




Original Article



Regional Inequities in Metabolic Dysfunction–associated Steatotic Liver Disease Burden and Care Quality in High-burden Settings: Implications for Health Systems

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Received: February 13, 2026 | Revised: April 26, 2026 | Accepted: May 07, 2026 | Published online: June 22, 2026

Abstract

Background and Aims: Metabolic dysfunction–associated steatotic liver disease (MASLD) is increasing rapidly, yet regional differences in burden and care quality remain unclear. This study aimed to compare regional incidence, mortality, and disability; evaluate care quality; identify key determinants; and project future incidence. **Methods:** We analyzed the Global Burden of Disease 2023 estimates of MASLD incidence, deaths, and disability-adjusted life years from 1990 to 2023 by age, sex, country, and region. Age-standardized rates were assessed using joinpoint regression. A composite Quality of Care Index (QCI) was derived through principal component analysis. Gradient boosting models with SHapley Additive exPlanations interpretation identified key predictors, and Bayesian age–period–cohort models generated incidence projections. **Results:** In 2023, South and East Asia had the largest numbers of new cases, while North Africa and the Middle East and Andean Latin America recorded the highest age-standardized incidence, mortality, and disability rates. Eastern Europe and Andean Latin America showed sustained increases in mortality and disability despite moderate incidence growth. QCI values were lowest in South Asia, Western Sub-Saharan Africa, and Eastern Europe. High body mass index and fasting plasma glucose were prominent contributors in comparative risk attribution analyses, and machine learning models identified age and calendar year as the strongest predictors of modeled burden patterns. Incidence is projected to continue increasing

through 2050, particularly in India and China. **Conclusions:** MASLD burden and care quality vary widely across regions. Low-QCI regions show higher mortality and disability, unfavorable metabolic risk profiles, and delayed detection patterns. Strengthening prevention, early case finding, fibrosis assessment, and treatment access may slow MASLD progression.

Citation of this article: Zhang K, Kan C, Sheng S, Xu W, Han F, Chen J, *et al.* Regional Inequities in Metabolic Dysfunction–associated Steatotic Liver Disease Burden and Care Quality in High-burden Settings: Implications for Health Systems. *J Clin Transl Hepatol* 2026. doi: 10.14218/JCTH.2026.00127.

Introduction

Metabolic dysfunction–associated steatotic liver disease (MASLD) has emerged as one of the most rapidly increasing contributors to liver-related morbidity worldwide.^{1–4} Its rise closely parallels global increases in obesity, impaired glucose metabolism, and clustered metabolic abnormalities.^{3–7} Over the past three decades, the distribution of MASLD has shifted markedly across regions due to population aging, changing lifestyles, and unequal health system performance.^{8,9} Although global prevalence continues to increase, the impact is highly uneven, with some regions experiencing rapidly expanding incidence and others facing worsening mortality or disability.

Despite these pronounced differences, comparative research remains limited. Few studies have provided long-term, region-wide assessments of MASLD incidence, mortality, and disability using standardized analytic frameworks. Even less is known about how demographic structure, metabolic risk exposures, and quality of care jointly shape regional patterns of disease burden. Large variations in diagnostic capacity, early detection, and access to metabolic risk management may either amplify or mitigate disease progression, yet the

Keywords: Metabolic dysfunction–associated steatotic liver disease; Global Burden of Disease; Quality of Care Index; Metabolic risk factors.

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contribution of these structural factors at a regional scale remains poorly understood.

Understanding regional inequalities in MASLD is essential for guiding prevention strategies and resource allocation. Age-standardized indicators offer a robust foundation for comparing disease patterns across diverse populations, but long-term evaluations using globally standardized data are scarce. Moreover, wide differences in care quality across countries may influence both disease detection and outcomes, further contributing to regional disparities. These gaps highlight the need for comprehensive, region-focused assessments of MASLD burden and its structural determinants.

In this study, we conducted a region-focused analysis of MASLD burden using the Global Burden of Disease (GBD) 2023 framework, with particular attention to regions and countries with relatively high burden or marked inequalities in outcomes and care quality. Building on previous MASLD burden research, we evaluated regional patterns of incidence, mortality, disability, and care quality, identified major associated factors using interpretable machine learning, and projected future incidence trends through 2050.

Methods

Data sources and study design

This population-based study was conducted using GBD 2023 estimates. All analyses were based on publicly available GBD 2023 estimates and were conducted in accordance with relevant GBD data use and publication requirements. Data were accessed through the GBD 2023 results platform and related IHME data resources. In GBD 2023, the underlying disease category remains non-alcoholic fatty liver disease (NAFLD) and has not yet been fully recoded to align with the updated MASLD definition. Therefore, although we used the term MASLD in this manuscript to reflect current clinical terminology, all estimates were derived from GBD 2023 NAFLD-related data. Incidence, deaths, and disability-adjusted life years (DALYs) for MASLD were extracted by year, sex, age group, country, and region from 1990 to 2023. GBD 2023 synthesizes data from vital registration, cancer and liver registries, surveys, hospital records, and published sources using a unified Bayesian framework with uncertainty propagation. Estimates are presented with 95% uncertainty intervals (UIs). In addition, comparative risk assessment estimates for major metabolic risk factors were obtained from GBD 2023. Within the GBD framework, attributable burden is estimated by integrating population exposure distributions, relative risks, and theoretical minimum-risk exposure levels to derive population-attributable fractions for specific risk–outcome pairs. These estimates reflect population-level attributable burden rather than individual-level causation.

DALYs

DALYs are a summary measure of total disease burden and are calculated as the sum of years of life lost due to premature death and years lived with disability. Higher DALY values indicate greater health loss attributable to disease.

Temporal trend analysis

To quantify long-term temporal trends, we applied joinpoint regression models to selected age-standardized rates. Western Europe was selected for the age-standardized incidence rate (ASIR) analysis because it showed the largest increase in age-standardized incidence from 1990 to 2023 among the examined regions. Eastern Europe was selected for the age-

standardized mortality rate (ASMR) and age-standardized disability-adjusted life year rate (ASDR) analyses because it showed the largest increases in age-standardized mortality and DALY rates during the same period. Therefore, the joinpoint analysis was designed to characterize the most prominent temporal increases in incidence and severe outcomes rather than to provide joinpoint models for all GBD regions. Joinpoint regression identifies statistically significant changes in temporal trends by fitting a series of connected log-linear segments and testing changes in slope using permutation methods. For each segment, we calculated the annual percent change (APC) with 95% confidence intervals, and for the overall study period, we computed the average annual percent change (AAPC) as a weighted average of the segment-specific APCs according to segment length.^{10,11} Sex-specific models were also fitted to examine differences by sex. A two-sided *P*-value < 0.05 was considered statistically significant. Joinpoint analysis was performed using the Joinpoint Regression Program.

Quality of Care Index (QCI)

To evaluate MASLD-related quality of care, we constructed a composite QCI at the regional and national levels using four indicators derived from GBD 2023 estimates: the mortality-to-incidence ratio (MIR), DALY-to-prevalence ratio (DPR), years of life lost-to-incidence ratio (YLR), and prevalence-to-incidence ratio (PIR). Each indicator was calculated for all countries and regions in 2023 and standardized to have a mean of zero and a standard deviation of one. Principal component analysis (PCA) was then applied to capture the shared variance structure among these indicators.¹² The proportion of variance explained by each principal component was recorded. PC1 and PC2 refer to the first and second principal components in PCA. PC1 represents the largest proportion of variance explained by the included indicators, whereas PC2 represents the second largest proportion of variance, independent of PC1. PC1 was used to construct the QCI because it captured the dominant shared variation across MIR, DPR, YLR, and PIR. The PC1-derived score was rescaled to a 0–100 range, with higher scores indicating better quality of care. PC2 was not incorporated into the QCI score but was examined to describe the secondary axis of variation in the PCA structure. To further characterize the QCI structure, we computed Pearson correlation coefficients for MIR, DPR, YLR, and PIR and examined the loadings of PC1 and PC2 across regions.

Machine learning analysis and SHapley additive ex-Planations (SHAP) interpretation

Gradient boosting tree models were developed using the XG-Boost framework in selected high-burden or high-inequality GBD regions. For incidence models, we included South Asia, Western Sub-Saharan Africa, and North Africa and the Middle East because these regions represented large incident case numbers, marked increases in incident cases, or high ASIRs. For DALY models, we included Western Europe, Andean Latin America, and Eastern Europe because these regions showed high DALY burden, high age-standardized DALY rates, or prominent increases in age-standardized DALY rates. The analytical unit was region-year-age group-sex. Predictors included age (treated as a continuous variable or age-group midpoint), sex, calendar year, and log-transformed population size. Eighty percent of observations were used for training and 20% for internal validation. Hyperparameters, including learning rate, maximum tree depth, number of trees, and subsampling fraction, were tuned by five-fold cross-validation. Model performance was assessed internally us-

ing the coefficient of determination and root mean squared error. The machine-learning analysis was intended primarily to characterize relative variable importance and model-based patterning in representative high-burden settings rather than to generate a comprehensive prediction model for all GBD regions or for clinical or operational use.^{13,14} SHAP values were computed for all predictors to interpret the fitted models. SHAP is a model interpretation method that quantifies how much each predictor contributes to the model output for a given observation. In this study, average absolute SHAP values were used to rank variable importance, and SHAP dependence plots were generated for major predictors to visualize their associations with predicted burden.

