Understanding NASH as a metabolic disease

Guideline recommendations for NAFLD/NASH diagnosis and management

Novo Nordisk’s commitment to Liver Health

Understanding NASH as a metabolic disease

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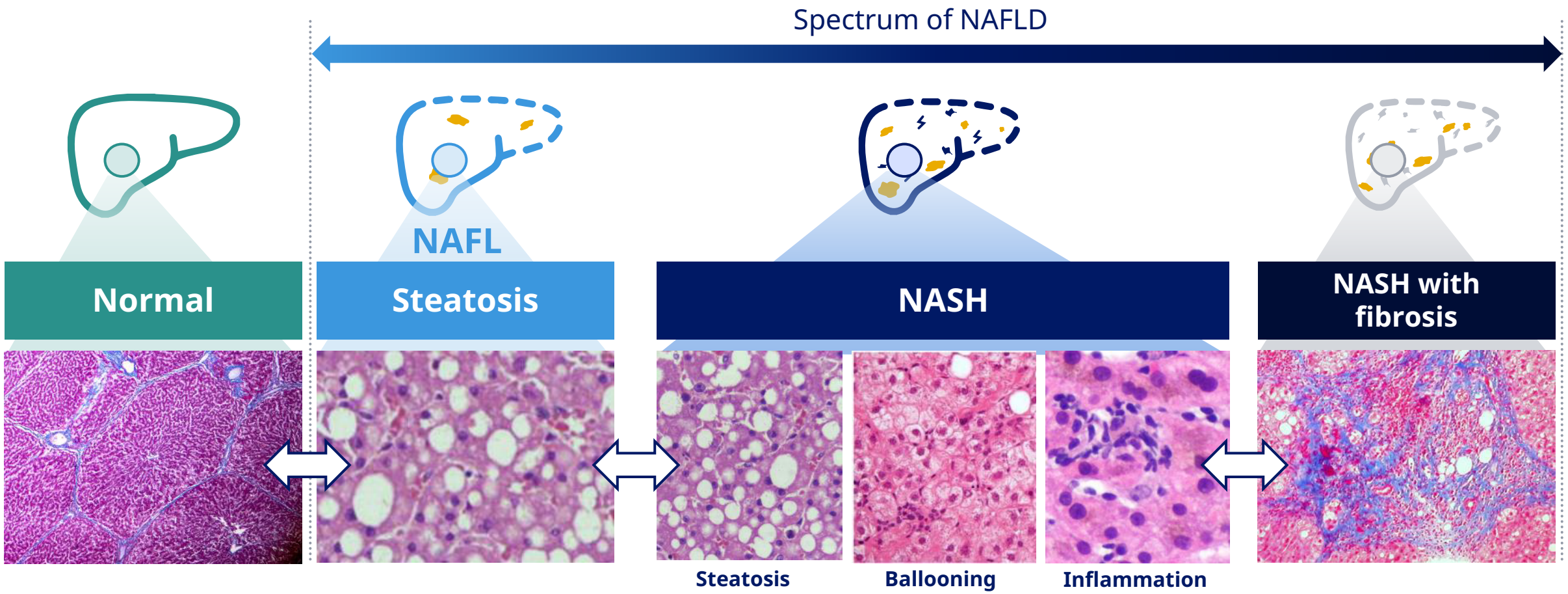
NASH is the progressive form of NAFLD



