



Prevalence of liver fibrosis in the general population (the LiverScreen project): a multinational European cohort study

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Summary

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Background Small scale, single-country studies suggest that undiagnosed liver fibrosis is prevalent in the general population; however, its true burden and main risk factors remain unclear. We aimed to assess the prevalence of undiagnosed liver fibrosis and its relationship with metabolic factors or alcohol consumption in a large prospective population-based multinational cohort study.

Methods We enrolled individuals from the general population who were aged 40 years and older across 35 sites, including primary health centres and screening units, and their 16 affiliated tertiary hospitals in nine European countries. Liver fibrosis was estimated using the liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE). A positive test was defined as an LSM of 8 kPa and greater or an alanine aminotransferase concentration of at least 1.5 the upper limit of normal, or a combination of both. Individuals with at least one criterion were referred for hepatology consultation to confirm chronic liver disease with fibrosis. The primary outcome was the prevalence of LSM of 8 kPa and greater.

Findings We enrolled 30 199 individuals (mean age 58 years; 57% [17 203 of 30 199] women, 89% [24 440 of 27 481] White) from nine European countries. Metabolic factors were present in 70% (21 084 of 30 024) of participants, and 59% (15 107 of 25 488) of participants reported alcohol use, with 6.1% (1771 of 29 081) of participants reporting harmful consumption. The positive screening rate was 6.9% with a prevalence of 4.6% with an LSM of 8 kPa and greater. Elevated LSM was strongly associated with obesity, type 2 diabetes, and harmful alcohol use. Of the participants referred, 61% (1491 of 2457) completed a hepatology evaluation, and chronic liver disease with fibrosis was confirmed in 32% (477 of 1491) of participants, yielding an overall estimated prevalence of 1.6% (477 of 30 199). Steatotic liver disease accounted for 93% (443 of 477) of cases.

Interpretation Undiagnosed liver fibrosis is common in the general population in Europe and is primarily driven by metabolic factors and alcohol consumption. Early detection is pivotal as it could allow personalised interventions that can prevent progression to cirrhosis and complications.

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Introduction

Chronic liver disease is the 12th leading cause of death worldwide, responsible for 2.3 million deaths in 2021.¹ Liver fibrosis—the main hallmark of chronic liver disease—progresses silently over decades and often remains undetected until cirrhosis with complications develops later in life.² Given that morbidity and mortality increase substantially when cirrhosis develops, early

identification of fibrosis is pivotal, offering an opportunity to intervene before complications arise and, thereby, potentially improve patient outcomes.³

Early detection has gained importance with the development of novel therapeutics targeting moderate and severe fibrosis in patients with metabolic dysfunction-associated steatotic liver disease (MASLD).^{4,5} Despite the development of accurate non-invasive fibrosis tests⁶ such

Research in context

Evidence before this study

Chronic liver disease is a leading cause of premature mortality worldwide. Liver fibrosis—the principal determinant of disease progression—is often undetected until advanced stages when there is little hope for cure. Although non-invasive tests and guideline recommendations for earlier detection are increasingly available, population-level evidence to support liver fibrosis screening in the general population remains to be poor. We searched PubMed on Oct 20, 2025, using the search terms “liver fibrosis screening”, “assessment of liver fibrosis”, and “liver fibrosis tests”, together with “general population”. We searched for prospective studies published between Jan 1, 2010, to Oct 20, 2025, for English-language studies assessing liver fibrosis screening in unselected populations using invasive or non-invasive methods. Of the 605 records identified, 66 contained relevant information and were assessed in detail. Most studies were excluded because they were restricted to selected high-risk populations, had small sample sizes, did not report relevant prevalence estimates, or lacked protocolised confirmatory diagnostic assessment of chronic liver disease following screening.

Added value of this study

This is the largest prospective population-based liver fibrosis screening study that has included more than 30 000 individuals from nine European countries. Unlike previous studies, screen-positive participants underwent complete hepatology

evaluation. Metabolic risk factors and alcohol use were present in more than 70% of the population. Type 2 diabetes and harmful alcohol use were the strongest predictors of positive screening and confirmed chronic liver disease, with a clear dose–response to elevated liver stiffness (≥ 8 kPa), which rose from 1.3% (no risk factors) to 21.0% (four metabolic factors) and 37.0% when combined with harmful alcohol use. Notably, nearly half of referred participants had lower liver stiffness measurements at hepatology assessment, underscoring the importance of confirmatory testing for accurately establishing a diagnosis of chronic liver disease. Overall, the prevalence of chronic liver disease with fibrosis in the screened population was 1.6%.

Implications of all the available evidence

Early detection of liver fibrosis is essential to enable timely, personalised interventions that can prevent disease progression. However, confirmatory testing is crucial to accurately diagnose chronic liver disease. Future screening strategies should be adapted to local epidemiological patterns and health-care system capacities to maximise effectiveness and equity in liver disease prevention. Given the high prevalence of metabolic and alcohol-related risk factors in the general population, effective screening approaches should extend beyond narrowly defined high-risk groups and include a broad segment of the population.

as liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE), liver fibrosis remains vastly underdiagnosed and most patients are diagnosed late at a symptomatic, decompensated stage.⁷ Increased LSM values are associated with advanced liver fibrosis and a high probability of liver-related outcomes such as complications of portal hypertension, hepatocellular carcinoma, and liver-related death.⁸ Despite having a similar age-standardised mortality rate as lung cancer and a higher prevalence than colorectal cancer, there are no population-wide screening programmes for the early detection of cirrhosis.⁹ Previous studies have estimated liver fibrosis using non-invasive tests but they are all single-country studies and do not incorporate structured hepatology evaluation or liver biopsy for diagnostic confirmation of people with increased LSM, limiting its ability to accurately define chronic liver disease with fibrosis or differentiate aetiologies.^{10,11} Thus, robust data on the estimated prevalence of undiagnosed liver fibrosis across different countries and health-care settings are required to justify and inform any future systematic screening initiatives.^{3,9}

The nomenclature of steatotic liver disease is based on the presence of steatosis and metabolic or alcohol risk factors and recognises three subtypes: (1) MASLD usually related to type 2 diabetes and obesity; (2) MASLD with

moderately high alcohol consumption (MetALD); and 3) alcohol-related liver disease secondary to very high alcohol use regardless of concomitant metabolic dysfunction.¹² MASLD affects approximately one-third of adults globally and harmful alcohol use remains to be a large contributor to liver-related mortality.¹³ Although interactions between alcohol and cardiometabolic risk factors have been studied in high-risk cohorts, population-based data clarifying their relative contributions to hepatic fibrosis are still low. Therefore, we aimed to assess the prevalence of undiagnosed liver fibrosis and its associated risk factors in the LiverScreen study, incorporating a comprehensive confirmatory assessment for individuals across a large European adult population with positive screening results.