Forecasting

Future incidence trends were projected using a Bayesian age-period-cohort (BAPC) model that simultaneously accounts for age, period, and cohort effects. Country-level BAPC projections were performed for selected countries rather than for all high-burden countries. Countries were selected to represent large incident case numbers, prominent European burden patterns, and high-income comparator settings. China and India were selected because they had the largest numbers of incident cases. The Russian Federation, Germany, and the United Kingdom were selected because they represented countries with prominent mortality, DALY burden, or temporal increases in Eastern and Western Europe. The United States was included as a high-income comparator with substantial MASLD burden. The BAPC framework is useful for separating disease patterns associated with aging, calendar time, and generational differences while accounting for uncertainty in future estimates. The model applied a Poisson likelihood with log-linear predictors and incorporated second-order random walk priors to generate smooth temporal trajectories. Posterior estimates were derived using integrated nested Laplace approximation, and model performance was assessed through the Deviance Information Criterion and posterior predictive checks. ASIRs from 2024 to 2050 were forecast with corresponding 95% credible intervals.¹⁵

Statistical analysis

All analyses were performed in R version 4.3.3. Estimates are presented with 95% UIs, and a two-sided *P*-value < 0.05 was considered statistically significant.

Results

Regional burden

In 2023, South Asia had the highest number of MASLD incident cases, reaching 10,832,255 (95% UI, 9,880,875–11,898,537). In this region, adults aged 15–49 years accounted for the largest share of new cases, totaling 8,284,204 (7,261,742–9,419,189). Western Europe recorded the highest numbers of deaths and DALYs, with 16,679 deaths (13,097–21,282) and 388,889 DALYs (298,115–495,849). In Western Europe, individuals aged 70 years and older had the highest mortality burden, reaching 8,884 deaths (6,368–11,803), whereas those aged 50–69 years had the highest DALYs, totaling 200,552 (128,936–282,676). From 1990 to 2023, Western Sub-Saharan Africa showed the largest increase in MASLD incidence cases, while Andean Latin America showed the largest increase in the number of MASLD-related deaths and DALYs (Fig. 1; Supplementary Figs. 1 and 2).

North Africa and the Middle East showed the highest ASIR

at 1,027.14 (954.81–1,098.29), consistently higher among men. Andean Latin America had the highest ASMR and ASDR at 6.09 (4.72–7.71) and 152.29 (114.07–194.74). ASMR was higher in women, whereas ASDR was higher in men. From 1990 to 2023, Western Europe had the largest increase in ASIR, while Eastern Europe had the largest increases in ASMR and ASDR (Fig. 1; Supplementary Figs. 1 and 2).

Temporal trends

This section reports the APC and AAPC for ASIR in Western Europe, and for ASMR and ASDR in Eastern Europe from 1990 to 2023, with a focus on gender differences. In Western Europe, ASIR increased steadily over the study period, with an overall AAPC of 0.6562%. The APC values were 0.90% in 1990–1997, 1.02% in 1997–2005, 0.61% in 2005–2015, and 0.14% in 2015–2023, indicating a gradual slowing in recent years. The AAPC was slightly higher in females (0.6674%) than in males (0.6494%). In Eastern Europe, ASMR showed a substantial rise, with an overall AAPC of 3.1386%. The APC values were 11.03% in 1990–1995, –6.66% in 1995–1998, 9.93% in 1998–2005, and 0.23% in 2005–2023. The AAPC was slightly higher in females (3.1819%) than in males (2.8827%). ASDR in Eastern Europe also rose markedly, with an overall AAPC of 3.4249%. The APC values were 12.99% in 1990–1995, –6.99% in 1995–1998, 11.32% in 1998–2005, and –0.18% in 2005–2023, indicating periods of rapid increase followed by a modest decline in recent years. Females again showed a slightly higher AAPC (3.6232%) compared with males (3.1761%) (Fig. 2).

Country-level burden and inequalities

In 2023, China in East Asia had the highest number of MASLD incident cases, totaling 9,375,312 (95% UI, 8,606,110–10,162,838). In South Asia, India contributed the largest number of new cases, reaching 8,340,905 (7,594,359–9,156,269). China also recorded the highest numbers of deaths and DALYs, with 14,192 deaths (11,531–17,456) and 353,221 DALYs (287,916–432,219). Within Western Europe, Germany had the highest mortality burden and DALYs, reporting 4,543 deaths (3,462–5,861) and 106,899 DALYs (79,442–139,816).

Kuwait in North Africa and the Middle East exhibited the highest ASIR at 1,174.48 (1,096.85–1,245.62). Egypt had the highest ASMR in the region, reaching 7.88 (5.45–10.98), whereas in Andean Latin America, Bolivia reported the highest ASMR at 6.68 (4.40–9.77). Mexico in Central Latin America recorded the highest ASDR at 192.10 (143.42–249.15), while Bolivia had the highest ASDR within Andean Latin America at 169.89 (113.88–248.18). From 1990 to 2023, Mexico experienced the largest increase in ASIR. Within Western Europe, the United Kingdom showed the greatest rise in ASIR. The Russian Federation in Eastern Europe exhibited the steepest increases in both ASMR and ASDR over the study period.

Risk factor contributions to ASMR and ASDR

Analysis of ASMR from 1990 to 2023 across five regions—Eastern Europe, Andean Latin America, Western Europe, North Africa and the Middle East, and South Asia—showed a clear shift toward metabolic risks, particularly high body mass index (BMI) and high fasting plasma glucose (FPG). In Eastern Europe, ASMR attributable to metabolic risks rose from 0.03 (0.02–0.05) to 0.07 (0.05–0.10), a 133.33% increase. High BMI increased by 100%, and high FPG increased by 200%. Andean Latin America showed even sharper growth, with ASMR due to metabolic risks rising by

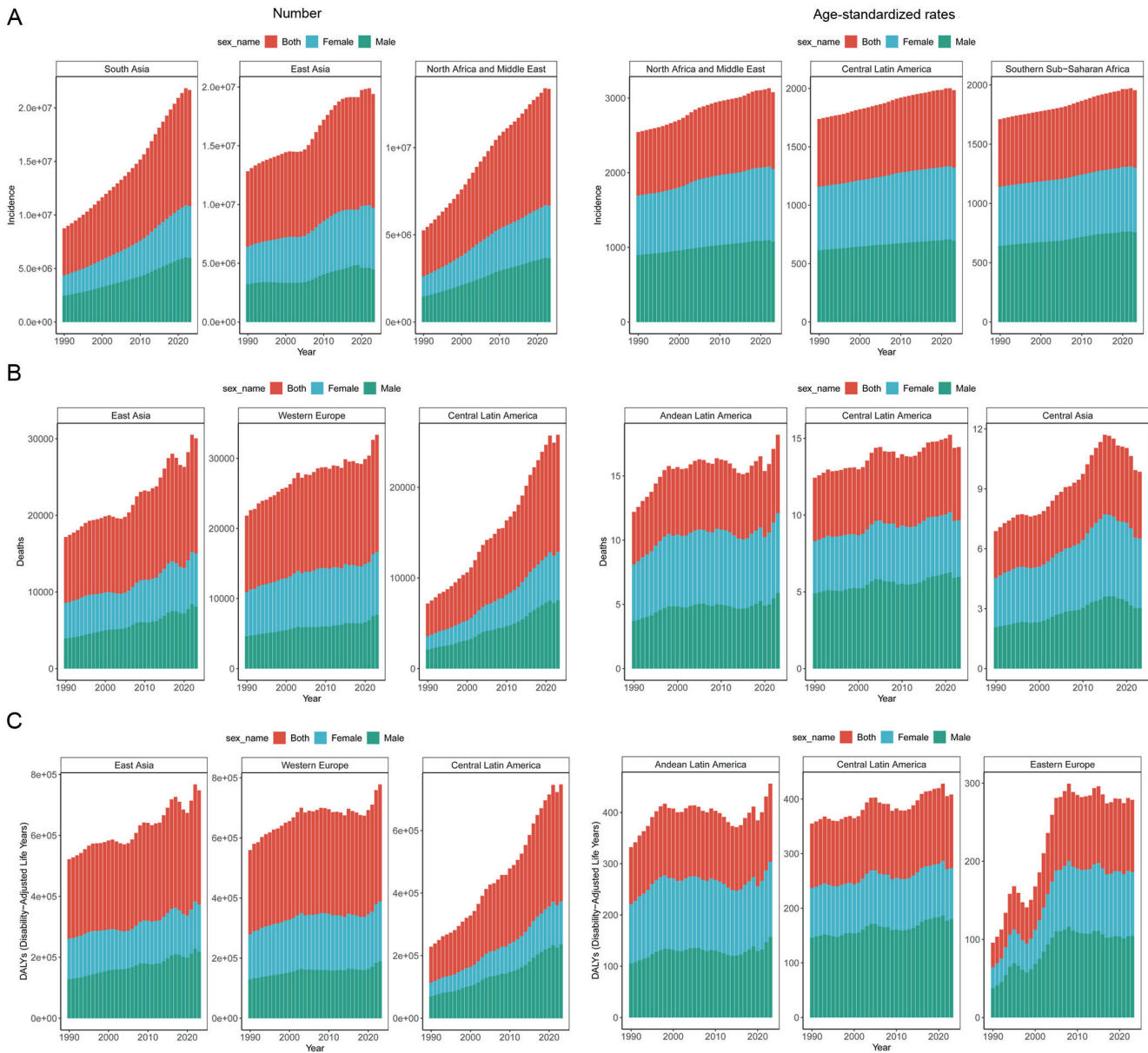


Fig. 1. Burden of MASLD in incidence, deaths, and DALYs. (A) Incidence; (B) Deaths; (C) DALYs. MASLD, metabolic dysfunction-associated steatotic liver disease; DALYs, disability-adjusted life years.