NAFLD, nonalcoholic fatty liver disease; NAFL, nonalcoholic fatty liver; NASH, nonalcoholic steatohepatitis.
Chalasani N et al. Hepatology 2018;67:328–57.
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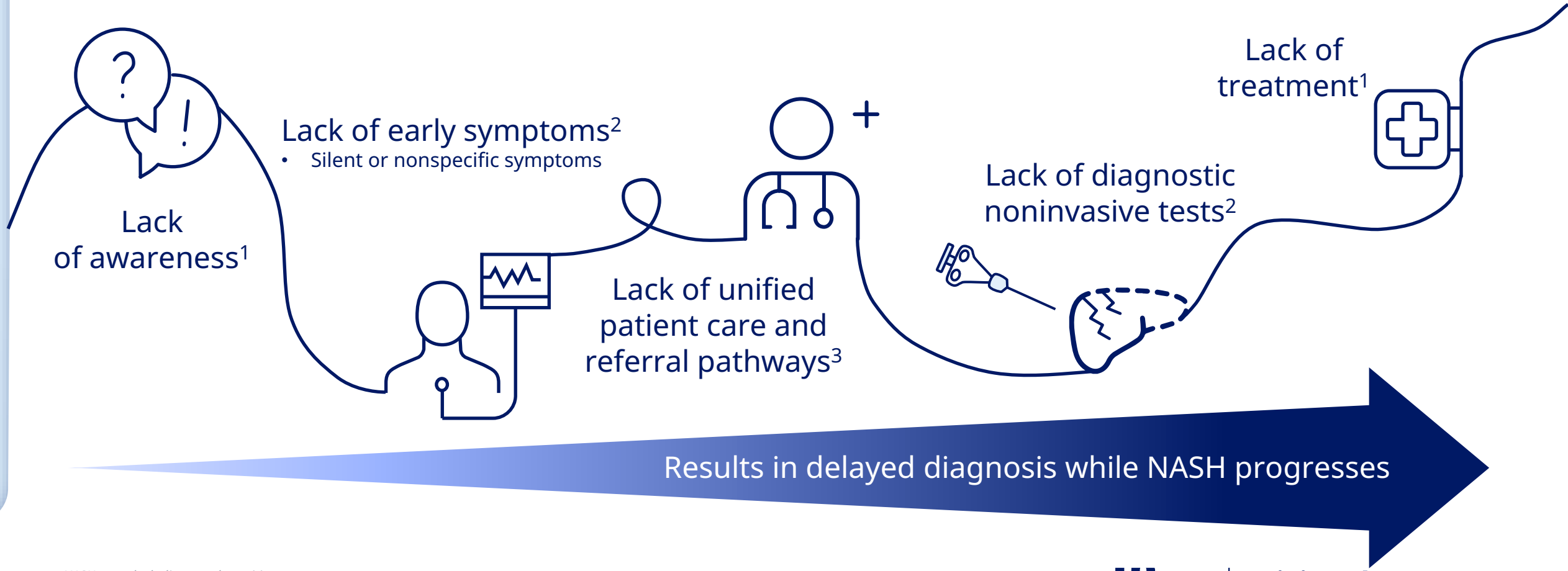
Patients living with NASH have unspecific symptoms and are often undiagnosed until later stages of disease



NASH, nonalcoholic steatohepatitis.

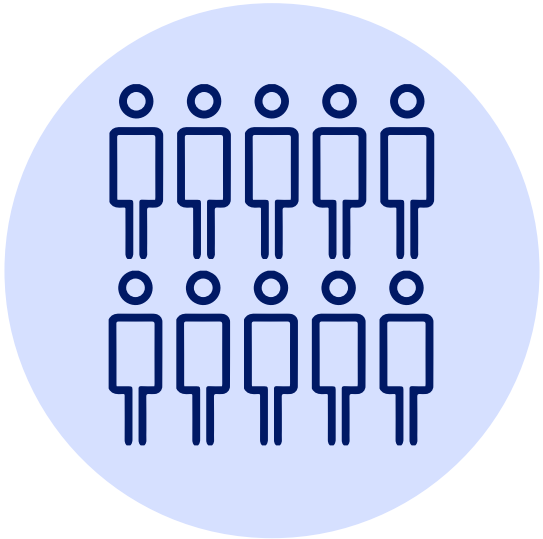
1. Ratziu V et al. J Hepatol 2015;62(1 Suppl):S65–75; 2. Ofosu A et al. Ann Gastroenterol 2018;31:288–95; 3. Lazarus JV et al. Nat Rev Gastroenterol Hepatol. 2021;18:717–29.