Methods

Study design

This prospective population-based multinational cohort study was carried out across 35 sites, including primary health-care centres and screening units and 16 associated tertiary hospitals across nine European countries: Spain, Denmark, Italy, Slovakia, Croatia, UK, France, The Netherlands, and Germany (appendix pp 8–10). Details on site selection have been provided in the appendix (p 3).

The primary objectives were to assess the prevalence of liver fibrosis, as estimated by an elevated LSM of 8 kPa or

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above, and evaluate the relationship between LSM (≥ 8 kPa) and metabolic risk factors, alcohol consumption, and the interaction between both metabolic risk factors and alcohol in a random population aged 40 years or older across Europe.

The study was approved by the individual ethics committees (appendix p 7) and is reported in accordance with the STROBE guidelines for observational studies (appendix pp 30–31).

Participants

We invited individuals from the general population to participate via three different methods: (1) a random selection of people attending primary health-care centres for a regular health check-up or follow-up (Spain, Croatia, France, and Germany); (2) a random selection of social security numbers or ZIP codes followed by online letter invitations or phone calls (Denmark, Spain, Italy, UK, The Netherlands); and (3) individuals who participated in existing population screening programmes or occupational health checks (Spain, Germany, Slovakia, and France). For details on recruitment procedures by site and country, see the appendix (pp 8–10).

The inclusion criteria were participants aged 40 years and older, and who were able to give informed consent. The exclusion criteria were known chronic liver disease (except liver steatosis), mental incapacity, language barrier, insufficient social support or any other reason

considered by the investigator to preclude adequate conduct of the study, and major extrahepatic diseases that could impair short-term prognosis, such as malignancy, congestive heart failure (New York Heart Association Grade 4), chronic obstructive pulmonary disease (GOLD >3), and advanced chronic kidney disease (serum creatinine >3 mg/dL or undergoing renal replacement therapy). Participants with a positive screening test were subsequently referred to a second visit with an hepatologist to confirm the presence of chronic liver disease. All participants gave written informed consent to participate in the study.

Procedures

At the screening visit, trained nurses carried out the examinations, following standard operating procedures. Visits included a medical history and measurement of weight, height, waist and hip circumferences, blood pressure, and blood tests for liver biochemistry, in addition to blood glucose, glycated haemoglobin, lipid profile, and serum creatinine. Alcohol drinking pattern was based on self-reported alcohol consumption using standardised alcohol questionnaires, including weekly alcohol intake and the Alcohol Use Disorders Identification Test-Concise (AUDIT-C) questionnaire. Harmful alcohol use was defined as current consumption of standard drink units of 14 units or more per week for women and 21 units or more per week for men. Diagnostic criteria for metabolic dysfunction (arterial hypertension, dyslipidaemia, type 2 diabetes, and people with overweight or people with obesity) and alcohol consumption patterns definition are reported in the appendix (p 4).

We estimated liver fibrosis using LSM by VCTE with the FibroScan device (Echosens, Paris, France) according to the instructions by the manufacturer (appendix p 5). VCTE was done following a minimum fasting period of 3 h. Measurements were considered reliable if at least ten valid readings were obtained and met one of the following criteria: an IQR range-to-median ratio (IQR/P50) of 30% or lower for median liver stiffness (P50 ≥ 7.1 kPa), or a P50 of less than 7.1 kPa regardless of the IQR. Measurements that did not meet these criteria were classified as unreliable. VCTE failure was defined as the inability to obtain any valid LSM. We recorded all study data in an electronic database called REDCap (version 13.7.1), Vanderbilt University, TN, USA) on servers hosted by and located in the Region of Southern Denmark, using pseudonymised data. Gender information was not assessed and sex and ethnicity variables were self-reported by participants at study entry using a prespecified question in the REDCap electronic case report form (appendix p 5). Ethnicity data were not collected for participants in the Slovakian cohort because this site did not use the REDCap questionnaire and, therefore, did not request or collect ethnicity data.

We defined a positive screening test as an LSM of at least 8.0 kPa or an alanine aminotransferase (ALT) of at

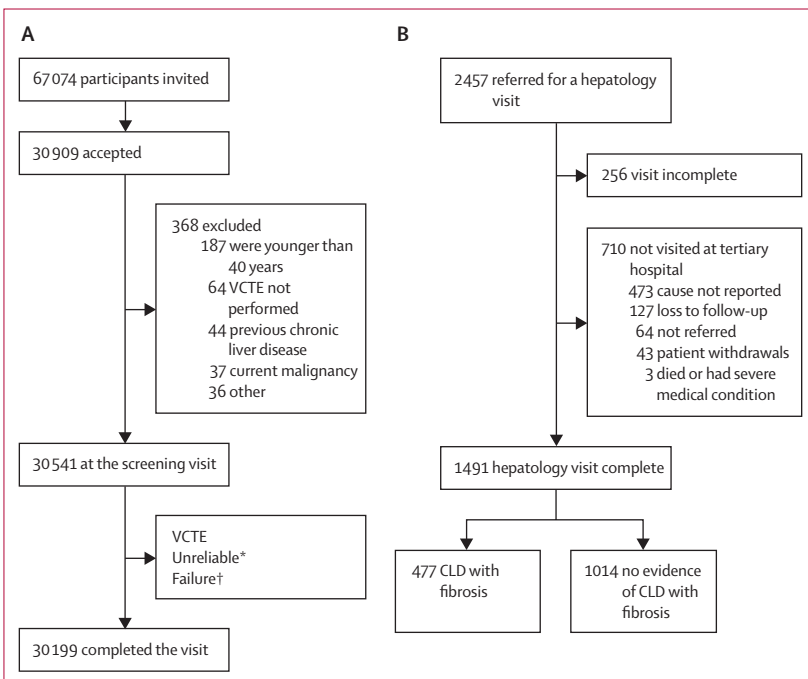


Figure 1: Trial profile

The invitation and enrolment process for the screening visit (A), and referral for hepatology consultation and final evaluation (B). CLD=chronic liver disease. VCTE=vibration-controlled transient elastography. *273 (0.9%) of 30541 participants had an interquartile range-to-median ratio (IQR/P50) of at least 30% for median liver stiffness (P50 ≥ 7.1 kPa). †For 69 (0.2%) of 30541 participants, we could not obtain any valid liver stiffness measurement.

least 1.5 upper limit of normal (ULN). Participants meeting at least one of the two criteria were referred for hepatology consultation to assess the presence, staging, and aetiology of chronic liver disease. We selected a threshold of 8.0 kPa to define elevated LSM because an LSM of less than 8 kPa is associated with a very low probability of fibrosis^{14,15} and liver-related events.^{8,16} We also included an ALT-based criterion to identify participants with possible liver inflammation that might be missed with VCTE alone.^{17,18} Individuals with unreliable or failed LSM were also referred for further evaluation.

