

# Treatment advances and optimal models of MAFLD care

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Burnet Institute

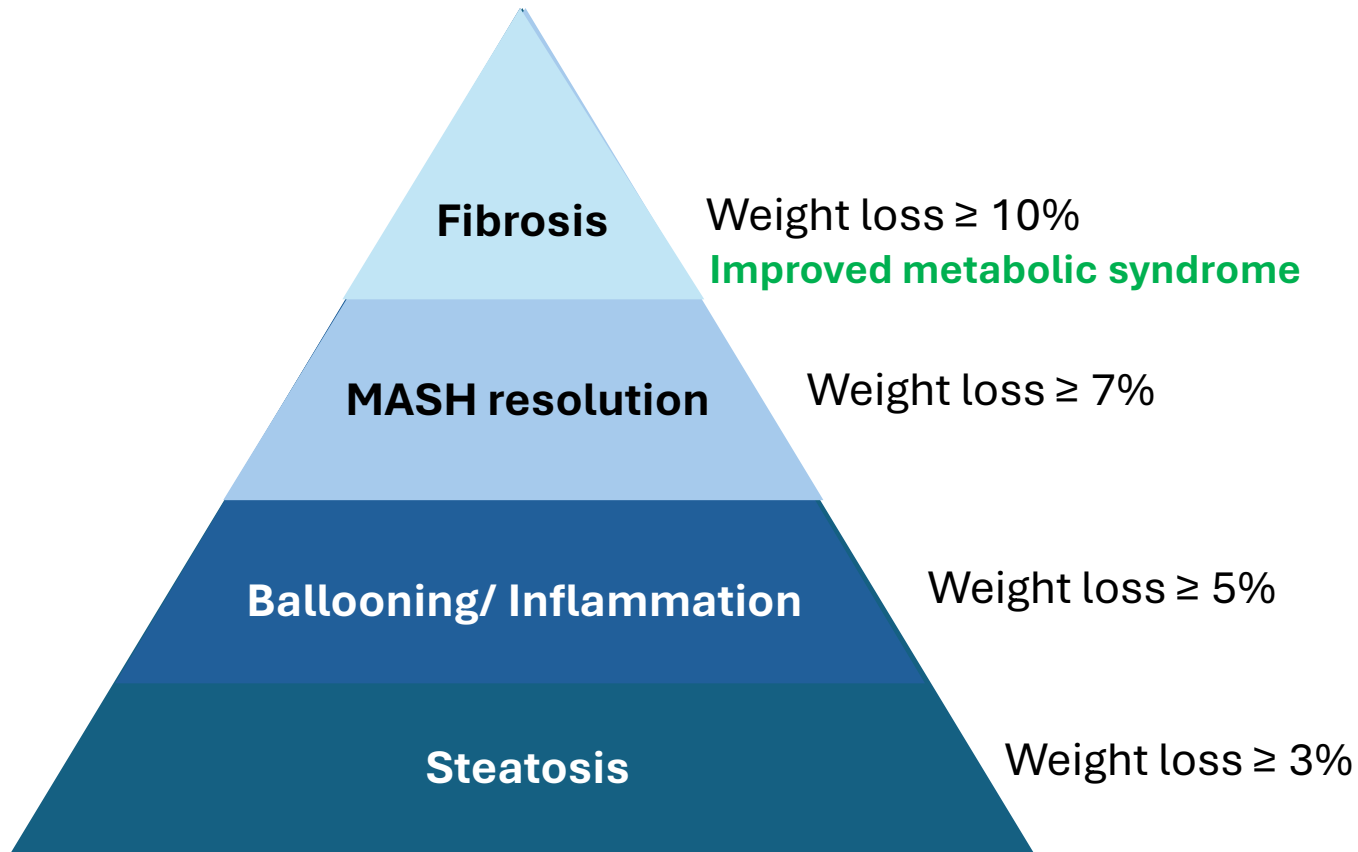
GESA



# Treatment

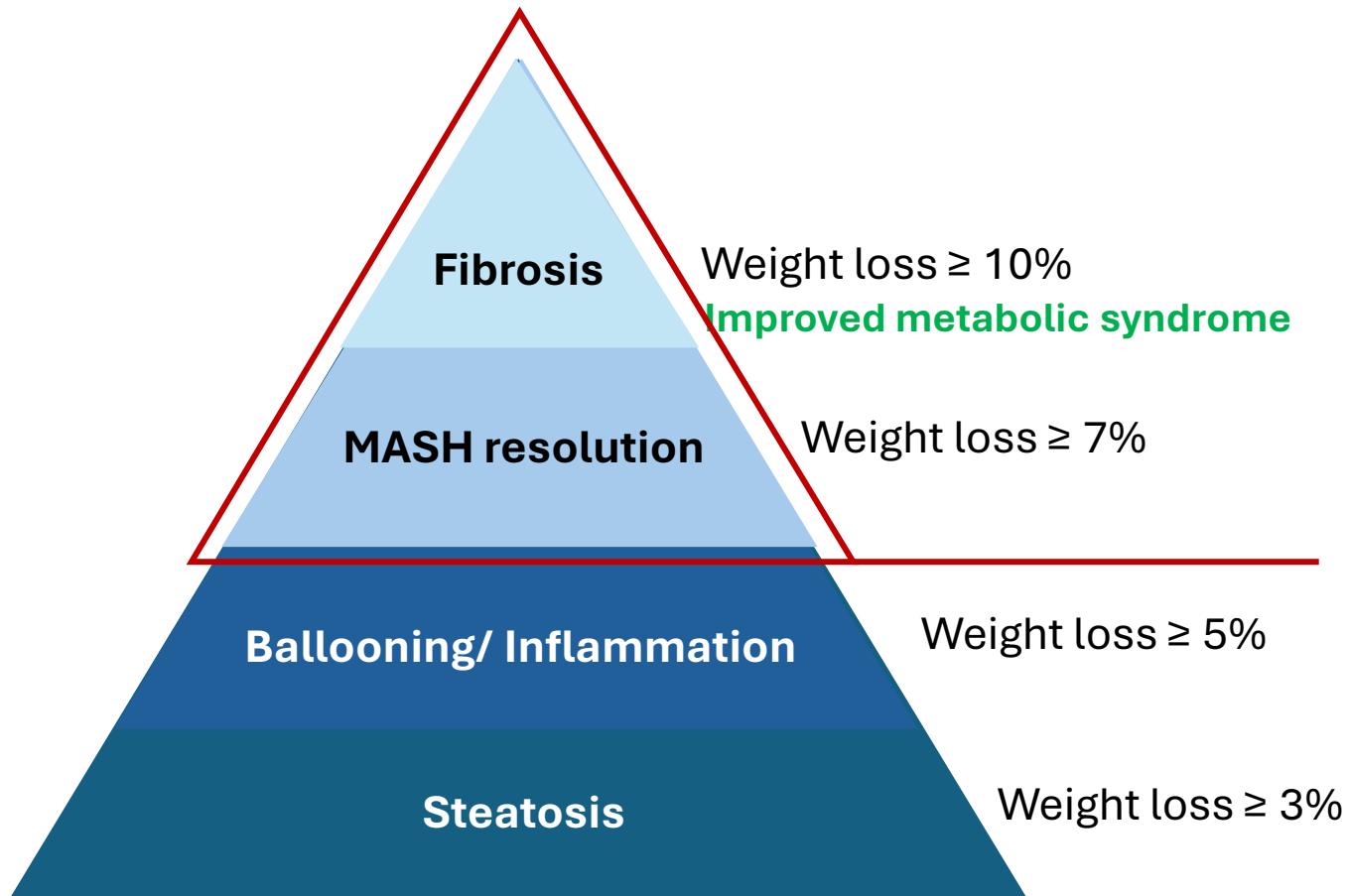


# Weight loss is the mainstay of treatment



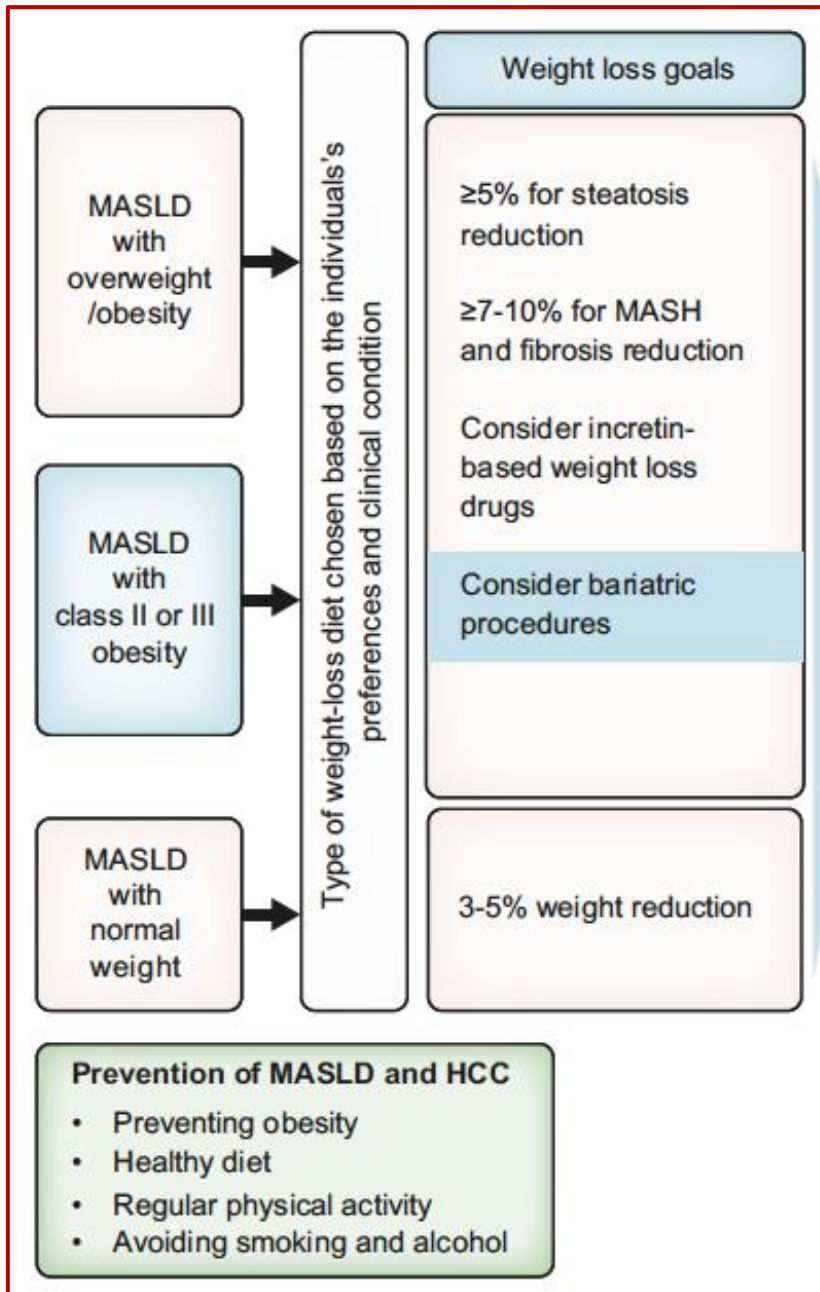
- Metabolic dysfunction associated fatty liver disease (MAFLD) is closely associated with obesity and the metabolic syndrome