Patients with NASH have a higher burden of health-related comorbidities

11.2 M (68%)
with hypertension

11.9 M (72%)
with dyslipidemia

11.7 M (71%)
with MetS



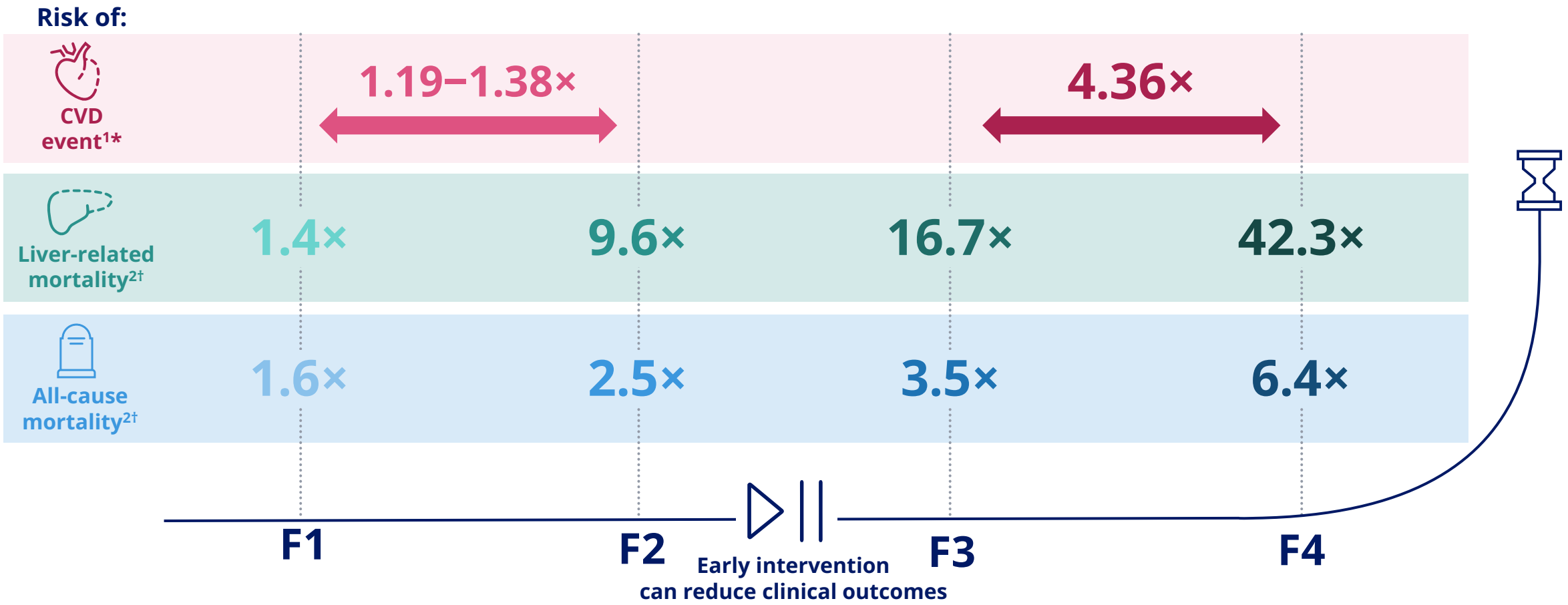
US patients living with
NASH
16.5 M

13.5 M (82%)
with obesity

7.8 M (47%)
with T2D

M, million; MetS, metabolic syndrome; NASH, nonalcoholic steatohepatitis; T2D, type 2 diabetes.
Younossi ZM et al. Hepatology 2016;64:73–84.

NASH-driven fibrosis progression increases risk of cardiovascular events and liver-related and all-cause mortality



*Compared with patients with F1–F2. †Compared with patients with F1.
CVD, cardiovascular disease; F, fibrosis stage; NASH, nonalcoholic steatohepatitis.
1. Dulai PS et al. Hepatology 2017;65:1557–65; 2. Ekstedt M et al. Hepatology 2015;61:1547–54.