200%, and both high BMI and high FPG increasing by 250%. Western Europe experienced similar patterns. ASMR attributable to metabolic risks increased from 0.05 (0.03–0.07) to 0.11 (0.07–0.16), a 120% rise. High BMI increased by 200%, and high FPG rose by 133.33%. North Africa and the Middle East showed a 108.7% increase in ASMR due to metabolic risks (0.23 to 0.48), with high FPG rising by 107.14%. South Asia showed a more modest overall increase, but ASMR attributable to high FPG still doubled from 0.03 to 0.06 (Fig. 3). ASDR patterns mirrored ASMR trends. In Eastern Europe, ASDR attributable to metabolic risks increased by 113.51%. In Andean Latin America, ASDR rose by 190.70%, with high BMI increasing by 212.5%. Western Europe showed a 117.76% increase in ASDR attributable to metabolic risks, while high FPG rose by 101.49%. North

Africa and the Middle East experienced a 115.47% increase, with high BMI rising by 129.68%. South Asia showed a 130.86% increase in ASDR attributable to metabolic risks, and high FPG increased by 94.81% (Fig. 3).

Regional variations in MASLD quality of care

Geographic distribution of QCI: Across the six examined regions, MASLD-related quality of care showed clear spatial heterogeneity, with QCI values varying widely within and between regions. In South Asia, Bhutan recorded the highest QCI at 85.85, while Nepal, Pakistan, and India scored much lower (25.80–27.83), revealing a strong gradient in which smaller high-performing countries outpaced larger populations facing heavier metabolic burdens. Western Europe showed a generally favorable profile, though notable

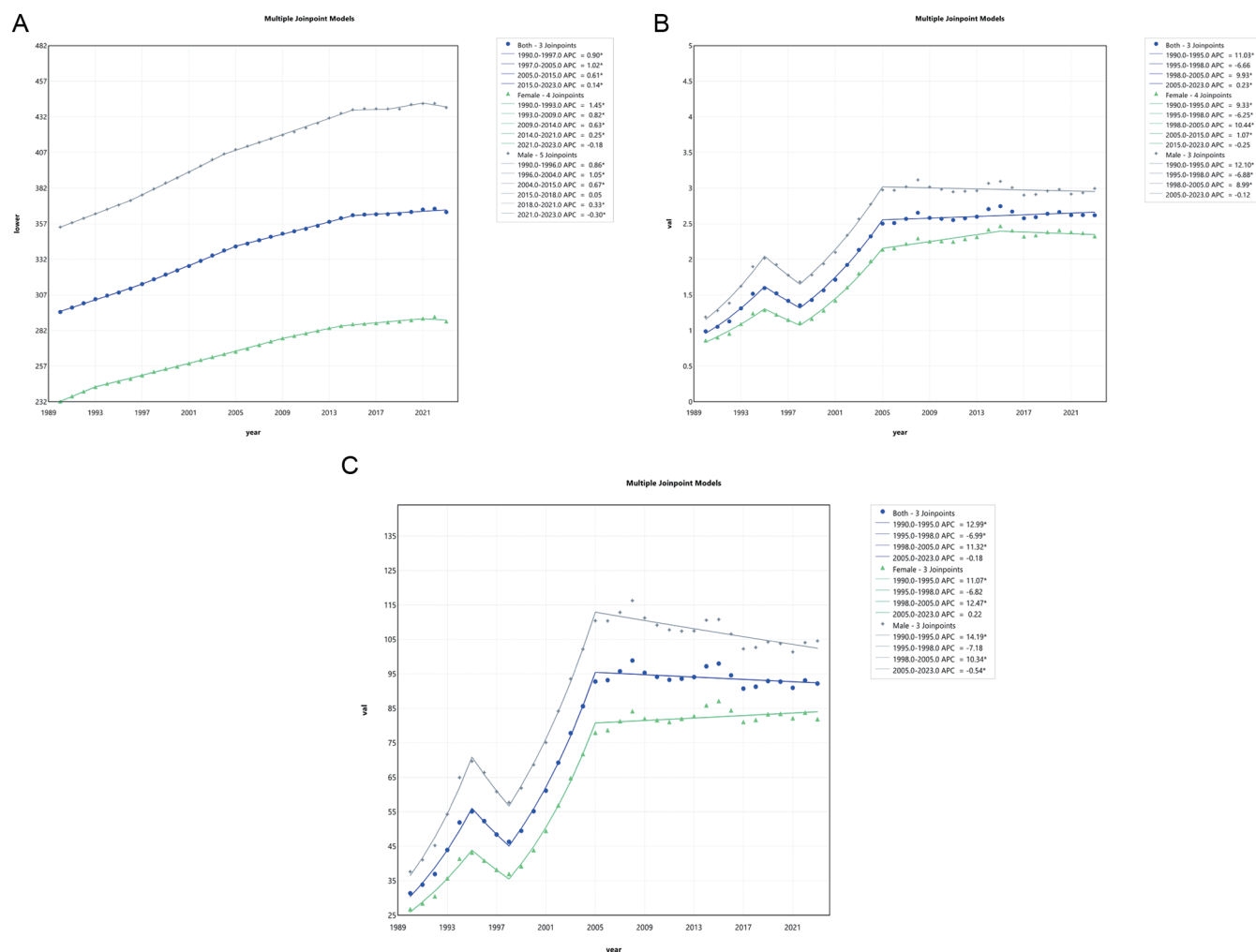


Fig. 2. Joinpoint analysis of temporal trends in MASLD ASIR, ASMR, and ASDR from 1990 to 2023. (A) ASIR in Western Europe. Joinpoint regression showing changes in ASIR for the total population, males, and females, with each segment representing a period defined by a distinct APC. The overall trend is summarized by the average AAPC. (B) ASMR and (C) ASDR in Eastern Europe. MASLD, metabolic dysfunction-associated steatotic liver disease; ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life-year rate; APC, annual percent change; AAPC, average annual percent change.

intra-regional differences persisted. In Western Sub-Saharan Africa, QCI ranged from very low levels in Mali, Niger, and Benin to moderate levels in Liberia, Cameroon, and Mauritania, reflecting structural inequities linked to limited diagnostic capacity and health system constraints. Andean Latin America exhibited a narrower distribution, with Peru and Ecuador performing better and Bolivia consistently scoring lower. In North Africa and the Middle East, Egypt achieved the highest QCI at 90.50, whereas Afghanistan, Kuwait, and Jordan ranked among the lowest. Eastern Europe overall remained low performing, with Moldova reaching a moderate QCI of 74.50, in contrast to persistently low values in Latvia, Estonia, and Belarus (Fig. 4; Supplementary Figs. 3 and 4).

Regional correlation patterns: Correlation analyses across regions revealed consistent relationships among QCI indicators. MIR and DPR showed uniformly strong positive correlations, with *r* values ranging from 0.9593 in Andean Latin America to 0.9883 in Eastern Europe, all *P* < 0.001, indicating that higher mortality relative to incidence was consistently linked to greater disability burden relative to prevalence. In contrast, YLR showed more variable associations.

Eastern Europe displayed minimal correlations between YLR and other indicators, while moderate positive correlations with MIR and DPR were observed in Western Europe, Western Sub-Saharan Africa, and Andean Latin America, suggesting partial alignment between acute fatality burden and disability accumulation.

PIR showed mainly negative or weak correlations with MIR, DPR, and YLR across most regions. The strongest inverse correlation was observed between PIR and DPR in Andean Latin America (*r* = -0.7462, *P* ≤ 0.001), whereas weak positive correlations appeared in South Asia. PIR also showed minimal association with YLR in some regions, indicating that chronic case accumulation and early fatality patterns often operate independently (Fig. 4; Supplementary Figs. 3 and 4; Supplementary Table 1).

Principal component structure of MASLD: PCA revealed a stable two-component structure across all examined regions. PC1 explained approximately 49%–80% of the total variance in MIR, DPR, YLR, and PIR, whereas PC2 explained an additional 15%–35% of the variance. PC1 was therefore used as the basis for QCI construction because it captured the dominant shared variation among the four

Eastern Europe

Risk Factors Ranking Change (1990–2023)				
ASMR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
0.04 (0.02, 0.07)	1 All risk factors	1 All risk factors	0.08 (0.06, 0.12)	100.00%
0.03 (0.02, 0.05)	2 Metabolic risks	2 Metabolic risks	0.07 (0.05, 0.10)	133.33%
0.02 (0.01, 0.03)	3 High body-mass index	3 High body-mass index	0.04 (0.02, 0.07)	100.00%
0.01 (0.01, 0.02)	4 High fasting plasma glucose	4 High fasting plasma glucose	0.03 (0.02, 0.05)	200.00%
0.01 (0.00, 0.02)	5 Smoking	5 Smoking	0.02 (0.01, 0.04)	100.00%
0.01 (0.00, 0.02)	6 Tobacco	6 Tobacco	0.02 (0.01, 0.04)	100.00%
0.01 (0.00, 0.02)	7 Behavioral risks	7 Behavioral risks	0.02 (0.01, 0.04)	100.00%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Risk Factors Ranking Change (1990–2023)				
ASDR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
0.97 (0.46, 1.47)	1 All risk factors	1 All risk factors	2.02 (1.50, 2.76)	108.21%
0.74 (0.48, 1.07)	2 Metabolic risks	2 Metabolic risks	1.58 (1.03, 2.31)	113.51%
0.47 (0.20, 0.78)	3 High body-mass index	3 High body-mass index	1.03 (0.45, 1.77)	119.15%
0.32 (0.20, 0.51)	4 High fasting plasma glucose	4 High fasting plasma glucose	0.89 (0.46, 1.09)	115.62%
0.30 (0.09, 0.53)	5 Behavioral risks	5 Behavioral risks	0.60 (0.19, 1.01)	100.00%
0.30 (0.09, 0.53)	6 Smoking	6 Smoking	0.60 (0.19, 1.01)	100.00%
0.30 (0.09, 0.53)	7 Tobacco	7 Tobacco	0.60 (0.19, 1.01)	100.00%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Andean Latin American

