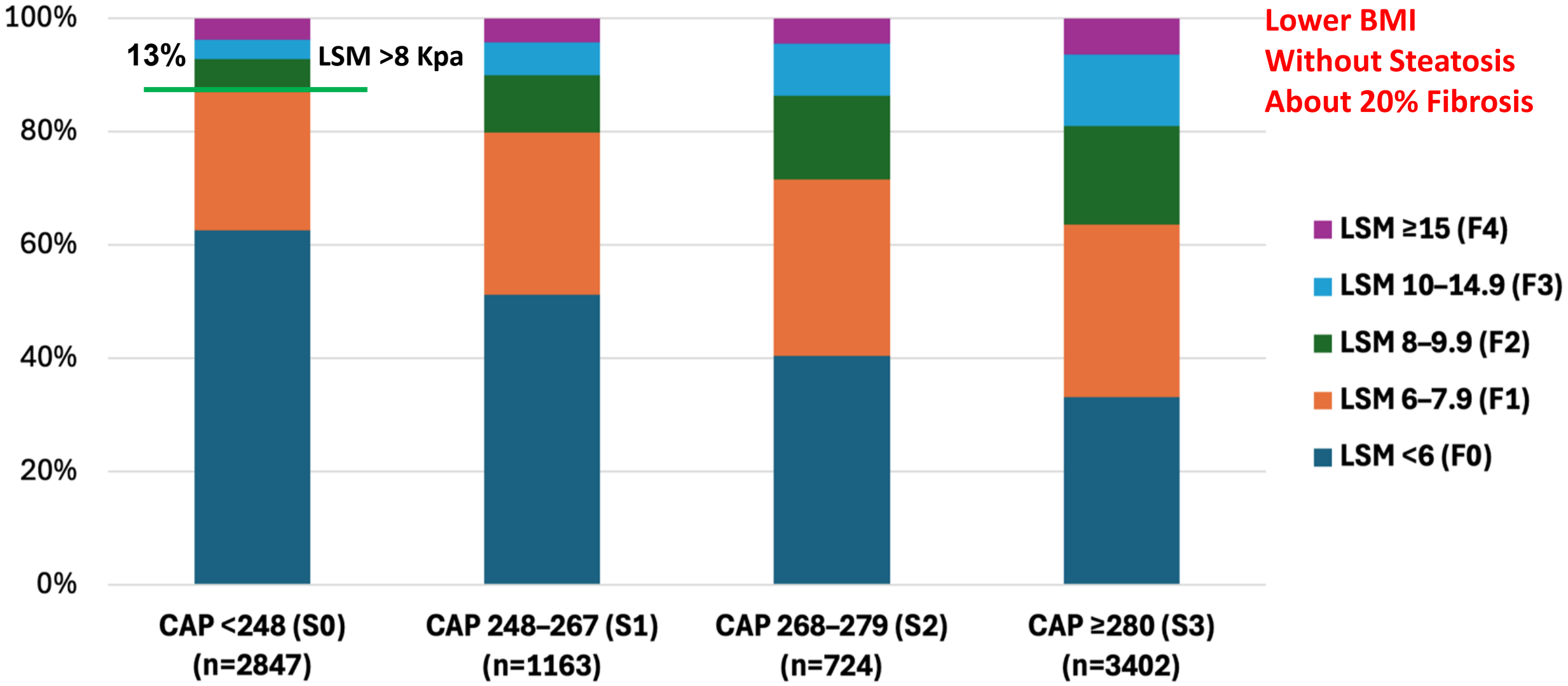
- **Obesity (OR 1.98)**
- **Dyslipidaemia (OR 1.21)**
- **Reduced eGFR (OR 1.23)**
- **T2D ≥10 years (OR 1.12)**
- ***BMI <25: 19% significant fibrosis***

Fibrosis Evaluation in T2D

4th Complication in T2 DM

Asish Kumar et al
The Lancet Regional Health - Southeast Asia 2026;47: 100753
https://doi.org/10.1016/j.lansea.2026.100753

Distribution of Fibrosis Stages Across Steatosis Grades



Lower BMI
Without Steatosis
About 20% Fibrosis

Asish Kumar et al Dia-Fib Study April 2026
*The Lancet Regional Health - Southeast Asia 2026;47: 100753*https://doi.org/10.1016/j.lansea.2026.100753

Mental health

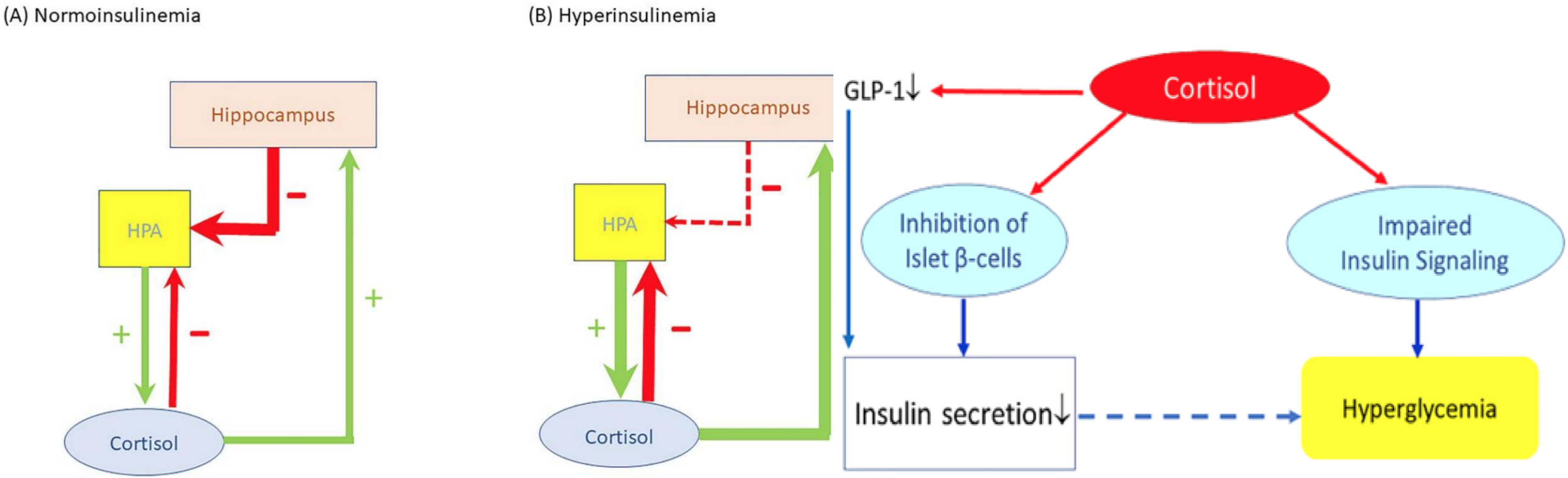
Mental Health / Stress : Increased Cortisol : Insulin resistance

Stress : HPA Axis - Increased Cortisol (One third population in developed world)

- Insulin resistance (gluco-neo-genesis/insulin antagonism at IRS-Hyperglycemia :
- More Insulin Production – Lipogenesis
- Cortisol - Linked to abdominal and visceral Obesity

Jansen et al Int. J. Mol. Sci. 2022, 23, 8178 1- 19

Insulin & Cortisol Balance by bio-feed back mechanism
Balanced Homeostatic state



Jansen et al Int. J. Mol. Sci. 2022, 23, 8178 1- 19

Sleep

American Medicine of Sleep medicine :