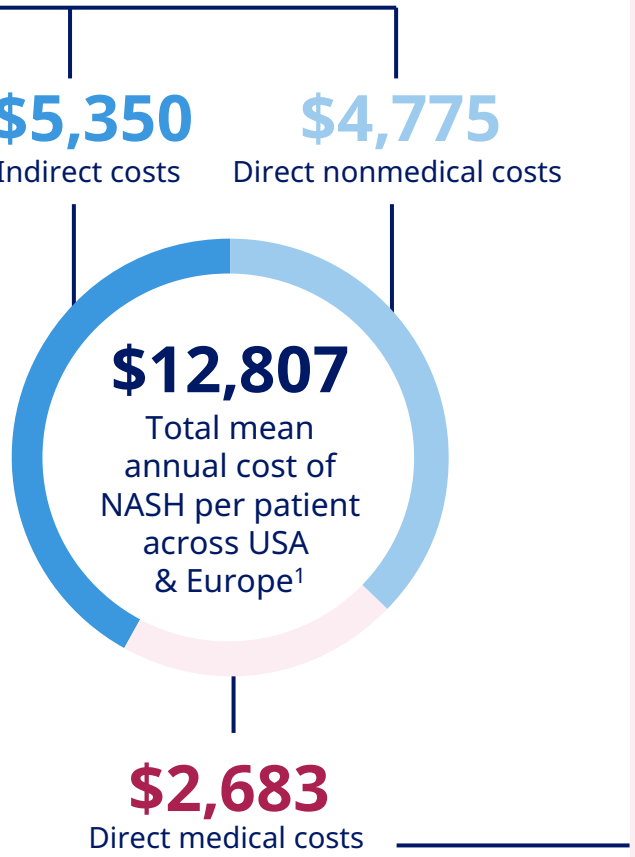
Patients living with NASH have a higher economic burden

Nonmedical and indirect costs

Caregivers account for the majority of direct nonmedical costs

Other costs include **transport, disability allowances, alternative therapies, home alteration, and OTC remedies**

Indirect costs are very high globally, accounting for **productivity loss**



Direct medical costs

The primary direct cost is medicines

There are **up to 27 different drugs** to treat NASH comorbidities

Other costs include **"off-label" prescribing of medication, hospitalizations and surgical procedures**

Costs for patients with advanced fibrosis were higher than for those with early-stage fibrosis

All costs converted from Danish Kroner values on October 12, 2022.
NASH, nonalcoholic steatohepatitis; OTC, over-the-counter.
1. O'Hara J et al. JHEP Rep 2020;2:100142.

Guideline recommendations for NAFLD/NASH diagnosis and management

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Professional associations have developed guidelines/guidance on NAFLD/NASH management