Risk Factors Ranking Change (1990–2023)				
ASMR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
0.05 (0.03, 0.07)	1 All risk factors	1 All risk factors	0.13 (0.08, 0.19)	160.00%
0.04 (0.02, 0.07)	2 Metabolic risks	2 Metabolic risks	0.12 (0.07, 0.18)	200.00%
0.02 (0.01, 0.04)	3 High fasting plasma glucose	3 High body-mass index	0.07 (0.02, 0.12)	250.00%
0.02 (0.01, 0.04)	4 High body-mass index	4 High fasting plasma glucose	0.07 (0.04, 0.10)	250.00%
0.01 (0.00, 0.02)	5 Smoking	5 Smoking	0.01 (0.00, 0.03)	0.00%
0.01 (0.00, 0.02)	6 Tobacco	6 Tobacco	0.01 (0.00, 0.03)	0.00%
0.01 (0.00, 0.02)	7 Behavioral risks	7 Behavioral risks	0.01 (0.00, 0.03)	0.00%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Risk Factors Ranking Change (1990–2023)				
ASDR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
0.86 (0.65, 1.06)	1 All risk factors	1 All risk factors	2.06 (1.56, 3.13)	171.53%
0.80 (0.46, 1.39)	2 Metabolic risks	2 Metabolic risks	2.50 (1.42, 3.78)	190.70%
0.48 (0.17, 0.99)	3 High body-mass index	3 High body-mass index	1.50 (0.85, 2.33)	212.50%
0.44 (0.25, 0.73)	4 High fasting plasma glucose	4 High fasting plasma glucose	1.25 (0.77, 1.92)	184.09%
0.16 (0.05, 0.35)	5 Tobacco	5 Tobacco	0.24 (0.06, 0.53)	50.00%
0.16 (0.05, 0.35)	6 Smoking	6 Smoking	0.24 (0.06, 0.53)	50.00%
0.16 (0.05, 0.35)	7 Behavioral risks	7 Behavioral risks	0.24 (0.06, 0.53)	50.00%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Western Europe

Risk Factors Ranking Change (1990–2023)				
ASMR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
0.06 (0.04, 0.09)	1 All risk factors	1 All risk factors	0.13 (0.08, 0.19)	119.67%
0.05 (0.03, 0.07)	2 Metabolic risks	2 Metabolic risks	0.11 (0.07, 0.16)	120.00%
0.03 (0.02, 0.05)	3 High fasting plasma glucose	3 High fasting plasma glucose	0.07 (0.05, 0.10)	133.33%
0.02 (0.01, 0.04)	4 High body-mass index	4 High body-mass index	0.06 (0.02, 0.09)	200.00%
0.02 (0.01, 0.04)	5 Smoking	5 Smoking	0.03 (0.01, 0.06)	50.00%
0.02 (0.01, 0.04)	6 Tobacco	6 Tobacco	0.03 (0.01, 0.06)	50.00%
0.02 (0.01, 0.04)	7 Behavioral risks	7 Behavioral risks	0.03 (0.01, 0.06)	50.00%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Risk Factors Ranking Change (1990–2023)				
ASDR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
1.41 (1.05, 2.19)	1 All risk factors	1 All risk factors	2.80 (1.38, 4.10)	161.44%
1.07 (0.72, 1.65)	2 Metabolic risks	2 Metabolic risks	2.33 (1.54, 3.29)	117.76%
0.67 (0.47, 0.90)	3 High fasting plasma glucose	3 High fasting plasma glucose	1.36 (0.92, 1.93)	101.49%
0.51 (0.16, 0.90)	4 High body-mass index	4 Behavioral risks	1.23 (0.50, 2.05)	141.16%
0.51 (0.16, 0.90)	5 Smoking	5 Behavioral risks	0.74 (0.22, 1.37)	45.10%
0.51 (0.16, 0.90)	6 Tobacco	6 Smoking	0.74 (0.22, 1.37)	45.10%
0.48 (0.18, 0.90)	7 High body-mass index	7 Tobacco	0.74 (0.22, 1.37)	54.17%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

North African and the Middle East

Risk Factors Ranking Change (1990–2023)				
ASMR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
0.26 (0.12, 0.44)	1 All risk factors	1 All risk factors	0.52 (0.31, 0.77)	100.00%
0.23 (0.12, 0.40)	2 Metabolic risks	2 Metabolic risks	0.48 (0.28, 0.71)	108.70%
0.14 (0.07, 0.22)	3 High fasting plasma glucose	3 High fasting plasma glucose	0.29 (0.19, 0.42)	107.14%
0.11 (0.04, 0.22)	4 High body-mass index	4 High body-mass index	0.27 (0.10, 0.47)	145.45%
0.04 (0.01, 0.10)	5 Tobacco	5 Tobacco	0.08 (0.02, 0.15)	100.00%
0.04 (0.01, 0.10)	6 Smoking	6 Smoking	0.08 (0.02, 0.15)	100.00%
0.04 (0.01, 0.10)	7 Behavioral risks	7 Behavioral risks	0.08 (0.02, 0.15)	100.00%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Risk Factors Ranking Change (1990–2023)				
ASDR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
5.98 (3.13, 9.72)	1 All risk factors	1 All risk factors	12.16 (7.36, 18.21)	103.34%
5.17 (2.65, 8.78)	2 Metabolic risks	2 Metabolic risks	11.14 (6.46, 16.41)	115.47%
2.83 (1.55, 4.80)	3 High fasting plasma glucose	3 High body-mass index	6.50 (2.59, 11.20)	129.68%
2.81 (0.99, 5.47)	4 High body-mass index	4 High fasting plasma glucose	6.41 (4.06, 8.65)	128.11%
1.13 (0.30, 2.46)	5 Behavioral risks	5 Behavioral risks	1.89 (0.51, 3.90)	67.26%
1.13 (0.30, 2.46)	6 Tobacco	6 Tobacco	1.89 (0.51, 3.90)	67.26%
1.13 (0.30, 2.46)	7 Smoking	7 Smoking	1.89 (0.51, 3.90)	67.26%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

South Asia

Risk Factors Ranking Change (1990–2023)				
ASMR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
0.05 (0.03, 0.08)	1 All risk factors	1 All risk factors	0.09 (0.06, 0.14)	80.00%
0.03 (0.02, 0.05)	2 Metabolic risks	2 Metabolic risks	0.08 (0.05, 0.11)	166.67%
0.03 (0.02, 0.05)	3 High fasting plasma glucose	3 High fasting plasma glucose	0.05 (0.04, 0.10)	100.00%
0.02 (0.01, 0.04)	4 Tobacco	4 Tobacco	0.02 (0.01, 0.04)	0.00%
0.02 (0.01, 0.04)	5 Behavioral risks	5 Behavioral risks	0.02 (0.01, 0.04)	0.00%
0.02 (0.01, 0.04)	6 Smoking	6 Smoking	0.02 (0.01, 0.04)	0.00%
0.00 (0.00, 0.00)	7 High body-mass index	7 High body-mass index	0.02 (0.01, 0.03)	8
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Risk Factors Ranking Change (1990–2023)				
ASDR per 100,000(95% UI)	1990 Rank	2023 Rank	Percent Change	
1.22 (0.72, 1.94)	1 All risk factors	1 All risk factors	2.23 (1.46, 3.42)	82.79%
0.81 (0.48, 1.29)	2 Metabolic risks	2 Metabolic risks	1.87 (1.17, 2.82)	130.86%
0.77 (0.46, 1.24)	3 High fasting plasma glucose	3 High fasting plasma glucose	1.50 (0.90, 2.31)	84.81%
0.48 (0.14, 0.93)	4 Behavioral risks	4 Behavioral risks	0.47 (0.13, 1.00)	-2.08%
0.48 (0.14, 0.93)	5 Tobacco	5 Tobacco	0.47 (0.13, 1.00)	-2.08%
0.48 (0.14, 0.93)	6 Smoking	6 Smoking	0.47 (0.13, 1.00)	-2.08%
0.06 (0.02, 0.11)	7 High body-mass index	7 High body-mass index	0.47 (0.17, 0.88)	683.33%
0.00 (0.00, 0.00)	8 Alcohol use	8 Alcohol use	0.00 (0.00, 0.00)	0.00%

Fig. 3. Changes in MASLD-related ASMR and ASDR attributable to metabolic risks, high BMI, and high FPG from 1990 to 2023 across selected regions. Color shading indicates the relative magnitude of percentage change, with darker shading representing larger increases. MASLD, metabolic dysfunction-associated steatotic liver disease; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life-year rate; DALYs, disability-adjusted life years; BMI, body mass index; FPG, fasting plasma glucose.

indicators. PC1 was mainly dominated by MIR and DPR, forming a mortality–disability axis separating high-burden from better-performing systems. PC2 was not included in the QCI calculation but was interpreted as an exploratory component describing residual variation in chronicity and survival patterns. PC2 was primarily defined by PIR, and in some regions, particularly North Africa and the Middle East, YLR also contributed to PC2, adding a dimension related to acute fatality burden. PCA biplots showed consistent clustering patterns: MIR and DPR loaded strongly along the positive PC1 axis, while PIR projected orthogonally onto PC2, typically in the opposite direction. YLR occupied intermediate positions, aligning with PC1 in some regions and PC2 in others. These results indicate that mortality, disabil-

ity, and chronicity form distinct but complementary dimensions shaping regional MASLD care-quality variation (Fig. 4; Supplementary Figs. 3 and 4).

