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Global burden of metabolic dysfunction-associated steatotic liver disease from 1990 to 2021 and the prediction for the next 10 years

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ABSTRACT

Objective: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a leading cause of chronic liver disease worldwide. Although the update of the MASLD practice guidelines and the approval of Resmetirom have brought new progress in the prevention and treatment of MASLD, this disease still has not received sufficient attention and remains a major public health issue.
Methods: Age-standardized incidence (ASIR), prevalence (ASPR), mortality (ASMR), and disability-adjusted life years (ASDR) rates of MASLD from 1990 to 2021 were extracted from the Global Burden of Disease 2021. The estimated annual percentage change was calculated using linear regression. Six time-series models were used for training and comparison, and the optimal model was selected to predict the disease burden from 2022 to 2031.
Results: Globally, the ASIR, ASPR, ASMR, and ASDR all exhibited upward trends. Regionally, Western Europe showed the fastest growth in ASIR and ASPR. Eastern Europe showed the fastest growth in ASMR and ASDR, whereas the high-income Asia Pacific demonstrated the most pronounced decline. The hybrid model best predicted ASIR (615.70/100,000) and ASPR (15,275.60/100,000) for 2031, the Neural Network Autoregressive model optimized ASMR (1.64/100,000), and Prophet projected ASDR to decline to 42.08/100,000.
Conclusions: The MASLD burden has increased globally and is projected to continue escalating. It is suggested that the MASLD screening be integrated into the non-communicable diseases program and be prioritized for monitoring in high-burden areas.

1. Introduction

With recent changes in lifestyle, the number of obese individuals and diabetic patients has continued to rise, and metabolic dysfunction-associated steatotic liver disease (MASLD) has emerged as one of the major chronic liver diseases, affecting approximately 30 % of the global population (Riazi et al., 2022). Notably, the incidence and prevalence of MASLD vary significantly across countries and even within different

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; GBD, Global Burden of Disease; DALYs, disability-adjusted life years; ICD, International Statistical Classification of Diseases and Related Health Problems; CI, confidence interval;; NNAR, Neural Network Autoregressive; BSTS, Bayesian Structural Time Series; ETS, Exponential Smoothing; SARIMA, Seasonal Autoregressive Integrated Moving Average; ASIR, age-standardized incidence rate; ASPR, age-standardized prevalence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; EAPC, estimated annual percentage change.

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regions of the same country, with Latin America, the Middle East, and North Africa showing markedly higher rates compared to other areas (Younossi et al., 2023). In 2023, to address the limitations and stigmatization associated with the previous terminology, multiple international liver research associations decided to introduce the term “metabolic dysfunction-associated steatotic liver disease” to replace the former designation of “non-alcoholic fatty liver disease” (NAFLD) (Kanwal et al., 2024). MASLD is defined as the coexistence of hepatic steatosis with at least one cardiometabolic risk factor in the absence of other identifiable causes (Kanwal et al., 2024). Although there are differences in the definitions between the two terms, multiple studies (Hagström et al., 2024a; Ratziu and Boursier, 2024; Song et al., 2024) have demonstrated that the populations identified using the MASLD criteria largely overlap with those previously classified as NAFLD. Therefore, this study will uniformly adopt the term MASLD.

Although hepatic steatosis itself shows limited correlation with liver pathology (Zeigerer, 2021), the pathological progression of MASLD is complex, with 20 %–30 % of cases potentially advancing to metabolic dysfunction-associated steatohepatitis, a severe manifestation of MASLD characterized by hepatocyte injury, inflammation, and progression to fibrosis, cirrhosis, and ultimately hepatocellular carcinoma (Kanwal et al., 2021; Llovet et al., 2023). MASLD has become the fastest-growing cause of liver-related mortality and a major contributor to end-stage liver disease, primary liver cancer, and the increasing demand for liver transplantation (Younossi et al., 2019). Recent updates to the European Association for the Study of the Liver, European Association for the Study of Diabetes, and European Association for the Study of Obesity joint guidelines and the American Association for the Study of Liver Diseases practice guidelines have provided clearer and more standardized recommendations for the prevention, screening, diagnosis, and management of MASLD (*Diabetologia.*, 2024). Additionally, the approval of resmetirom, the first pharmacologic agent for treating MASH, represents a significant advancement in clinical care (Chen et al., 2025). However, MASLD remains underrecognized as a major non-communicable disease, and targeted national strategies and policy-level responses are still lacking.