- Adolescent sleep duration8-10 hours
- Adults not less than 7 hours

Ding C et al . Sleep and obesity .J Obesity Metab Syndr 2018;27: 4-24

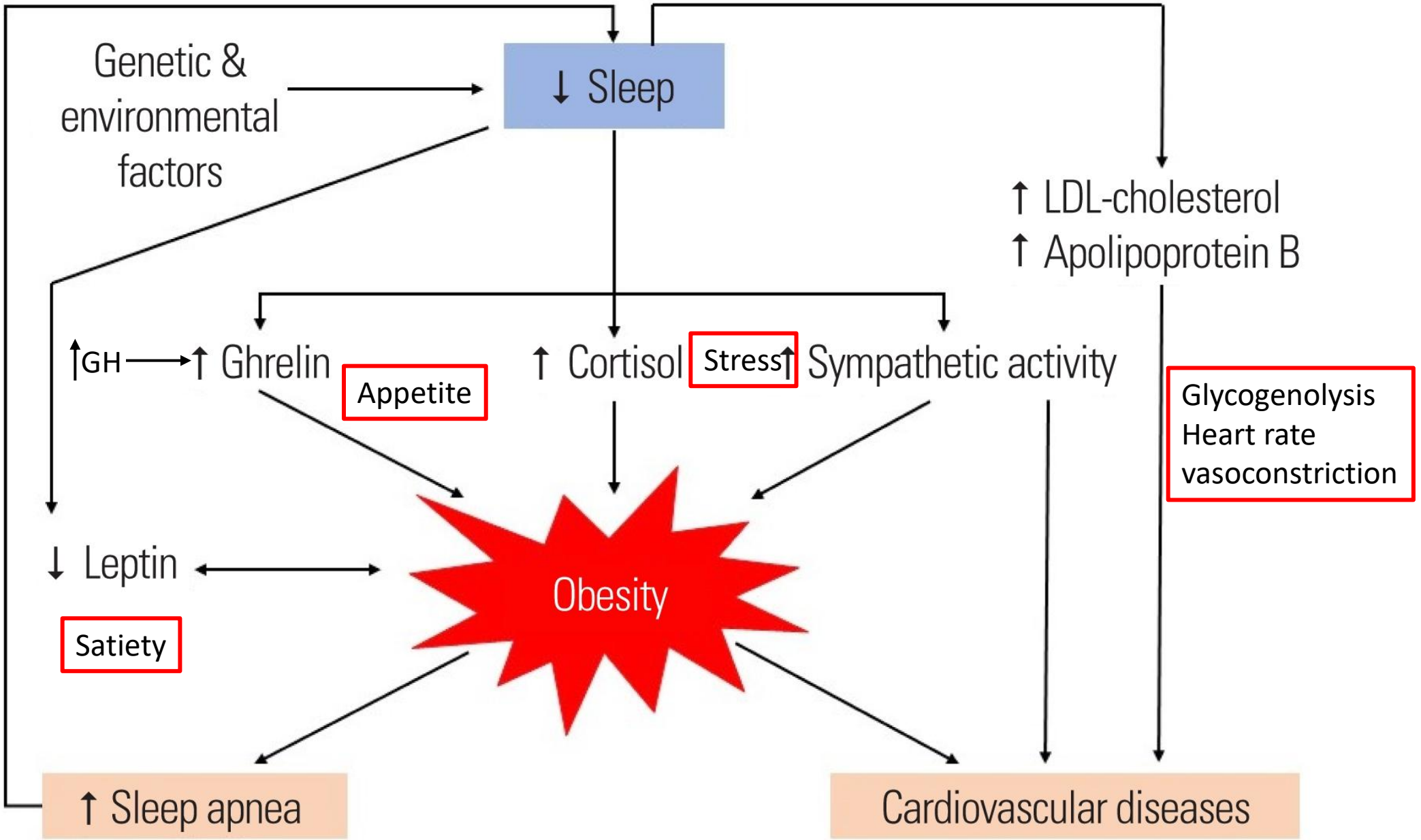
Insomnia is prevalent in Population

In China: meta-analysis of 17 cross-sectional population-based studies:

- **One in six adults had insomnia** *Cao XL et al. PLoS One 2017;12:e0170772.*

Multiple studies and surveys: Sleep debt :

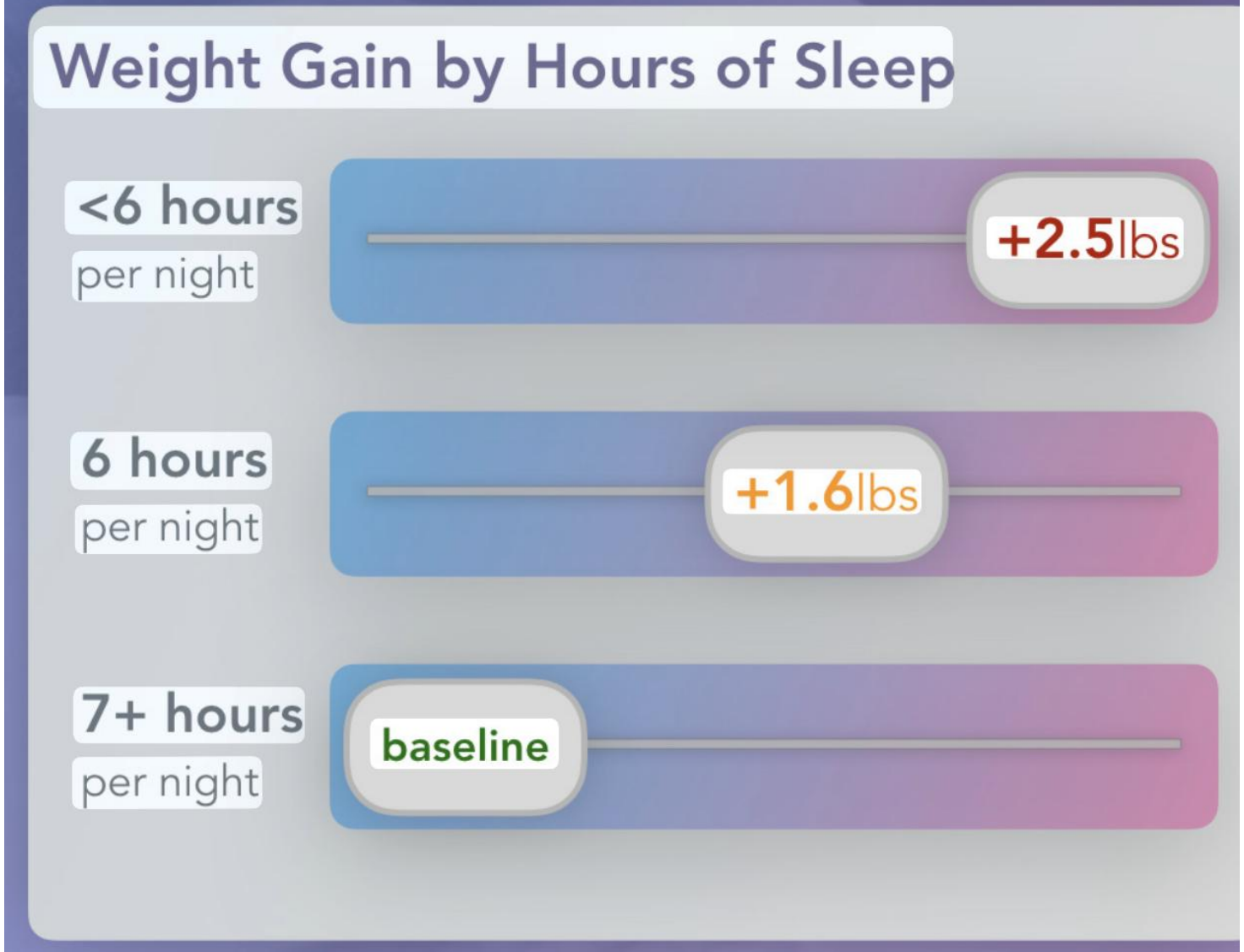
- **Increased snacking, binge intake of food, increased saturated fats , less physical activities**



Ding C et al . Sleep and obesity .J Obesity Metab Syndr 2018;27: 4-24

Sleep & Weight Gained

Nurses who slept 6 or fewer hours per night gained significantly more weight over the study.



Protect Your Liver -Healthy Liver

Protect Your Liver

Life style modification

Diet

Exercise recommendation

Behavior therapy : Sleep & mental health

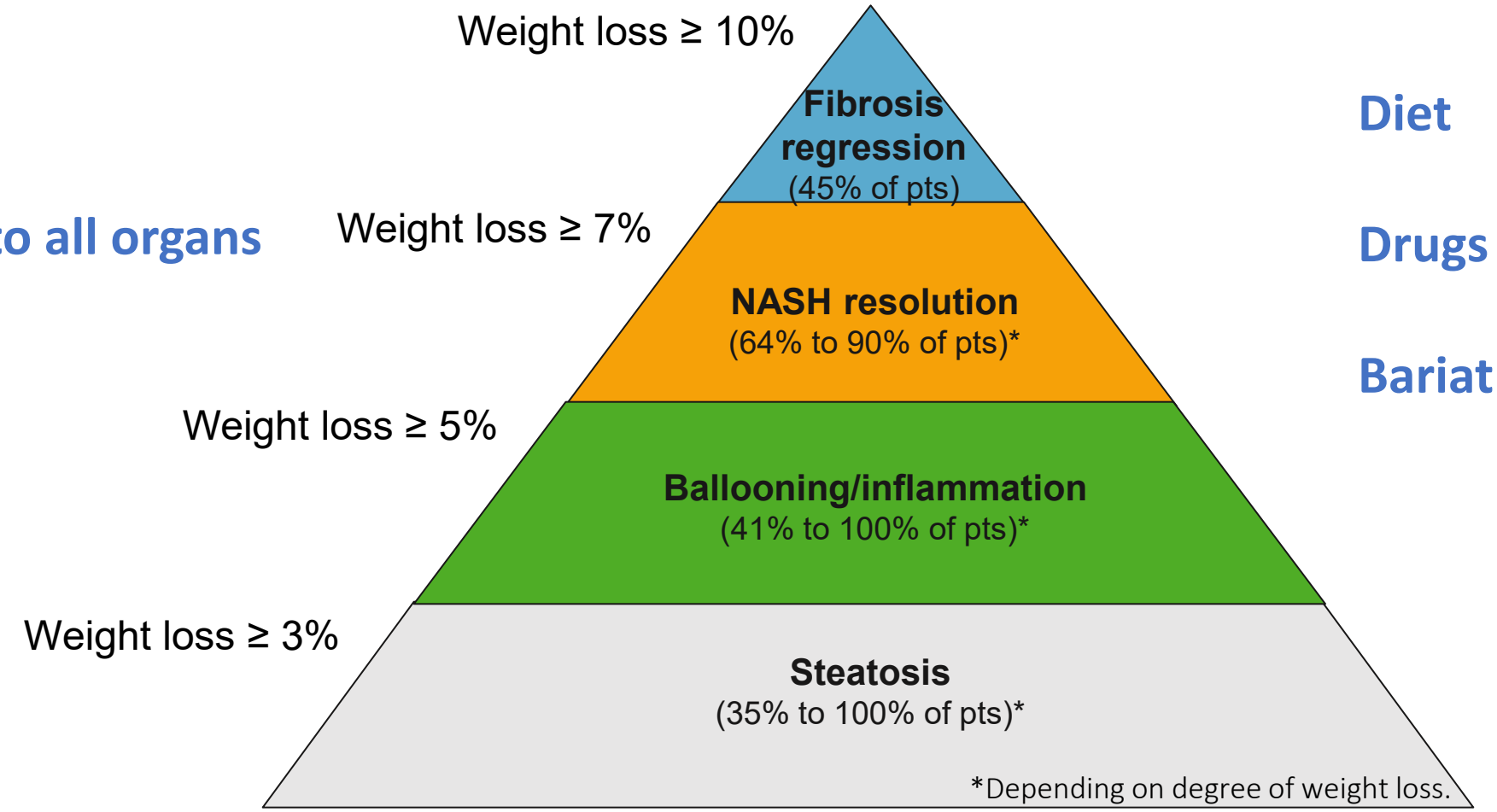
Pharmacologic therapies

Bariatric/Endoscopic surgery

Percentage of Weight Loss Associated With Histological Improvement of Fat in Liver