Predictors and patterning of MASLD incidence and DALY burden

Machine-learning predictors of MASLD incidence: XG-Boost–SHAP analyses consistently identified age as the strongest predictor of MASLD incidence in South Asia, Western Sub-Saharan Africa, and North Africa and the Middle East, while population size contributed little to incidence variation. In South Asia, age showed a nonlinear pattern with two major peaks: a substantial rise among young adults aged 20–30 years and a second increase around 60–70 years. SHAP val-

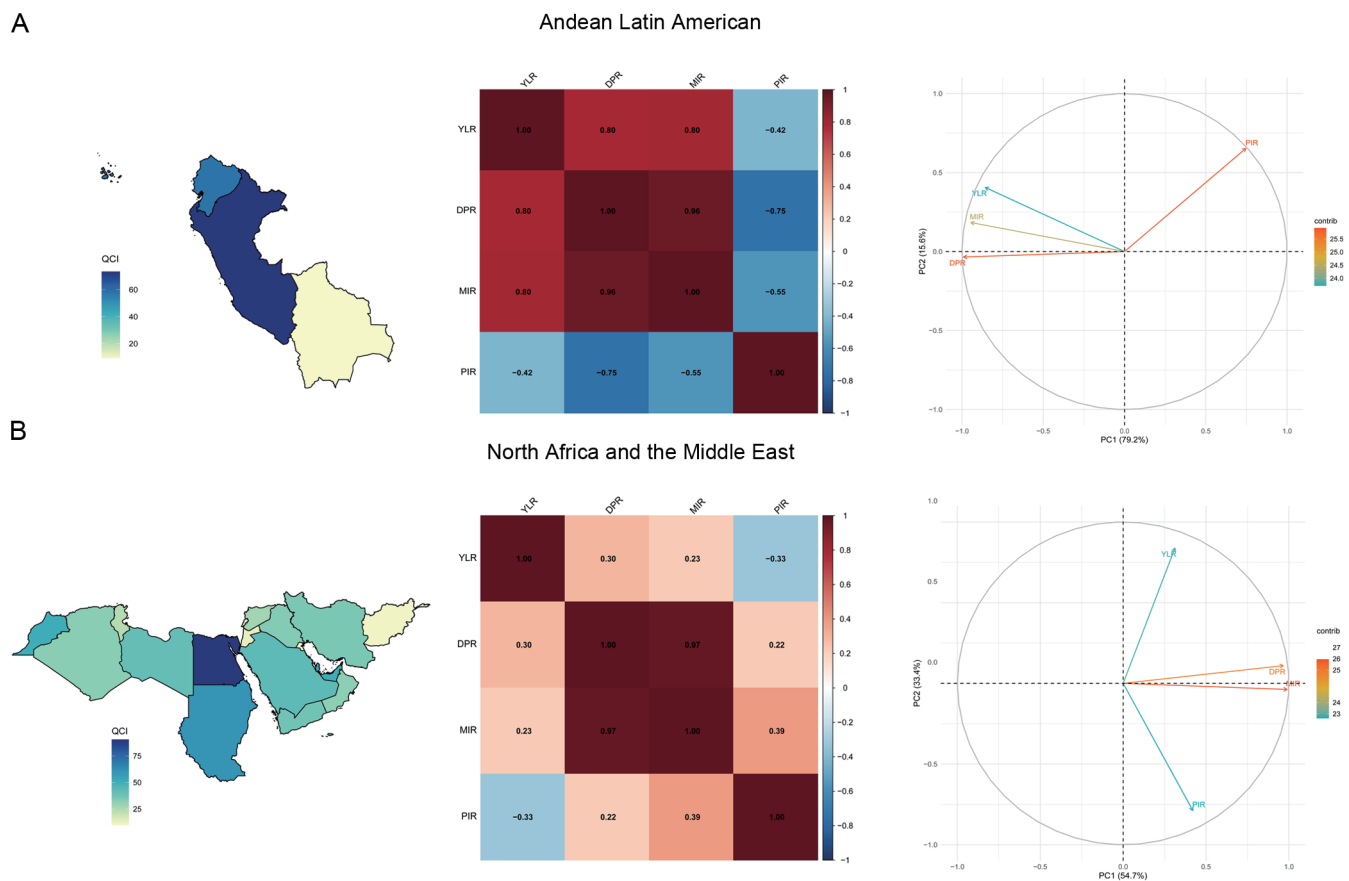


Fig. 4. Quality of Care Index map, correlation matrix, and PCA variable contributions in Andean Latin America (A) and North Africa and the Middle East (B). DALYs, disability-adjusted life years; DPR, DALY-to-prevalence ratio; MIR, mortality-to-incidence ratio; PCA, principal component analysis; PIR, prevalence-to-incidence ratio; QCI, Quality of Care Index; YLR, life lost-to-incidence ratio.

ues became negative after age 80, indicating lower predicted incidence in the oldest groups. Year was the second most influential determinant, with steadily increasing SHAP values from 1990 to 2023 and further increases projected to 2050, reflecting ongoing metabolic transition. Sex made a moderate contribution, with male sex consistently increasing predicted incidence and female sex showing negative SHAP values.

Western Sub-Saharan Africa demonstrated a similar hierarchy of predictors. Age again dominated, with SHAP values peaking near 600 among individuals aged 20–25 years before declining and turning negative after age 75. Sex exerted a stronger effect than year in this region, with males showing marked positive contributions. Temporal trends revealed steady historical increases and sharper rises in forecast years. Population size remained near zero across all observations.

In North Africa and the Middle East, age exerted an even stronger influence, with SHAP values reaching 1,000–1,400 for individuals aged 15–30 years and gradually declining through midlife before becoming negative in the oldest groups. Year again served as a major driver, shifting from negative SHAP values in the early 1990s to consistently positive values after 2020. Sex effects were present but smaller in magnitude, with males showing generally positive contributions. Across all regions, the negligible influence of population size confirms that MASLD incidence is shaped primarily by age structure, sex-specific risk patterns, and temporal progression rather than demographic scale (Supplementary Fig. 5).

Machine-learning predictors of MASLD DALYs: For

MASLD-related DALYs, SHAP analyses also identified age as the predominant determinant in Western Europe, Andean Latin America, and Eastern Europe, followed by year and sex, while population size again showed minimal impact. In Western Europe, older age groups generated strong positive SHAP values and accounted for most DALY burden, while younger and middle-aged adults contributed little. Year showed mild increases historically with attenuation in forecast years. Sex effects were modest, with male sex producing slightly higher predicted DALYs.

In Andean Latin America, age effects were even more pronounced. SHAP values were strongly negative among individuals aged 15–40 years but shifted to positive contributions after age 50, peaking at ages 80–100. This pattern highlights the overwhelming concentration of disability burden in late life. Calendar year showed a gradual rise from 1990 to 2010, a plateau thereafter, and renewed increases in 2020–2050 projections, indicating worsening disability burden. Sex contributed moderate variability, with females showing positive SHAP values and males showing negative contributions.

Eastern Europe demonstrated a similar but more sharply defined nonlinear relationship. SHAP values were strongly negative among young adults, increased rapidly after age 40, and peaked around 55–65 years, remaining positive in older ages. Year was the second strongest contributor, moving from negative SHAP values in the early 1990s to strong positive values in projected years, indicating a growing DALY burden. Male sex consistently increased predicted DALYs, while

female sex reduced them. Population size again showed negligible predictive value (Fig. 5). Together, these findings show that MASLD incidence and DALYs are shaped primarily by age distribution and temporal progression, with sex adding further heterogeneity across regions.

Forecasting ASIR to 2050

Across the six selected countries, BAPC models projected a continued rise in MASLD ASIR through 2050, although the magnitude and trajectory varied across settings. India showed the steepest increase, reaching 649.3 per 100,000 (532.3–766.3) by 2050. China is projected to reach an ASIR of 726.1 (536.8–915.3) by 2050, representing the highest predicted level among all countries analyzed. The Russian Federation is also expected to experience a substantial rise, with ASIR reaching 552.1 (453.8–650.5) by 2050. In Germany, ASIR is projected to reach 437.1 (348.2–526.0) by 2050, whereas the United Kingdom shows a similar pattern, with a predicted ASIR of 497.8 (393.0–602.5). The United States is expected to show a more moderate but steady increase, reaching 426.9 (337.2–516.5) by 2050 (Fig. 6).

Discussion

This study demonstrates large and persistent regional inequalities in MASLD burden and care quality. Incidence, mortality, and disability showed distinct geographic patterns, likely reflecting differences in metabolic exposure, demographic structure, diagnostic capacity, and health system performance. As obesity and diabetes continue to rise, MASLD has become an increasingly important cause of illness, highlighting the need for region-specific prevention, early detection, and care strategies.