The hepatology consultation to confirm the presence of chronic liver disease with fibrosis consisted of a comprehensive evaluation including biochemical testing for viral, metabolic, and immune diseases; abdominal ultrasound; repeat VCTE to confirm elevated LSM; and, if participants consented, liver biopsy as part of standard clinical care. Definitions of chronic liver disease aetiologies have been shown in the appendix (p 5). Pathology was analysed blindly using digitalised central reading by two pathologists (AD and SD; appendix pp 5–6).

We defined chronic liver disease with fibrosis as presence of at least one of the following criteria: (1) any stage of fibrosis (F1=mild fibrosis, ≥F2=significant fibrosis, ≥F3=advanced fibrosis, and ≥F4=cirrhosis) confirmed by biopsy; (2) abdominal ultrasound with at least two of the following findings typical of chronic liver disease with fibrosis: heterogeneous parenchyma, enlarged right liver lobe, enlarged left liver lobe including caudate lobe, irregular liver surface, rounded edges, extrahepatic venous collaterals, spleen length greater than 13 cm, or ascites; and (3) an LSM of at least 10 kPa on VCTE performed at the hepatology visit.¹⁹ We selected a threshold of 10 kPa to diagnose chronic liver disease with fibrosis in the absence of liver biopsy as this threshold is associated with high risk of liver-related outcomes across aetiologies and is recommended in clinical guidelines for the diagnosis of possible compensated advanced chronic liver disease.¹⁶ Adverse events were systematically assessed and recorded at both visits.

Statistical analysis

Quantitative variables were described using either mean and SD (normal distributed variables) or median (P50) and IQR (skewed variables). Categorical variables were described using frequencies and percentages. Categorisation of continuous variables was done using well established cutoff points (eg, BMI 25 kg/m² and 30 kg/m²) or close to a quartile or median (eg, aged ≥60 years). We applied univariable and multivariable logistic regression models to assess the association between selected variables and LSM using different cutoff points (8 kPa, 10 kPa, and 15 kPa), adjusted by age, sex, and country. We selected the following predictor variables based on existing evidence: obesity, type 2 diabetes, arterial

| | Overall cohort (N=30 199) |
|-------------------------------------|------------------------------|
| Age (years) | 58 (10) |
| Sex | |
| Female | 17 203 (57%) |
| Male | 12 996 (43%) |
| Ethnicity | |
| White | 24 440 (89%) |
| African | 1171 (4.2%) |
| Latin-American | 985 (3.6%) |
| Asian | 537 (2.0%) |
| Mixed | 94 (0.3%) |
| Other | 140 (0.5%) |
| Smoking | 4273 (15%) |
| BMI (kg/m ²)* | 27 (5) |
| Normal | 10 259 (34%) |
| Overweight | 11 857 (40%) |
| Obese | 8065 (26%) |
| Abdominal obesity† | 14 071 (47%) |
| Metabolic risk factors | |
| Arterial hypertension | 10 488 (35%) |
| Type 2 diabetes | 3140 (10%) |
| Dyslipidaemia | 16 031 (53%) |
| At least one metabolic risk factor | 21 084 (70%) |
| Harmful alcohol use‡ | 1771 (6.1%) |
| Glucose (mg/dL) | 99 (27) |
| Glycated haemoglobin (%) | 5.6 (0.8) |
| Total cholesterol (mg/dL) | 205 (43) |
| HDL cholesterol (mg/dL) | 59 (16) |
| LDL cholesterol (mg/dL) | 124 (37) |
| Triglycerides (mg/dL) | 106 (75) |
| AST (IU/L) | 24 (9) |
| ALT (IU/L) | 22 (13) |
| GGT (IU/L) | 22 (19) |
| AP (IU/L) | 72 (24) |
| Platelet count (10 ⁹ /L) | 247 (61) |

Continuous variables with normal distribution are expressed as mean (SD) and non-normal variables are expressed as P50 (IQR). ALT=alanine aminotransferase. AP=alkaline phosphatase. AST=aspartate aminotransferase. GGT=gamma-glutamyl-transpeptidase. *BMI categories used: normal (BMI <25.0 kg/m²); overweight (BMI ≥25.0 kg/m² and <29.9 kg/m²); obese (BMI ≥30.0 kg/m²); Asian origin BMI ≥25.0 kg/m². †Abdominal obesity was defined as a waist circumference of at least 88 cm for women and 102 cm for men. ‡Harmful alcohol use was defined as individuals who reported current alcohol consumption equal to or greater than 14 units per week for women and 21 units per week for men. For the participants in whom the standard drinking units questionnaire was not available, the Alcohol Use Disorders Identification Test-Concise (AUDIT-C) responses were changed to units. Missing data: ethnicity (9% missing); smoking (6% missing); alcohol consumption (4% missing); glucose (11% missing); glycated haemoglobin (39% missing); total cholesterol (10% missing); HDL cholesterol (12% missing); LDL cholesterol (14% missing); triglycerides (10% missing); AST (13% missing); ALT (9% missing); GGT (10% missing); AP (16% missing); and platelet count (16% missing). Ethnicity data were not collected for participants from the Slovakian cohort.

Table 1: Baseline characteristics

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See Online for appendix

hypertension, dyslipidaemia, harmful alcohol use, and standard liver tests. A similar approach was used with chronic liver disease with fibrosis as the dependent variable. In this case, all the explanatory variables corresponded to the baseline visit. All the logistic regression models provided adjusted odds ratios (aORs) and 95% CI on tables or figures (forest plots). We determined the optimal LSM cutoff at the screening visit to detect chronic liver disease with fibrosis by maximising the product of sensitivity and specificity.²⁰ No imputation was done for missing data, as most of the missing values were due to centre-specific data collection policies (eg, analyse only ALT and no AST, or fasting glucose and no glycated haemoglobin). All tests were two-sided and statistical significance was defined as a p value of less than 0.05. The statistical analysis was performed with Stata (version 19).

The sample size was calculated to assess the usefulness of VCTE as a screening method for detecting substantial liver fibrosis. Because liver biopsy remains the gold standard for fibrosis staging, the calculation considered the number of biopsies required to assess concordance between biopsy and VCTE. We first estimated the population prevalence of LSM at least 8 kPa to be 6%.^{16,17} Assuming that half of the participants with elevated LSM would agree to have a liver biopsy performed, with a 5% of bilateral alpha error and a statistical power of 95%, we would need to screen a minimum of 28 887 participants to obtain histological scores from at least 450 biopsies.

The LiverScreen study is registered on ClinicalTrials.gov (NCT03789825) and is completed, and the protocol was published in 2022.²¹

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between May 2, 2018, and Dec 19, 2024, 67 074 individuals were invited and 30 909 participants from nine European countries prospectively accepted (figure 1). The participation rate according to the recruitment method and country has been shown in the appendix (pp 8–10). A total of 368 participants were excluded due to the predefined exclusion criteria and, in addition, 342 participants had unreliable or failed LSM at the screening visit. Therefore, the primary outcome was assessed in 30 199 participants (figure 1) with a mean age of 58 years; 57% (17 203 of 30 199) were women, and 89% (24 440 of 30 199) were White. The characteristics of the overall study population and those of the participants categorised by country, sex, age, and recruitment method have been shown in table 1 and the appendix (pp 11–15).