- **Caloric restriction** and following a **Mediterranean diet** recommended by EASL and Australian guidelines

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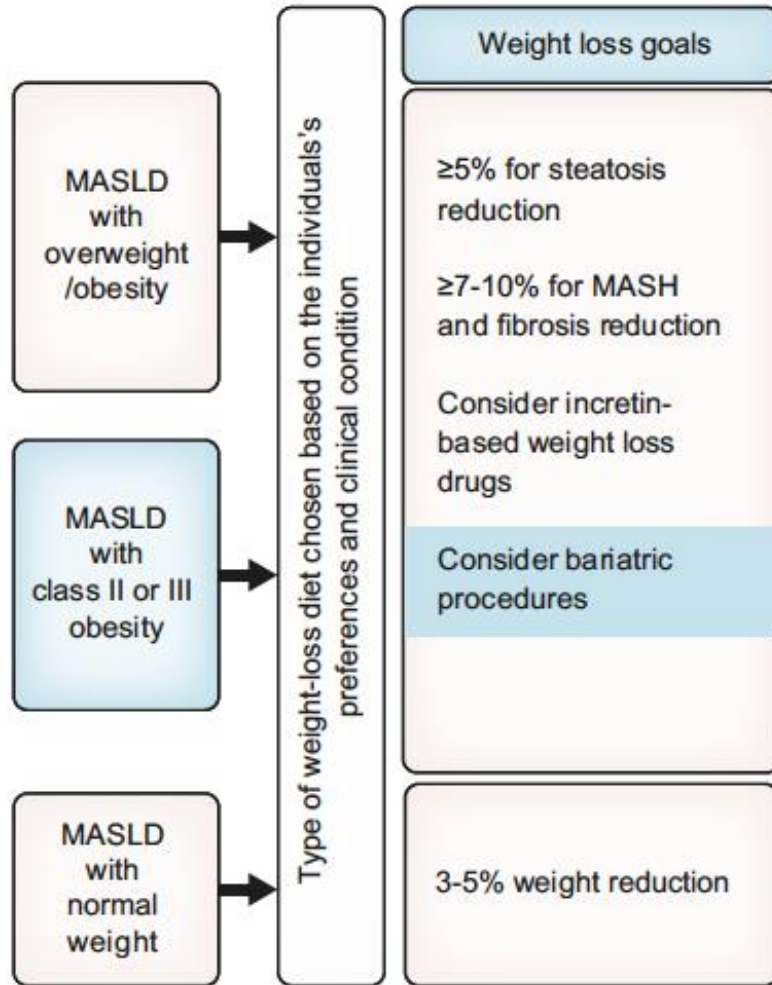
- Metabolic dysfunction associated fatty liver disease (MAFLD) is closely associated with obesity and the metabolic syndrome
- **Caloric restriction** and following a **Mediterranean diet** recommended by EASL and Australian guidelines
- **BUT weight loss is difficult to achieve and maintain**

