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Global burden of metabolic dysfunction-associated steatotic liver disease, 2010 to 2021

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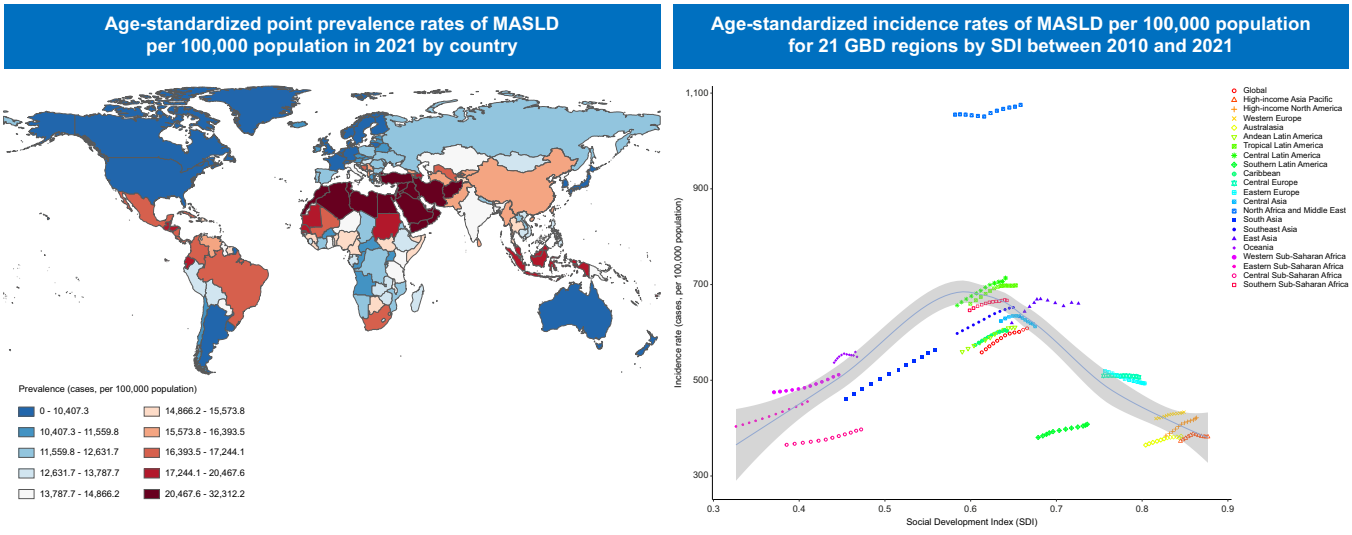
Graphical abstract



Highlights:

- MASLD is a global health concern, with the highest prevalence reported in Kuwait, Egypt, and Qatar.
- Men have a higher prevalence of MASLD than women, with the peak age of prevalence differing between sexes.
- Raising awareness about MASLD risk factors and prevention is crucial worldwide, particularly in China, Sudan, and India.

Impact and implications:

This research provides a comprehensive analysis of the global burden of MASLD, highlighting its rising prevalence and incidence, particularly in countries with varying sociodemographic indices. The findings are significant for both clinicians and policymakers, as they offer critical insights into the regional disparities in MASLD burden, which can inform targeted prevention and intervention strategies. However, the study's reliance on modeling and available data suggests cautious interpretation, and further research is needed to validate these findings in clinical and real-world settings.

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Global burden of metabolic dysfunction-associated steatotic liver disease, 2010 to 2021☆

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Background & Aims: This study used the Global Burden of Disease data (2010–2021) to analyze the rates and trends of point prevalence, annual incidence, and years lived with disability (YLDs) for metabolic dysfunction-associated steatotic liver disease (MASLD) in 204 countries.

Methods: Total numbers and age-standardized rates per 100,000 population for MASLD prevalence, annual incidence, and YLDs were compared across regions and countries by age, sex, and sociodemographic index (SDI). Smoothing spline models were used to evaluate the relationship between the burden of MASLD and SDI. Estimates were reported with uncertainty intervals (UI).

Results: Globally, in 2021, the age-standardized rates per 100,000 population of point prevalence of MASLD were 15,018.1 cases (95% UI 13,756.5–16,361.4), annual incidence rates were 608.5 cases (598.8–617.7), and YLDs were 0.5 (0.3–0.8) years. MASLD point prevalence was higher in men than women (15,731.4 *vs.* 14,310.6 cases per 100,000 population). Prevalence peaked at ages 45–49 for men and 50–54 for women. Kuwait (32,312.2 cases per 100,000 people; 95% UI: 29,947.1–34,839.0), Egypt (31,668.8 cases per 100,000 people; 95% UI: 29,272.5–34,224.7), and Qatar (31,327.5 cases per 100,000 people; 95% UI: 29,078.5–33,790.9) had the highest prevalence rates in 2021. The largest increases in age-standardized point prevalence estimates from 2010 to 2021 were in China (16.9%, 95% UI 14.7%–18.9%), Sudan (13.3%, 95% UI 9.8%–16.7%) and India (13.2%, 95% UI 12.0%–14.4%). MASLD incidence varied with SDI, peaking at moderate SDI levels.

Conclusions: MASLD is a global health concern, with the highest prevalence reported in Kuwait, Egypt, and Qatar. Raising awareness about risk factors and prevention is essential in every country, especially in China, Sudan and India, where disease incidence and prevalence are rapidly increasing.