Of the 30 199 participants, 2075 (6.9%) participants screened positive: 1376 (4.6%) participants with an LSM of 8 kPa and greater, of whom 171 (0.6%) participants also exhibited increased ALT, and 699 (2.3%) participants with ALT levels of at least 1.5 ULN but normal LSM values. The median LSM in the whole series was 4.6 kPa (range 1.5–75.0 kPa; IQR 1.8 kPa), whereas the median value for the participants with an LSM of 8 kPa and greater was 10.2 kPa (IQR 4.0 kPa). The prevalence of LSM values of 10 kPa and greater was 2.5% and 0.8% for 15 kPa and greater. The prevalence of increased LSM and the mean LSM values by country have been shown in the appendix (p 17).

Elevated LSM correlated with several demographic and clinical factors including age and male sex, and metabolic risk factors such as dyslipidaemia, arterial hypertension, people who are overweight or people with obesity, and type 2 diabetes, and harmful alcohol use (figure 2). The number of metabolic risk factors also correlated with elevated LSM. Although we observed a prevalence of an LSM of 8 kPa and greater in 1.3% of participants without

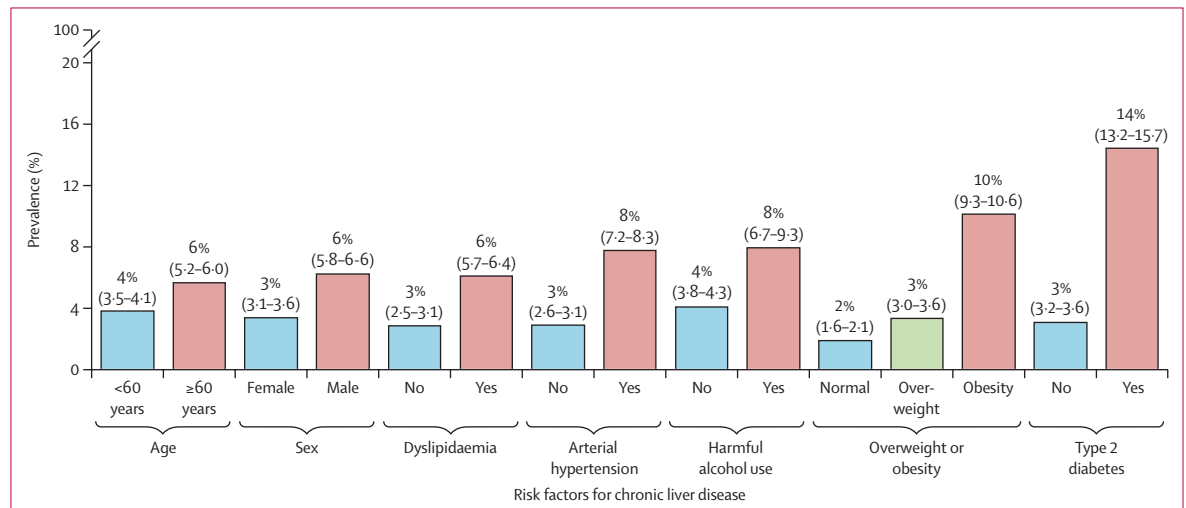


Figure 2: Prevalence of liver stiffness measurement (LSM; ≥8 kPa) according to age, sex, and presence or absence of metabolic conditions and harmful alcohol use. Data show the prevalence of LSM of 8 kPa and greater and 95% CI in brackets for each condition.

metabolic risk factors and without evidence of harmful alcohol consumption, the prevalence increased stepwise to 2.2%, 5.2%, 9.4%, and 20.7% among participants with one, two, three, or four metabolic risk factors (figure 3). The presence of harmful alcohol use was associated with an additional increase in the prevalence of elevated LSM, beyond that conferred by metabolic risk factors alone (1.9%, 6.5%, 9.3%, 15.3%, and 37.1% in the case of zero, one, two, three, and four metabolic risk factors, respectively; figure 3). Although current harmful alcohol use was associated with increased LSM, former alcohol use, either low or harmful, showed no association (appendix pp 18, 26). Similar associations were observed when analysing LSM 10 kPa and 15 kPa cutoffs (appendix p 18). Type 2 diabetes and harmful alcohol consumption in combination showed the strongest association with increased LSM (table 2). In addition, we observed a progressive increase in the prevalence of LSM of at least 8 kPa across increasing BMI categories (appendix p 18). Similarly, median LSM values increased progressively with the number of metabolic conditions present and showed a further elevation in individuals who also reported harmful alcohol use (appendix p 19).

The laboratory variables associated with increased LSM were elevated concentrations of ALT, aspartate aminotransferase (AST), gamma-glutamyl-transpeptidase (GGT), alkaline phosphatase, glycated haemoglobin, total cholesterol, and triglycerides, in addition to a lower platelet count and HDL cholesterol (appendix p 20). On multivariable analysis that included both clinical and laboratory variables, the following binary predictors were independently associated with an increased LSM (≥ 8 kPa): age, male sex, harmful alcohol use, people who were overweight or people with obesity, type 2 diabetes, arterial hypertension, and increased ALT and GGT values (figure 4). Analyses using the same variables modelled as continuous predictors yielded similar results (appendix p 21). Country-specific analyses yielded similar findings (appendix p 22). Findings remained unchanged after excluding individuals in whom VCTE measurements could be less reliable (BMI ≥ 36 kg/m² or an ALT ≥ 100 IU/L; appendix p 23). Factors associated with an increased LSM of 10 kPa and greater or 15 kPa and greater on multivariable analyses were similar (appendix p 27).