AGA Clinical Care Pathway 2021

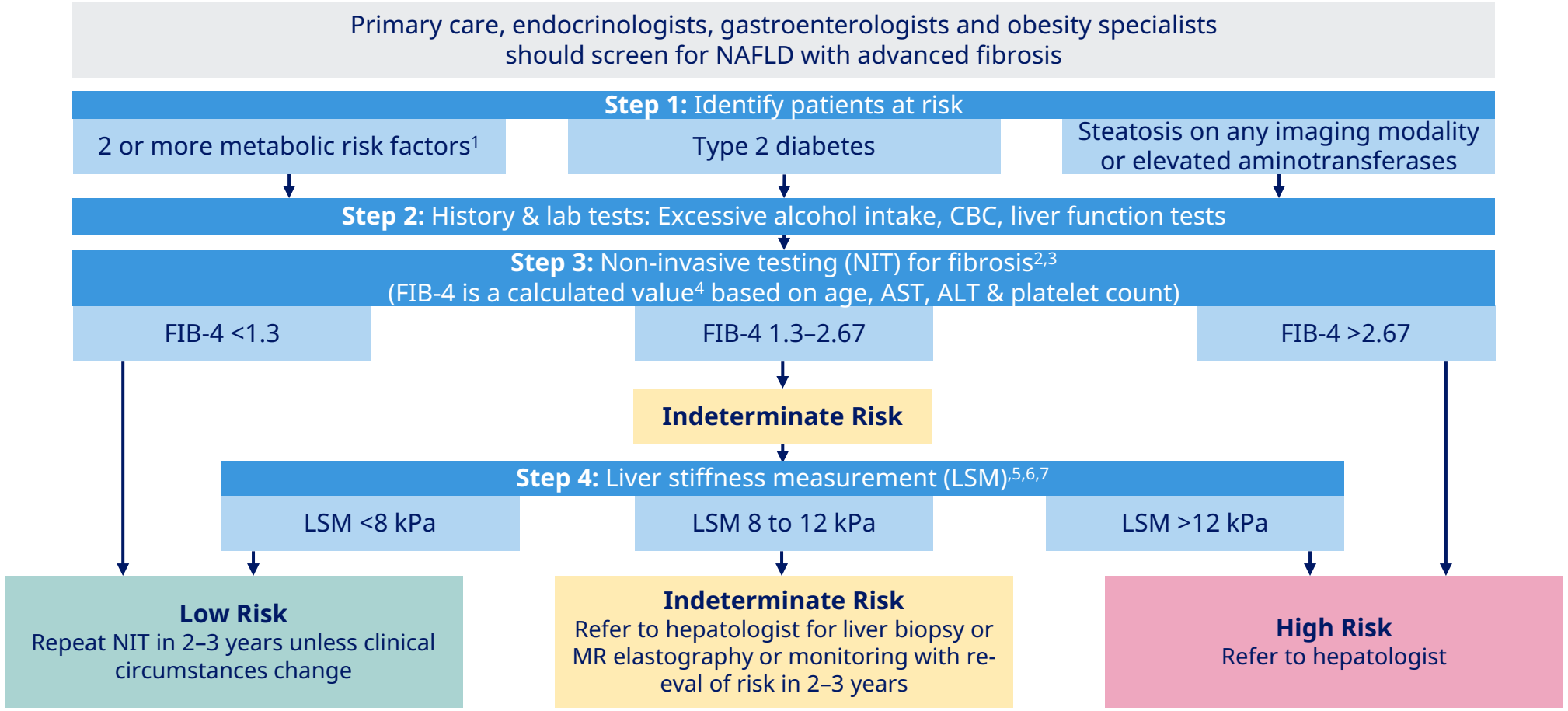
EASL Clinical Practice Guideline 2021

AASLD Practice Guidance Practice 2023

AACE Clinical Practice Guideline 2022

AGA Clinical Care Pathway 2021

Screening for advanced fibrosis related to NAFLD/NASH

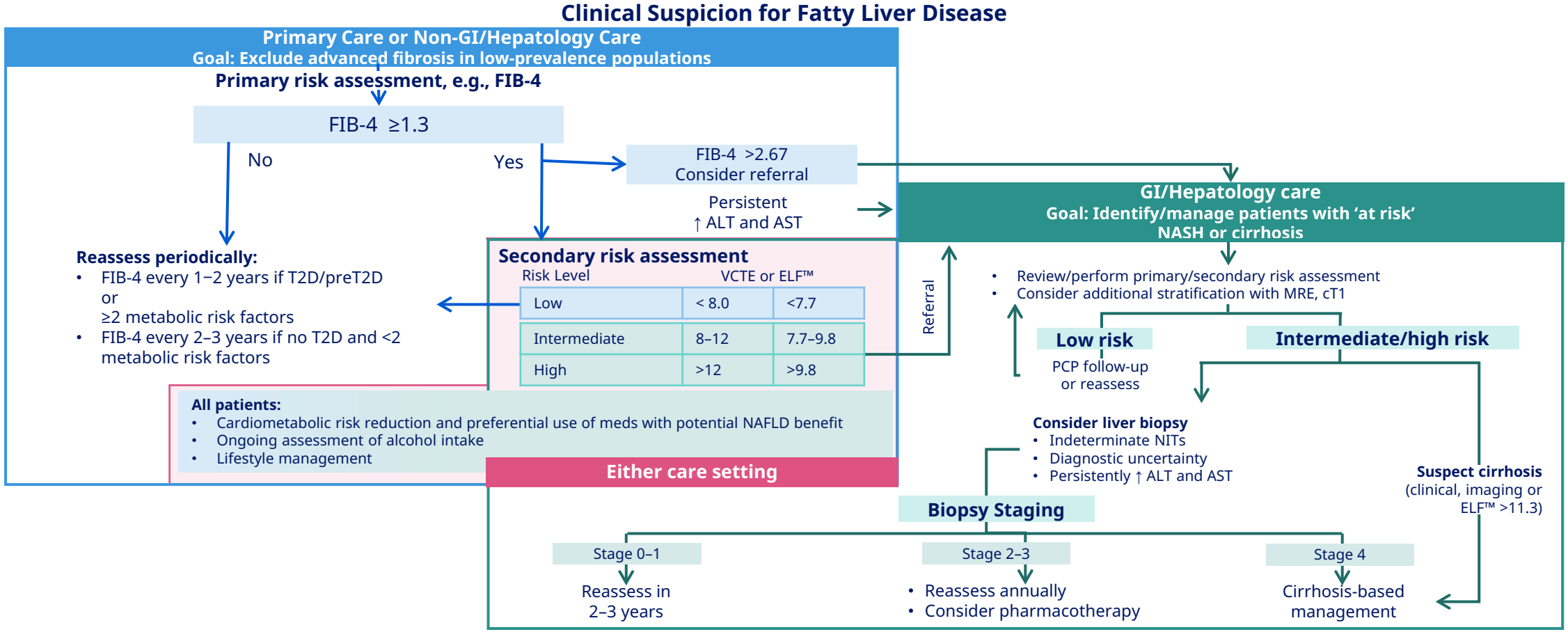


1. Metabolic risk factors: central obesity, high triglycerides, low HDL cholesterol, hypertension, prediabetes, or insulin resistance. 2. For patients age >65, use FIB-4 <2.0 as the lower cutoff. Higher cutoff does not change. 3. Other NITs derived from routine laboratories can be used instead of FIB-4. 4. Many online FIB-4 calculators are available such as https://www.mdcalc.com/fibrosis-4-fib-4-index-liver-fibrosis. 5. Ultrasound acceptable if vibration-controlled transient elastography (VCTE, FibroScan®) is unavailable. Consider referral to hepatologist for patients with hepatic steatosis on ultrasound who are indeterminate or high risk based on FIB-4. 6. LSM values are for VCTE (FibroScan®). Other techniques such as bidimensional shear wave elastography or point shear wave elastography can also be use used to measure LSM. Proprietary commercially available blood NITs may be considered for patients considered indeterminate or high risk based on FIB-4 or APRI, or where LSM unavailable. 