Assessing the disease burden of MASLD can be approached through multiple methodologies. In traditional research paradigms, scholars predominantly rely on meta-analyses to estimate the disease’s prevalence and mortality rates (Ye et al., 2020; Li et al., 2022; Quek et al., 2023). However, while this analytical approach demonstrates robust data-processing capabilities, it suffers from obvious limitations: on one hand, study data often exhibit significant heterogeneity; on the other hand, factors such as positive-result bias, language bias, and omission of grey literature may introduce publication bias into the findings. In contrast, the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) — led by the Institute for Health Metrics and Evaluation — provides a more systematic evaluation framework. It utilizes advanced statistical models to adjust for data uncertainty and statistical noise, ultimately delivering optimized estimates rather than raw data outputs (Quek et al., 2023). Importantly, the Institute for Health Metrics and Evaluation annually updates each GBD dataset, enabling continuous refinement of analytical results and progressive improvements in accuracy and comprehensiveness (GBD, 2018). The latest iteration, GBD 2021, optimizes data sources and quality by incorporating new datasets and more granular demographic information, superseding all prior versions (*Lancet*, 2024). At present, there are limited studies using time-series models to predict the disease burden of MASLD, and most of them adopt a single model. Considering the complexity of global data, using more types of time series models can better capture the data characteristics and achieve more accurate predictions.

This study analyzed the global burden of MASLD from 1990 to 2021 using data obtained from GBD 2021, advancing our understanding of the evolving complex disease patterns across regions over time. Additionally, in order to achieve better predictions, six time-series models were trained and compared. The optimal models were selected to predict the burden of MASLD in the next decade. This provided evidence-based references for policymakers and public health researchers, guiding the formulation of prevention, control and disease management strategies for MASLD.

2. Materials and methods

2.1. Data sources

This study extracted comprehensive data on the incidence, prevalence, mortality, and disability-adjusted life years (DALYs) of MASLD in 204 countries and regions from the Global Health Data Exchange platform (https://vizhub.healthdata.org/gbd-results/) from 1990 to 2021, including absolute case numbers, age-standardized rates, and their corresponding 95 % uncertainty intervals. As MASLD is a relatively new clinical concept, it has not yet been formally integrated into the International Statistical Classification of Diseases and Related Health Problems (ICD) system. Relevant studies recommend updating ICD terminology by retaining the coding previously used for NAFLD; thus, this study employs the code K76.0 to represent MASLD (Hagström et al., 2024b). Ethical approval was not required as this study used publicly available data.

2.2. Statistical analysis

2.2.1. Age-standardized rates

In this study, the age-standardized incidence rate (ASIR), age-standardized prevalence rate (ASPR), age-standardized mortality rate (ASMR), and age-standardized disability-adjusted life years rate (ASDR) were calculated using the direct method, with reference to the GBD world standard population structure for standardization (Collaborators GDaI., 2024).

2.2.2. Temporal trends

To evaluate long-term trends, linear regression analysis was applied to estimate the annual percentage change (EAPC) in ASRs. This formula is expressed as follows:

$$\ln(\text{ASR}) = \alpha + \beta x + \varepsilon$$

where x represents the calendar year, α denotes the intercept, β indicates the slope, and ε is the error term. The EAPC and its 95 % confidence interval (CI) were derived from this model.

$$\text{EAPC} = 100 \times \left(e^{\beta} - 1\right)$$

If the EAPC and its 95 % CI were both above 0, the ASR was considered to exhibit a significant upward trend over time. If the EAPC and its 95 % CI were both below 0, the ASR was classified as having a significant downward trend. If the 95 % CI included 0, the temporal change in the ASR was deemed statistically non-significant (Sun et al., 2024).

2.2.3. Predictive models

This study compared six commonly used time series models for disease burden assessment: Neural Network Autoregressive (NNAR), Bayesian Structural Time Series (BSTS), Prophet, Exponential Smoothing (ETS), Seasonal Autoregressive Integrated Moving Average (SARIMA), and a hybrid model. (Table S1) The NNAR model is a time series forecasting model based on neural networks, capable of capturing nonlinear relationships in time series data and suitable for non-stationary series (Luo et al., 2022). The BSTS model, a stochastic state-space model, combines structural time-series models with Bayesian inference, making it ideal for complex time-series data with multiple components (Feroze, 2020). At its core, Prophet uses an additive regression model that decomposes time-series data into trend, seasonality, and holiday effects, facilitating an understanding of each component's contribution to predictions (Zhang et al., 2024a). The ETS model generates forecasts by assigning exponentially decreasing weights to past data, allowing it to adapt flexibly to data trends (Yang et al., 2023). The SARIMA model can capture both long-term trends and short-term fluctuations in time-series data, as well as handle seasonality, making it perfect for analyzing periodic data (Yang et al., 2023). Given that single models often struggle to simultaneously capture trends, seasonality, and nonlinear features, a hybrid model was developed. This hybrid model combines SARIMA, ETS, Seasonal-Trend Decomposition Procedure Based on Loess decomposition, and NNAR models, using an averaging method to achieve greater robustness and computational efficiency (Zhang et al., 2024a).