# EASL MAS(F)LD Treatment guidelines 2024



Recommendations to all MASLD		Implementation
<p><b>Diet quality</b></p> <ul style="list-style-type: none"> <li>Mediterranean diet</li> <li>Minimising processed meat, ultra-processed foods and sugar-sweetened beverages</li> <li>Increasing unprocessed/ minimally processed foods</li> </ul>	<p><b>Physical activity</b></p> <ul style="list-style-type: none"> <li>Tailored to the individual's preference and ability</li> <li>&gt;150 min/week of moderate- or 75 min/week of vigorous-intensity physical activity</li> <li>Minimising sedentary time</li> </ul> <p><b>Other lifestyle habits</b></p> <ul style="list-style-type: none"> <li>Smoking: avoidance</li> <li>Alcohol: discouraged or avoidance in advanced fibrosis or cirrhosis</li> </ul>	<ul style="list-style-type: none"> <li>Multidisciplinary care</li> <li>Lifestyle evaluation during healthcare visits</li> <li>Affordable structured lifestyle interventions</li> <li>Individualised plan depending on the patient's preferences and economic constraints</li> <li>Behavioural therapy</li> </ul>
<p><b>MASH cirrhosis</b></p> <ul style="list-style-type: none"> <li>Lifestyle adapted to the severity of liver disease and nutritional status</li> <li>Sarcopenia or decompensated cirrhosis: high-protein diet and late-evening snack</li> <li>Compensated cirrhosis with obesity: moderate weight reduction plus high-protein intake and physical activity</li> </ul>		
<p><b>Long-term goals:</b></p> <p>Quality of life and survival Cardiometabolic benefits Prevention of cirrhosis, HCC, T2D, cardiovascular disease</p>		

# EASL MASLD Treatment guidelines 2024

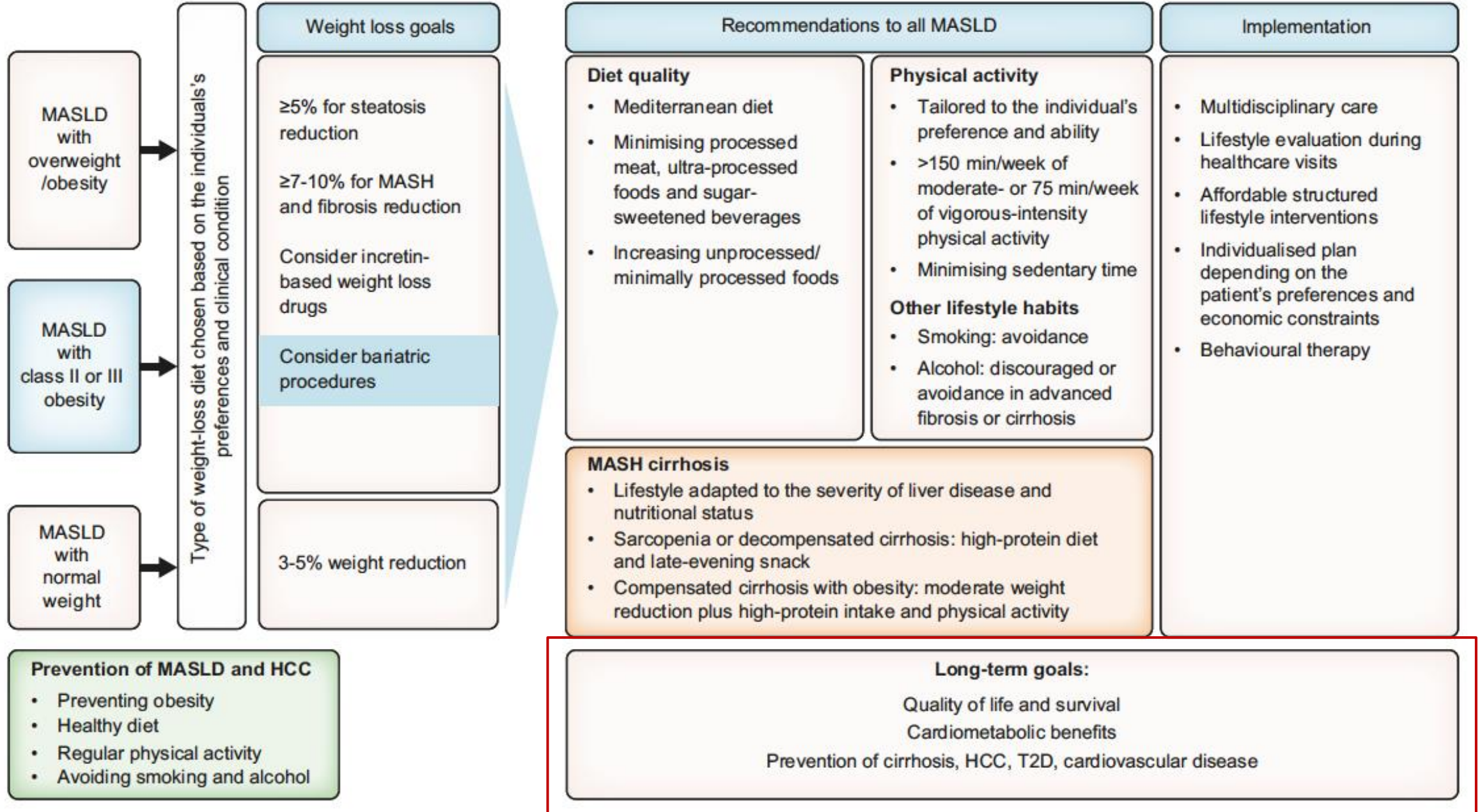


- Prevention of MASLD and HCC**
- Preventing obesity
  - Healthy diet
  - Regular physical activity
  - Avoiding smoking and alcohol

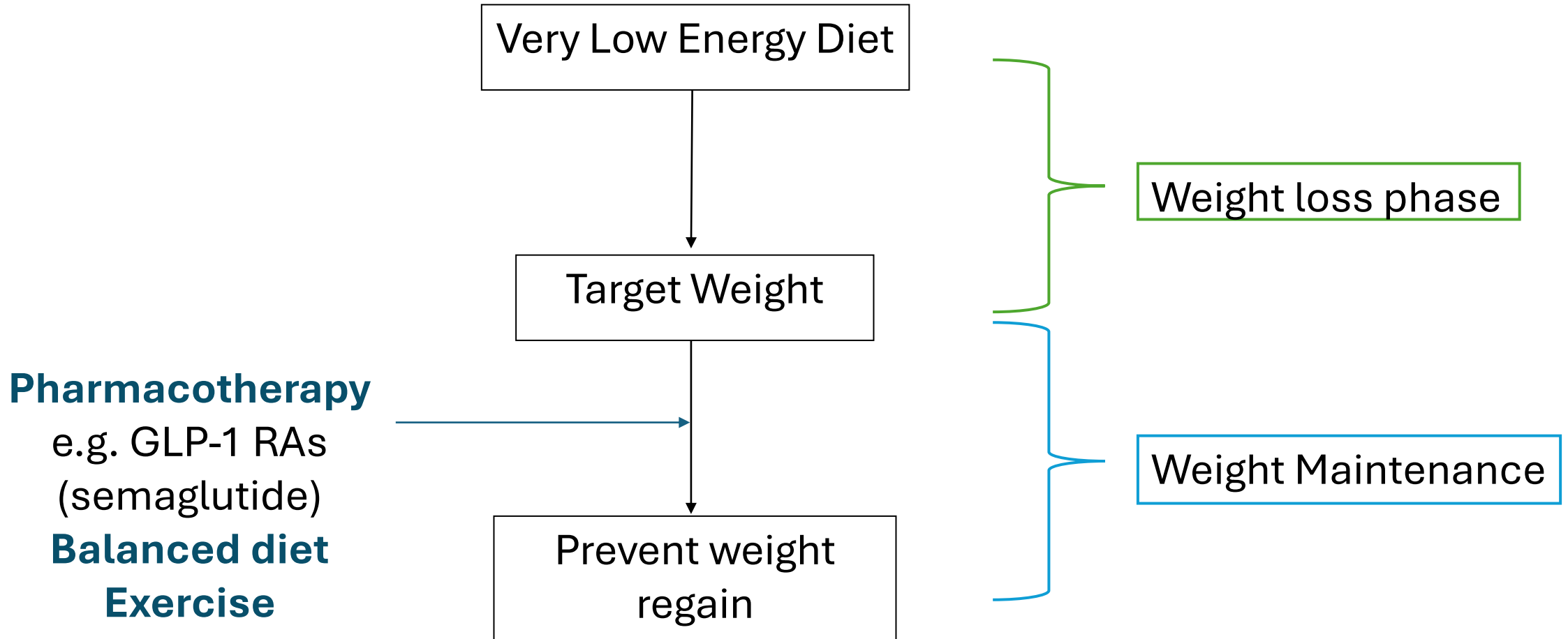
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- Quality of life and survival
  - Cardiometabolic benefits
  - Prevention of cirrhosis, HCC, T2D, cardiovascular disease