- Analysis of data from 4 randomized studies

Benefit to all organs



Exercise

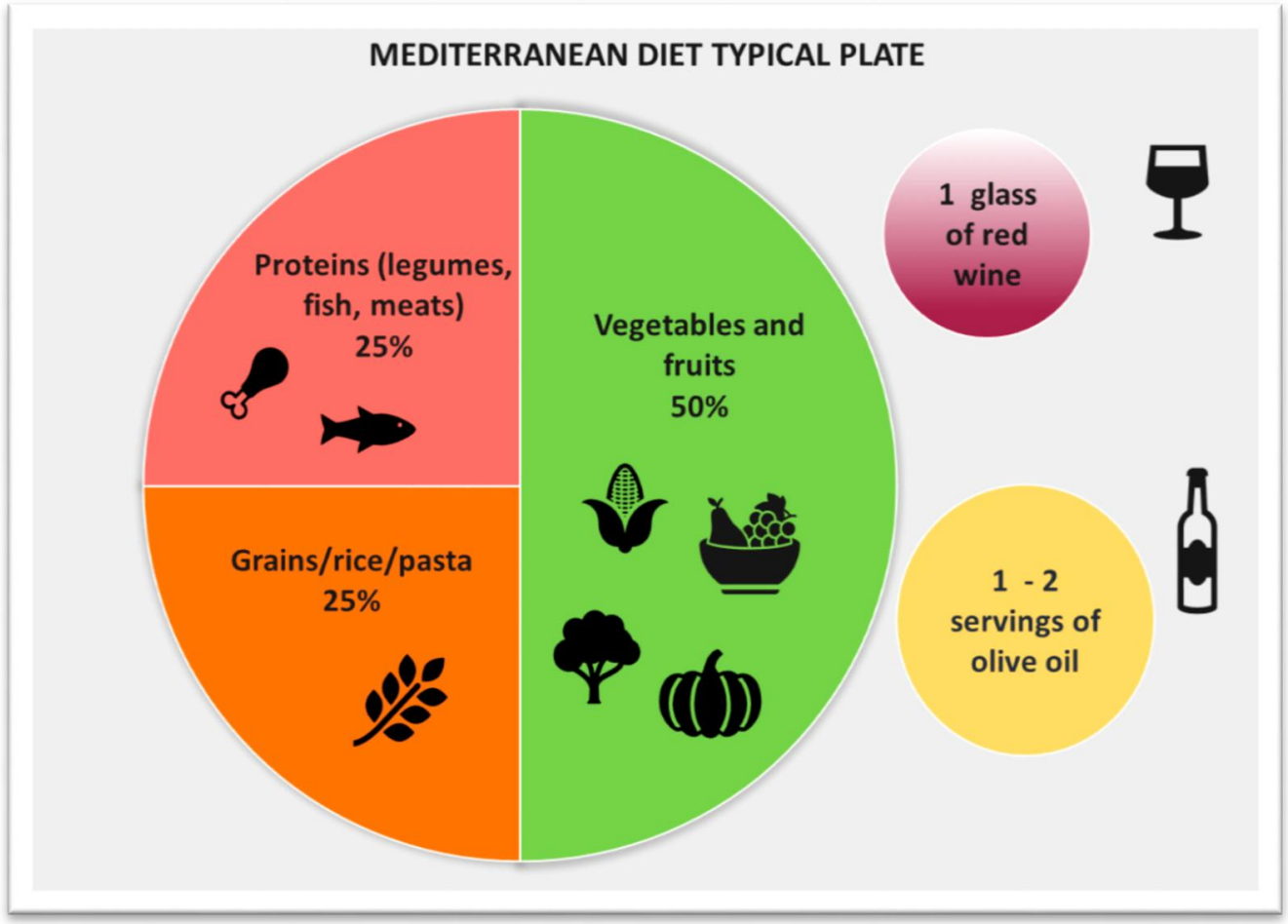
Diet

Drugs

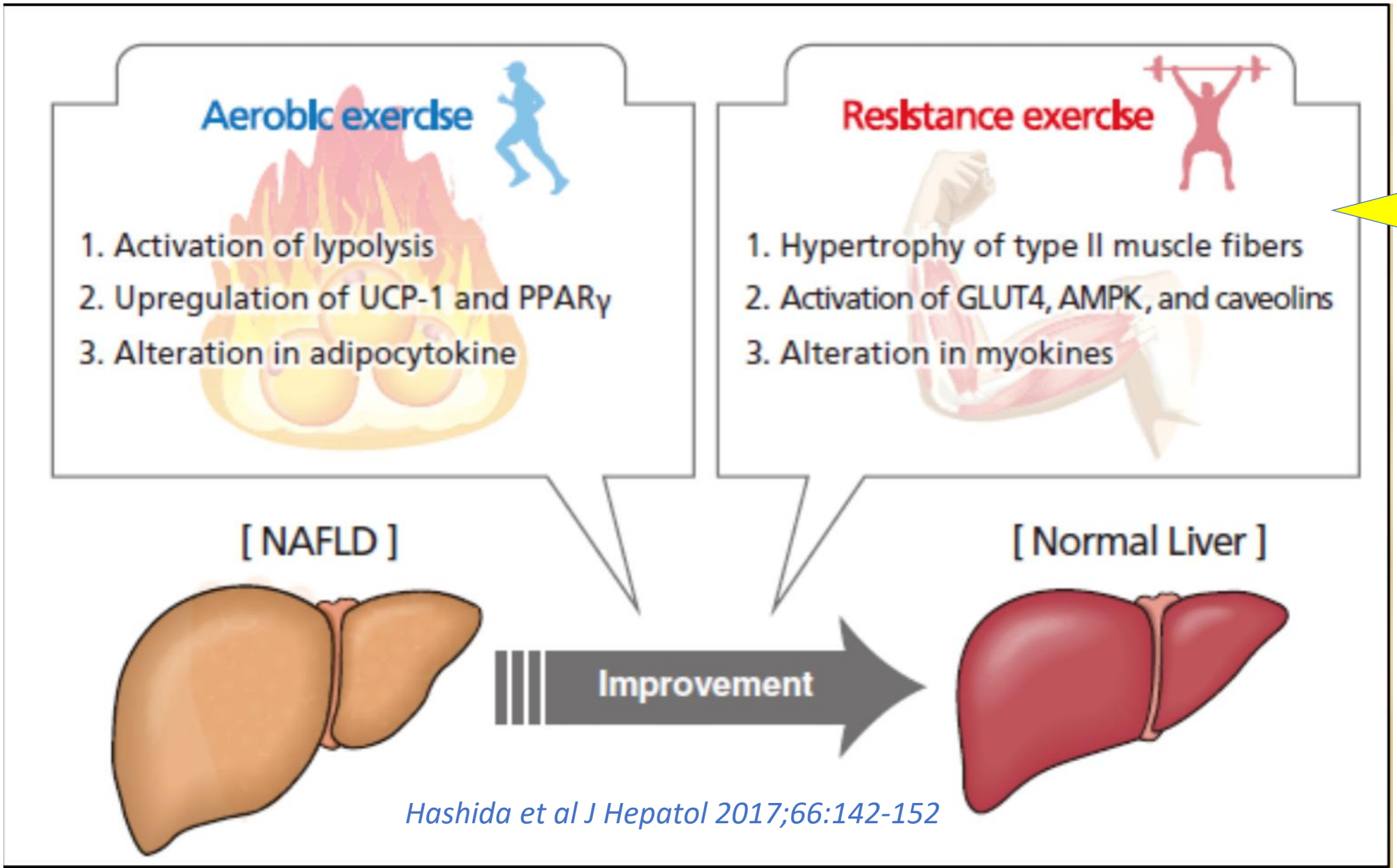
Bariatric interventions

Hannah WN, et al. Clin Liver Dis. 2016;20:339-350.

Mediterranean diet



Aerobic or Resistance Exercise



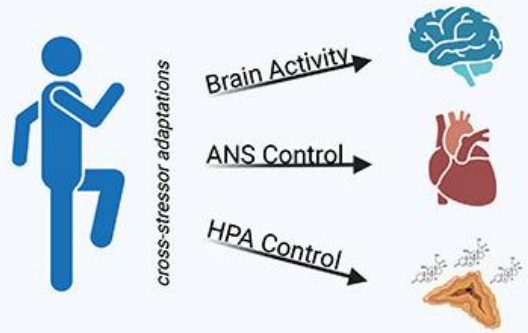
Equally effective,

Hashida et al J Hepatol 2017;66:142-152

Effects of a Year-Long Aerobic Exercise Intervention on Neuroendocrine, Autonomic, and Neural Correlates of Stress, Emotion, and Cardiovascular Disease Risk in Midlife Adults

Aims

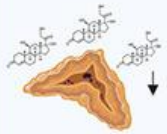
According to the "Cross-Stressor Adaptation Hypothesis"[1] aerobic exercise may down-regulate stress- and emotion-related neurophysiology



Our registered trial (NCT03841669)[2,3] tested the following cross-stressor predictions at the levels of the brain, autonomic nervous system (ANS), and hypothalmic-pituitary-adrenal (HPA) axis

- ↓ Subjective Stress & Affective Reactivity
- ↓ Brain Patterns for Stress & Negative Emotion
- ↑ Brain Patterns for Emotion Regulation

- ↓ Cardiovascular Reactivity to Stressors
- ↑ Parasympathetic Cardiac Activity



- ↓ Cumulative Cortisol Output

Trial Design

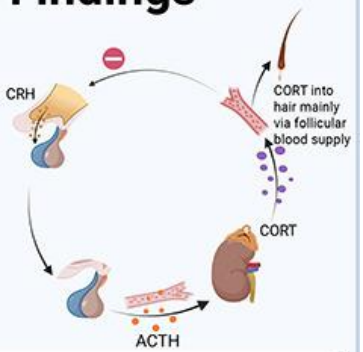
N = 130
(26-58yr | 68% female)

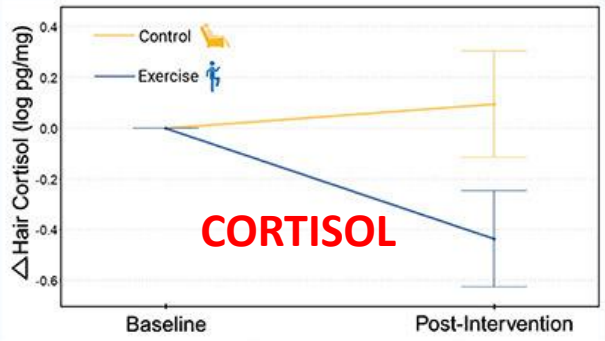
Exercise	Control
	
N = 64	N = 66
1 yr moderate-to-vigorous aerobic exercise for 150 min per wk	1 yr health information only (no change in behavior)

ITT and Per Protocol Analyses

Main Findings

Exercise reduced cumulative cortisol (measured in hair)





Note. ITT BGD = -0.62 (95% CI: -1.14 to -0.10) p_{FDR} = 0.04. Replicated in per protocol analyses.