According to the consensus, the data was divided into a training set and a test set in a ratio of 8:2 (Zhang et al., 2024b). Data on ASIR, ASPR, ASMR, and ASDR for MASLD from 1990 to 2015 were used as the training set to train six time-series models. The data from 2016 to 2021 were used as the test set to calculate the models' root mean square error, R-squared, and mean absolute error to evaluate their performance. The root mean square error measures the average magnitude of the error, the mean absolute error represents the average of absolute errors, and the R-squared indicates the proportion of variance in the dependent variable that is predictable from the independent variables (Zhang et al., 2024a). Given that the scales and ranges of these indicators are different, the *Z*-normalized composite index was calculated to achieve comparability and fairness. Finally, the model with the highest Z value was selected as the optimal model for predicting the disease burden of MASLD from 2022 to 2031.

All statistical analyses and visualizations were implemented using R software (version 4.3.0).

3. Results

3.1. Global and regional age-standardized rates for metabolic dysfunction-associated steatotic liver disease

3.1.1. Incidence

Globally, the ASIR rose from 475.54 per 100,000 in 1990 to 593.28 per 100,000 in 2021. The EAPC of ASIR from 1990 to 2021 was 0.73, indicating an upward trend. Among the 21 GBD regions, North Africa and the Middle East had the highest ASIR of 1037.64 per 100,000 in 2021. ASIR showed growth across all regions, with significant increases in East Asia and Western Europe, while growth was slower in Central Sub-Saharan Africa. (Fig. 1, Fig. 2, and Table S1).

3.1.2. Prevalence

Globally, the ASPR rose from 12,085.09 per 100,000 in 1990 to 15,018.07 per 100,000 in 2021. From 1990 to 2021, the global ASPR exhibited a significant upward trend, with an EAPC of 0.73. Regionally, in 2021, North Africa and the Middle East had the highest ASPR at 27,686.69, approximately three times higher than the lowest ASPR in high-income Asia-Pacific. While all regions showed rising ASPR trends, the most pronounced increases occurred in Western Europe, with the