# EASL MASLD Treatment guidelines 2024



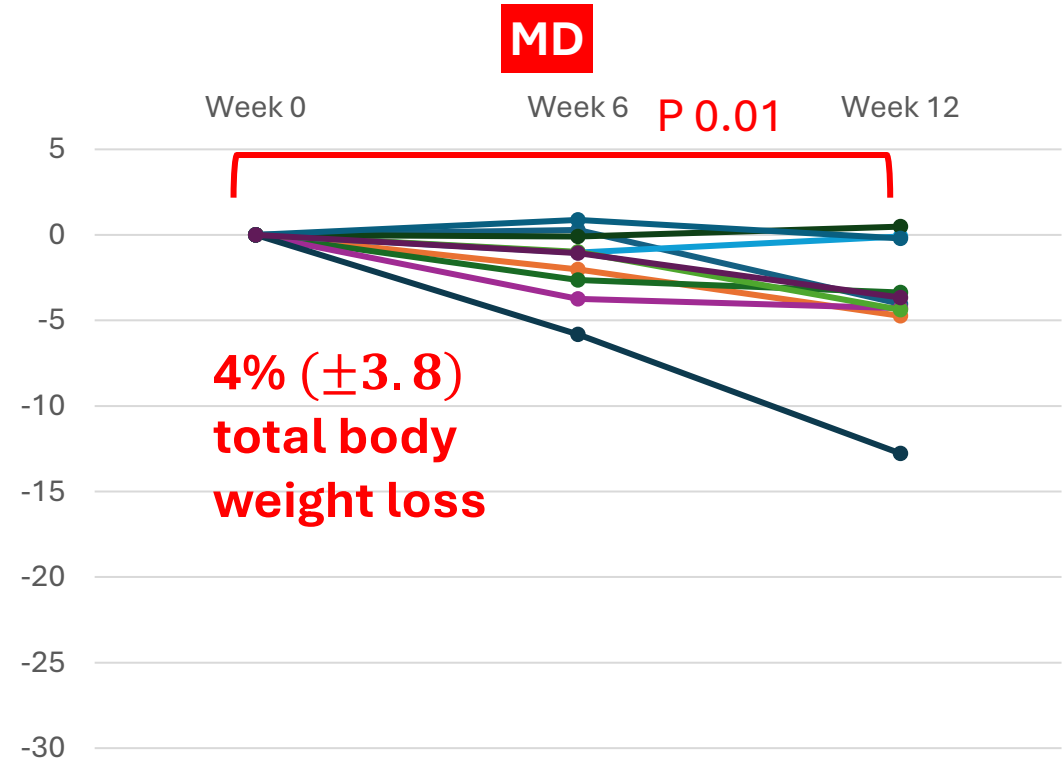
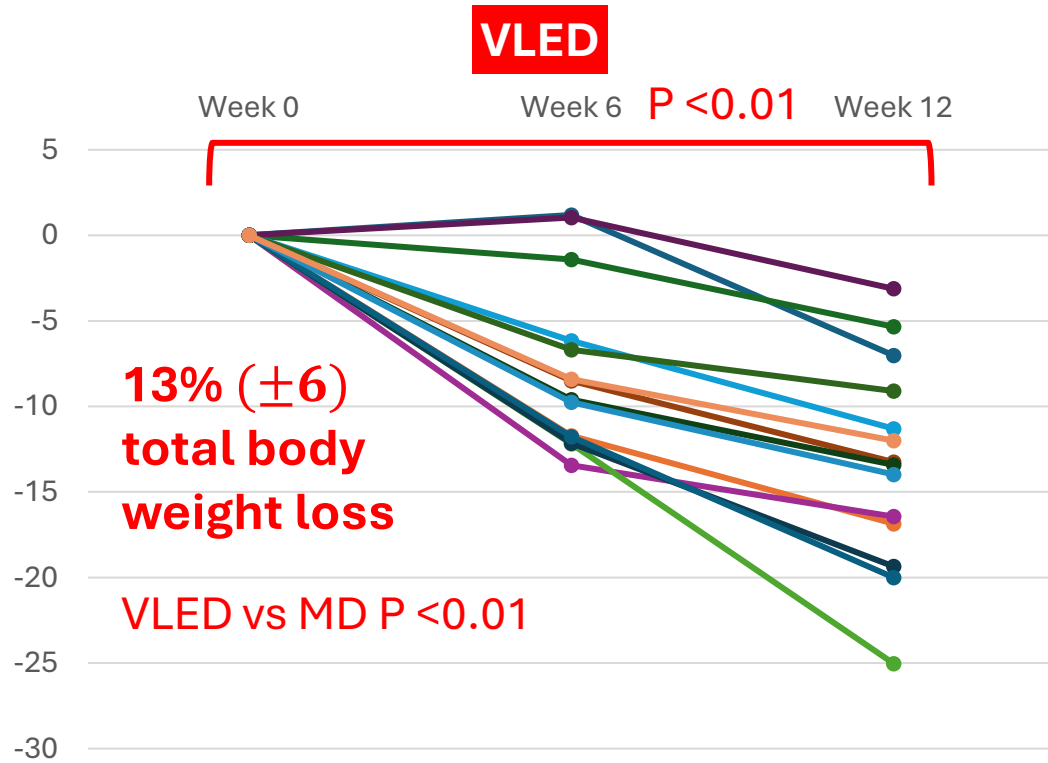
# Medical management of obesity