Introduction

Non-alcoholic fatty liver disease (NAFLD), recently renamed as metabolic dysfunction-associated fatty liver disease (MAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD), has rapidly become the most common chronic liver disease worldwide, with an estimated 38% of the global adult population currently affected.[1,2] For simplicity, we opted for using the term MASLD throughout this manuscript. MASLD is closely linked to obesity, type 2 diabetes, hypertension, and other metabolic risk abnormalities.[3] MASLD may progress from metabolic dysfunction-associated hepatic steatosis to metabolic dysfunction-associated steatohepatitis (MASH) with varying levels of fibrosis, cirrhosis, and hepatocellular carcinoma (HCC).[4]

The Global Burden of Diseases (GBD) study is an important epidemiological research project led by the Institute for Health

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Metrics and Evaluation at the University of Washington, USA.[5,6] The GBD study is considered one of the most extensive burden of disease studies conducted to date.[7] While Paik *et al.*[8] have recently utilized the GBD database to investigate the disease burden of MASLD, it is important to underline that their analysis was conducted using the previous 2019 GBD data and did not explore the relationships between the sociodemographic index (SDI) and the disease burden of MASLD.

The global incidence and prevalence rates of MASLD have notably increased in the past decades. This increase in the global prevalence and incidence rates of MASLD is closely linked to modern dietary patterns, decreased physical activity, and rapid urbanization. MASLD is not only associated with liver disease but data suggests that it is also contributing to various extrahepatic complications, such as cardiovascular disease, type 2 diabetes, chronic kidney disease, and certain types of extrahepatic cancers, which further increase the patient's risk of disability.[9–11] MASLD is recognized as a significant risk factor likely to be attributed to the rise in years lived with disability (YLDs), but needs further research to provide evidence for these hypotheses.[12] Genetic susceptibility also plays a role in MASLD development, with some genetic variants, such as Patatin-like phospholipase domain-containing protein 3, Transmembrane 6 superfamily member 2, and Membrane-bound O-acyltransferase domain-containing 7, identified as risk factors for increased hepatic fat accumulation and disease progression.[13] The most updated data from the GBD 2021 was published in mid-May 2024, offering detailed information on various diseases and injuries over different time frames.[14] Utilizing the GBD 2021 dataset can enhance our understanding of the updated global, regional and national burden of MASLD.

Cases and methods

Data sources

Data for this study were obtained from the GBD 2021 database. The database draws from 328,938 data sources and disaggregates data by key demographic variables such as age, sex, location, and socioeconomic groups. Health disparities can be identified through further analysis. GBD 2021 encompasses the global burden of disease assessments for 204 countries (or regions) from 1990 to 2021. The data were generated from the GBD study results, publicly available at https://vizhub.healthdata.org/gbd-results/. This study used the GBD data (2010–2021) to analyze the rates and trends of point prevalence, annual incidence, and YLDs for MASLD in 204 countries.

Definition

The study uses various disease burden indicators, including the rates of prevalence, incidence, mortality, and YLDs, to illustrate the impact of diseases on population health and the extent of their lethal hazards. Incidence refers to the frequency of new cases, reflecting the effect of the disease on population health. YLDs are a measure of the burden of disease that quantify the effects of health conditions on an individual's life. The calculation method for YLDs involves multiplying the number of people with a specific disease or health condition within a given period by the disability weight of that disease or health condition. Therefore, YLDs provide an indicator of the burden of disease, reflecting the impact of specific diseases or health conditions on the quality of life. The GBD study incorporates global disease burden data from 2010 to 2021. NAFLD is defined by the presence of hepatic steatosis (>5% hepatic steatosis) without significant alcohol consumption or other known liver disease causes. In 2020, the term MAFLD was proposed by a group of researchers to emphasize the disease's link with metabolic dysfunction, requiring hepatic steatosis along with criteria such as overweight/obesity, type 2 diabetes, or metabolic dysregulation.[15] In 2023, the term MASLD was proposed by three pan-national scientific associations. MASLD is defined as steatotic liver disease (SLD) in the presence of one or more cardiometabolic risk factor(s), and the absence of harmful alcohol intake.[1] The GBD study employs the SDI as a composite measure to quantify the health-related socioeconomic development of regions. This index is derived from three key indicators: fertility rates among young women (under 25 years), educational attainment (average years of schooling for individuals ≥15 years), and economic prosperity (lag-distributed income per capita).[16] The SDI is computed as the geometric mean of these three components, each normalized to a scale of 0–1. To facilitate comparative analyses, the GBD 2021 study categorizes the 204 countries into five quintiles – low, low-middle, middle, high-middle, and high – based on their SDI values in 2021.[16]