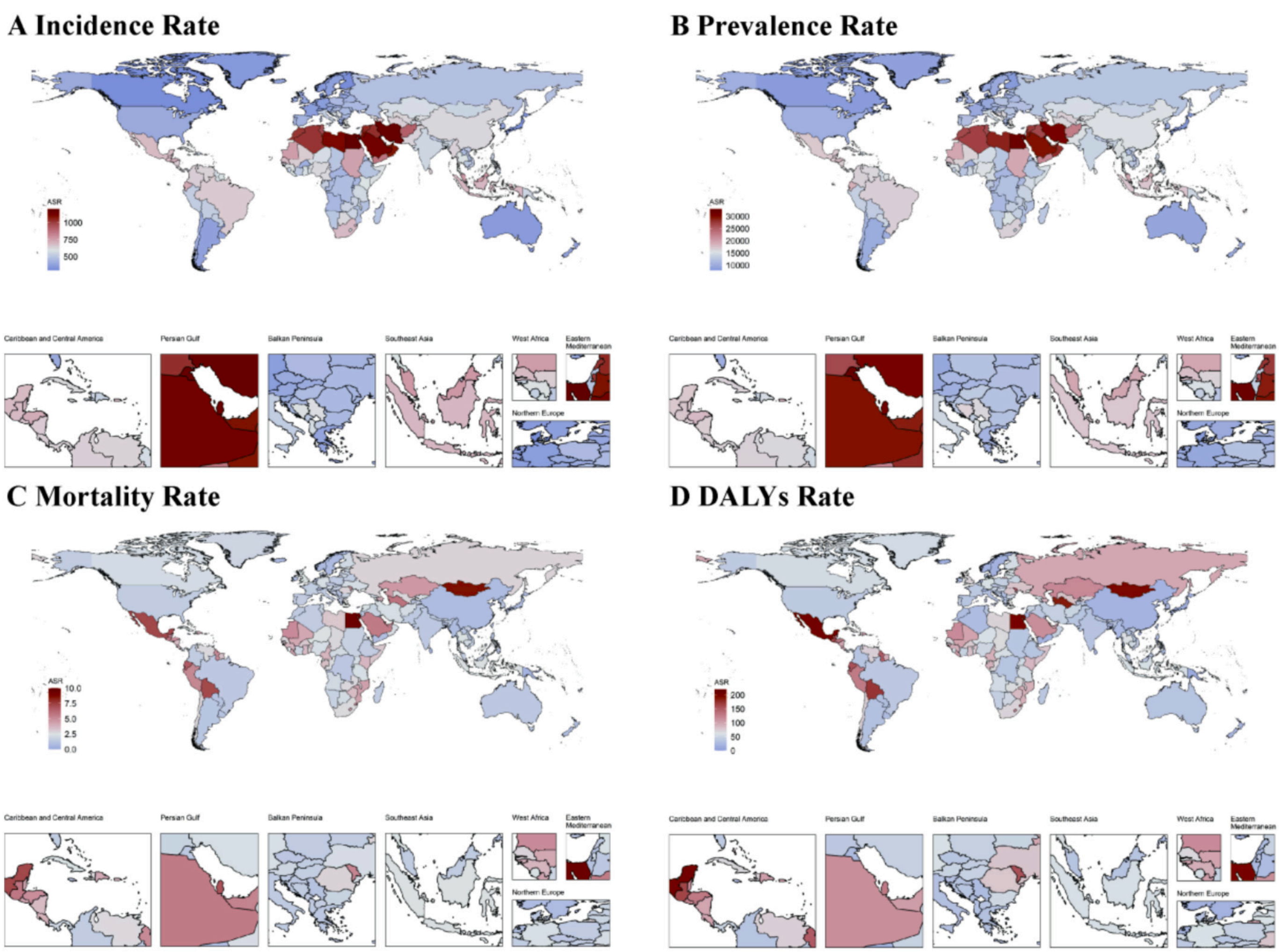

Fig. 1. Global age-standardized incidence, prevalence, mortality and disability-adjusted life years rates of metabolic dysfunction-associated steatotic liver disease in 2021. Abbreviations: DALYs, disability-adjusted life years