Synopsis

- Results add to our prior trial evidence that aerobic exercise improves brain age and cardiorespiratory fitness →
- In line with "cross-stressor hypothesis," 1yr of exercise reduced a stress-related biomarker - hair cortisol - that relates to cardiovascular health[4]
- The potential stress-buffering effects of aerobic exercise not seen for brain or ANS outcomes

[1]Sothmann et al (1996) Exerc Sport Sci Rev; 24: 267-87.[2]Molina-Hidalgo et al (2023) BMJ Open; 13: e077905.[3]Funded by P01 HL040962.
[4]Kuckuck et al (2024) J Intern Med; 295: 2-19. Made in BioRender.

Gianaros PJ et al >J Sports and health Sciences https://doi.org/10.1016/j.jshs.2026.101135 - 16th March 2026

Exercise decreases Cortisol & IR

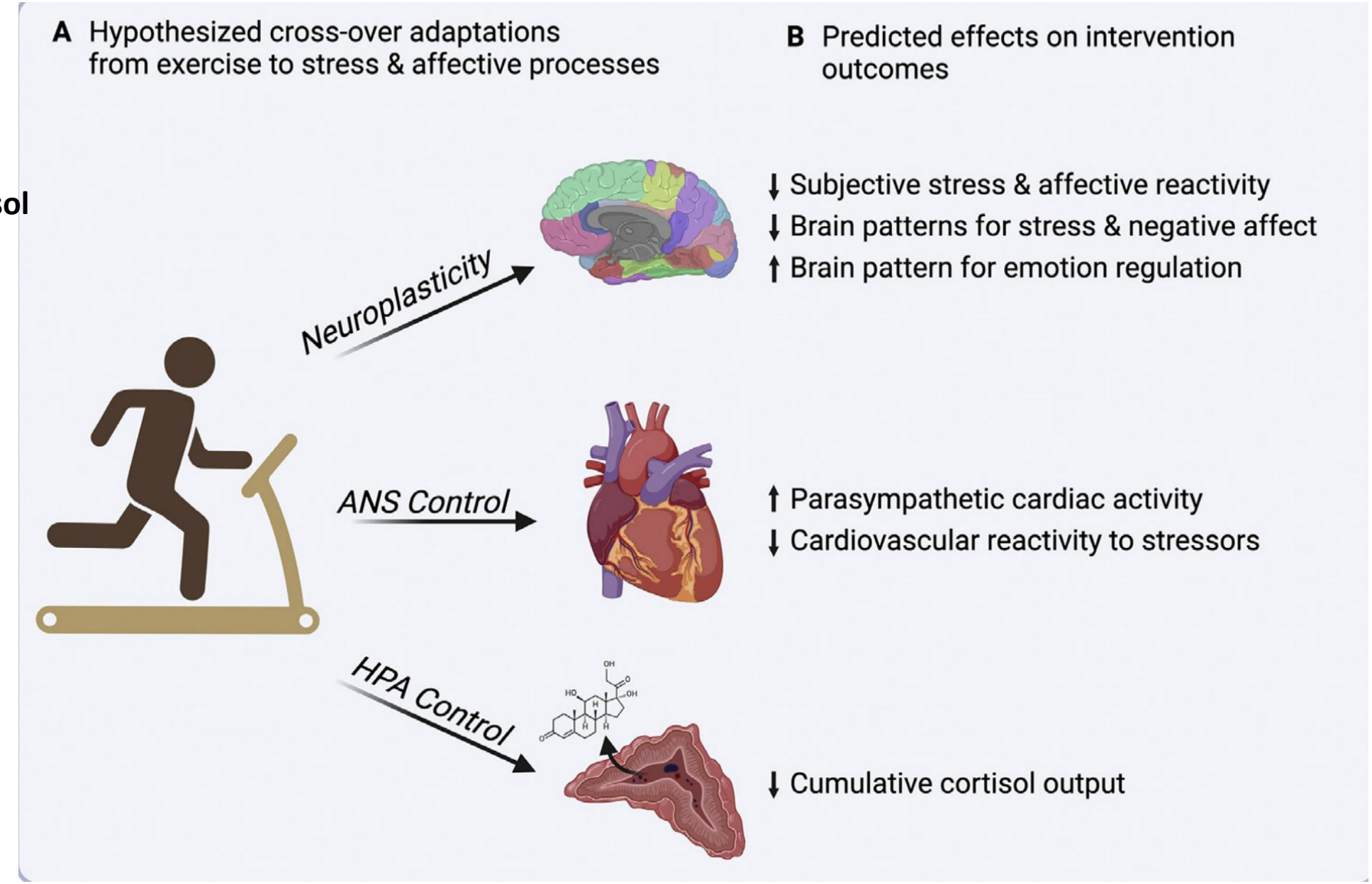
Inflammatory cytokines

Increase Endorphins_

Improve glucose uptake

Improves brain function

Cardio vascular function



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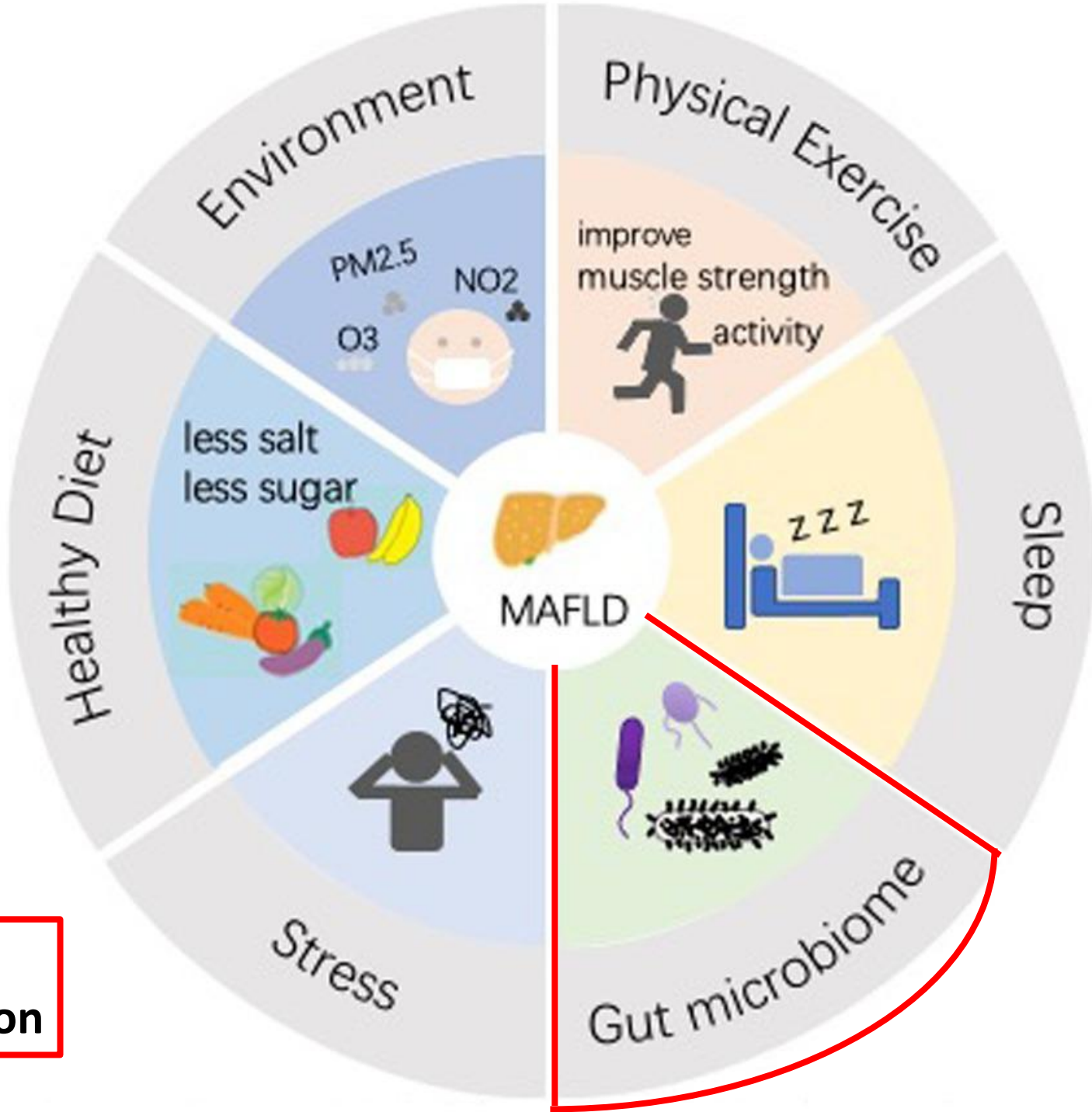
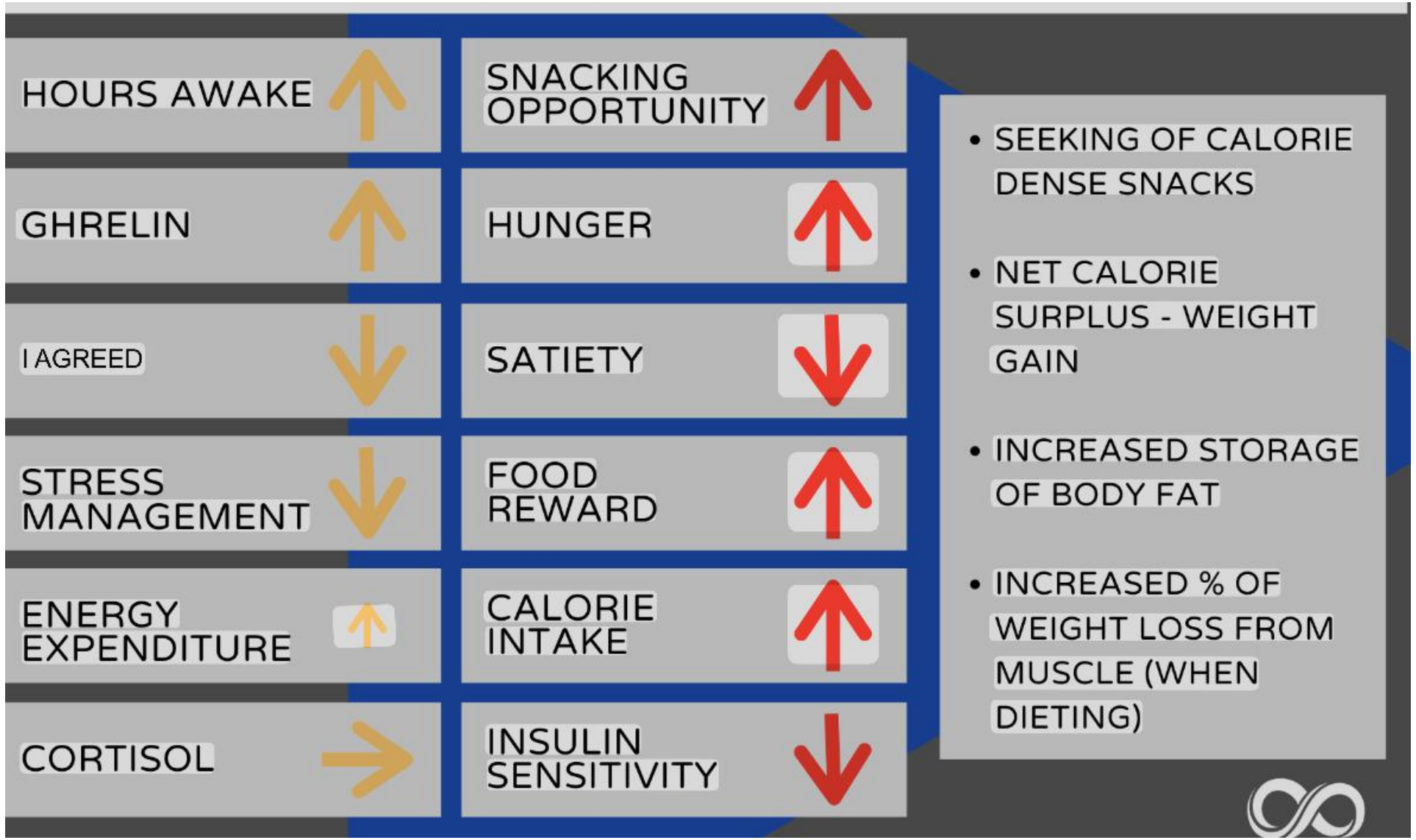
Healthy Interventions
Healthy Liver