Statistical analysis

The prevalence and trends of MASLD were assessed through a range of statistical analysis methods. Initially, the point prevalence of MASLD per 100,000 population was calculated to indicate disease prevalence at a specific time; annual incidence was used to track new cases annually; and YLDs, determined by disease prevalence and associated disability weights, gauged the impact on quality of life. Disability weights, which represent the magnitude of health loss associated with specific health outcomes, are used to calculate YLDs for these outcomes in each population. The weights are measured on a scale from 0 to 1, where 0 equals a state of full health and 1 equals death (https://ghdx.healthdata.org/record/ihme-data/gbd-2021-disability-weights). All estimates were accompanied by a 95% uncertainty interval (UI) to account for statistical variability in the forecast. The UI is widely used in GBD research, as it not only captures statistical uncertainty (such as sampling error) but also includes other sources of uncertainty (such as model selection and parameter estimation). Subsequently, a regression model was used to analyze the changing burden of MASLD from 2010 to 2021, identifying countries and regions with notable growth or decline. Furthermore, a comparison of MASLD burden across different countries and regions was conducted, evaluating variations among age groups, sexes, and SDI levels to investigate the effect of economic development and lifestyle changes on the rates of prevalence, incidence, and YLDs of MASLD. Smoothing spline models were used to evaluate the relationship between the burden of MASLD and SDI for the 21 regions and 204 countries and territories. The expected values were determined through a calculation that considers the SDI and disease rates across all locations.[16] We fitted smooth splines using the Locally Weighted Scatterplot Smoothing method, which automatically determines the degree, number, and location of nodes (knots) based on the data and the span parameter.[16] The statistical

computing software R (Version 3.5.2, R Foundation for Statistical Computing, Vienna, Austria) was utilized to perform procedures for analysis and graphic representation.

Results

Global level for MASLD

Table 1 shows the prevalence, incidence, and YLD rates of MASLD in the general population for males and females in 2021. Additionally, it shows the percentage change in age-standardized rates (ASRs) per 100,000 population between 2010 and 2021 across various GBD regions. The global prevalence of MASLD in 2021 was approximately 1.27 billion (95% UI 1,157,934,071–1,380,435,423) with an ASR of 15,018.1 cases (95% UI 13,756.5–16,361.4) per 100,000 population, representing an 11.2% increase (95% UI 10.5%–11.8%) in ASRs from 2010 to 2021. The global incidence of MASLD was about 48.35 million (95% UI 47,612,534–49,094,010) with an ASR of 608.5 cases (95% UI 598.8–617.7) per 100,000 population, reflecting a 3.2% increase (95% UI 2.1%–4.2%). YLDs were reported at 44,089 (95% UI 29,048–65,849) with an ASR of 0.5 years (95% UI 0.3–0.8) per 100,000 population (Table 1).

Regional level for MASLD

In 2021, the highest age-standardized point prevalence rates of MASLD per 100,000 population were in North Africa and the Middle East (27,686.7 cases, 95% UI 25,586.9–29,914.6), Central Latin America (16,984.0 cases, 95% UI 15,536.5–18,533.6), and Tropical Latin America (16,662.7 cases, 95% UI 15,244.9–18,205.5). The lowest ASRs per 100,000 population of MASLD were in High-income North America (10,056.0 cases, 95% UI 9,187.3–10,925.6), Australasia (9,468.2 cases, 95% UI 8,665.5–10,349.4), and high-income Asia Pacific (8,885.7 cases, 95% UI 8,148.4–9,666.7) (Table 1). High-income North America refers specifically to the United States and Canada. The high-income Asia-Pacific region refers to economically developed countries and territories within the Asia-Pacific area. These nations typically have high *per capita* income levels and well-established healthcare systems. Specific countries and regions in this category include Japan, South Korea, and Singapore.

Similarly, the highest age-standardized incidence rates per 100,000 population were in North Africa and the Middle East (1,075.5 cases, 95% UI 1049.6–1103.8), Central Latin America (713.6 cases, 95% UI 691.5–734.9), and Tropical Latin America (698.1 cases, 95% UI 624.4–797.7). The lowest incidence rates per 100,000 population of MASLD were observed in Central Sub-Saharan Africa (397.2 cases, 95% UI 333.7–486.3), Australasia (383.2 cases, 95% UI 368.0–400.4), and high-income Asia Pacific (381.9 cases, 95% UI 367.1–397.2) (Table 1).

The highest ASRs of YLDs per 100,000 population were in Andean Latin America (1.7 years, 95% UI 1.0–2.4), Central Latin America years (1.5 years, 95%UI 1.0–2.3), and Eastern Europe (1.1 years, 95% UI 0.7–1.8). The lowest ASRs of YLDs per 100,000 population were in East Asia (0.3 years, 95% UI 0.2–0.4), Central Sub-Saharan Africa (0.3 years, 95% UI 0.2–0.5), and Oceania (0.2 years, 95% UI 0.1–0.3) (Table 1).

The highest percentage change in the age-standardized prevalence rate of MASLD per 100,000 population from 2010 to 2021 was an increase observed in East Asia (+16.6%, 95% UI 14.5%–18.5%), South Asia (+12.0%, 95%UI 10.9–12.9%) and Southern Latin America (+7.2%, 95% UI 4.3%–9.9%). The highest percentage change in the age-standardized annual incidence of MASLD per 100,000 population from 2010 to 2021 was an increase observed in East Asia (+10.7%, 95% UI 9.1%–12.6%), Southern Latin America (+8.9%, 95% UI 5.6%–12.1%), and Western Europe (+6.4%, 95% UI 5.0%–8.0%). In addition, the highest increase in age-standardized years lived with disability from MASLD per 100,000 population from 2010 to 2021 was in North Africa and Middle East (+23.5%, 95% UI 14.3%–31.7%), High-income North America (+21.1%, 95% UI 15.9%–26.3%) and South Asia (+20.8%, 95% UI 15.0%–26.6%) (Table 1).