We referred 2457 participants for a hepatology consultation: 2075 (84%) participants because of screening positive, 342 (14%) participants because of unreliable or failed VCTE, and 40 (2%) due to investigator's oversight. Of the 2457 participants, 1491 (61%) completed the follow-up evaluation (figure 1). Excluding the three countries with the lowest follow-up evaluation rates (Germany [40%], Slovakia [25%], and The Netherlands [15%]), the hepatology visit completion rate was 76% (1276 of 1674). Overall, there was a reduction in LSM values at the hepatology visit compared with those at the screening visit, particularly in participants

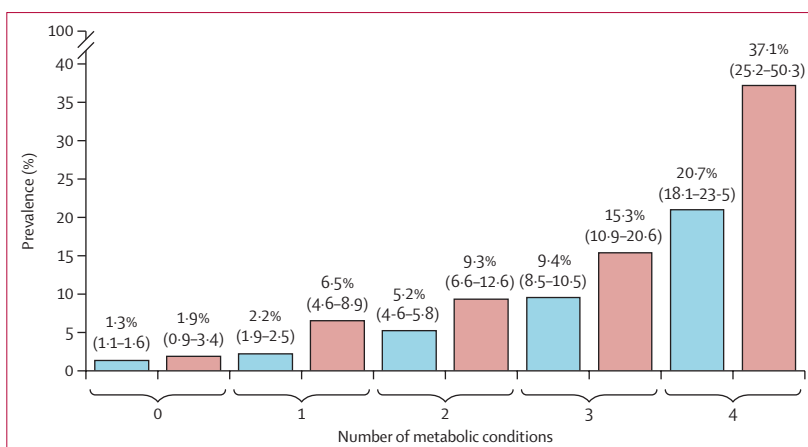


Figure 3: Prevalence of liver stiffness measurement (LSM; ≥ 8 kPa) according to the number of metabolic conditions and its association with harmful alcohol use

The numbers equate to the following: 0 is no metabolic condition; 1 is one metabolic condition; 2 is two metabolic conditions; 3 is three metabolic conditions; 4 is four metabolic conditions. The blue bars indicate no harmful alcohol use and pink bars indicate harmful alcohol use. Data show the prevalence of LSM of 8 kPa and greater and 95% CI in brackets for each condition. Odds ratios for the association between harmful alcohol use and LSM of 8 kPa and greater were calculated within each stratum of metabolic conditions, comparing participants with harmful alcohol use to those without harmful alcohol use but with the same number of metabolic conditions. The odds ratio was 1.41 in participants with no metabolic conditions, 2.97 in those with one metabolic condition, 1.79 in those with two metabolic conditions, 1.62 in those with three metabolic conditions, and 1.79 in those with four metabolic conditions. The interaction between harmful alcohol use and the number of metabolic conditions was not statistically significant, with a p value of 0.072.

with normal liver enzymes, fewer risk factors, and for individuals whose LSM values were only slightly increased over the threshold of 8 kPa (appendix p 23). Of the 1491 participants who completed the second visit, a liver biopsy was done in 331 (22%) participants. The main reasons for not doing a liver biopsy were decrease in LSM to 8 kPa or lower at the second visit in 715 (48%) of 1491 participants, and lack of consent for biopsy in 234 (16%) participants. A diagnosis of chronic liver disease with fibrosis was made in 477 of 1491 participants, almost one-third (32%) of individuals who completed the evaluation for liver disease, which represents an overall estimated prevalence of chronic liver disease with fibrosis of at least 1.6% (477 of 30 199 participants), considering that more than one-third of individuals who screened positive were not evaluated further (figure 1). Most of the participants with a liver biopsy had fibrosis (273 [82%] of 331 participants), and 93 (28%) participants had advanced liver fibrosis (58 participants with F3 liver fibrosis and 35 participants with F4 liver fibrosis). In participants who met the chronic liver disease criteria but did not have biopsy confirmation, 102 (50%) of 204 participants had an LSM of 10 kPa and greater but no ultrasound evidence of chronic liver disease, 70 (34%) participants fulfilled the ultrasound criteria of chronic liver disease only, and 32 (16%) participants exhibited both an LSM of 10 kPa and greater and ultrasound criteria indicative of chronic liver disease. Presence and severity of liver fibrosis on liver biopsy with respect to LSM values at screening and at the hepatology consultation has been shown in the

| | LSM \geq 8 kPa | | LSM \geq 10 kPa | | LSM \geq 15 kPa | |
|--|------------------|-----------|-------------------|-----------|-------------------|----------|
| | n (aOR) | 95% CI | n (aOR) | 95% CI | n (aOR) | 95% CI |
| No risk factors | 340 (1 [ref]) | .. | 167 (1 [ref]) | .. | 54 (1 [ref]) | .. |
| Type 2 diabetes | 106 (3.4) | 2.7–4.3 | 67 (4.0) | 3.0–5.4 | 28 (4.8) | 3.0–7.8 |
| Harmful alcohol use | 52 (2.6) | 1.9–3.5 | 29 (2.8) | 1.9–4.2 | 15 (4.8) | 2.7–8.7 |
| Obesity | 386 (3.8) | 3.3–4.5 | 186 (3.6) | 2.9–4.5 | 45 (2.6) | 1.8–3.9 |
| Type 2 diabetes and harmful alcohol use | 18 (12.5) | 7.2–21.6 | 12 (14.2) | 7.4–27.0 | 6 (20.9) | 8.6–51.2 |
| Type 2 diabetes and obesity | 273 (11.7) | 9.8–14.0 | 168 (12.7) | 10.1–16.0 | 57 (11.5) | 7.7–17.0 |
| Harmful alcohol use and obesity | 40 (5.6) | 4.0–8.0 | 26 (7.0) | 4.5–10.8 | 9 (7.9) | 3.8–16.3 |
| Type 2 diabetes, harmful alcohol use and obesity | 30 (25.9) | 16.3–41.1 | 17 (22.5) | 12.8–39.4 | 5 (18.7) | 7.2–48.7 |

Data are n (aOR) and 95% CI, adjusted by age, sex, and country. aOR=adjusted odds ratio. LSM=liver stiffness measurement.

Table 2: Logistic regression analysis of individual and combined risk factors with increased LSM (\geq 8, \geq 10, and \geq 15 kPa)

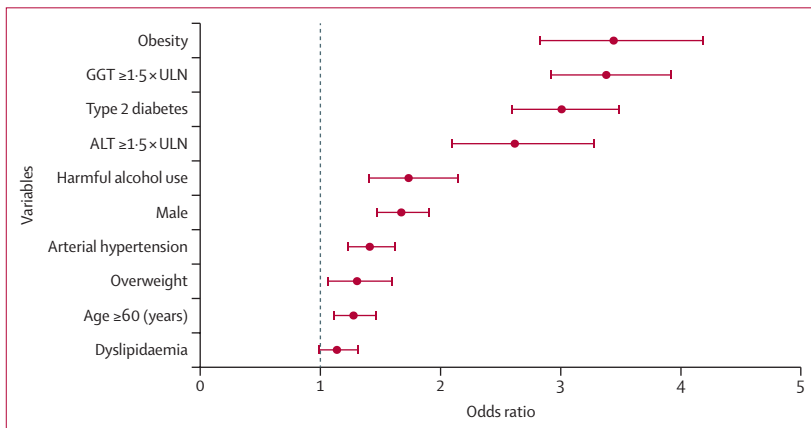


Figure 4: Multivariable analysis of factors related to increased liver stiffness measurement (LSM; \geq 8 kPa)
 Values shown are adjusted odds ratio and 95% CI, adjusted by country, sex, and all variables included in the model. ALT=alanine aminotransferase. GGT=gamma-glutamyl-transpeptidase. ULN=upper limit of normal.

appendix (p 24). The decrease in LSM values at the hepatology visit compared with LSM values at screening was observed in all fibrosis stages. We found chronic liver disease with fibrosis in 13% (47 of 439) of participants who at screening had an ALT of at least 1.5 ULN without increased LSM, 39% (305 of 773) participants with an LSM of 8 kPa and greater alone, and 67% (80 of 119) participants meeting both screening criteria. Most individuals with chronic liver disease had steatotic liver disease (93% of 477 participants), of whom 73% had MASLD, 15% with MetALD, and 5% with alcohol-related liver disease, while the remaining cases were due to miscellaneous causes and only four individuals had viral hepatitis (appendix p 24). Of the 342 participants with unreliable or failed VCTE, 153 (45%) were evaluated, and 21 (14%) of 153 participants had chronic liver disease with fibrosis.