Gut Flora and Diet
Influence energy extraction

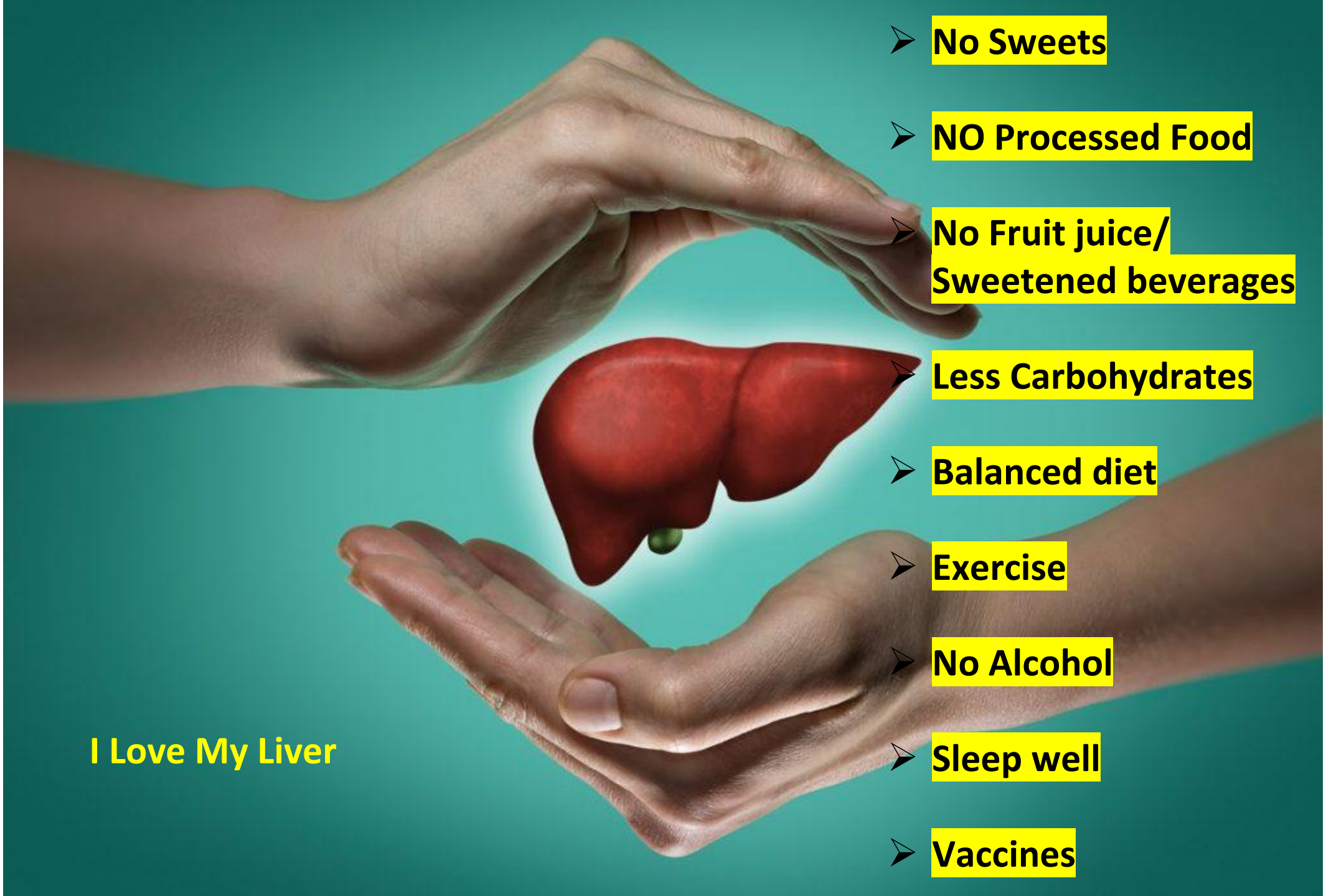
Impact of Sleep on Body weight



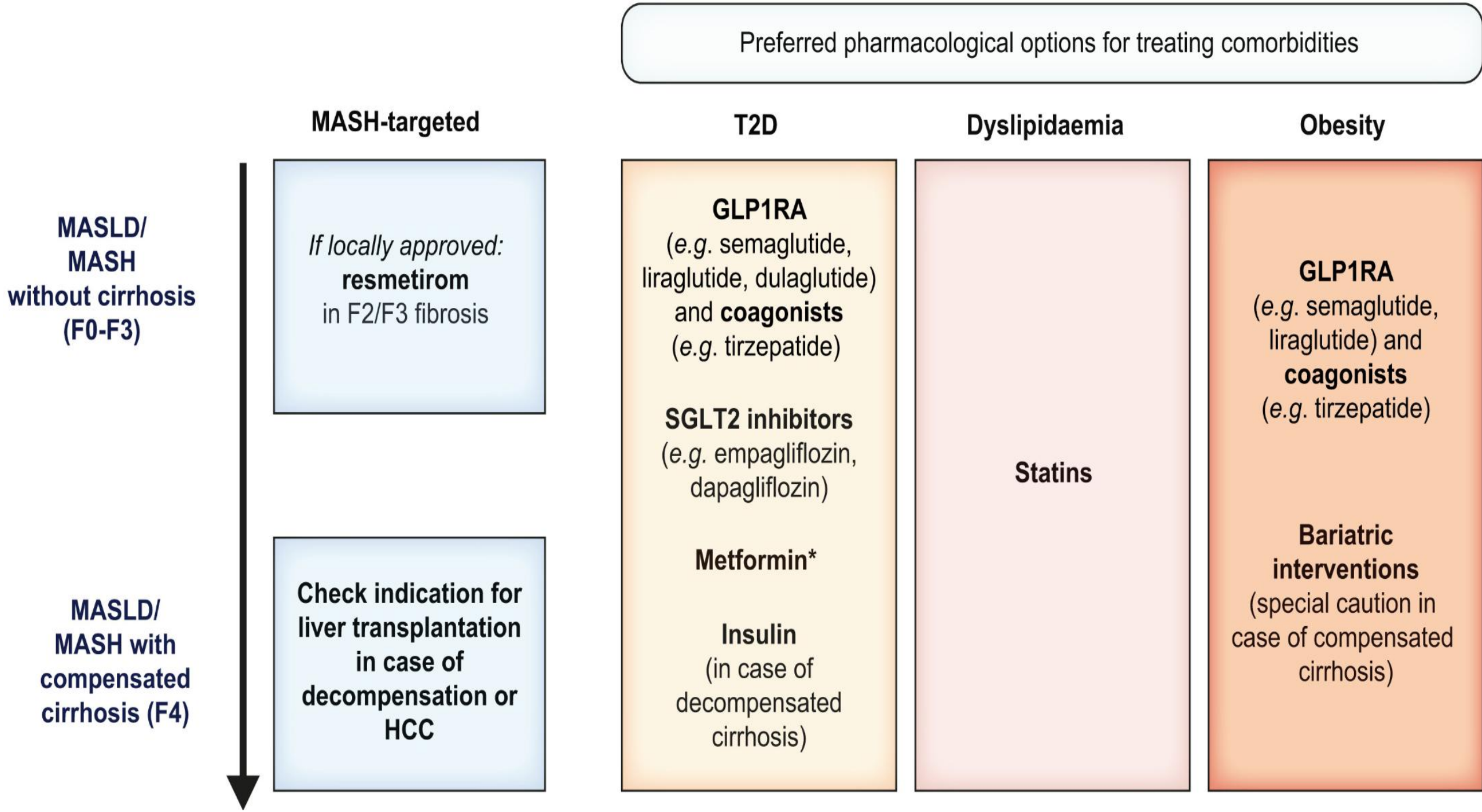
Hepatitis :

