



Updates in nonalcoholic fatty liver disease

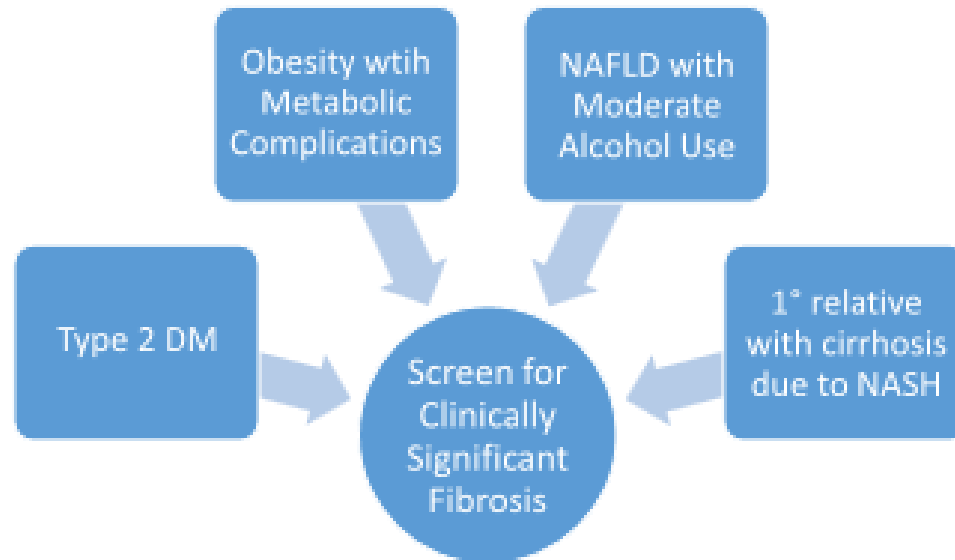
Definition and Epidemiology

- ▶ In parallel with the obesity epidemic and rising metabolic comorbidities, the prevalence of NAFLD has reached 25% worldwide
- ▶ NAFLD encompasses a spectrum of conditions defined by hepatic steatosis without significant contributions from secondary causes, such as alcohol, Medications, or inborn errors of metabolism
- ▶ Patients with NAFLD experience both increased liver- related mortality and overall mortality, with the most common cause of death being cardiovascular disease, followed closely by cancer

screening

- ▶ screening for
 1. type 2diak
 2. obesity with
 3. individuals g/d in wor
 4. and in first
- ▶ also recomr tested for:

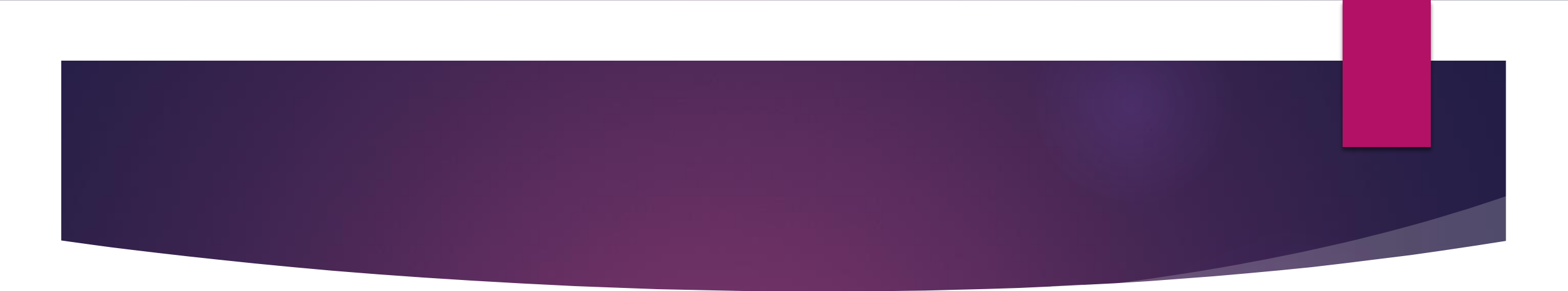
1. T2DM, and
2. obesity-based adiposity-based chronic disease should be assessed for the presence and severity of NAFLD