Among the participants who completed the liver disease evaluation, the prevalence of chronic liver disease with fibrosis was higher among those with metabolic conditions and harmful alcohol use (appendix p 27). Type 2 diabetes and harmful alcohol use were the two conditions associated with the highest prevalence of chronic liver disease with fibrosis. Among participants

referred for hepatology evaluation, individuals in whom chronic liver disease with fibrosis was confirmed had a higher baseline LSM compared with participants in whom it was not confirmed (11.0 vs 8.5 kPa). The optimal LSM cutoff value at screening for predicting histological liver fibrosis was 10.3 kPa (Se 60% and Sp 73%; appendix p 28) whereas the optimal cutoff value for predicting chronic liver disease with fibrosis was 10.0 kPa (Se 63% and Sp 75%; appendix p 28). LSM values at screening had a higher accuracy to diagnose chronic liver disease with fibrosis than liver enzymes alone or FIB-4 (appendix p 29). The prevalence of chronic liver disease with fibrosis in participants with LSM at screening between 8 kPa and 9.9 kPa was 27% (115 of 429) versus 56% (284 of 504) in participants with LSM at screening of at least 10 kPa.

Discussion

In this large multinational cohort study of 30 199 individuals, who were randomly selected from the general population from nine European countries, we found that 4.6% of participants had an increased LSM using VCTE, and 2.9% had an increased ALT, indicative of possible undiagnosed chronic liver disease. We subsequently confirmed that at least 1.6% of the whole population had chronic liver disease with fibrosis. The presence and number of metabolic conditions, including obesity, type 2 diabetes, dyslipidaemia, and arterial hypertension were strongly associated with increased LSM, and coexistence of harmful alcohol use further increased this association.

This study shows a high overall prevalence of metabolic conditions, including being overweight or people with obesity, type 2 diabetes, arterial hypertension, and dyslipidaemia, in addition to current alcohol consumption of any amount (70% of participants had at least one metabolic risk factor, and 59% reported any alcohol consumption, respectively), closely matching national estimates and supporting the representativeness of the cohort. The prevalence of harmful alcohol use (6.1%) was slightly lower than WHO estimates, possibly reflecting both non-standardised alcohol reporting across

For more on the national estimates see <https://ec.europa.eu/eurostat>

studies and under-reporting of alcohol consumption.²² Among individual factors, obesity and type 2 diabetes showed the strongest correlation with elevated LSM, whereas the combination of alcohol consumption and type 2 diabetes showed the strongest association across risk factor combinations.

MASLD was by far the most common aetiology of chronic liver disease with fibrosis, followed by MetALD and alcohol-related liver disease. Together, these three aetiologies accounted for 93% of all chronic liver disease with fibrosis, underscoring the importance of metabolic conditions and alcohol consumption as primary drivers of chronic liver disease with fibrosis in European countries. These findings are consistent with a modelling study suggesting that MASLD will become the leading cause of decompensated cirrhosis and liver cancer in the near future.²³ Nevertheless, the importance of alcohol as a major aetiological factor of chronic liver disease cannot be overstated, given that alcohol consumption remains to be the highest in Europe among all continents, and is increasing in many countries.²⁴ Moreover, under-reporting of alcohol consumption is a well recognised limitation that can bias the estimated prevalence of SLD subcategories, likely leading to an underestimation of the true contribution of alcohol.²⁵ The low prevalence of hepatitis B as an aetiological factor of chronic liver disease in this study could be explained by the effect of the universal hepatitis B vaccination in all the included countries.

Abnormalities in liver tests, particularly ALT and AST have for long been associated with the presence of chronic liver disease of various aetiologies.²⁶ Our findings show that, although most liver tests were associated with LSM elevation, ALT and GGT had the strongest association. Nevertheless, it is important to emphasise that increased ALT in the absence of increased LSM, was associated with chronic liver disease with fibrosis in only 13% of cases, compared with 67% when increased ALT occurred together with increased LSM. In some countries, including the USA, GGT is not systematically used as a liver test. However, recent studies from 2021 have shown that GGT is an excellent biomarker of liver fibrosis.²⁷ Our results confirm these findings and support the use of GGT in the assessment of fibrosis.

Our study underscores the asymptomatic nature of chronic liver disease, and the importance of imaging or blood-based testing for case finding patients before decompensation. There are effective treatments to reverse type 2 diabetes, obesity, and harmful alcohol use. Furthermore, the two approved pharmacological agents to treat metabolic dysfunction-associated steatohepatitis, resmetirom and semaglutide, have been approved for moderate or advanced hepatic fibrosis but not cirrhosis.^{4,5} Therefore, early diagnosis followed by a therapy targeted at reversing disease aetiology could potentially prevent the progression to decompensated cirrhosis or liver

cancer but requires proof in randomised controlled studies.

Our findings provide relevant information for any future screening strategies for liver fibrosis. Screening efforts should primarily target individuals with established risk factors, particularly type 2 diabetes, obesity, and harmful alcohol use, although these conditions are prevalent in a large proportion of the adult population. In such populations, an initial screening test should be followed by confirmatory evaluation supported by well-structured organisational and logistical systems to ensure adherence to repeated assessment.³ In this study, LSM was applied as the initial screening test; however, in nearly half of participants with an initial LSM of 8 kPa and greater, the values fell below this threshold at the follow-up assessment consistent with previous reports showing declines in 33–45% of cases on repeat assessment.²⁸ In our cohort, individuals with a healthier liver profile—characterised by low liver enzyme concentrations, few risk factors, and slight or moderate increase in baseline LSM values—were most likely to show such decreases, suggesting that test–retest variability of VCTE and regression to the mean are important contributors, particularly in low-prevalence populations.²⁸

Nevertheless, lifestyle changes between visits that were not captured could also have contributed. Importantly, rather than implying that LSM is ineffective as a screening tool, these findings highlight the need for structured confirmatory pathways to minimise false-positive diagnoses in population-based screening and ensure accurate identification of individuals with previously unrecognised liver fibrosis. An alternative approach to a single LSM measurement is a stepwise strategy using blood-based risk scores, such as guideline-recommended FIB-4, followed by confirmatory LSM before specialist referral. In our cohort, FIB-4 underperformed compared with LSM for detecting chronic liver disease, suggesting that this is not a good method for fibrosis screening in a low-prevalence population. Whether blood-based tests specifically developed for general population screening (eg, LiverRisk, LiverPRO, SAFE, MAF-5, or CLivD) could be more suitable as first-line tools and deserve further study.^{29–33} Future studies should define optimal referral pathways combining blood-based and imaging-based non-invasive tests and evaluate their cost-effectiveness and health-system impact. Ultimately, randomised controlled trials are needed to determine whether population-based fibrosis screening improves clinical outcomes. Finally, our findings suggest that when using LSM with VCTE for fibrosis screening in the general population, a threshold of 10 kPa identifies substantial fibrosis (\geq F2) more accurately than 8 kPa, despite the reduction in sensitivity. This finding has implications for the potential use of LSM by VCTE as surrogate of fibrosis for pharmacological treatment indication or guidance in the future, indicating that confirmatory testing is likely to be

required before treatment initiation when fibrosis is identified through general population screening.