National level for MASLD

The national age-standardized point prevalence rates of MASLD in 2021 ranged from 8,133.5 to 32,312.2 cases per 100,000 population. The countries with the highest age-standardized point prevalence rates per 100,000 population in 2021 were Kuwait (32,312.2 cases, 95% UI 29,947.1–34,839.0), Egypt (31,668.8 cases, 95% UI 29,272.5–34,224.7), and Qatar (31,327.5 cases, 95% UI 29,078.5–33,790.9), whereas Canada (8,492.3 cases, 95% UI 7,739.8–9,305.5), Finland (8,358.5 cases, 95% UI 7,620.0–9,180.6), and Japan (8,133.5 cases, 95% UI 7,457.7–8,837.4) had the lowest age-standardized point rates of MASLD (Fig. 1 and Table S1).

The highest national age-standardized annual incidence rates per 100,000 population of MASLD in 2021 were observed in Brazil (1,407.1 cases, 95% UI 1221.7–1,659.1), Qatar (1,358.6 cases, 95% UI 1,284.0–1,448.6), and Saudi Arabia (1,333.3 cases, 95% UI 1,187.2–1,516.0), with the lowest national age-standardized annual incidence rates reported in Japan (349.0 cases, 95% UI 330.3–371.7), Finland (336.1 cases, 95% UI 311.9–370.0), and Canada (333.4 cases, 95% UI 316.0–350.6) (Fig. 2 and Table S2). In addition, the highest ASRs of YLDs per 100,000 population were in Mexico (2.2 years, 95% UI 1.4–3.4), Mongolia (2.1 years, 95% UI 1.3–3.2), and Ecuador (1.9 years, 95% UI 1.2–2.8). The lowest ASRs of YLDs per 100,000 population were in Timor-Leste (0.2 years, 95% UI 0.1–0.2), Yemen (0.1 years, 95% UI 0.1–0.2), and Papua New Guinea (0.1 years, 95% UI 0.1–0.2) (Fig. S1 and Table S3).

The percentage change in age-standardized point prevalence rates per 100,000 population from 2010 to 2021 differed substantially between countries, with the largest increases in China (16.9%, 95% UI 14.7%–18.9%), Sudan (13.3%, 95% UI 9.8%–16.7%), and India (13.2%, 95% UI 12.0%–14.4%) (Fig. S2 and Table S4). The largest increases for percentage change in age-standardized annual incidence rates per 100,000 population from 2010 to 2021 were in Haiti (11.9%, 95% UI 4.6%–18.8%), Argentina (11.6%, 6.8%–16.4%), and Germany (11.6%, 6.7%–16.1%) (Fig. S3 and Table S5). The largest increases for percentage change in ASRs of YLDs per 100,000 population in 204 countries and territories between 2010 and 2021 were in Turkmenistan (36.4%, 95% UI 19.0%–55.0%), Nepal (35.4%, 95% UI 22.8%–50.1%) and Equatorial Guinea (33.4%, 95% UI 17.0%–50.6%) (Fig. S4 and Table S6).

Age and sex patterns

In 2021, the global age-standardized point prevalence rates of MASLD were higher in men (15,731.4 cases, 95% UI

Table 1. Total numbers and global and regional rates of prevalence, incidence, and YLDs from MASLD in the general population in 2021.