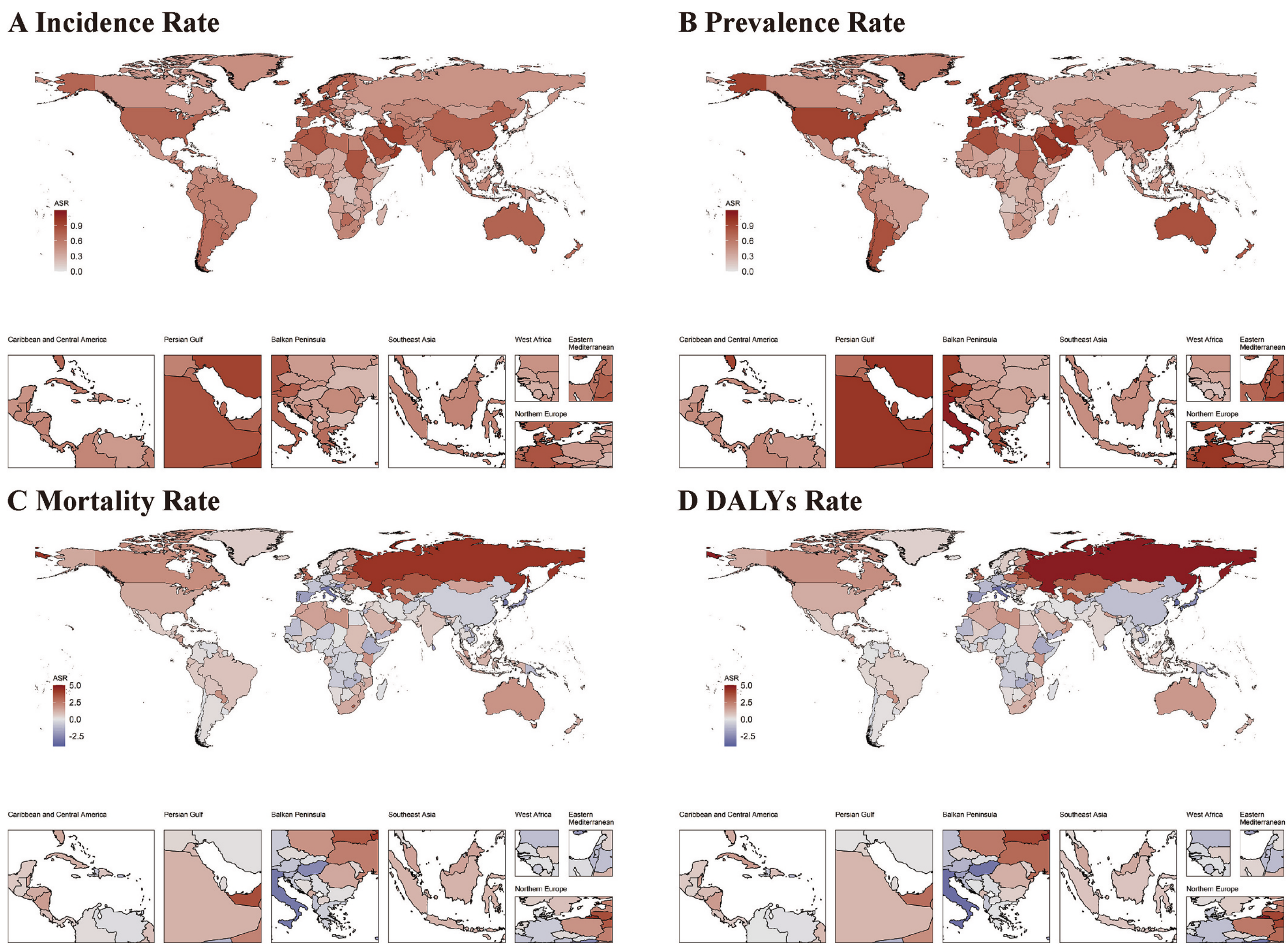

Fig. 2. The estimated annual percentage changes of the global age-standardized incidence, prevalence, mortality and disability-adjusted life years rates of metabolic dysfunction-associated steatotic liver disease from 1990 to 2021. Abbreviations: DALYs, disability-adjusted life years

EAPC of 0.98. In contrast, Central Sub-Saharan Africa had the slowest growth at 0.28. (Fig. 1, Fig. 2, and Table S2).

3.1.3. Mortality

According to the analysis, it was found that the ASMR showed a modest rise over this period globally, with an EAPC of 0.19, increasing from 1.53 per 100,000 in 1990 to 1.62 per 100,000 in 2021. Regionally, ASMR declined in high-income Asia Pacific, Western Europe, East Asia, Oceania, Central Sub-Saharan Africa, and Western Sub-Saharan Africa, whereas it remained stable in the Caribbean and Eastern Sub-Saharan Africa. Notably, Eastern Europe exhibited the most pronounced upward trend. (Fig. 1, Fig. 2, and Table S3).

3.1.4. DALYs

From 1990 to 2021, the global ASDR demonstrated a gradual increase, with an EAPC of 0.16. The ASDR rose from 40.20 per 100,000 population in 1990 to 42.40 per 100,000 population in 2021. Among the 21 GBD regions, declining trends in ASDR were observed in high-income Asia Pacific, Western Europe, East Asia, Oceania, Central Sub-Saharan Africa, and Western Sub-Saharan Africa, while Southern Latin America and Eastern Sub-Saharan Africa remained stable. All other regions showed upward trends, with Eastern Europe displaying the most significant increase. (Fig. 1, Fig. 2, and Table S4)

3.2. Predictions

According to the results of the model training, the hybrid model demonstrated superior performance for ASIR and ASPR, with *Z*-scores of 2.26 and 2.82, respectively. For ASMR, the NNAR model was optimal ($Z = 2.78$), and for ASDR, Prophet performed the best ($Z = 4.33$) (Fig. 3, Table S6). The model's prediction results indicate that, over the next decade, ASIR, ASPR, and ASMR are projected to rise, with ASIR showing the most significant upward trend, reaching 615.70 per 100,000 by 2031. ASPR and ASMR are expected to increase more gradually, reaching 15,275.60 per 100,000 and 1.64 per 100,000 by 2031. On the contrary, the ASDR is projected to decline to 42.08 by 2031. (Fig. 4).

4. Discussion

Based on our analysis, the global ASIR and ASPR rates of MASLD exhibited sustained upward trends from 1990 to 2021, consistent with the trajectories observed during 1990–2019 (Wang et al., 2022). However, there were significant differences in growth patterns and disease burdens across different regions. In less developed areas such as North Africa and the Middle East, ASIR, and ASPR were higher. This is generally consistent with the growth trajectories of global obesity rates, type 2 diabetes, and metabolic syndrome, especially in North Africa and the Middle East, where these are prevalent diseases (Younossi et al., 2023). The growth trend was particularly evident in regions such as Western Europe and North America. This might be attributed to the