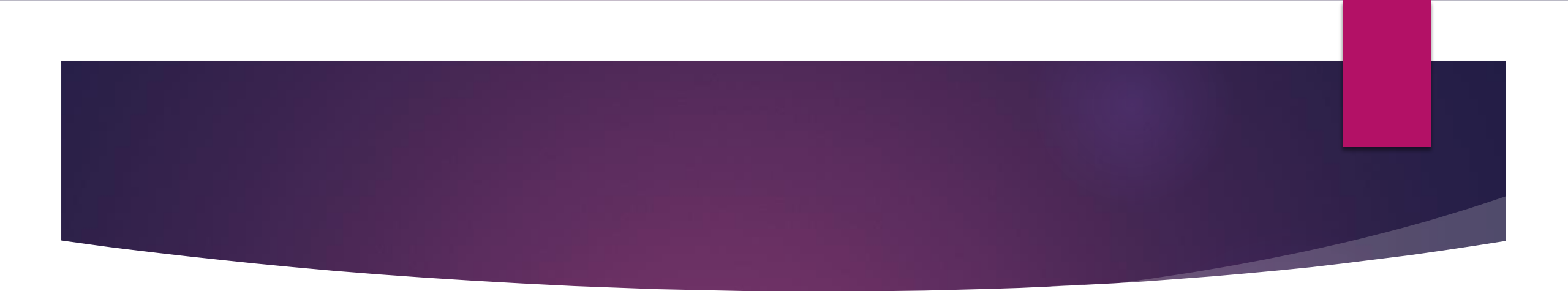


up to 21–39

Approach

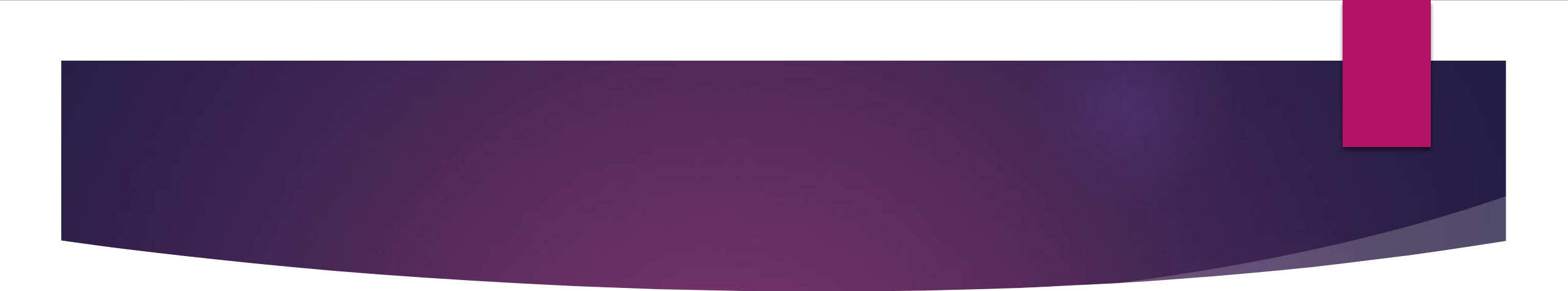
- ▶ The initial step identifies patients with NAFLD at greatest risk for clinically significant fibrosis:
 1. T2DM
 2. 2 or more metabolic risk factors (central obesity, dyslipidemia, hypertension, and pre-diabetes)
 3. incidental findings of hepatic steatosis or elevated aminotransferases
- ▶ The FIB-4 score is an easy-to-calculate, noninvasive measure of liver fibrosis based on age, alanine aminotransferase, aspartate aminotransferase, and platelet count.
- ▶ assessment with liver stiffness measurement (LSM) using vibration-controlled transient elastography

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- ▶ FIB-4 score of <1.3 : very low risk for advanced hepatic fibrosis The pathway recommends these individuals undergo repeat noninvasive testing with laboratory testing in 2–3 years.
 - ▶ An indeterminate FIB-4 score of 1.3–2.67: necessitates further risk assessment with LSM.
 - ▶ LSM <8 kPa are at low risk for advanced fibrosis, and repeat noninvasive testing is recommended in 2–3 years.
 - ▶ Patients with an LSM > 8 kPa should be referred to hepatology with management by a multidisciplinary team
 - ▶ FIB-4 score > 2.67 : increased risk for advanced fibrosis and should be referred to hepatology for management, ideally by a multidisciplinary team.