	Prevalence			Incidence			YLDs		
Regions	No. (95% UI, cases)	ASRs per 100,000 population (95% UI, cases)	Percentage change in ASRs per 100,000 population (95% UI, %)	No. (95% UI, cases)	ASRs per 100,000 population (95% UI, cases)	Percentage change in ASRs per 100,000 population (95% UI, %)	No. (95% UI, years)	ASRs per 100,000 population (95% UI, years)	Percentage change in ASRs per 100 000 population (95% UI, %)
Global	1,267,867,997 (1,157,934,071–1,380,435,423)	15,018.1 (13,756.5–16,361.4)	11.2 (10.5–11.8)	48,353,272 (47,612,534–49,094,010)	608.5 (598.8–617.7)	3.2 (2.1–4.2)	44,089 (29,048–65,849)	0.5 (0.3–0.8)	0.8 (-2.4 to 3.9)
Andean Latin America	9,737,655 (8,884,038–10,649,706)	14,984.8 (13,708.4–16,361.5)	4.1 (1.9–6.1)	399,223 (393,163–405,283)	610.6 (583.1–647.4)	-2.8 (-5.8 to 0.5)	996 (627–1,467)	1.7 (1.0–2.4)	8.1 (-2.2 to 18.4)
Australasia	3,778,619 (3,457,855–4,124,388)	9,468.2 (8,665.5–10,349.4)	5.8 (3.2–8.7)	117,958 (116,015–119,902)	383.2 (368.0–400.4)	5.4 (1.7–9.2)	261 (169–372)	0.5 (0.4–0.8)	16.6 (9.0 to 24.6)
Caribbean	8,111,960 (7,440,860–8,804,729)	15,650.7 (14,340.1–16,986.2)	3.4 (1.9–4.9)	287,884 (283,459–292,309)	603.1 (568.1–639.4)	3.5 (0.3–6.5)	453 (295–675)	0.9 (0.6–1.3)	15.6 (8.8 to 23.2)
Central Asia	15,204,171 (13,885,517–16,673,758)	16,120.1 (14,735.3–17,604.5)	7.1 (5.6–8.6)	583,559 (574,644–592,474)	612.4 (563.3–673.7)	-6.1 (-9.3 to -2.7)	908 (572–1,379)	1.1 (0.7–1.6)	16.3 (8.5 to 24.4)
Central Europe	20,606,023 (18,822,096–22,372,105)	12,731.5 (11,618.6–13,852.6)	5.2 (3.9–6.4)	569,426 (560,221–578,631)	506.2 (492.2–522.3)	-7.4 (-8.9 to -5.7)	1,211 (763–1,851)	0.6 (0.4–1.0)	6.8 (0.6 to 12.4)
Central Latin America	44,693,566 (40,900,171–48,782,244)	16,984.0 (15,536.5–18,533.6)	6.2 (4.8–7.6)	1,786,199 (1,759,467–1,812,932)	713.6 (691.5–734.9)	-1.4 (-3.0 to -0.3)	3,929 (2,514–5,904)	1.5 (1.0–2.3)	14.2 (8.1 to 20.9)
Central Sub-Saharan Africa	10,850,618 (9,833,003–11,986,283)	11,870.6 (10,844.9–12,943.4)	5.6 (3.1–8.5)	549,883 (541,760–558,005)	397.2 (333.7–486.3)	-0.4 (-4.0 to 3.6)	183 (118–298)	0.3 (0.2–0.5)	11.2 (-0.8 to 23.3)
East Asia	301,408,386 (274,406,342–328,824,040)	15,596.2 (14,262.4–16,999.3)	16.6 (14.5–18.5)	9,905,423 (9,743,925–10,066,921)	660.4 (625.4–699.0)	10.7 (9.1–12.6)	6,226 (4,124–9,154)	0.3 (0.2–0.4)	-1.6 (-10.0 to 8.9)
Eastern Europe	34,696,290 (31,695,847–37,763,371)	12,293.9 (11,254.5–13,359.2)	4.3 (2.3–6.0)	1,035,050 (1,017,952–1,052,148)	493.5 (454.6–543.7)	-7.8 (-10.0 to -5.6)	3,298 (2,028–5,370)	1.1 (0.7–1.8)	-3.2 (-9.3 to 4.1)
Eastern Sub-Saharan Africa	37,304,081 (34,041,055–41,466,666)	13,162.1 (12,037.1–14,400.2)	6.5 (5.5–7.5)	1,953,106 (1,925,028–1,981,184)	455.5 (440.7–471.3)	-0.9 (-2.4 to 0.6)	841 (566–1,240)	0.5 (0.3–0.7)	6.1 (-2.3 to 14.8)
High-income Asia Pacific	24,694,242 (22,636,602–26,784,254)	8,885.7 (8,148.4–9,666.7)	6.4 (3.5–8.9)	728,246 (715,952–740,540)	381.9 (367.1–397.2)	5.8 (3.5–8.1)	1,933 (1,260–2,786)	0.4 (0.3–0.7)	-20.1 (-24.6 to -15.0)
High-income North America	48,995,595 (44,673,054–53,423,290)	10,056.0 (9,187.3–10,925.6)	4.5 (3.0–5.8)	1,635,646 (1,609,457–1,661,835)	421.6 (402.2–444.2)	-0.6 (-2.0 to 0.9)	3,833 (2,450–5,799)	0.7 (0.4–1.0)	21.1 (15.9 to 26.3)
North Africa and Middle East	164,312,589 (151,441,885–179,050,648)	27,686.7 (25,586.9–29,914.6)	6.0 (5.3–6.9)	6,578,946 (6,480,051–6,677,840)	1,075.5 (1,049.6–1,103.8)	-2.8 (-4.6 to -0.9)	2,600 (1,703–3,871)	0.6 (0.4–0.8)	23.5 (14.3 to 31.7)
Oceania	1,625,693 (1,483,817–1,796,525)	15,182.7 (13,936.2–16,584.7)	2.1 (–0.0 to 4.4)	76,654 (75,506–77,802)	549.0 (507.1–603.1)	-5.8 (-9.5 to -1.6)	18 (12–28)	0.2 (0.1–0.3)	-3.7 (-11.8 to 3.8)
South Asia	249,790,702 (227,865,117–273,237,523)	14,158.3 (12,940.9–15,445.1)	12.0 (10.9–12.9)	10,765,351 (10,602,018–10,928,683)	563.3 (518.2–614.2)	1.3 (-0.5 to 3.4)	4,837 (3,193–7,249)	0.3 (0.2–0.5)	20.8 (15.0 to 26.6)
Southeast Asia	115,103,788 (104,841,848–125,940,613)	15,691.7 (14,308.3–17,127.2)	5.7 (4.6–6.7)	4,606,197 (4,535,042–4,677,353)	651.9 (635.1–669.3)	-0.7 (-2.1 to 0.6)	2,553 (1,682–3,822)	0.4 (0.3–0.6)	8.2 (-1.2 to 17.0)
Southern Latin America	8,080,745 (7,374,984–8,823,030)	10,292.5 (9,394.6–11,265.4)	7.2 (4.3–9.9)	283,022 (278,411–287,634)	408.1 (377.8–443.1)	8.9 (5.6–12.1)	511 (315–788)	0.6 (0.4–0.9)	9.6 (-2.6 to 23.4)
Southern Sub-Saharan Africa	11,781,789 (10,763,174–12,907,446)	15,937.2 (14,572.6–17,388.0)	7.1 (5.6–8.8)	532,714 (524,679–540,749)	666.8 (616.9–722.6)	1.9 (-0.5 to 4.3)	346 (232–499)	0.6 (0.4–0.8)	-1.0 (-7.9 to 6.1)
Tropical Latin America	42,870,511 (39,161,072–46,852,272)	16,662.7 (15,244.9–18,205.5)	3.8 (2.2–5.7)	1,584,118 (1,559,329–1,608,907)	698.1 (624.4–797.7)	-3.0 (-5.1 to -0.9)	1,306 (823–2,056)	0.5 (0.3–0.8)	11.0 (5.0 to 16.2)