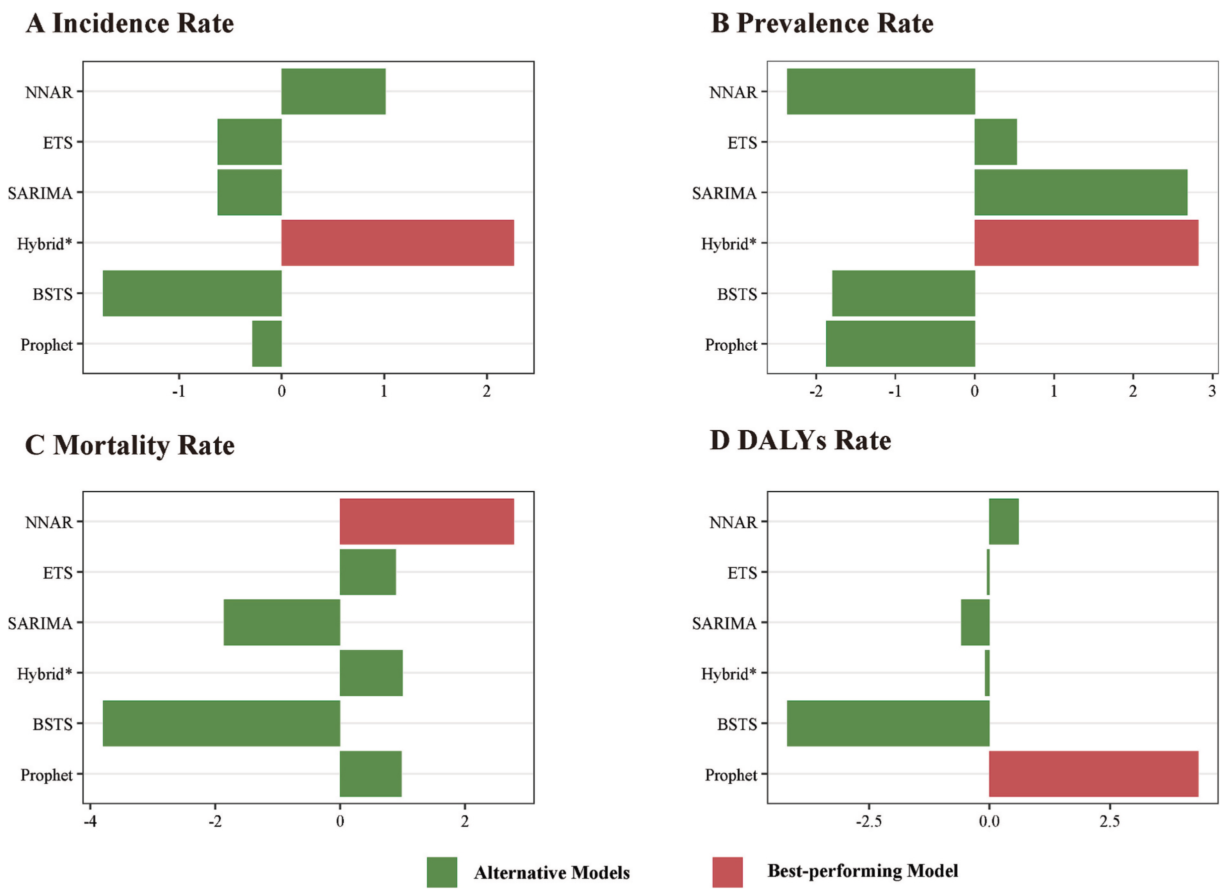

Fig. 3. The *Z*-normalized composite index of the prediction model for the disease burden of metabolic dysfunction-associated steatotic liver disease. (Test data: 2016–2021). Abbreviations: DALYs, disability-adjusted life years.

prevalence of fast food culture and the convenience of modern life that have led to a decrease in physical activity, creating a favorable environment for the development of MASLD.

Over the 32-year study period, global ASMR and ASDR for MASLD showed modest increases. Perhaps the insufficient understanding of the MASLD and limitations in screening protocols have exacerbated its burden. Even in regions with relatively robust healthcare resources, MASLD is often perceived as a “benign” condition, leading to delayed interventions and underprioritization in clinical practice (Lazarus et al., 2022). In the process of economic transformation in Eastern Europe, the lifestyle has undergone great changes, the traditional healthy diet pattern has been broken, and alcohol consumption is more common in some countries (Jasilionis et al., 2020). Although the MASLD definition excludes heavy alcohol consumption, low doses of alcohol intake may still accelerate the disease process in people with underlying metabolic disorders. In contrast, high-income Asia Pacific, Western Europe, and East Asia demonstrated improving trends. These regions have developed economies, abundant medical resources, and well-established medical security systems and public health policies. It is worth noting that in some parts of sub-Saharan Africa, the ASMR and ASDR have decreased. This phenomenon may be attributed to the increased international aid and the growing emphasis on public health by local governments in recent years.