# DARWIN study: RCT of VLED vs MD for MASH

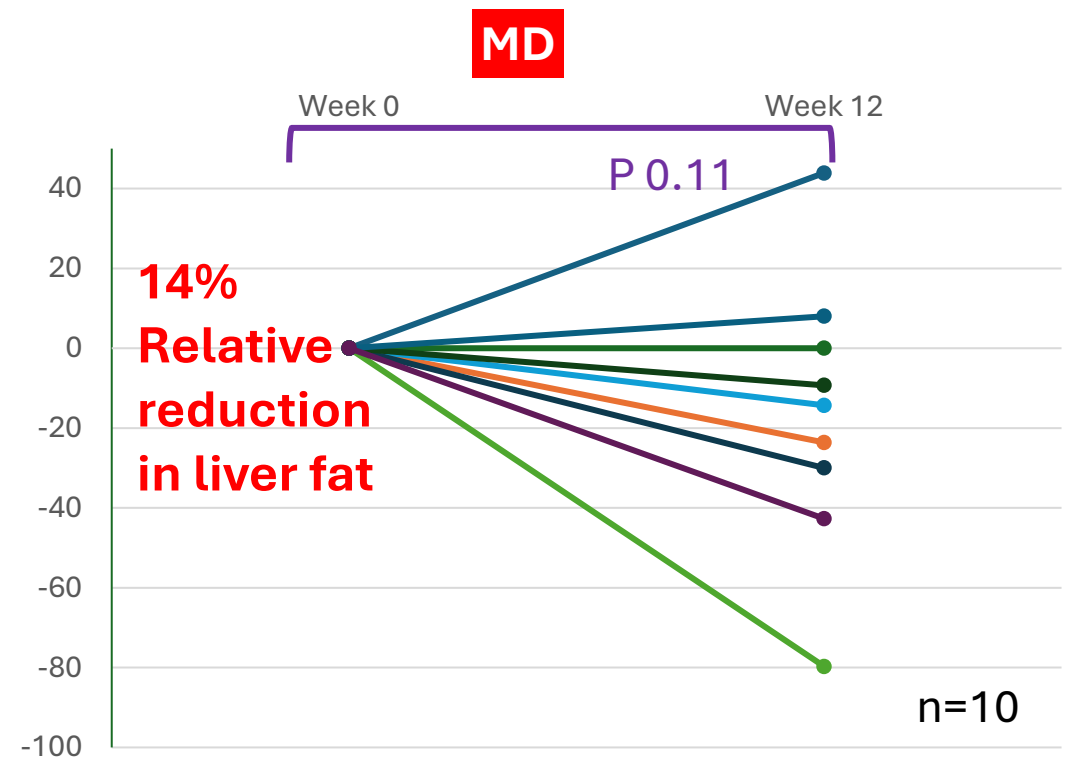
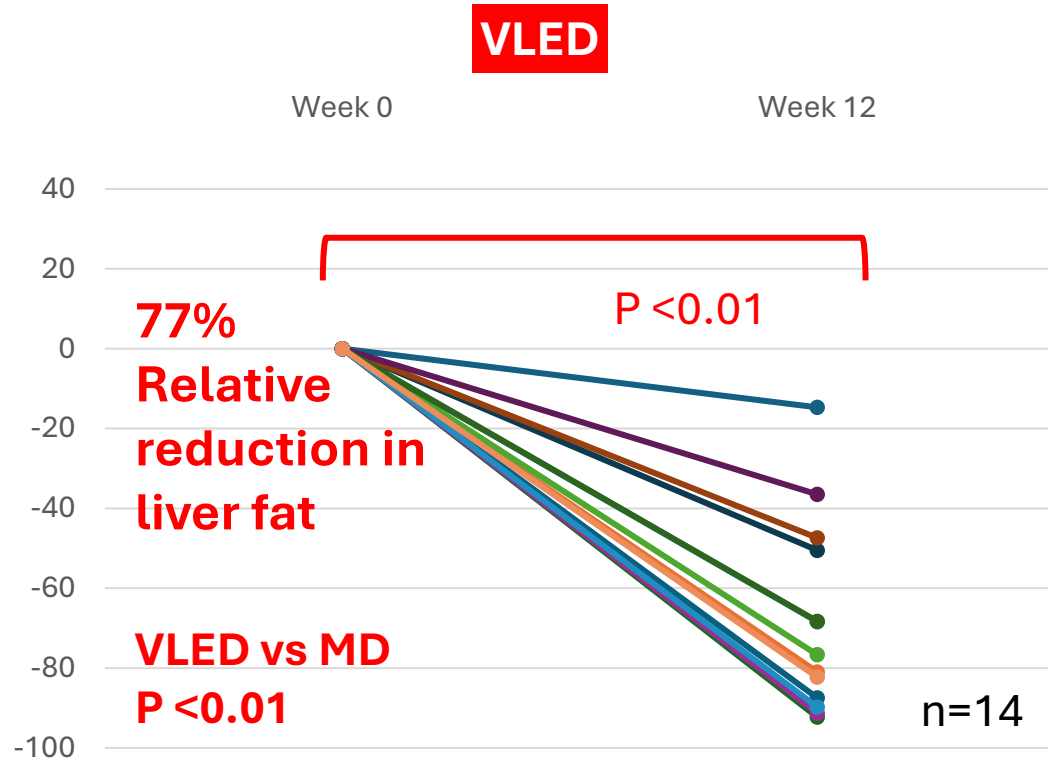
## VLED: greater weight loss at wk 12



Week 12	VLED	MD	P-value
Clinically significant weight loss (>10% TBWL)	71% (n=10)	10% (n=1)	< 0.01

# VLED: greater reduction in MR-liver fat at wk 12

## Improved biochemical parameters

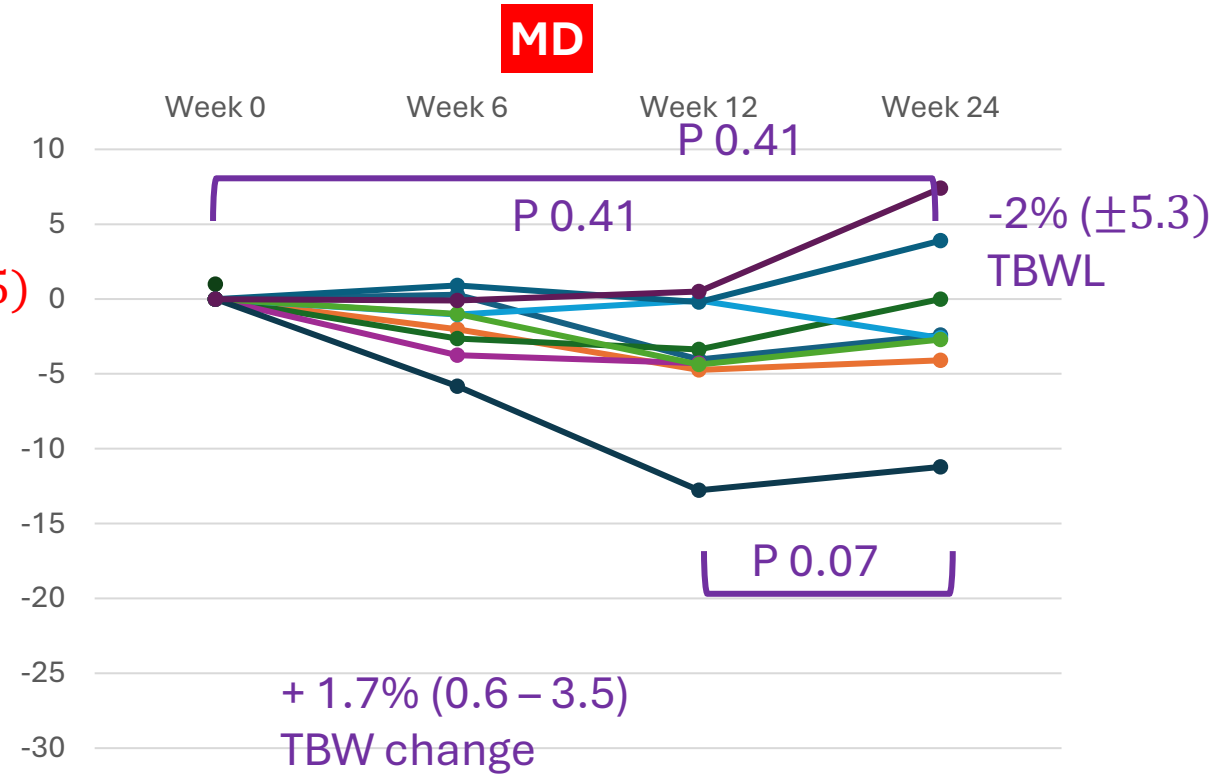
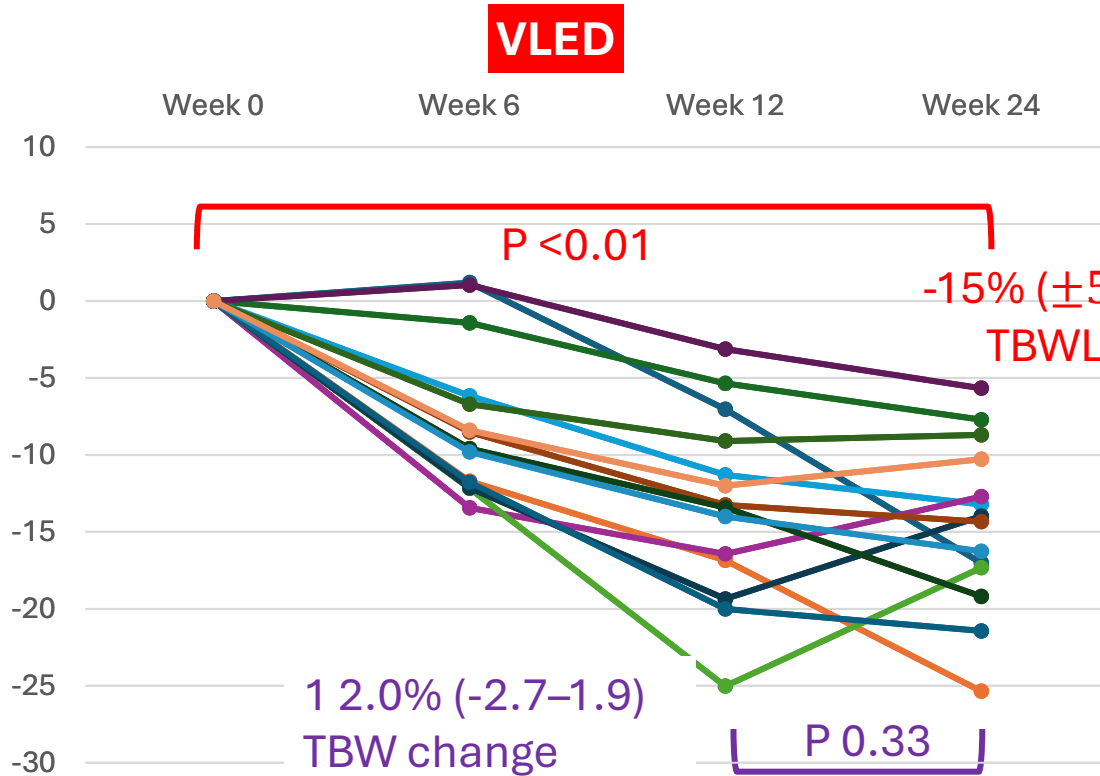