(*continued on next page*)

Table 1. (*continued*)

Regions	Prevalence			Incidence			YLDs		
	No. (95% UI, cases)	ASRs per 100,000 population (95% UI, cases)	Percentage change in ASRs per 100,000 population (95% UI, %)	No. (95% UI, cases)	ASRs per 100,000 population (95% UI, cases)	Percentage change in ASRs per 100,000 population (95% UI, %)	No. (95% UI, years)	ASRs per 100,000 population (95% UI, years)	Percentage change in ASRs per 100 000 population (95% UI, %)
Western Europe	66,258,939 (60,940,043–71,561,630)	10,841.8 (9,939.0–11,802.0)	7.0 (5.9–8.2)	1,871,635 (1,841,743–1,901,527)	433.3 (426.6–441.9)	6.4 (5.0–8.0)	6,556 (4,227–9,738)	0.8 (0.5–1.3)	-12.2 (-16.2 to -7.7)
Western Sub-Saharan Africa	47,962,036 (43,856,187–53,002,936)	14,936.8 (13,659.3–16,347.6)	6.2 (5.3–7.2)	2,501,856 (2,465,846–2,537,866)	511.6 (490.5–534.7)	4.3 (2.5–6.1)	1,289 (889–1,875)	0.6 (0.4–0.9)	9.0 (-2.4 to 19.0)

For males and females, and percentage changes of ASRs per 100,000 population between 2010 and 2021 by Global Burden of Disease regions (generated from data available at https://vizhub.healthdata.org/gbd-results/). ASRs, age-standardized rates; MASLD, metabolic dysfunction-associated steatotic liver disease; UI, uncertainty interval.

14,392.7–17,167.4 per 100,000 population) than women (14,310.6 cases, 95% UI 13,114.9–15,573.6 per 100,000 population). The number of prevalent cases also rose with age, peaking in the 45–49 age group for men and in the 50–54 age group for women, and then decreased as age advanced in both sexes (Fig. 3 and Table S7). Regarding the number of incident cases at different ages in MASLD, the number for men peaked at ages 15–19 years, then gradually declined; for women, the number peaked at ages 20–24, followed by a gradual decline (Fig. S5 and Table S8). Regarding the YLDs across different ages in MASLD, the YLDs for men peaked at ages 65–69. Similarly, for women, the YLDs peaked at ages 65–69, followed by a gradual decline thereafter (Fig. S6 and Table S9).

Observed burden of MASLD compared with that expected by SDI

The incidence rates of MASLD peaked at moderate levels of social development and were lower at both low and high levels of social development. Some regions, such as North Africa and the Middle East, had higher than expected incidence rates, while more developed regions, such as Australasia, had lower than expected incidence rates (Fig. 4). The observed MASLD incidence rates were higher than expected, indicating that in certain regions, the actual incidence surpassed the rates predicted based on the SDI and disease rates of the region. Similarly, for countries, MASLD incidence rates peaked at moderate levels of social development and were lower at both low and high levels of social development. Countries such as Afghanistan, Yemen, and Sudan showed higher than expected incidence rates, whereas Australia, Canada, and Finland had lower than expected rates (Fig. 5).

Fig. S7 shows the age-standardized prevalence rates of MASLD from 2010 to 2021 across GBD regions, grouped by the SDI. The overall trend indicates that MASLD prevalence rates peaked at moderate levels of social development and were lower at both low and high levels. Some regions, such as North Africa and the Middle East, showed higher than expected prevalence rates of MASLD, while Southern Latin America showed lower than expected prevalence rates. Similarly, countries, such as Egypt, Kuwait, and Qatar, had higher than expected prevalence rates of MASLD, whereas Japan, Canada, and Finland had lower than expected rates (Fig. S8).

Fig. S9 illustrates the age-standardized YLD rates from MASLD per 100,000 population across GBD regions, grouped by the SDI for 2010–2021. The trends indicate that YLD rates also peaked at moderate levels of social development and decreased at lower and higher levels. Some regions, such as Central Latin America, had higher than expected YLD rates, while East Asia showed lower than expected YLD rates. Similarly, countries such as Egypt, Mexico, and Qatar had higher than expected YLD rates, whereas Japan, Singapore, and Sweden had lower than expected YLD rates (Fig. S10).