In terms of model performance, the hybrid model performed the best in predicting ASIR and ASPR, which may be related to the advantages of integrating different models. The hybrid model can capture long-term trends and seasonal fluctuations of data through SARIMA, while Prophet was used to deal with abrupt points, and NNAR’s neural network structure was used to enhance the fitting ability of nonlinear relationships (Perone, 2022). The incidence and prevalence of MASLD are affected by the interlocking of many factors, and the change patterns of these factors over time are complex, making it difficult for a single model to describe them fully. However, the mixed model can effectively integrate the ability of different models to capture characteristics such as trends and cycles, and provide a guarantee for accurate prediction. Notably, NNAR and Prophet outperformed the hybrid model in predicting ASMR and ASDR, respectively. The relatively weaker performance of the hybrid model may stem from its equal-weight approach during modeling, which might underperform compared to the standalone NNAR or Prophet models. NNAR excels in handling nonlinear relationships (Kalantari, 2021), making it suitable for MASLD mortality prediction, which involves complex pathological mechanisms and nonlinear medical intervention effects. ASDR, reflecting disease-induced premature mortality and disability, is influenced more by long-term disease burden, seasonal metabolic syndrome exacerbations, and policy intervention timing. Prophet, adept at handling data with trend changes, seasonality, and holiday effects (Xie et al., 2021), stood out in ASDR prediction by flexibly responding to interventions, unlike traditional models that might underestimate change speeds owing to rigid time-series structures. Overall, the hybrid, NNAR and Prophet models provide viable options for future MASLD and other chronic disease burden predictions.

Predictions show a sustained rise in ASIR, likely because, despite obesity and diabetes prevention policies in some countries, the global metabolic risk factor epidemic remains uncontrolled. This is especially true in rapidly urbanizing areas, where high-calorie diets, sedentary lifestyles, and aging populations may further drive up MASLD’s ASIR. The gradual increase in ASPR and ASMR could stem from public health education, boosting health awareness and improving lifestyles. Additionally, advances in medical technology and treatments for MASLD and