	VLED	MD	P-value
Normalization of liver fat ( $\leq 5\%$ steatosis)	46% (n=6)	10% (n=1)	< 0.01

# VLED and semaglutide vs MD

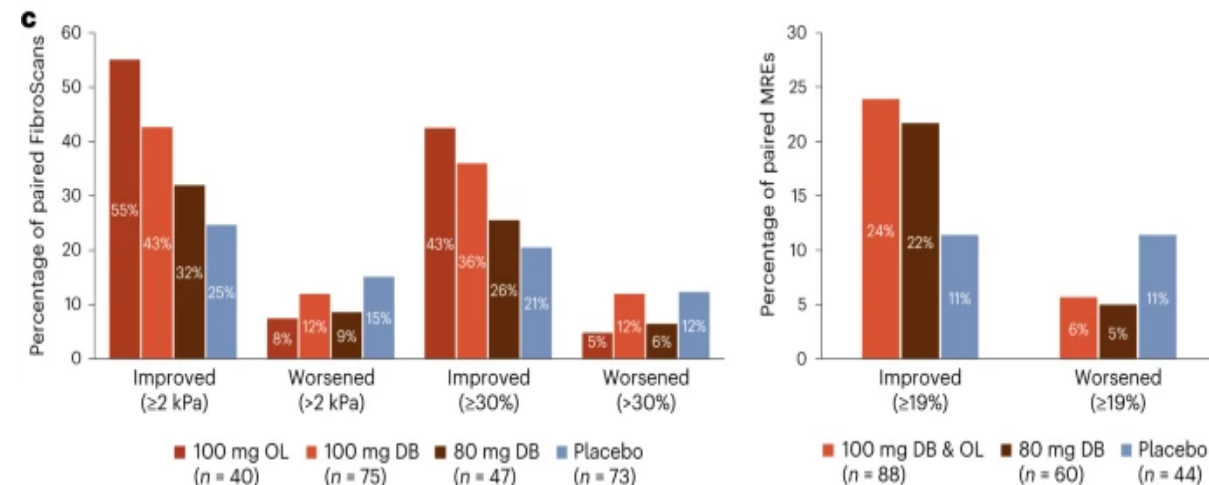
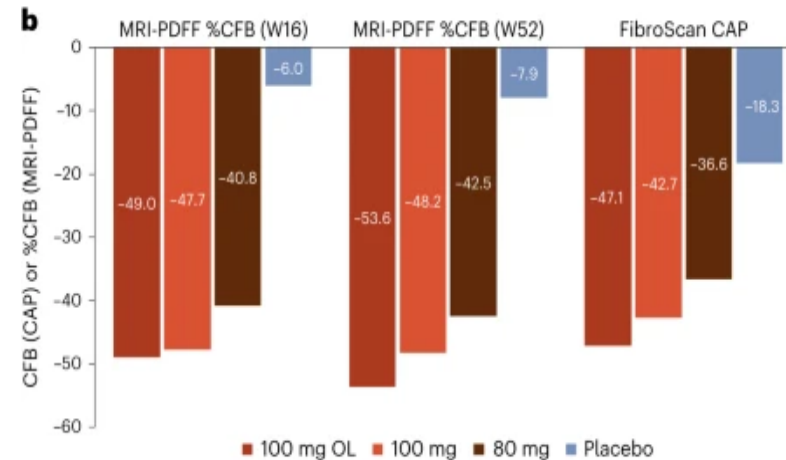
VLED: weight loss maintained from wk 12 to 24

Liver fat reduction also maintained in VLED/ semaglutide group



# Medications: Resmetiron

- Liver B thyroid receptor thyromimetic
- MAESTRO-NASH phase III trial
- **Approved in USA March 2024**
- Reduced steatohepatitis and fibrosis
- Lipids and LFTs improved
- No impact obesity or T2DM
- NOT for use in cirrhosis
- No long-term outcome data yet
- GI side effects (30%), once daily oral



# Other medications

- **GLP-1 agonists** (eg: semaglutide)
  - Glucose dependent insulinotropic polypeptide agonists
  - Safe to use in MAFLD, including in compensated cirrhosis
  - Histological benefits more inflammation, not fibrosis resolution
  - Seem to have an anorectic effect that helps with weight loss
  - Also central effects- “reduces the noise around food thinking”
- **Dual and triple acting GLP-1 plus lipogenesis inhibitors** (eg: tirzepatide)
  - Equal or greater weight loss to bariatric surgery
- SGLT2 inhibitors and metformin safe but not effective in MAFLD



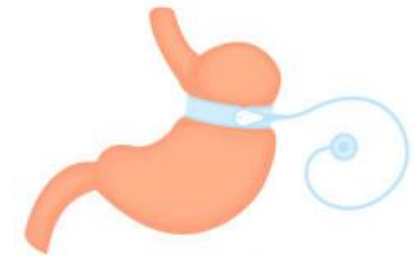
# Bariatric surgery

- Bariatric surgery shown to reduce T2DM, improve cardiovascular risk, reduce liver outcomes
  - Sleeve gastrectomy
  - Diverting gastro-intestinal bypass (eg Roux en Y)
- 30% improved or resolved fibrosis with Roux en Y
- **Eg: BRAVES study** 55% improved histology
  - No change in fibrosis
- **Medicare:** BMI > 40; OR BMI > 35 and comorbidity (eg: T1DM)
- In those with compensated cirrhosis, careful evaluation required
- Endoscopic bariatric procedures have insufficient data currently in MAFLD