- **Vaccination : HBV, HAV (HEV)**
- **HBV : UIP , Health care , Obese , Alcoholics**
- **Screening in house hold contacts**
- **HAV : Non-immune Children /Obese Children**

Drugs & CAMS



- No Sweets
- NO Processed Food
- No Fruit juice/ Sweetened beverages
- Less Carbohydrates
- Balanced diet
- Exercise
- No Alcohol
- Sleep well
- Vaccines


Preferred pharmacological options for treating comorbidities
MASH-targeted
T2D
Dyslipidaemia
Obesity
MASLD/ MASH without cirrhosis (F0-F3)
MASLD/ MASH with compensated cirrhosis (F4)
If locally approved: resmetirom in F2/F3 fibrosis
Check indication for liver transplantation in case of decompensation or HCC
GLP1RA (e.g. semaglutide, liraglutide, dulaglutide) and coagonists (e.g. tirzepatide)
SGLT2 inhibitors (e.g. empagliflozin, dapagliflozin)
Metformin*
Insulin (in case of decompensated cirrhosis)
Statins
GLP1RA (e.g. semaglutide, liraglutide) and coagonists (e.g. tirzepatide)
Bariatric interventions (special caution in case of compensated cirrhosis)

WHO and FDA & EMA may license three mor drugs to treat Obesity 2026

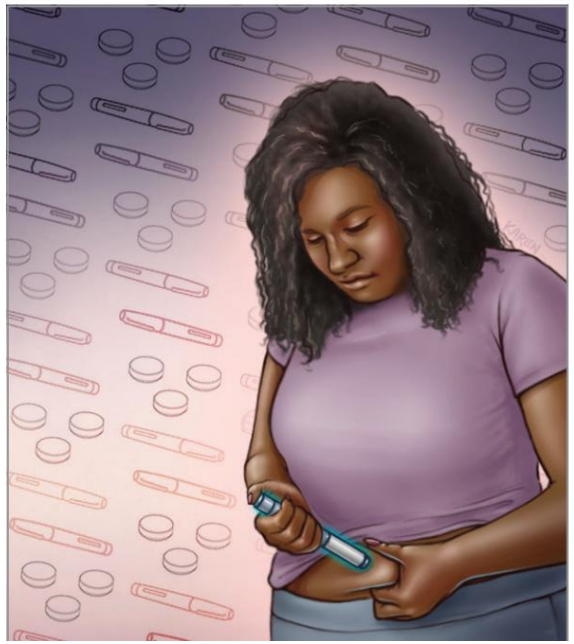
Data on 3 New GLP-1 Drugs for Weight Loss That May Be Approved This Year

Rita Rubin, MA

The approval of 3 new weight-loss medication options—2 injectables and a pill—is expected in the US this year. As the World Health Organization recently emphasized in its first guideline on the use of GLP-1 therapies to treat obesity, the medications, when prescribed, should be used alongside behavioral support focused on a healthy diet and physical activity.

Medical News website

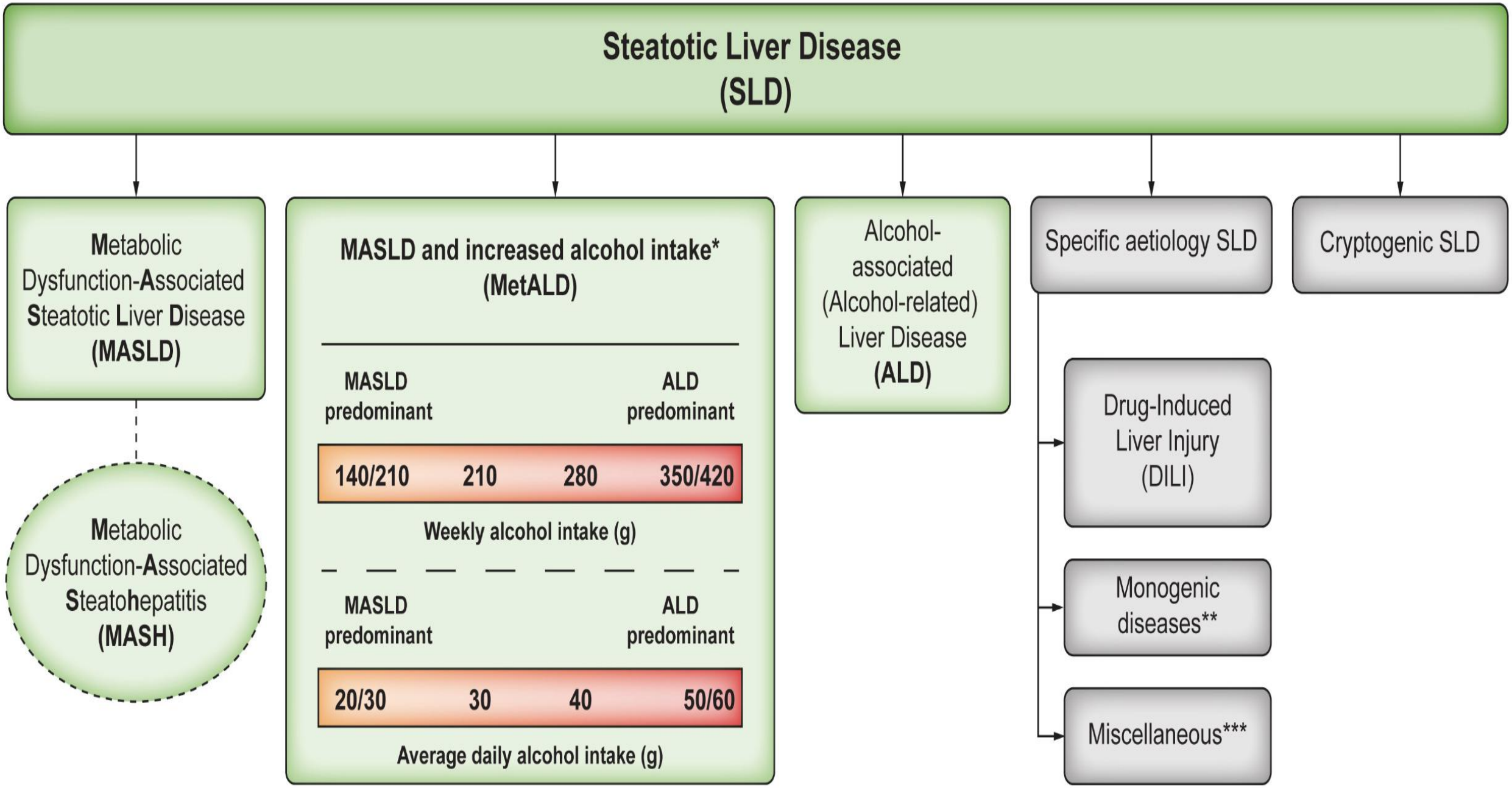
One of the anticipated injectables combines semaglutide, the glucagon-like peptide 1 (GLP-1) receptor agonist in the weight-loss drug marketed as Wegovy and the



High dose Injectable Semaglutide 7.2 mg/SC/week :