In 2023, South Asia and East Asia reported the largest numbers of new cases, while North Africa and the Middle East had the highest ASIR, and Andean Latin America had the highest ASMR and ASDR. These patterns suggest that rapid metabolic transition has outpaced improvements in screening, fibrosis assessment, and integrated liver–metabolic care in many settings. Joinpoint results indicated sustained increases in ASMR and ASDR in Eastern Europe, followed by stabilization at high levels in recent years, possibly reflecting persistent gaps in early diagnosis and integrated care. Countries with high deaths and DALYs but relatively lower incidence may indicate delayed case finding and later-stage detection. Regional variation may also be influenced by differences in diagnostic awareness, access to imaging or laboratory testing, reporting systems, and healthcare infrastructure, rather than true disease burden alone. Although non-invasive fibrosis assessment, including transient elastography and serum biomarkers, can improve early detection and risk stratification, access remains uneven across regions, potentially contributing to poorer outcomes in low-QCI settings.^{16–18} Persistent increases in obesity and diabetes further underscore the need for stronger metabolic prevention and earlier detection. Although incidence growth has slowed in Western Europe, mortality and disability remain prominent in Eastern Europe and Andean Latin America. Latin American settings deserve particular attention because Andean Latin America had the highest regional ASMR and ASDR, and Mexico had the highest ASDR in 2023. These patterns may reflect cumulative metabolic risk, delayed fibrosis detection, limited access to non-invasive liver assessment, and insufficient integration of liver care with diabetes and cardiometabolic services.

Differences in care quality also shape regional variation. QCI analysis showed clear inequalities across regions. Low

QCI scores in South Asia, Western Sub-Saharan Africa, and Eastern Europe were associated with patterns suggestive of limited screening capacity, delayed diagnosis, and weaker chronic care systems. However, these associations should not be interpreted as direct evidence of causality. The geographic pattern, with Bhutan and Egypt achieving high QCI while many larger countries in South Asia and Western Sub-Saharan Africa remain well below average, suggests that differences in diagnostic capacity and referral pathways may contribute to meaningful variation in QCI performance. PCA results provided additional insight into the structure of the QCI indicators. PC1, which was used to construct the QCI, was influenced mainly by MIR and DPR and reflected the dominant mortality–disability axis. PC2 represented the second-largest and independent axis of variation and was mainly influenced by PIR, suggesting an additional chronicity–survival dimension within the PCA structure. These patterns align with current guidelines, which highlight early case finding and risk stratification as essential components of MASLD care.

Risk factor attribution analysis reinforced the importance of metabolic exposure at the population level. Between 1990 and 2023, ASMR and ASDR attributable to metabolic risks increased substantially in most regions, with high BMI and high FPG as the leading contributors. However, the GBD comparative risk assessment framework estimates population-level attributable burden rather than individual-level causality. Attributable burdens for different metabolic risks should not be interpreted as mutually exclusive or directly additive because these exposures may be correlated, share causal pathways, or have bidirectional relationships with MASLD progression. Metabolic dysfunction may promote MASLD progression, while established liver disease may alter metabolic status, increase healthcare contact, and affect the likelihood of diagnosis and risk-factor recognition. Differences in income level, diagnostic capacity, and access to liver assessment may further shape these regional patterns. Genetic susceptibility may also contribute to individual and regional differences in MASLD risk and progression. Recent evidence suggests that genetic variation can influence metabolic syndrome, which is closely linked to MASLD susceptibility. These findings support more refined risk stratification frameworks that integrate metabolic, demographic, clinical, and, where available, genetic information.^{19,20}

Machine learning analysis provided complementary evidence on patterning rather than causation. Age was the strongest predictor of incidence and DALYs in all regions, and calendar year also showed substantial contributions. SHAP values describe the relative contribution of predictors within the fitted model and should therefore be interpreted as measures of model-based importance rather than causal effects. SHAP profiles showed that young and middle-aged adults had the highest incremental risk for incidence. DALYs were concentrated in older adults, especially in Western Europe, Eastern Europe, and Andean Latin America, reflecting long-term injury and progression to advanced fibrosis. Rising SHAP values for calendar year suggest that long-term metabolic deterioration has a greater influence on MASLD burden than short-term demographic change. Sex differences varied across regions. Male sex increased incidence in most settings, while DALY contributions differed by sex, likely reflecting variation in obesity, diabetes, care access, and metabolic clustering. Population size contributed little in all models, showing that age structure, temporal trends, and sex-specific risk patterns are more influential than demographic scale.

Future projections indicate continued growth in ASIR through 2050, especially in high-burden countries. India and

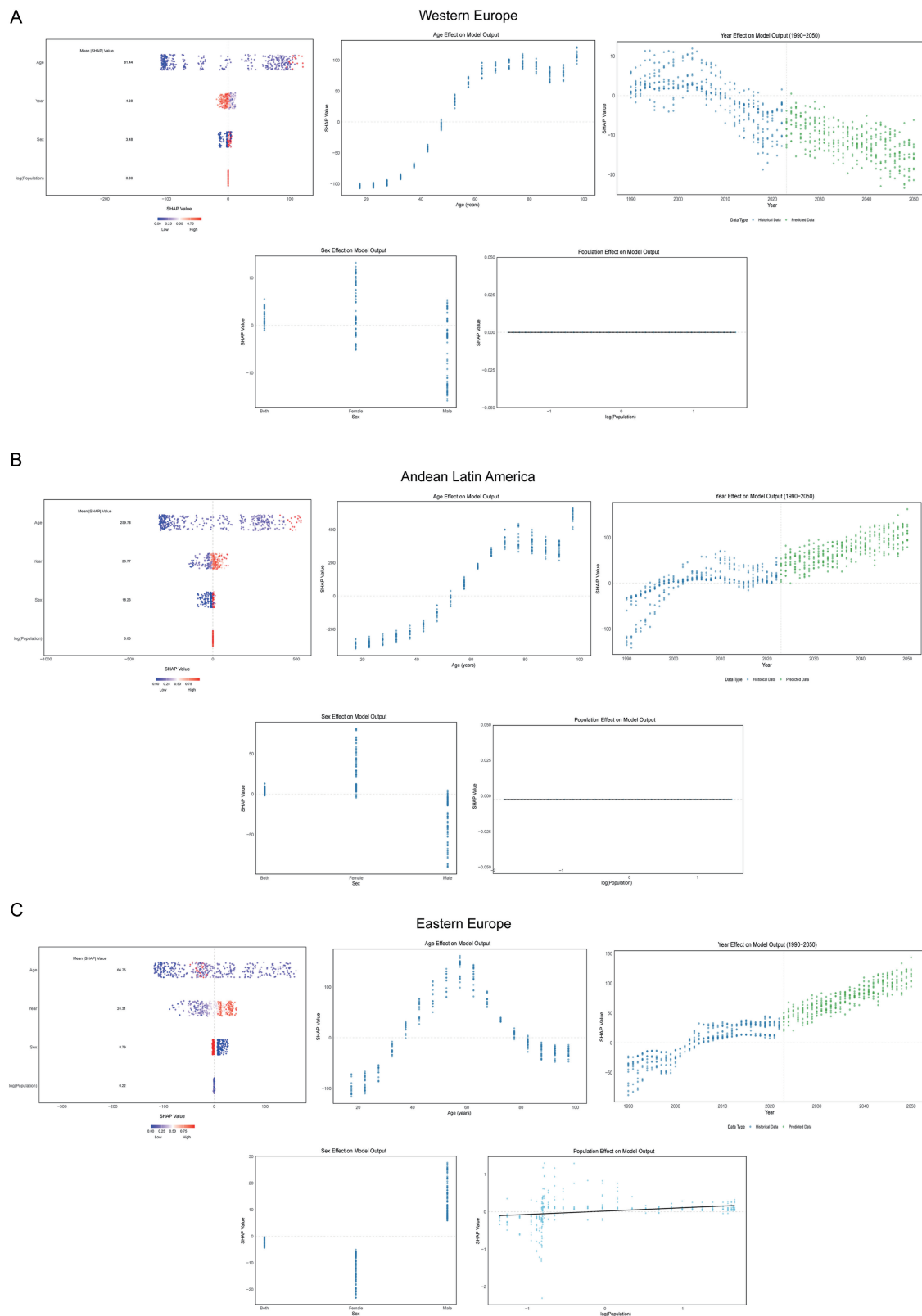


Fig. 5. SHAP-based machine learning interpretation of MASLD DALYs rates across three high-burden regions. (A) Western Europe: SHAP summary plot and the contributions of age, year, sex, and population size. (B) Andean Latin America. (C) Eastern Europe. SHAP, Shapley Additive exPlanations; MASLD, metabolic dysfunction-associated steatotic liver disease; DALYs, disability-adjusted life years.