## BARIATRIC SURGERY PROCEDURES



VERTICAL SLEEVE  
GASTRECTOMY



ADJUSTABLE  
GASTRIC BAND



ROUX-EN-Y  
GASTRIC BYPASS



MINI-GASTRIC  
BYPASS

# Prevention of MAFLD

- Primary versus secondary prevention
- Reduce risk of MAFLD, cirrhosis and HCC
- Broader impact on health of populations of healthy lifestyle
  - Healthy weight range
  - Mediterranean unprocessed high fibre diet
  - Exercise, active lifestyle
  - Minimise carcinogens smoking, alcohol
- Specific interventions for MALD
  - Reduce red meat consumption, sugar containing drinks
  - Coffee consumption
  - Statins, aspirin

# **Models of care and barriers to care**



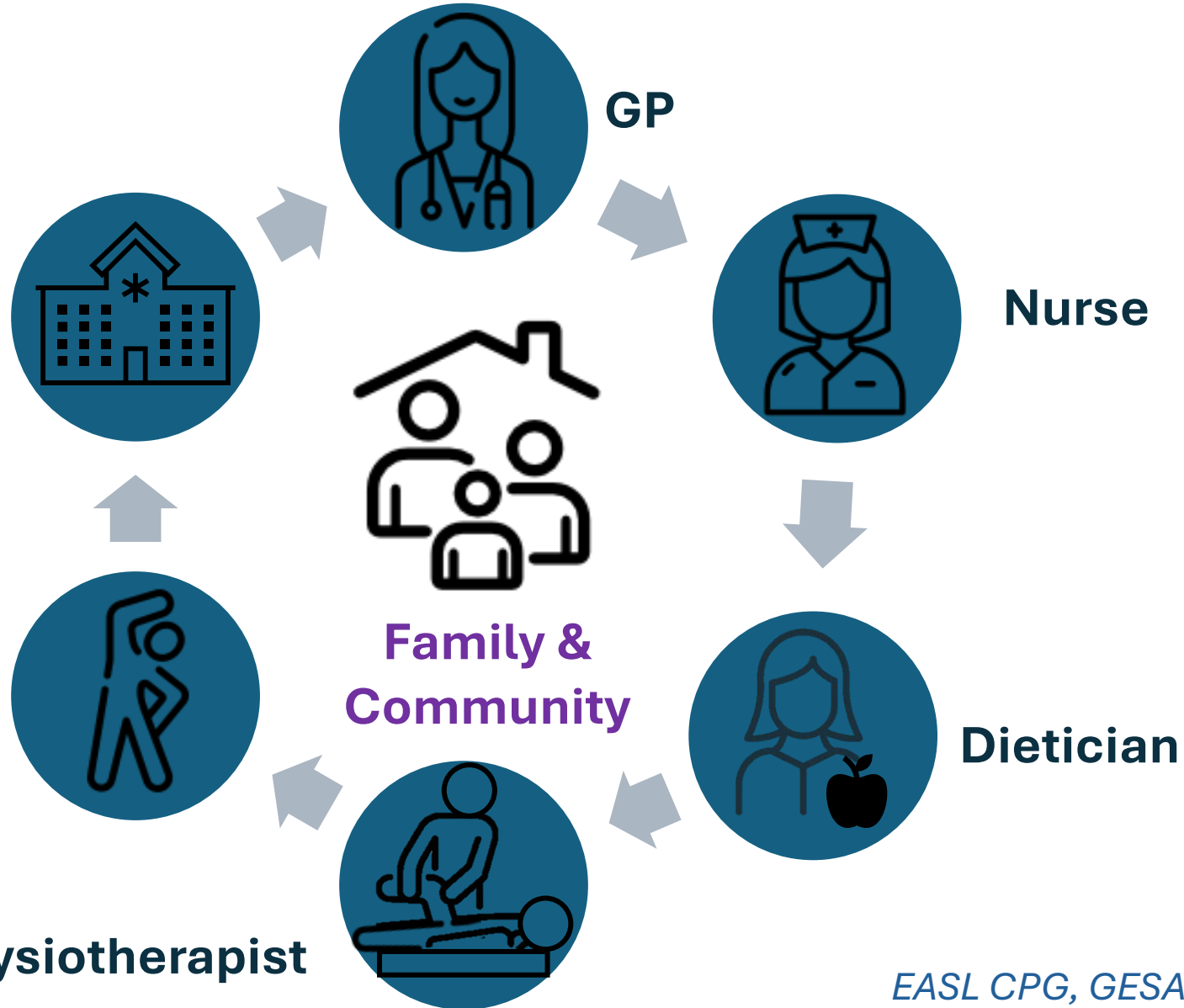
# MAFLD Multidisciplinary models of care

## Specialists

- Hepatologist
- +/- Bariatric surgeon
- +/- Endocrinologist
- +/- Cardiologist

Exercise  
physiologist

Physiotherapist



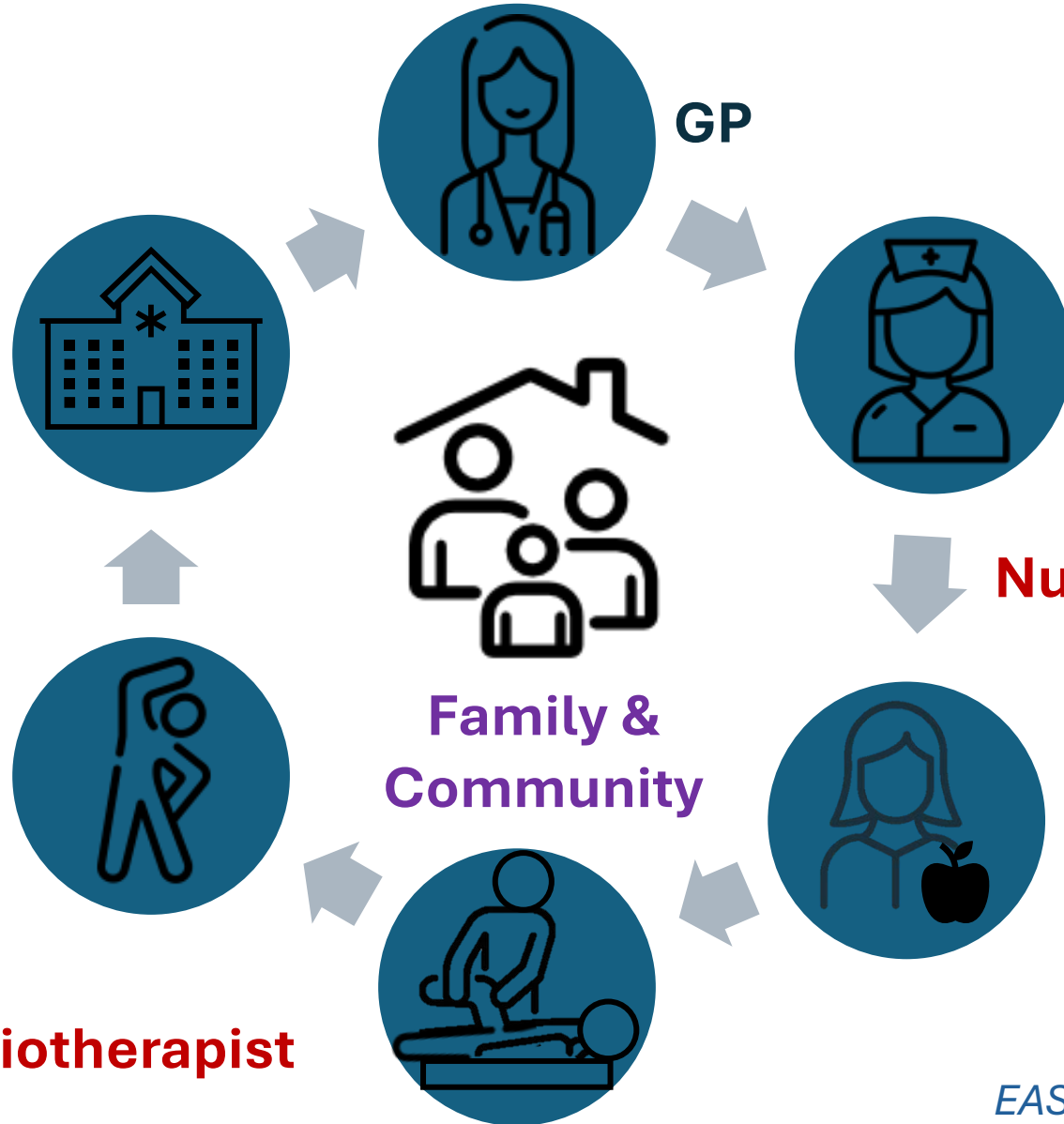
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**Exercise  
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## MASLD MDT:

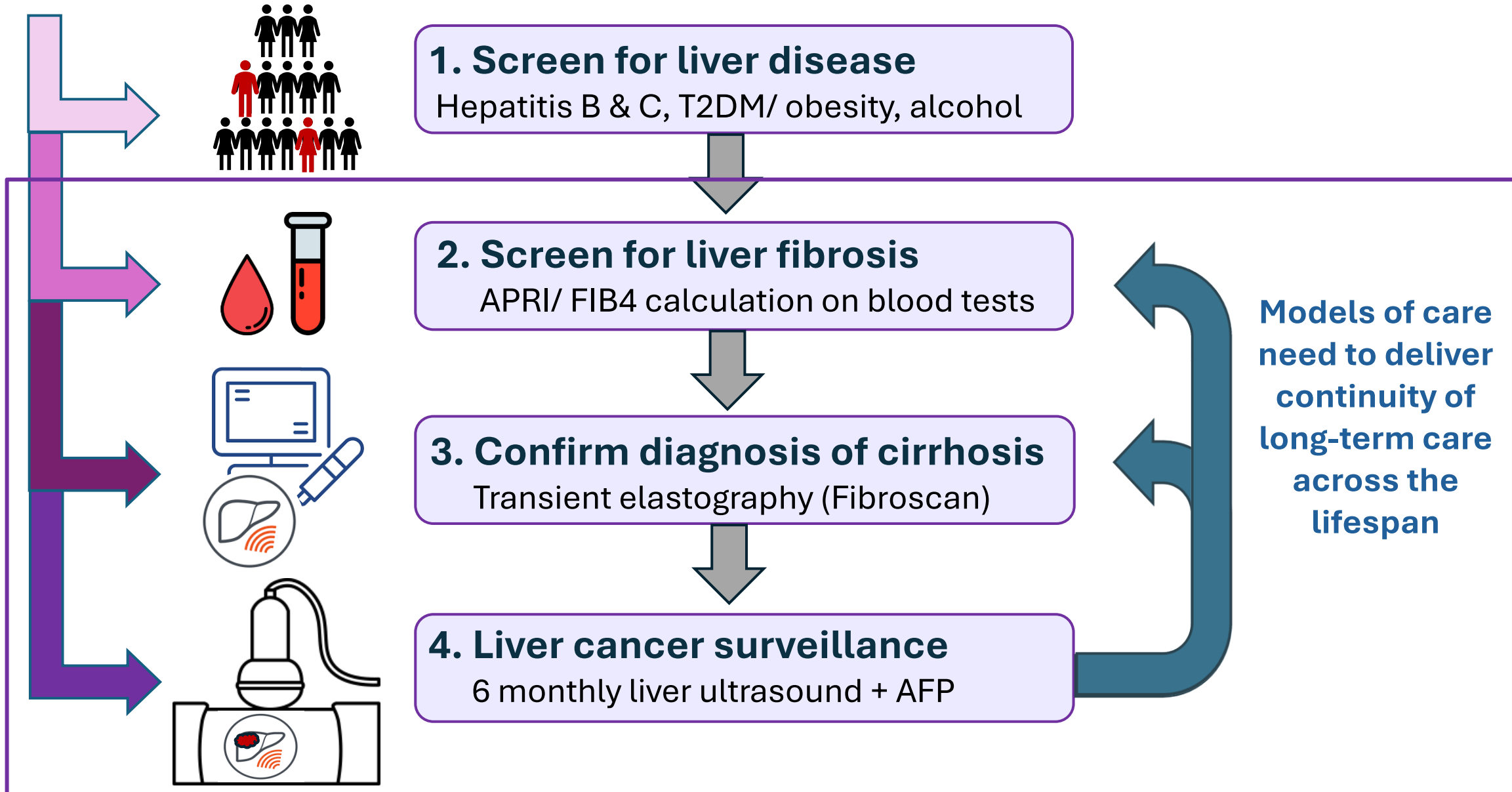
- **Inaccessible**
- **Only partially subsidized, or**
- **Not funded**

**Nurse**

**Dietician**



# Pathway of care for people with liver disease



# Barriers to MAFLD care

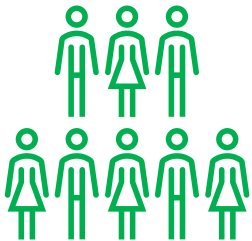


## INDIVIDUAL

- Time pressures
- Support networks
- Socioeconomic status
- Education level/ health literacy
- Access to health services
- Competing priorities

## ENVIRONMENT & POLICIES

- Access to exercise
- Access to fresh foods
- Alcohol industry
- Processed food and sugar industry
- Socioeconomic policies



## SOCIO-CULTURAL

- Cultural foods and eating behaviours
- Cultural attitudes to food
- Cultural health beliefs
- Cultural impact on body image
- Gender roles and norms

## HEALTH SYSTEM

- Medicare rebates for allied health
- Health staff & service coverage
- PBS rebates medications and access
- General practice model limitations
  - Ad hoc use by clients
  - 1-2 items for discussion
  - privatised
- Lack of chronic liver disease nurses
- No MBS item for liver check or MASLD



# Policy measures

Medicare rebate for more allied health sessions

Specific MBS item number for "healthy liver check"

Include MASLD in type 2 diabetes and cardiovascular checks

Regulate unhealthy processed food and drink marketing

Food industry reformulations, front of package nutrition labels

Subsidize availability of high-quality unprocessed healthy food

Public education to increase food and health literacy

Regulation and taxation alcohol, smoking

Invest in public transport and safe outdoor spaces for recreation

Subsidize gym and sporting club memberships

# Conclusions

Weight loss,  
mediterranean diet  
and exercise  
mainstay of therapy

Weight loss  
by any means  
beneficial in MASLD

Bariatric surgery  
effective

No treatments on  
PBS for MASLD

Need policy  
solutions to reduce  
MASLD

Need  
multidisciplinary  
models of care  
across lifespan



# Acknowledgements



**Dr Ann Farrell, PhD Scholar**



## **DARWIN Investigators**

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