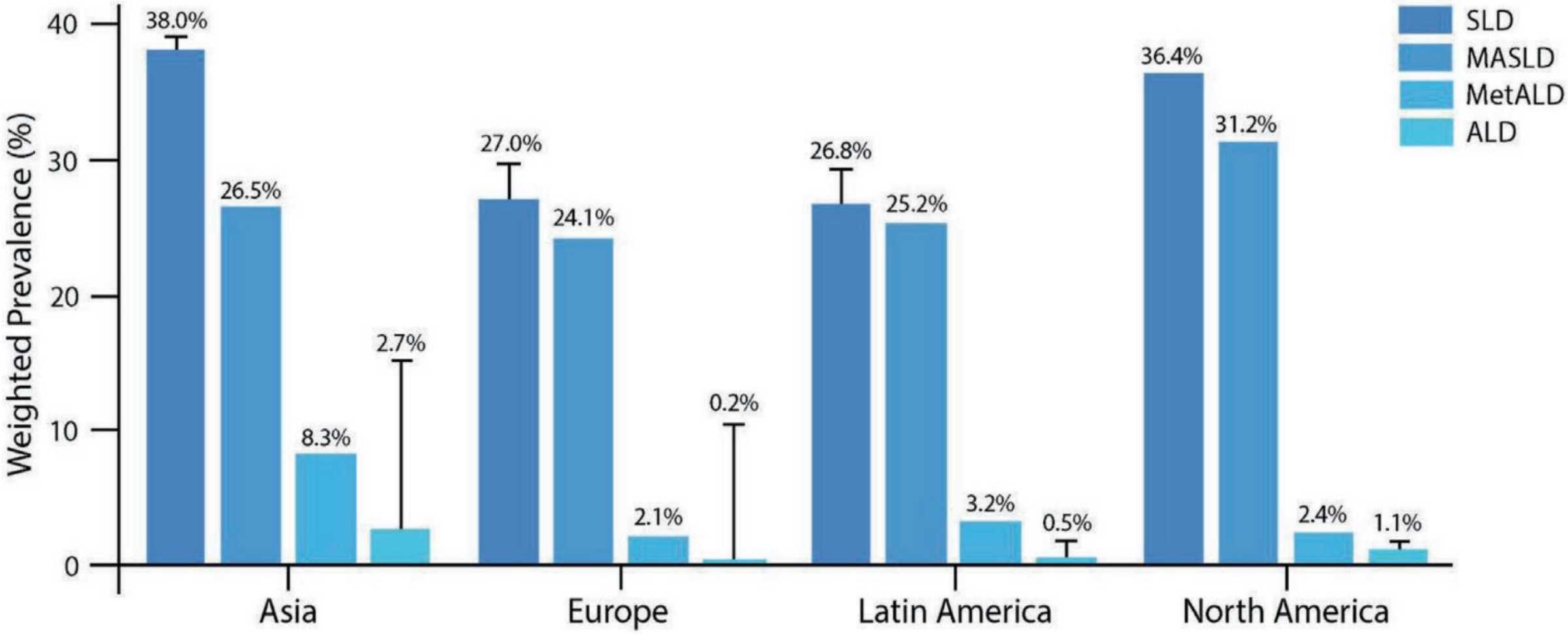
High dose oral Semaglutide Orfroglifron : 6 ,12, 36mg daily

Semaglutide+ Cagrilinide (Amylin) 2.4 mg + 2.4 mg S/C /Week


Steatotic Liver Disease
(SLD)
Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)
Metabolic Dysfunction-Associated Steatohepatitis (MASH)
MASLD and increased alcohol intake* (MetALD)
MASLD predominant
ALD predominant
140/210
210
280
350/420
Weekly alcohol intake (g)
MASLD predominant
ALD predominant
20/30
30
40
50/60
Average daily alcohol intake (g)
Alcohol-associated (Alcohol-related) Liver Disease (ALD)
Specific aetiology SLD
Drug-Induced Liver Injury (DILI)
Monogenic diseases**
Miscellaneous***
Cryptogenic SLD

World Obesity Federation (WOF):
2030: 1.1 billion Obese adults .
2060: Global Medical > ₹1544 trillion
(converted on 2/1/2025 at 1$ to ₹ 85)

Regional Prevalence of SLD, MASLD, Met-ALD, ALD

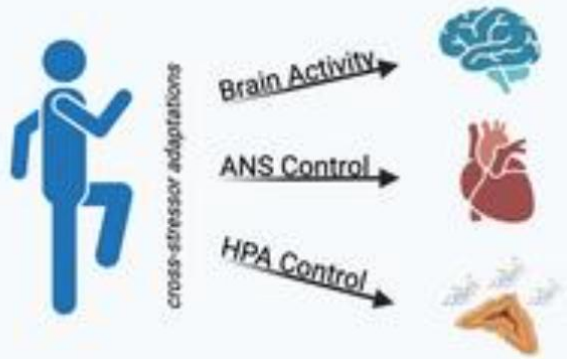


Liver International, 2025; 45:e70017 PP:1-18
https://doi.org/10.1111/liv.70017

Effects of a Year-Long Aerobic Exercise Intervention on Neuroendocrine, Autonomic, and Neural Correlates of Stress, Emotion, and Cardiovascular Disease Risk in Midlife Adults

Aims

According to the "Cross-Stressor Adaptation Hypothesis"[1] aerobic exercise may down-regulate stress- and emotion-related neurophysiology



Our registered trial (NCT03841669)[2,3] tested the following cross-stressor predictions at the levels of the brain, autonomic nervous system (ANS), and hypothalmic-pituitary-adrenal (HPA) axis

- ↓ Subjective Stress & Affective Reactivity
- ↓ Brain Patterns for Stress & Negative Emotion
- ↑ Brain Patterns for Emotion Regulation

- ↓ Cardiovascular Reactivity to Stressors
- ↑ Parasympathetic Cardiac Activity

- ↓ Cumulative Cortisol Output

Trial Design

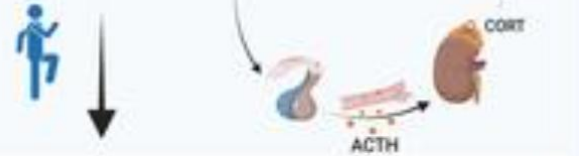
N = 130
(26-58yr | 68% female)

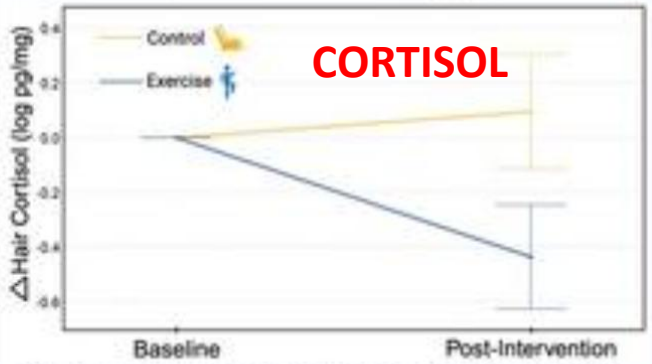
Exercise	Control
	
N = 64	N = 66
1 yr moderate-to-vigorous aerobic exercise for 150 min per wk	1 yr health information only (no change in behavior)

ITT and Per Protocol Analyses

Main Findings

Exercise reduced cumulative cortisol (measured in hair)



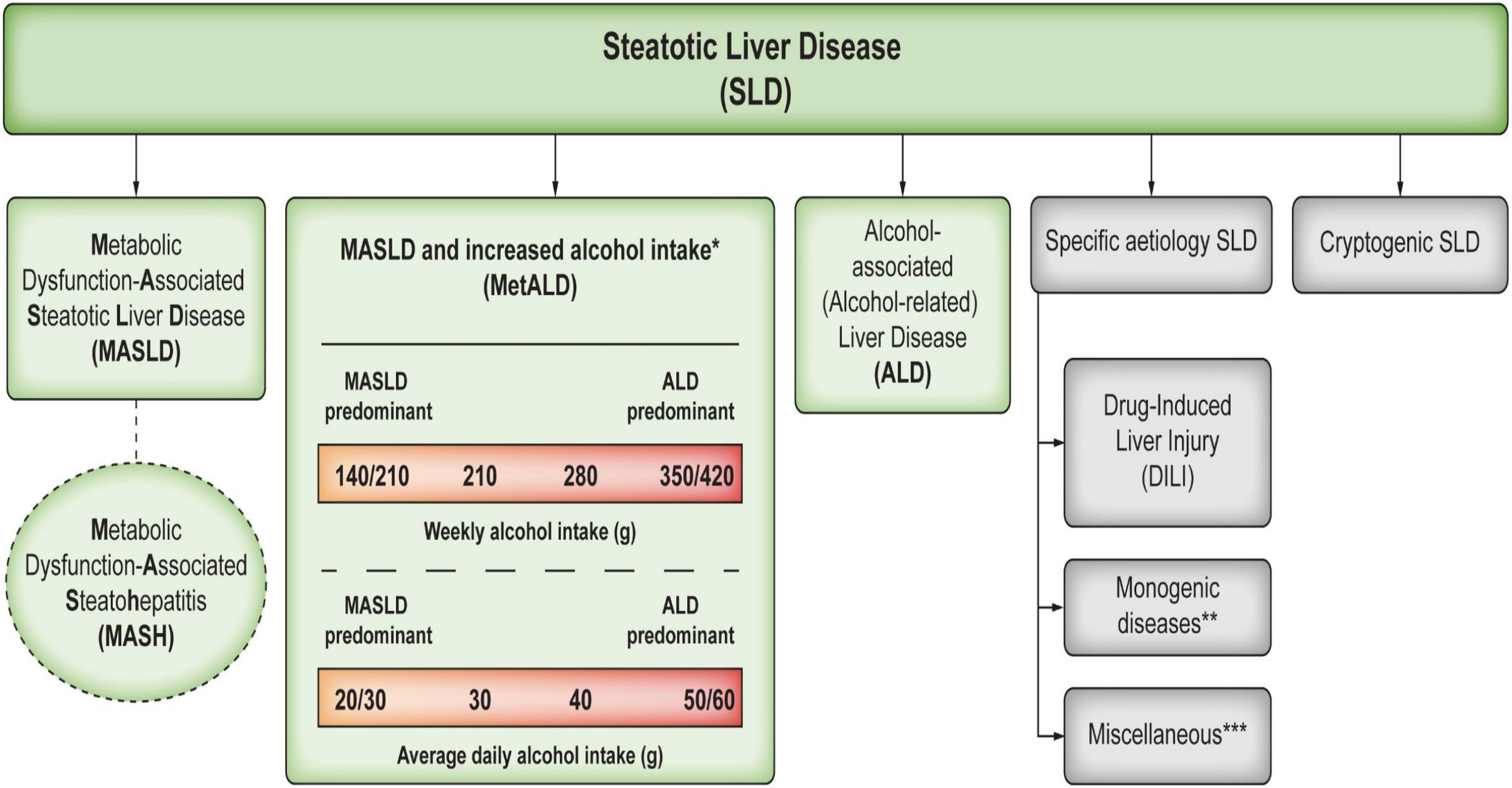


Note. ITT BGD = -0.62 (95% CI: -1.14 to -0.10) p_{ITT} = 0.04. Replicated in per protocol analyses.