Discussion

This study utilizes data from the GBD 2021 to examine the point prevalence and annual incidence of MASLD across 204 countries and regions from 2010 to 2021, along with trends in YLDs. The analysis of the GBD 2021 study highlights global prevalence patterns of MASLD and offers detailed insights into the

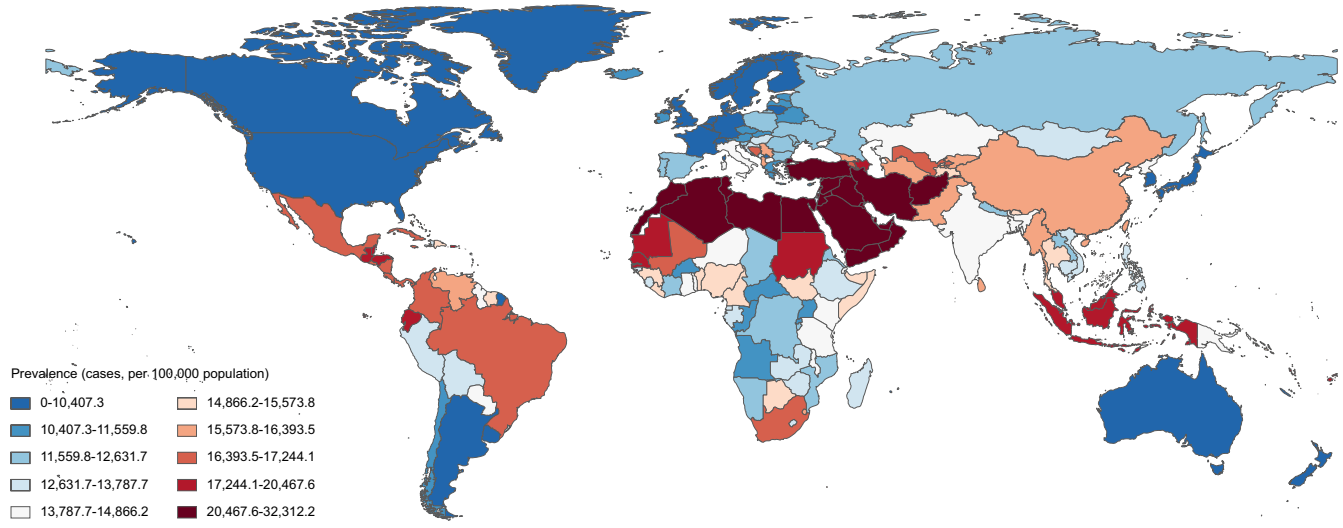

Fig. 1. Age-standardized point prevalence rates of MASLD per 100,000 population in 2021 by country.

burden of the disease across different sexes, ages, and SDI groups. Thus, the present analysis investigates the disease burden of MASLD using data from the most recent GBD period (2010–2021), providing an up-to-date analysis of this important health issue.

Our study offers several advantages over previously published research using the GBD database. Firstly, regarding data scope and time, Zhang *et al.*[17] selected the period from 1990 to 2021, while Danpanichkul *et al.*[18] focused on 2000–2019. We chose the period from 2010 to 2021 because the global burden of MASLD has significantly changed over the past decade. Selecting this time frame allows us to capture these changes. While GBD data has been available since 1990, MASLD-related data before 2010 is often scarce or lower in quality, so we focused on a more reliable period. Secondly, Zhang *et al.*[17] reported only on MASLD-related for disability-adjusted life years and mortality, which is entirely different from our study's focus on the rates of incidence, prevalence, and YLDs of MASLD.[17] Danpanichkul *et al.*[18] did not analyze incidence and YLDs. Allen *et al.*[19] provided a comprehensive review without specifically reporting updated rates of incidence, prevalence, or YLDs for MASLD. Lastly, regarding the geographical scope, our study provides a more detailed and updated analysis of MASLD burden in 204 countries and emphasizes the differences in disease prevalence and incidence among countries with different SDI levels.

In 2021, the global age-standardized point prevalence rate of MASLD was 15,018.1 cases per 100,000 people, with an annual incidence rate of 608.5 cases per 100,000. These findings highlight MASLD as a growing public health concern globally. Kuwait, Egypt, and Qatar have the highest prevalence of MASLD. This high prevalence of MASLD could be attributed