7. Eddowes et al. uses 8.2 and 12.1 kPa as cutoffs for LSM using VCTE. Validation of simple (rounded) cutoffs reported by Papatheodoridi et al.

Adapted from: Kanwal F et al. Gastroenterol. 2021;161:1657–69.

AASLD Practice Guidance 2023

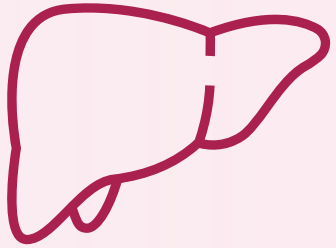
Clinical practice across caregiver spectrum



AASLD, American Association for the Study of Liver Diseases; ALT, alanine aminotransferase; AST, aspartate aminotransferase; cT1, corrected T1; ELF™, enhanced liver fibrosis; FIB-4, fibrosis-4 index; GI, gastroenterology; MRE, magnetic resonance elastography; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; PCP, primary care physician; T2D, type 2 diabetes; VCTE, vibration-controlled elastography.

Rinella ME et al. Hepatology. 2023;doi: 10.1097/HEP.0000000000000323.

Novo Nordisk's commitment to Liver Health



novo nordisk®

A global company with a heritage of patient-focused innovation

Novo Nordisk has a heritage of 100 years of innovation and leadership, primarily in diabetes care.

This has given us experience and capabilities that enable us to help in defeating other serious chronic diseases: hemophilia, growth disorders, obesity, and now nonalcoholic steatohepatitis.