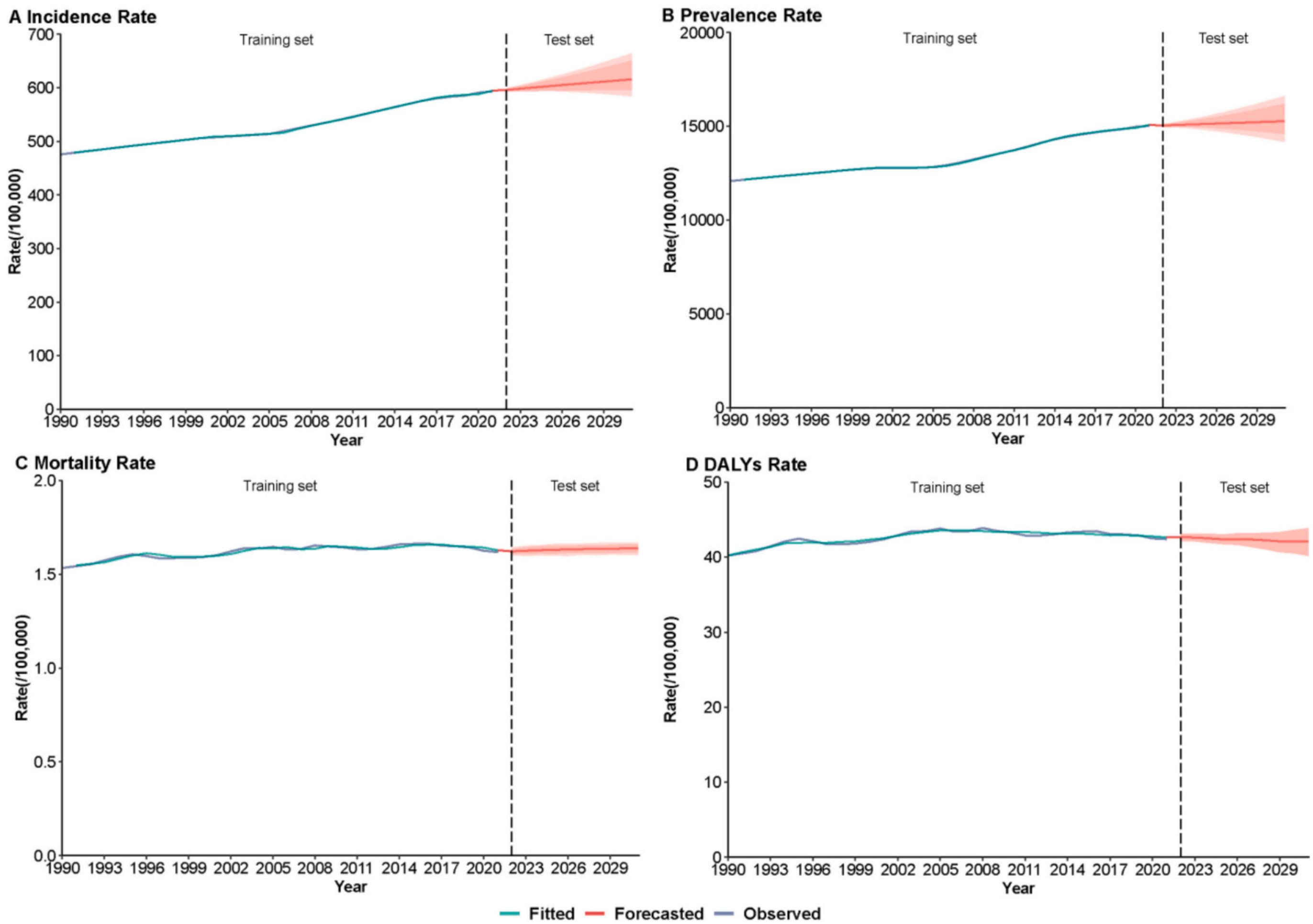

Fig. 4. The predicted results of disease burden of metabolic dysfunction-associated steatotic liver disease from 2022 to 2031. Abbreviations: DALYs, disability-adjusted life years

related complications can slow disease progression and reduce mortality rates. The slight decline in ASDR might be due to the strengthened prevention and treatment measures for MASLD-related comorbidities and the improvement in the management of liver disease complications. The development of specific treatment methods will also be a major driving force (Chen et al., 2025). However, the model inherently has uncertainties, including issues related to data quality, parameter estimation, and the future trends of relevant risk factors (*Lancet*, 2024). For instance, sudden public health events may disrupt routine medical care and increase the vulnerability of the MASLD population. Medical planning should prioritize optimizing the cardiovascular and metabolic risk management for all MASLD patients, and steadfastly invest in the primary prevention of obesity and diabetes at the societal level.

Regarding MASLD, the health department can incorporate MASLD screening into the prevention and control plan for non-communicable diseases, enabling early detection, management and treatment. The specific model can be adopted from the "Co-management of Doctors of Three Kinds" (Yang, 2024) in Xiamen, China, which involves collaboration among specialist physicians, traditional Chinese medicine practitioners and health managers for coordinated diagnosis and treatment. In areas with high disease burden, priority should be given to establishing "regional sentinel monitoring networks", where free testing sites are added at grassroots medical institutions, and relevant apps are developed to upload health data and provide AI risk warnings. For individuals identified as high-risk through the screening, a referral green channel should be provided. Given the global prevalence and complex mechanisms of MASLD, strengthening global cooperation in formulating prevention and treatment strategies is crucial.

The prominent advantage of this study lies in the use of the latest data from GBD and the training of six time series models, from which the optimal model was selected to predict the disease burden of MASLD in the next ten years. However, several limitations of this study should be considered when interpreting the results. Most importantly, data collection standards vary significantly across countries and regions. Some underdeveloped areas largely rely on statistical models that use predictive covariates, historical trends, or trends from neighboring countries, introducing uncertainties that may lead to underestimation or overestimation of the disease burden (Paik et al., 2021). Secondly, while the models can predict future disease burden based on historical data, they cannot fully account for potential breakthroughs in medical technology or changes in public health policies. These factors could significantly influence epidemiological trends of MASLD. At last, during the ICD-10 period, the code K76.0 was uniformly used for NAFLD. However, during the transition period of ICD-11, the code MASLD was gradually adopted instead. The dynamic adjustment of diagnostic labels may cause the interchange of MASLD and NAFLD over time, introducing classification bias and leading to an inaccurate increase or decrease in risk estimation. This type of bias cannot be completely eliminated, so the results of cross-period comparisons should be interpreted with greater caution.

5. Conclusion

MASLD has seen increases in ASIR and ASPR across all countries from 1990 to 2021, with over half experiencing rises in ASMR and ASDR. Model forecasts also suggest a persistently heavy disease burden over the next decade, making it a global public health concern. Future efforts to reduce the MASLD's health burden should focus on health policy reform, enhanced preventive care, and research collaboration, in line with international health goals and the well-being of all people.

CRediT authorship contribution statement

Zhuang Lin: Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Conceptualization. **Ruixin Zhang:** Writing – original draft, Visualization, Validation, Formal analysis, Data curation, Conceptualization. **Shuhao Ren:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Tingjuan He:** Writing – review & editing, Visualization, Validation, Conceptualization. **Hongfei Mi:** Writing – review & editing, Visualization, Software, Data curation, Conceptualization. **Wei Jiang:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization. **Chenghao Su:** Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2025.103248.

Data availability

Data will be made available on request.

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