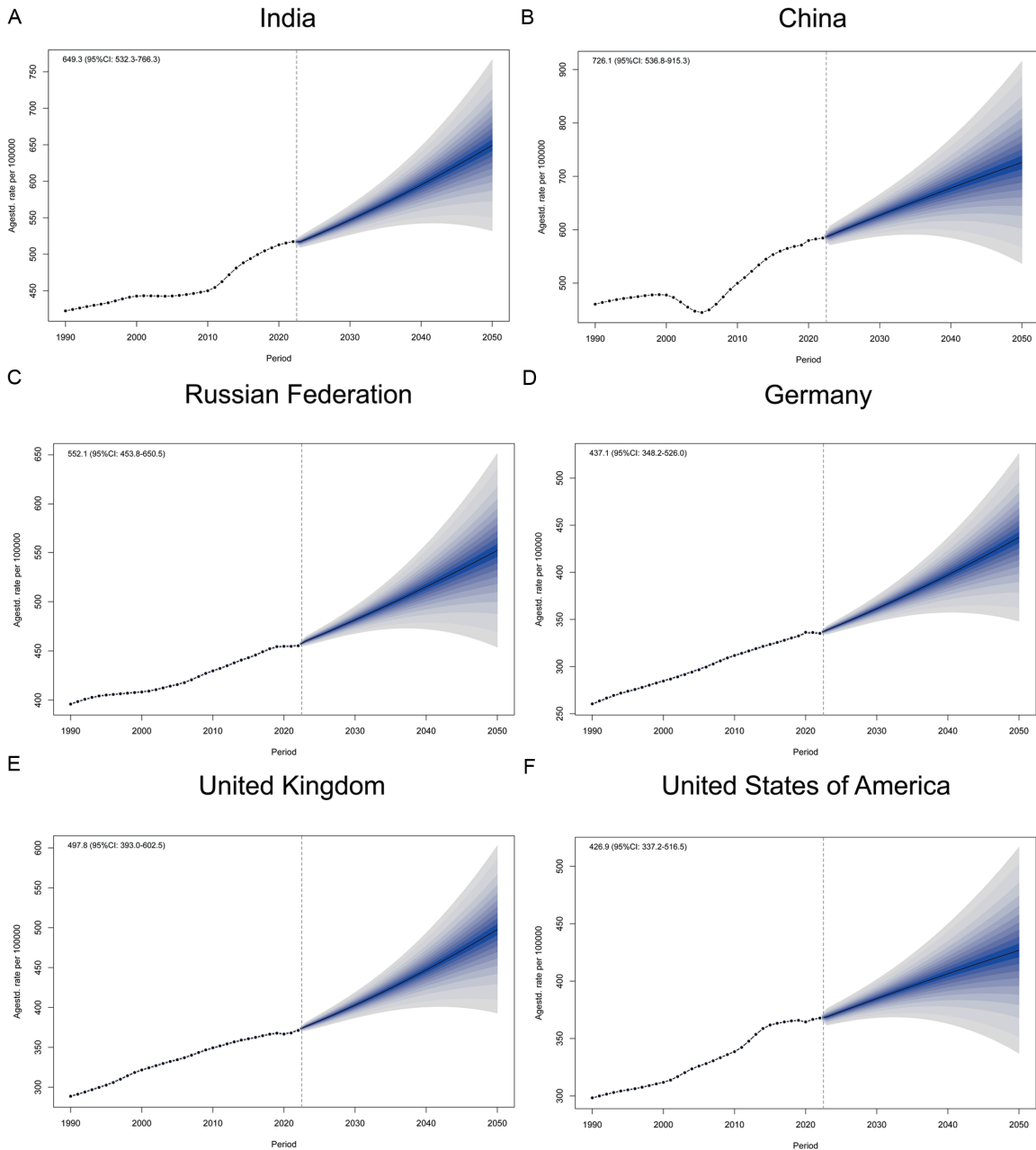


Fig. 6. BAPC projections of MASLD ASIR through 2050. Panels A to F show observed and projected ASIR for six high-burden countries. Black dots represent observed estimates from 1990 to 2023. Blue curves represent BAPC projections from 2024 to 2050, with uncertainty intervals shown as shaded areas. (A) India; (B) China; (C) Russian Federation; (D) Germany; (E) United Kingdom; (F) United States of America. BAPC, Bayesian age–period–cohort; MASLD, metabolic dysfunction-associated steatotic liver disease; ASIR, age-standardized incidence rate.

China are expected to experience the largest increases, reflecting rapid urbanization, rising obesity, and limited screening coverage.^{21–24} High-income countries are also projected to show rising incidence despite more advanced health systems, suggesting that current strategies for metabolic risk control are not sufficient to reverse long-term trends. These projections highlight the long-term consequences of current metabolic patterns and the need for sustained intervention.

These findings support region-specific strategies according to burden profile and QCI performance. In low-QCI regions, including South Asia, Western Sub-Saharan Africa,

and Eastern Europe, priorities should include strengthening basic diagnostic infrastructure, expanding early case finding, improving access to serum-based fibrosis scores and elastography where feasible, and integrating MASLD screening into diabetes and metabolic disease clinics. In regions with large incident case numbers, particularly South Asia and East Asia, prevention should focus on population-level metabolic risk control, including weight management, diabetes prevention, dietary improvement, and earlier detection in young and middle-aged adults. In Latin American settings with high ASDR, including Andean Latin America and Mexico,

health systems should prioritize fibrosis risk stratification, timely referral pathways for advanced liver disease, and cardiometabolic–liver care integration. In higher-QCI or high-income settings, priorities should include reducing residual gaps in fibrosis assessment, improving equitable access to emerging therapies such as resmetirom and GLP-1 receptor agonists, and ensuring long-term monitoring of patients at high risk of progression. Overall, MASLD care should be adapted to local burden profiles, QCI performance, and health system capacity.^{25–32}

This study has several limitations. First, although MASLD was used to reflect current clinical nomenclature, GBD 2023 fatty liver disease estimates remain based on NAFLD mappings and do not fully align with MASLD criteria, particularly regarding alcohol thresholds and metabolic definitions. Therefore, our findings should be interpreted as GBD-based NAFLD estimates discussed within an updated MASLD framework. Second, GBD risk attribution estimates population-level attributable burden rather than individual-level causality. Correlated metabolic risks, including high BMI and high FPG, may overlap or share pathways, so their attributable fractions should not be interpreted as directly additive or mutually exclusive. Third, the machine-learning analyses were exploratory, and SHAP results indicate model-based variable importance rather than causality. Fourth, temporal and regional patterns may partly reflect differences in diagnostic criteria, clinical awareness, access to imaging or laboratory testing, reporting systems, and case ascertainment. Because MASLD is often underdiagnosed, some geographic heterogeneity may reflect differences in detection and healthcare capacity rather than true disease burden alone. Finally, BAPC projections were performed for selected countries and should be viewed as representative examples rather than a complete assessment of all high-burden countries. These projections are based on historical age, period, and cohort patterns and cannot fully account for future changes in obesity, diabetes, diet, policy interventions, diagnostic expansion, or emerging therapies such as GLP-1 receptor agonists.

Conclusions

MASLD is a growing health challenge marked by wide regional inequalities in burden and care quality. South Asia and East Asia carry the largest numbers of new cases, whereas North Africa and the Middle East and Andean Latin America show disproportionately high age-standardized rates. Eastern Europe and Andean Latin America face high mortality and disability burdens, and Mexico shows particularly high ASDR within the broader Latin American context. Low-QCI regions, including South Asia, Western Sub-Saharan Africa, and Eastern Europe, require stronger diagnostic infrastructure, early case finding, and accessible fibrosis assessment. Regions with large incident case numbers need stronger metabolic prevention and better integration of MASLD screening into diabetes and metabolic disease care. Latin American settings with high disability burden require improved fibrosis risk stratification and referral pathways for advanced liver disease. Higher-QCI and high-income settings should focus on equitable access to fibrosis assessment, long-term monitoring, and emerging therapies. Tailoring these strategies to regional burden profiles, QCI performance, and health system capacity may help reduce severe MASLD outcomes and slow the rising burden through 2050.

Supporting information

Supplementary material for this article is available at <https://doi.org/10.14218/JCTH.2026.00127>.

doi.org/10.14218/JCTH.2026.00127.

Funding

This study was supported by grants from the National Natural Science Foundation of China (81974105 and 82370867), the Special Funds for the Taishan Scholars Project of Shandong Province (tsqn202211365), and the Clinical Research Project of Tongji Hospital, Tongji University (ITJ(QN)2301). The GBD Study was supported by the Bill & Melinda Gates Foundation.

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Conceived and designed the study (KZ, CK, SS, WX, FH, JC, XL, NH, YX, XS), collected, analyzed, and interpreted the data (KZ, WX, CK, FH, JC, SS), prepared the figures and tables (KZ, CK, WX, XL, FH), drafted the manuscript (KZ, CK), contributed to data interpretation and manuscript revision (NH), supervised the study, provided critical revisions, and approved the final version (YX, XS). All authors read and approved the final manuscript.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2024). Because this study used publicly available, aggregated GBD 2023 data without individual-level identifiers, ethics approval and informed consent were not required.

Data sharing statement

The data that support the findings of this study are available from GBD 2023 at <http://ghdx.healthdata.org/gbd-2023>.