1923 | Driving change for generations

Products marketed in
168
countries

Total net sales
140.8
billion DKK

Supplier of nearly
50%
of the world's insulin

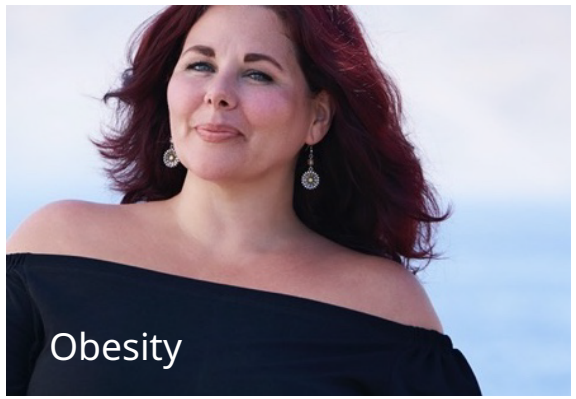
More than
34
million people use our diabetes care products

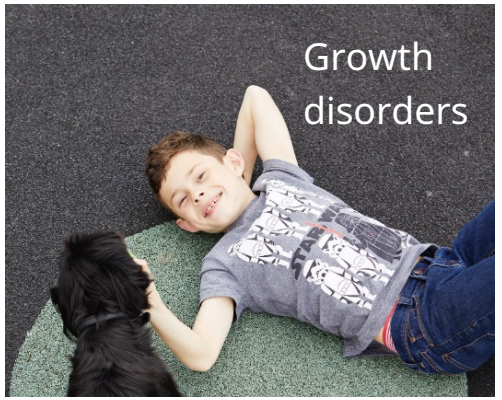
Affiliates in
80
countries

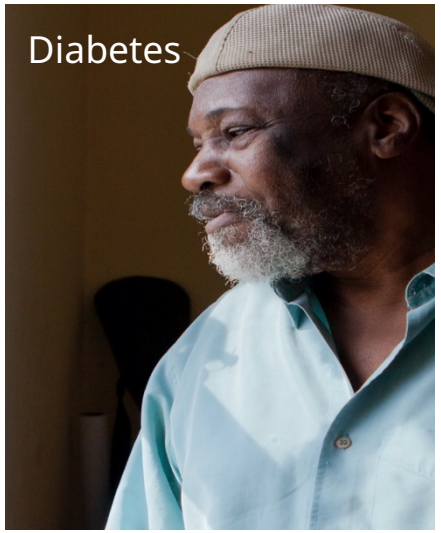
R&D centres in China, Denmark, India, UK and US

Strategic production sites in Denmark, Brazil, China, France and US

Over
55,000
employees







The world's 4th largest pharma company measured by market value[1]

1. https://companiesmarketcap.com/pharmaceuticals/largest-pharmaceutical-companies-by-market-cap/

Monotherapy or combination therapies for NASH should address the individual's disease stage and existing comorbidities

	NAFL	NASH without fibrosis	NASH with F1 & F2	NASH with F3 & F4
Outcomes	• Cardiovascular disease • Non-hepatic malignancies • Renal disease • Cerebrovascular disease	• Cardiovascular disease • Non-hepatic malignancies • Liver disease • Renal disease	• Liver disease • Cardiovascular disease • Hepatic and non-hepatic malignancies • Renal disease	• Liver disease • Cardiovascular disease • Hepatic and non-hepatic malignancies • Renal disease
Lifestyle modification				
± Drugs that can resolve steatohepatitis				
± Drugs that improve glycemic control/improve dyslipidemia/decrease CVD/ induce weight loss/lower malignancy risk				
± Drugs that prevent fibrosis progression				
± Drugs that reduce fibrosis				

Liver-specific

Metabolic benefits

CVD, cardiovascular disease; F, fibrosis stage; NAFL, nonalcoholic fatty liver; NASH, nonalcoholic steatohepatitis.

Vuppalanchi R et al. Nat Rev Gastroenterol Hepatol 2021;18:373–92.