The main strengths of this study include the evaluation of a large cohort of adults without known liver disease, randomly assigned from nine European countries, the standardised use of VCTE across all participating centres supported by structured training and identical devices, and the rigorous assessment of chronic liver disease among participants who screened positive. The rigorous assessment of chronic liver disease individuals who screened positive has been largely absent from previous population-based studies, limiting accurate estimation of the true prevalence of undiagnosed chronic liver disease with fibrosis. Almost two-thirds of participants with either increased LSM or ALT values underwent a comprehensive hepatology assessment to confirm or rule out the presence of chronic liver disease with fibrosis. Although this proportion was lower than that reported in established screening programmes, such as colorectal cancer screening (76–84%),³⁴ several structural and contextual factors likely contributed, including little integration with hepatology services at some centres, COVID-19-related disruptions and lower public awareness of chronic liver disease compared with cancer.

This study has some limitations that should be acknowledged. First, the generalisability of our findings is restricted by the demographic characteristics of the cohort, which was predominantly White and included only adults aged 40 years and older. Liver fibrosis patterns can differ in younger individuals and in ethnically diverse populations due to variations in genetic susceptibility, metabolic phenotypes, and lifestyle factors. Accordingly, our prevalence estimates should be applied with caution in other demographic settings, and further studies in more diverse populations are warranted. Second, serological markers of hepatitis C and B were not tested in all participants. The uncommon cases with hepatitis C or B and normal ALT and LSM could have been missed. Third, direct biomarkers of alcohol consumption, such as phosphatidylethanol, were not measured. Fourth, fewer liver biopsies were performed than anticipated, which was likely to be due to a combination of factors, including a reduction in LSM values at the time of hepatology visits in almost half of participants who were screened positive and the challenges in patient follow-up and referral imposed by the COVID-19 pandemic. Nevertheless, this study represents the largest general population cohort to date in which the greatest number of liver biopsies has been performed.

In summary, we found that almost 5% of the middle-aged general population across Europe exhibit evidence of possible liver fibrosis. As elevated LSM strongly associates with type 2 diabetes, obesity, and harmful alcohol use, risk factors that can be effectively treated by pharmaceutical and non-pharmaceutical interventions, there is a need for systematic strategies to ensure early case finding. MASLD, MetALD, and alcohol-related liver disease accounted for

more than 90% of confirmed chronic liver disease cases, which is a timely finding given the approval of therapies for MASLD and the emergence of pharmaceutical trials in alcohol-related liver disease and MetALD. These findings also highlight the importance and urgency of primary prevention measures to reduce the widespread prevalence of metabolic risk factors and harmful alcohol consumption across Europe.

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Contributors

All authors reviewed the manuscript, had access to and reviewed the results of the data analyses, and take responsibility for the fidelity of the report to the protocol. The study coordinator and statistician team (IGra, GP, PG, AS, JPi, EB, and AA) had full access to the complete dataset from all participating centres and verified the integrity of the data and the accuracy of the analyses. Each local principal investigator had access to, and takes responsibility for the accuracy and completeness of the data contributed by their centre (MTh, AK, PAng, SP, PT, WPB, DRou, LCas, IGrg, LS, JMP, FL, JS, RB, ET, ING, and RM). All authors approved the decision to submit the manuscript for publication. IG and MT designed the study, acquired data, developed the database, designed the statistical analyses and interpretation, and drafted and revised the

manuscript. LC designed the study, acquired data, designed the statistical analyses and interpretation, and drafted and revised the manuscript. GP designed the study, undertook statistical analyses and interpretation, and drafted and revised the manuscript. SP acquired data, designed the statistical analyses and interpretation, and drafted and revised the manuscript. AS acquired data, interpreted data, and contributed to manuscript drafting and revision. NF designed the study, interpreted data, and contributed to manuscript drafting and revision. PT, CC, KTB, HLS, MTO, SI, JM, VL, AM, SK, DJH, SA-S, JP, LAVK, AJ-M, LP, MZ, SNW, PRG, RH, and LI-S acquired data, interpreted data, and contributed to manuscript drafting and revision. AD and SD blindly read liver biopsies acquiring data, interpreted data, and contributed to manuscript drafting and revision. MS-B designed the study, designed the statistical analyses and interpretation, and drafted and revised the manuscript. AA, PAng, JPi, EB, MK, CF-P, AL, M-CG, HJK, and MP-G acquired data, interpreted data, and contributed to manuscript drafting and revision. ATM acquired data, interpreted data, participated in the formal analysis and methodology, and contributed to manuscript drafting and revision. AJ, EP, IA, LM, IV, JKH, VC, RG, BB, FP, PDK, DZ, KKS, DRoj, RK, MDM, AT, RH-I, JH, RL-M, and RMM acquired data, interpreted data, and contributed to manuscript drafting and revision. SG, MM, TK, PN, and PSK interpreted data and contributed to manuscript drafting and revision. RB acquired data, interpreted data, and contributed to manuscript drafting and revision. ING designed the study, acquired data, interpreted data, and contributed to manuscript drafting and revision. JMS, FL, ET, WPB, JMP, LS, IGr, DR, PA acquired data, interpreted data and contributed to manuscript drafting and revision. AK and LIC designed the study, interpreted the data, and contributed to manuscript drafting, and revision. PG designed the study, interpreted the data, and drafted and revised the manuscript.

Declaration of interests

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Data sharing

Data from this manuscript can be requested by qualified researchers. Before the use of the data, proposals need to be approved by all partners of the LiverScreen Consortium, and a data sharing agreement will need to be signed. Approval will depend on the scientific value of the proposal, compatibility with the original patient consent, and data protection legislation.