References

- [1] Targher G, Byrne CD, Tilg H. MASLD: a systemic metabolic disorder with cardiovascular and malignant complications. *Gut* 2024;73(4):691–702. doi:10.1136/gutjnl-2023-330595, PMID:38228377.
- [2] Kalligeros M, Vassilopoulos A, Vassilopoulos S, Victor DW, Mylonakis E, Noureddin M. Prevalence of Steatotic Liver Disease (MASLD, MetALD, and ALD) in the United States: NHANES 2017–2020. *Clin Gastroenterol Hepatol* 2024;22(6):1330–1332.e4. doi:10.1016/j.cgh.2023.11.003, PMID:37949334.
- [3] Younossi ZM, Golabi P, Price JK, Owringi S, Gundu-Rao N, Satchi R, *et al*. The Global Epidemiology of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis Among Patients With Type 2 Diabetes. *Clin Gastroenterol Hepatol* 2024;22(10):1999–2010.e8. doi:10.1016/j.cgh.2024.03.006, PMID:38521116.
- [4] Driessen S, Francque SM, Anker SD, Castro Cabezas M, Grobbee DE, Tushuizen ME, *et al*. Metabolic dysfunction-associated steatotic liver disease and the heart. *Hepatology* 2025;82(2):487–503. doi:10.1097/HEP.0000000000000735, PMID:38147315.
- [5] Younossi ZM, Kalligeros M, Henry L. Epidemiology of metabolic dysfunction-associated steatotic liver disease. *Clin Mol Hepatol* 2025;31(Suppl):S32–S50. doi:10.3350/cmh.2024.0431, PMID:39159948.
- [6] Guo T, Zheng S, Chen T, Chu C, Ren J, Sun Y, *et al*. The association of long-term trajectories of BMI, its variability, and metabolic syndrome: a 30-year prospective cohort study. *EClinicalMedicine* 2024;69:102486. doi:10.1016/j.eclinm.2024.102486, PMID:38370536.
- [7] Cusi K, Abdelmalek MF, Apovian CM, Balapattabi K, Bannuru RR, Barb D, *et al*. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association. *Diabetes Care* 2025;48(7):1057–1082. doi:10.2337/dci24-0094, PMID:40434108.
- [8] Kozlitina J, Sookoian S. Global Epidemiological Impact of PNPLA3 I148M on Liver Disease. *Liver Int* 2025;45(3):e16123. doi:10.1111/liv.16123, PMID:39373119.
- [9] Zhang H, Zhou XD, Shapiro MD, Lip GYH, Tilg H, Valenti L, *et al*. Global burden of metabolic diseases, 1990–2021. *Metabolism* 2024;160:155999.

- doi:10.1016/j.metabol.2024.155999, PMID:39151887.
- [10] GBD 2015 Healthcare Access and Quality Collaborators. GBD 2015 Healthcare Access and Quality Collaborators. Healthcare Access and Quality Index based on mortality from causes amenable to personal health care in 195 countries and territories, 1990-2015: a novel analysis from the Global Burden of Disease Study 2015. *Lancet* 2017;390(10091):231-266. doi:10.1016/S0140-6736(17)30818-8, PMID:28528753.
- [11] Ordunez P, Martinez R, Soliz P, Giraldo G, Mujica OJ, Nordet P. Rheumatic heart disease burden, trends, and inequalities in the Americas, 1990-2017: a population-based study. *Lancet Glob Health* 2019;7(10):e1388-e1397. doi:10.1016/S2214-109X(19)30360-2, PMID:31537369.
- [12] Pan Y, Liu Q, Zhang N, Peng S, Li X, Zhou F. Global assessment of leukemia care quality: insights from the quality of care index (QCI) from 1990 to 2021. *EClinicalMedicine* 2025;79:102996. doi:10.1016/j.eclinm.2024.102996, PMID:39802300.
- [13] Liang D, Wang L, Zhong P, Lin J, Chen L, Chen Q, *et al*. Perspective: Global Burden of Iodine Deficiency: Insights and Projections to 2050 Using XGBoost and SHAP: A Systematic Analysis. *Nutrients* 2025;16(3):100384. doi:10.1016/j.advnut.2025.100384, PMID:39914495.
- [14] Liang D, Wang L, Liu S, Li S, Zhou X, Xiao Y, *et al*. Global Incidence of Diarrheal Diseases-An Update Using an Interpretable Predictive Model Based on XGBoost and SHAP: A Systematic Analysis. *Nutrients* 2024;16(18):3217. doi:10.3390/nu16183217, PMID:39339819.
- [15] Liu Z, Xu K, Jiang Y, Cai N, Fan J, Mao X, *et al*. Global trend of aetiology-based primary liver cancer incidence from 1990 to 2030: a modelling study. *Int J Epidemiol* 2021;50(1):128-142. doi:10.1093/ije/dyaa196, PMID:33349860.
- [16] European Association for the Study of the Liver (EASL). European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO), European Association for the Study of the Liver (EASL). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). *J Hepatol* 2024;81(3):492-542. doi:10.1016/j.jhep.2024.04.031, PMID:38851997.
- [17] European Association for the Study of the Liver, European Association for the Study of Diabetes, European Association for the Study of Obesity. EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD): Executive Summary. *Diabetologia* 2024;67(11):2375-2392. doi:10.1007/s00125-024-06196-3, PMID:38869512.
- [18] Sah AK, Afzal M, Elshaikh RH, Abbas AM, Shalabi MG, Prabhakar PK, *et al*. Innovative Strategies in the Diagnosis and Treatment of Liver Cirrhosis and Associated Syndromes. *Life (Basel)* 2025;15(5):779. doi:10.3390/15050779, PMID:40430206.
- [19] Deprince A, Haas JT, Staels B. Dysregulated lipid metabolism links NAFLD to cardiovascular disease. *Mol Metab* 2020;42:101092. doi:10.1016/j.molmet.2020.101092, PMID:33010471.
- [20] Rao DS, Kumar A, Agarwal S, Elshaikh RH, Choudhary A, Choudhary RK, *et al*. The role of genetic variations in metabolic syndrome: insights into etiology, diagnosis, and management. *Ital J Med* 2025;19(1):1908. doi:10.4081/itjm.2025.1908.
- [21] Estes C, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, *et al*. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. *J Hepatol* 2018;69(4):896-904. doi:10.1016/j.jhep.2018.05.036, PMID:29886156.
- [22] Zhou J, Zhou F, Wang W, Zhang XJ, Ji YX, Zhang P, *et al*. Epidemiological Features of NAFLD From 1999 to 2018 in China. *Hepatology* 2020;71(5):1851-1864. doi:10.1002/hep.31150, PMID:32012320.
- [23] Fan JG, Kim SU, Wong VW. New trends on obesity and NAFLD in Asia. *J Hepatol* 2017;67(4):862-873. doi:10.1016/j.jhep.2017.06.003, PMID:28642059.
- [24] Le MH, Le DM, Baez TC, Wu Y, Ito T, Lee EY, *et al*. Global incidence of non-alcoholic fatty liver disease: A systematic review and meta-analysis of 63 studies and 1,201,807 persons. *J Hepatol* 2023;79(2):287-295. doi:10.1016/j.jhep.2023.03.040, PMID:37040843.
- [25] Noureddin M, Charlton MR, Harrison SA, Bansal MB, Alkhoury N, Loomba R, *et al*. Expert Panel Recommendations: Practical Clinical Applications for Initiating and Monitoring Resmetivir in Patients With MASH/NASH and Moderate to Noncirrhotic Advanced Fibrosis. *Clin Gastroenterol Hepatol* 2024;22(12):2367-2377. doi:10.1016/j.cgh.2024.07.003, PMID:39038768.
- [26] Do A, Zahrawi F, Mehal WZ. Therapeutic landscape of metabolic dysfunction-associated steatohepatitis (MASH). *Nat Rev Drug Discov* 2025;24(3):171-189. doi:10.1038/s41573-024-01084-2, PMID:39609545.
- [27] Huang DQ, Wong VW, Rinella ME, Boursier J, Lazarus JV, Yki-Järvinen H, *et al*. Metabolic dysfunction-associated steatotic liver disease in adults. *Nat Rev Dis Primers* 2025;11(1):14. doi:10.1038/s41572-025-00599-1, PMID:40050362.
- [28] Newsome PN, Ambery P. Incretins (GLP-1 receptor agonists and dual/triple agonists) and the liver. *J Hepatol* 2023;79(6):1557-1565. doi:10.1016/j.jhep.2023.07.033, PMID:37562748.
- [29] Kanwal F, Kramer JR, Li L, Yang YX, Cao Y, Yu X, *et al*. GLP-1 Receptor Agonists and Risk for Cirrhosis and Related Complications in Patients With Metabolic Dysfunction-Associated Steatotic Liver Disease. *JAMA Intern Med* 2024;184(11):1314-1323. doi:10.1001/jamainternmed.2024.4661, PMID:39283612.
- [30] Harrison SA, Browne SK, Suschak JJ, Tomah S, Gutierrez JA, Yang J, *et al*. Effect of pemvidutide, a GLP-1/glucagon dual receptor agonist, on MASLD: A randomized, double-blind, placebo-controlled study. *J Hepatol* 2025;82(1):7-17. doi:10.1016/j.jhep.2024.07.006, PMID:39002641.
- [31] Lin RT, Sun QM, Xin X, Ng CH, Valenti L, Hu YY, *et al*. Comparative efficacy of THR- β agonists, FGF-21 analogues, GLP-1R agonists, GLP-1-based polyagonists, and Pan-PPAR agonists for MASLD: A systematic review and network meta-analysis. *Metabolism* 2024;161:156043. doi:10.1016/j.metabol.2024.156043, PMID:39357599.
- [32] Xiang L, Wang G, Zhuang Y, Luo L, Yan J, Zhang H, *et al*. Safety and efficacy of GLP-1/FGF21 dual agonist HEC88473 in MASLD and T2DM: A randomized, double-blind, placebo-controlled study. *J Hepatol* 2025;82(6):967-978. doi:10.1016/j.jhep.2024.12.006, PMID:39709140.