Synopsis

- Results add to our prior trial evidence that aerobic exercise improves brain age and cardiorespiratory fitness
- In line with "cross-stressor hypothesis," 1yr of exercise reduced a stress-related biomarker - hair cortisol - that relates to cardiovascular health[4]
- The potential stress-buffering effects of aerobic exercise not seen for brain or ANS outcomes

[1]Sothmann et al (1996) Exerc Sport Sci Rev; 24: 267-87.[2]Molina-Hidalgo et al (2023) BMJ Open; 13: e077905.[3]Funded by P01 HL040962.
[4]Kuckuck et al (2024) J Intern Med; 295: 2-19. Made in BioRender.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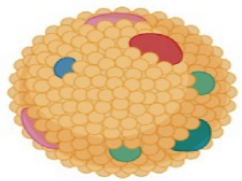
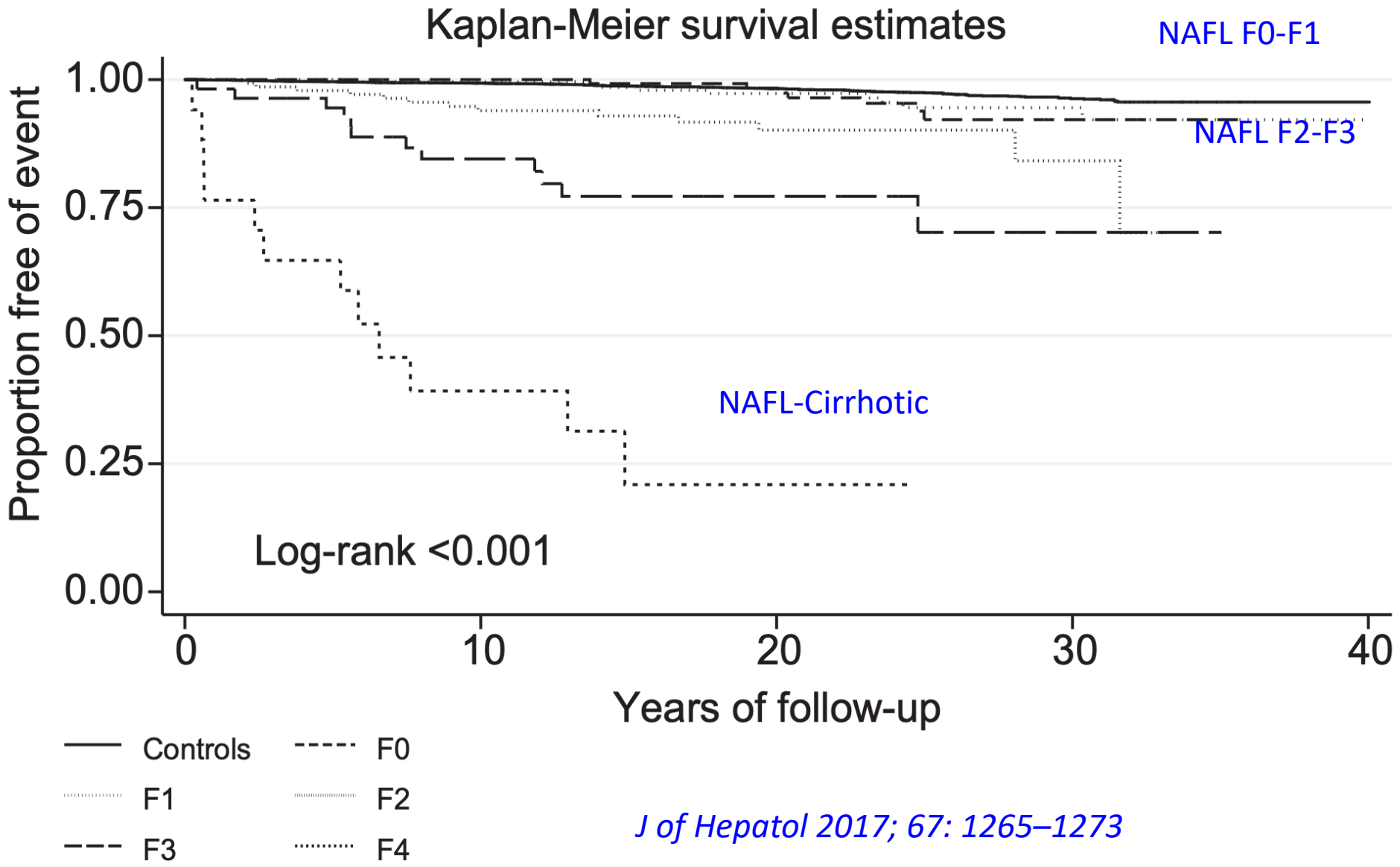
Specific aetiology SLD
Drug-Induced Liver Injury (DILI)
Monogenic diseases**
Miscellaneous***
Cryptogenic SLD

		Cardiometabolic criteria	Alcohol intake effect ⚠
1		BMI ≥ 25 kg/m2 [23 Asia] OR WC> 94 cm (M) 80 cm (F) OR ethnicity adjusted	Weight gain due to its high caloric content and its ability to alter fat metabolism
2		Fasting serum glucose ≥ 5.6 mmol/L OR 2-hour post-load glucose levels ≥ 7.8 mmol/L OR HbA1c ≥ 5.7% OR type 2 diabetes OR treatment for type 2 diabetes	Acute consumption can cause hyperglycemia. Overall effect on A1c is unclear and may depend on genetic and epigenetic factors
3		Blood pressure ≥ 130/85 mmHg OR specific antihypertensive drug treatment	Increase in blood pressure due to vasoconstriction, which raises peripheral vascular resistance.
4		Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] OR lipid lowering treatment	Increases triglyceride synthesis in the liver and reduces its degradation, contributing to hypertriglyceridemia
5		Plasma HDL-cholesterol ≤ 1.0 mmol/L (M) and ≤ 1.3 mmol/L (F) OR lipid lowering treatment	In the long term, it leads to an increase in HDL but also other atherogenic lipoproteins

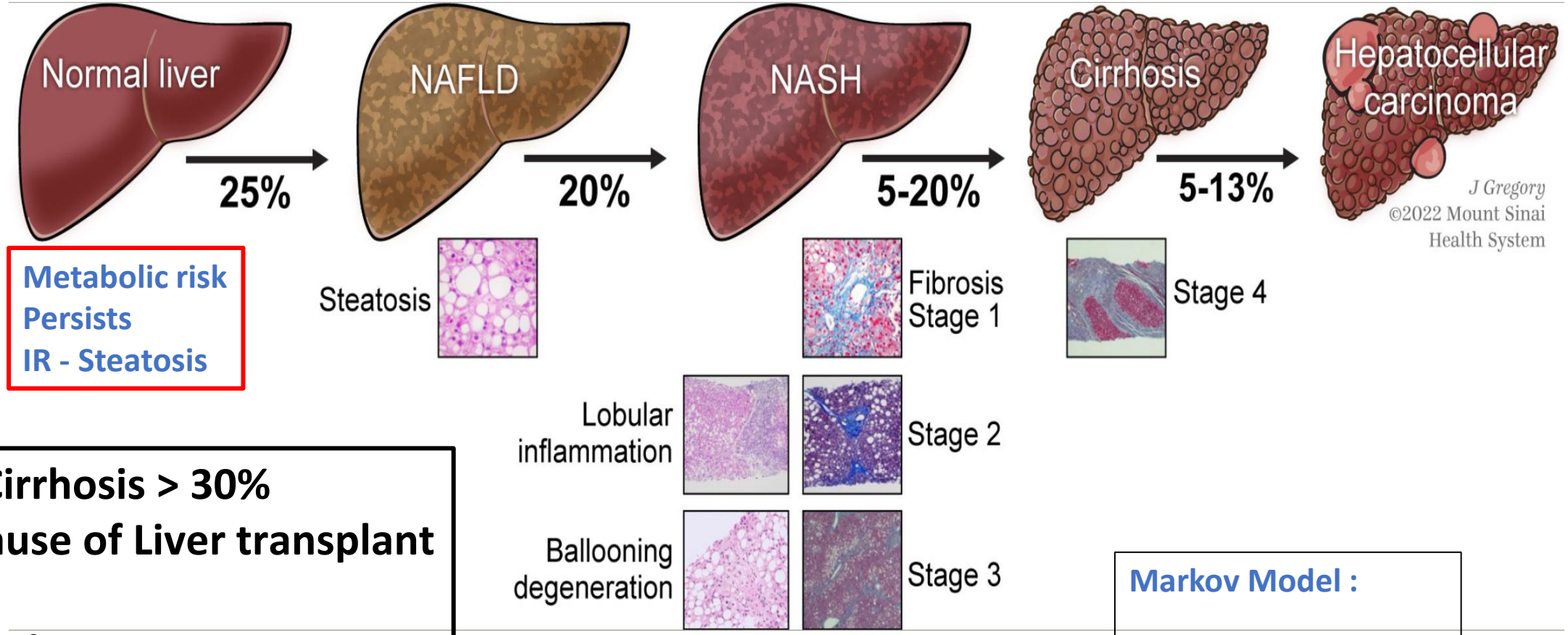
Fibrosis stage but not NASH predicts mortality and time to development of severe liver disease in biopsy-proven NAFLD

Hannes Hagström[1,2,3,*,†], Patrik Nasr[4,†], Mattias Ekstedt[4], Ulf Hammar[5], Per Stål[1,2,6], Rolf Hultcrantz[1,2,6], Stergios Kechagias[4]



J of Hepatol 2017; 67: 1265–1273

MASH – MAFLD Natural Course



Metabolic risk
Persists
IR - Steatosis

Cause of Cirrhosis > 30%
Leading cause of Liver transplant

Alcohol Cirrhosis : 40%

Markov Model :

By 2030:

- ***100 million MAFLD***
- ***27 million MASH***
- ***14 million F2***

Karim G & Bansal M touchREVIEWS in Endocrinology. 2023;19(1):60–70
EASL-EASD-EASO Guideline J hepatology . 2024; 81:492-542
INASL guideline JCEH 2023;13:273-302