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References

- Naghavi M, Ong KL, Aali A, et al, and the GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* 2024; **403**: 2100–32.
- Ginès P, Krag A, Abralles JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. *Lancet* 2021; **398**: 1359–76.
- Johansen S, Åberg F, Tsochatzis EA, Krag A. Screening for advanced steatotic liver disease. *Lancet Gastroenterol Hepatol* 2025; **10**: 842–54.
- Harrison SA, Bedossa P, Guy CD, et al, and the MAESTRO-NASH Investigators. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. *N Engl J Med* 2024; **390**: 497–509.
- Sanyal AJ, Newsome PN, Kliers I, et al, and the ESSENCE Study Group. Phase 3 trial of semaglutide in metabolic dysfunction-associated steatohepatitis. *N Engl J Med* 2025; **392**: 2089–99.
- Castera L, Rinella ME, Tsochatzis EA. Noninvasive assessment of liver fibrosis. *N Engl J Med* 2025; **393**: 1715–29.
- Nilsson E, Anderson H, Sargenti K, Lindgren S, Prytz H. Clinical course and mortality by etiology of liver cirrhosis in Sweden: a population based, long-term follow-up study of 1317 patients. *Aliment Pharmacol Ther* 2019; **49**: 1421–30.
- Lin H, Lee HW, Yip TCF, et al, and the VCTE-Prognosis Study Group. Vibration-controlled transient elastography scores to predict liver-related events in steatotic liver disease. *JAMA* 2024; **331**: 1287–97.
- Thiele M, Kamath PS, Graupera I, et al. Screening for liver fibrosis: lessons from colorectal and lung cancer screening. *Nat Rev Gastroenterol Hepatol* 2024; **21**: 517–27.
- Luo N, Zhang X, Huang J, Chen H, Tang H. Prevalence of steatotic liver disease and associated fibrosis in the United States: results from NHANES 2017–March 2020. *J Hepatol* 2024; **80**: e70–71.
- Man S, Deng Y, Ma Y, et al. Prevalence of liver steatosis and fibrosis in the general population and various high-risk populations: a nationwide study with 5.7 million adults in China. *Gastroenterology* 2023; **165**: 1025–40.
- Rinella ME, Lazarus JV, Ratziu V, et al, and the NAFLD Nomenclature consensus group. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *J Hepatol* 2023; **79**: 1542–56.
- Israelsen M, Francque S, Tsochatzis EA, Krag A. Steatotic liver disease. *Lancet* 2024; **404**: 1761–78.
- Roulot D, Costes JL, Buyck JF, et al. Transient elastography as a screening tool for liver fibrosis and cirrhosis in a community-based population aged over 45 years. *Gut* 2011; **60**: 977–84.
- Caballería L, Pera G, Arteaga I, et al. High prevalence of liver fibrosis among European adults with unknown liver disease: a population-based study. *Clin Gastroenterol Hepatol* 2018; **16**: 1138–45.
- de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII—renewing consensus in portal hypertension. *J Hepatol* 2022; **76**: 959–74.
- Kwo PY, Cohen SM, Lim JK. ACG clinical guideline: evaluation of abnormal liver chemistries. *Am J Gastroenterol* 2017; **112**: 18–35.
- Newsome PN, Cramb R, Davison SM, et al. Guidelines on the management of abnormal liver blood tests. *Gut* 2018; **67**: 6–19.
- Schwöpe RB, Katz M, Russell T, Reiter MJ, Lisanti CJ. The many faces of cirrhosis. *Abdom Radiol* 2020; **45**: 3065–80.
- Liu X. Classification accuracy and cut point selection. *Stat Med* 2012; **31**: 2676–86.
- Graupera I, Thiele M, Ma AT, et al, and the LiverScreen Consortium investigators. LiverScreen project: study protocol for screening for liver fibrosis in the general population in European countries. *BMC Public Health* 2022; **22**: 1385.
- WHO. Alcohol, health and policy response in the European Union in 2019. <https://www.who.int/europe/publications/m/item/alcohol-health-and-policy-response-in-the-european-union-in-2019> (accessed Dec 15, 2025).
- Le P, Tatar M, Dasarathy S, et al. Estimated burden of metabolic dysfunction-associated steatotic liver disease in US adults, 2020 to 2050. *JAMA Netw Open* 2025; **8**: e2454707–2454707.
- Karlsen TH, Sheron N, Zelber-Sagi S, et al. The EASL-Lancet Liver Commission: protecting the next generation of Europeans against liver disease complications and premature mortality. *Lancet* 2022; **399**: 61–116.
- Krag A, Torp N, Younossi ZM, Israelsen M. Reporting discrepancy of alcohol intake affecting estimated prevalence of MetALD and ALD. *Lancet Gastroenterol Hepatol* 2025; **10**: 282–84.
- Radcke S, Dillon JF, Murray AL. A systematic review of the prevalence of mildly abnormal liver function tests and associated health outcomes. *Eur J Gastroenterol Hepatol* 2015; **27**: 1–7.
- Chen LW, Huang MS, Shyu YC, Chien RN. Gamma-glutamyl transpeptidase elevation is associated with metabolic syndrome, hepatic steatosis, and fibrosis in patients with nonalcoholic fatty liver disease: a community-based cross-sectional study. *Kaohsiung J Med Sci* 2021; **37**: 819–27.
- Lindfors A, Strandberg R, Hagström H. Screening for advanced liver fibrosis due to metabolic dysfunction-associated steatotic liver disease alongside retina scanning in people with type 2 diabetes: a cross-sectional study. *Lancet Gastroenterol Hepatol* 2025; **10**: 125–37.
- Lindvig KP, Thorhauge KH, Hansen JK, et al. Development, validation, and prognostic evaluation of LiverPRO for the prediction of significant liver fibrosis in primary care: a prospective cohort study. *Lancet Gastroenterol Hepatol* 2025; **10**: 55–67.
- Sripongpun P, Kim WR, Mannalithara A, et al. The steatosis-associated fibrosis estimator (SAFE) score: a tool to detect low-risk NAFLD in primary care. *Hepatology* 2023; **77**: 256–67.
- Åberg F, Luukkonen PK, But A, et al. Development and validation of a model to predict incident chronic liver disease in the general population: the CLivD score. *J Hepatol* 2022; **77**: 302–11.
- Serra-Burriel M, Juanola A, Serra-Burriel F, et al, and the LiverScreen Consortium Investigators. Development, validation, and prognostic evaluation of a risk score for long-term liver-related outcomes in the general population: a multicohort study. *Lancet* 2023; **402**: 988–96.
- van Kleef LA, Francque SM, Prieto-Ortiz JE, et al. Metabolic Dysfunction-Associated Fibrosis 5 (MAF-5) score predicts liver fibrosis risk and outcome in the general population with metabolic dysfunction. *Gastroenterology* 2024; **167**: 357–67.
- Jørgensen SF, Larsen PT, Erichsen R, Andersen B, Rebolj M, Njor S. Adherence to follow-up and resource use after abnormal FIT-screening: evaluation of the Danish colorectal cancer screening program. *Endosc Int Open* 2024; **12**: e649–58.