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- ▶ the accuracy of the FIB-4 score varies with extremes of age. Thus, caution should be used in its interpretation for patients 65 years of age or above and those below 35 years of age given the risk of false-positive and false-negative results, respectively.
 - ▶ Additionally, patients with thrombocytopenia due to nonliver-related etiologies may have falsely elevated FIB-4 scores.
 - ▶ assessments or liver biopsy need to be considered if indicate

MEDICAL MANAGEMENT

- ▶ multidisciplinary approach can best address and prevent complications particularly given the high prevalence of nonhepatic metabolic comorbidities A multidisciplinary management plan may include:
 1. lifestyle modifications
 2. pharmacologic treatments
 3. endobariatric interventions.

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- ▶ Lifestyle modifications: improve cardiovascular risk factors
 1. weight loss: loss of 3%–5% of body weight
 2. Mediterranean diet (avoidance of fructose)
 3. Exercise (150–300 minutes of moderate-intensity or 75–150 minutes of vigorous-intensity aerobic exercise per week)
 - ▶ the greatest histologic improvement and fibrosis regression seen in patients with $\geq 10\%$ of body weight lost
 - restrict alcohol consumption

Pharmacologic therapies

- no FDA-approved medications for the treatment of NAFLD
- **Resmetirom**: a thyroid hormone receptor agonist, increases hepatic fat metabolism, decreases lipotoxicity, and decreases hepatic fat content
- **Obeticholic acid**: a farnesoid X receptor agonist, has been associated with significant improvement in hepatic fibrosis
- **(SGLT2) dapagliflozin**: work by decreasing renal glucose reabsorption and have been shown to reduce hepatic lipid content
- **(GLP1) semaglutide and liraglutide** :decrease post-prandial glucagon secretion, and increase post-prandial insulin secretion.
- **Dipeptidyl peptidase IV (DPP4) inhibitors**: including sitagliptin and vidagliptin, enhance GLP1activity
- **Lanifibranor**: is a pan peroxisome proliferator–activated receptor agonist that improves insulin sensitivity and has been associated with improvement in liver histology
- **Thiazolidinediones**: pioglitazone are peroxisome proliferator–activated receptor γ agonists that have been demonstrated to improve insulin sensitivity

Bariatric and endobariatric and metabolic therapies

- Bariatric surgery can improve NASH, hepatic fibrosis, and cardiovascular risk factors **but is not an established treatment** recommendation for NAFLD
- Complications of bariatric surgery include anastomotic leak and strictures, dumping syndrome, malabsorption, wound infection, gastroesophageal reflux disease, and vitamin deficiencies
- ▶ FDA-approved EBMTs(endobariatric and metabolic therapies) include the intragastric balloon and endoscopic sleeve gastrectomy.
- ▶ EBMTs have been associated with improvement in liver fibrosis, hepatic steatosis, and insulin resistance
- ▶ Side effects and complications of EBMTs include weight regain, pancreatitis, intraprocedural bleeding, and symptomatic gastroesophageal reflux disease

TABLE 2 Suggested pharmacologic agents for weight loss^[33]

Agent	Adverse effects	When to avoid
Semaglutide	Delayed gastric emptying, nausea, and vomiting Increased risk of pancreatitis and gallbladder disease	Personal or family history of medullary thyroid carcinoma History of multiple endocrine neoplasia type 2 Pregnancy
Liraglutide	Delayed gastric emptying, nausea, and vomiting Increased risk of pancreatitis and gallbladder disease	Personal or family history of medullary thyroid carcinoma History of multiple endocrine neoplasia type 2 Pregnancy
Phentermine/Topiramate ER	Tachycardia Constipation Dry mouth	History of cardiovascular disease Uncontrolled hypertension Pregnancy (topiramate is teratogenic)
Naltrexone-Bupropion ER	Headache Sleep disturbance Nausea Constipation Vomiting	Avoid in patients with seizure disorders or at risk for seizures Do not use with concomitant opiates
Phentermine	Cardiac effects including tachycardia and hypertension	History of cardiovascular disease

THANK YOU