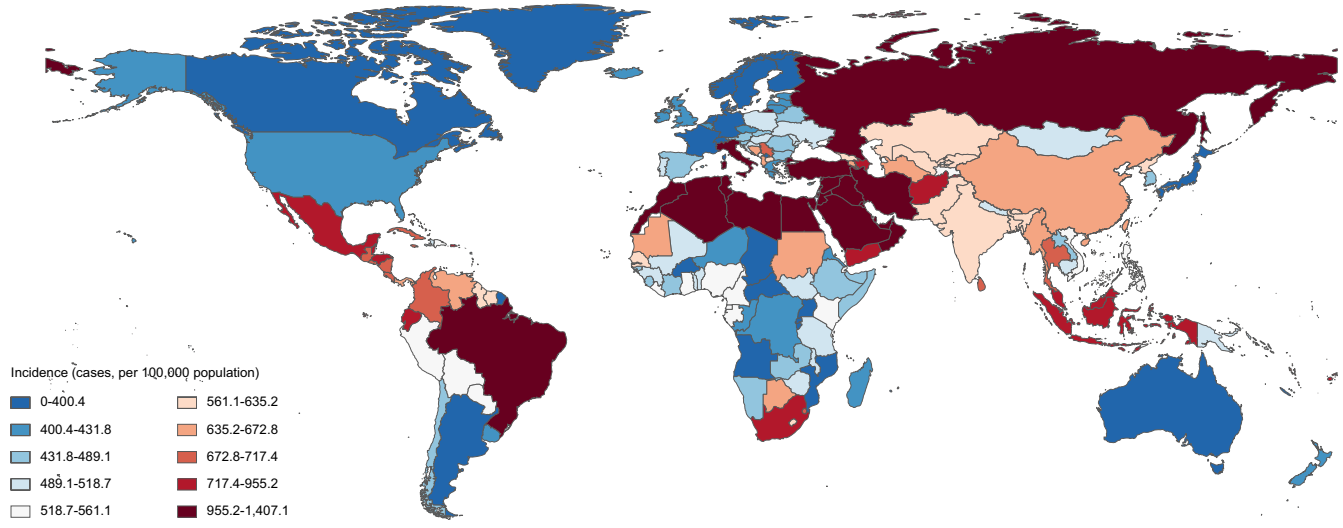

Fig. 2. Age-standardized annual incidence rates of MASLD per 100,000 people in 2021 by country.

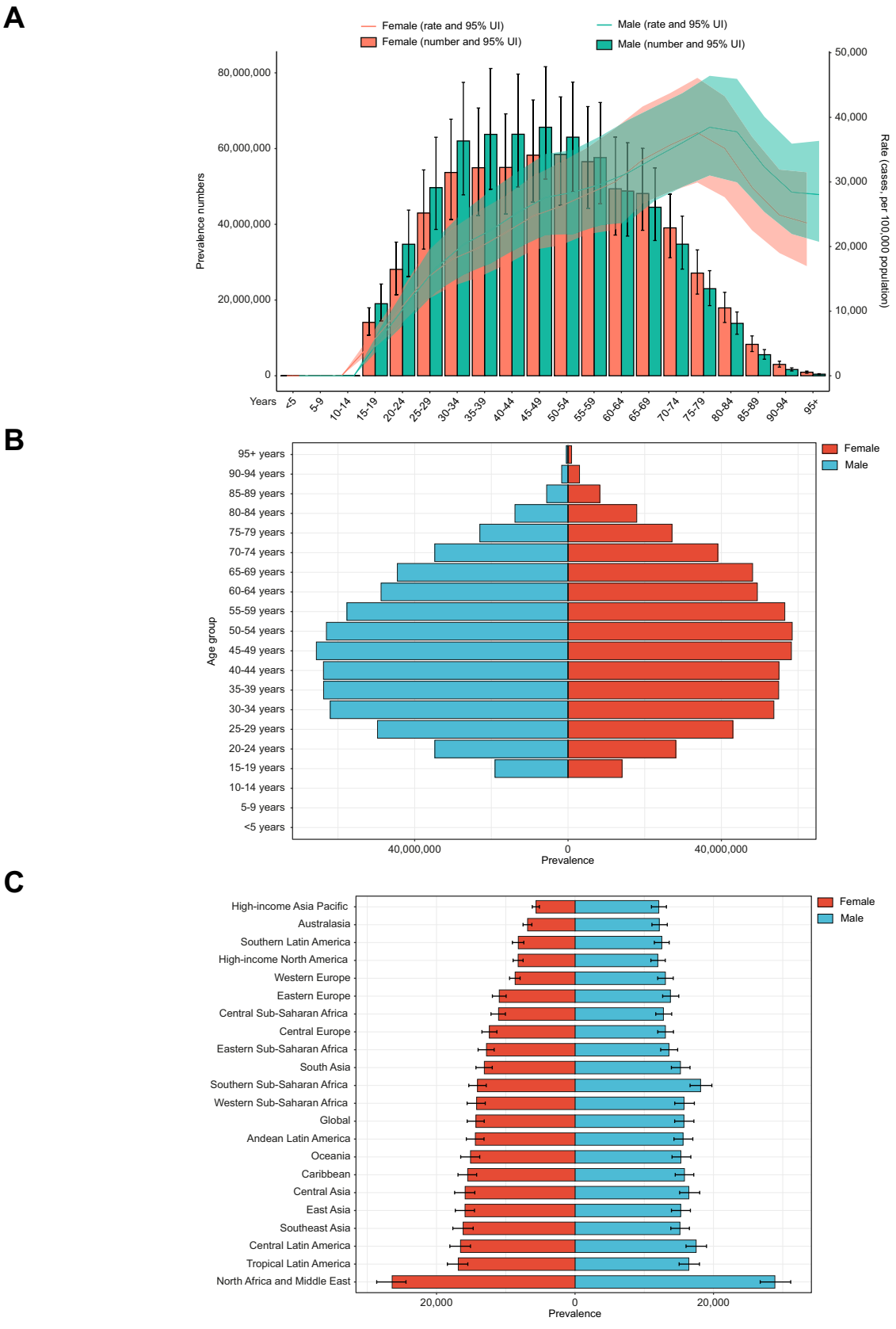

Fig. 3. Total number of prevalent cases and age-standardized point prevalence rates of MASLD per 100,000 population by age and sex in 2021. (A) Prevalence and rate of disease by age and sex. Dashed lines indicate 95% upper and lower uncertainty intervals (UIs). (B) Age and sex distribution of disease prevalence. (C) Regional distribution of disease prevalence by sex.

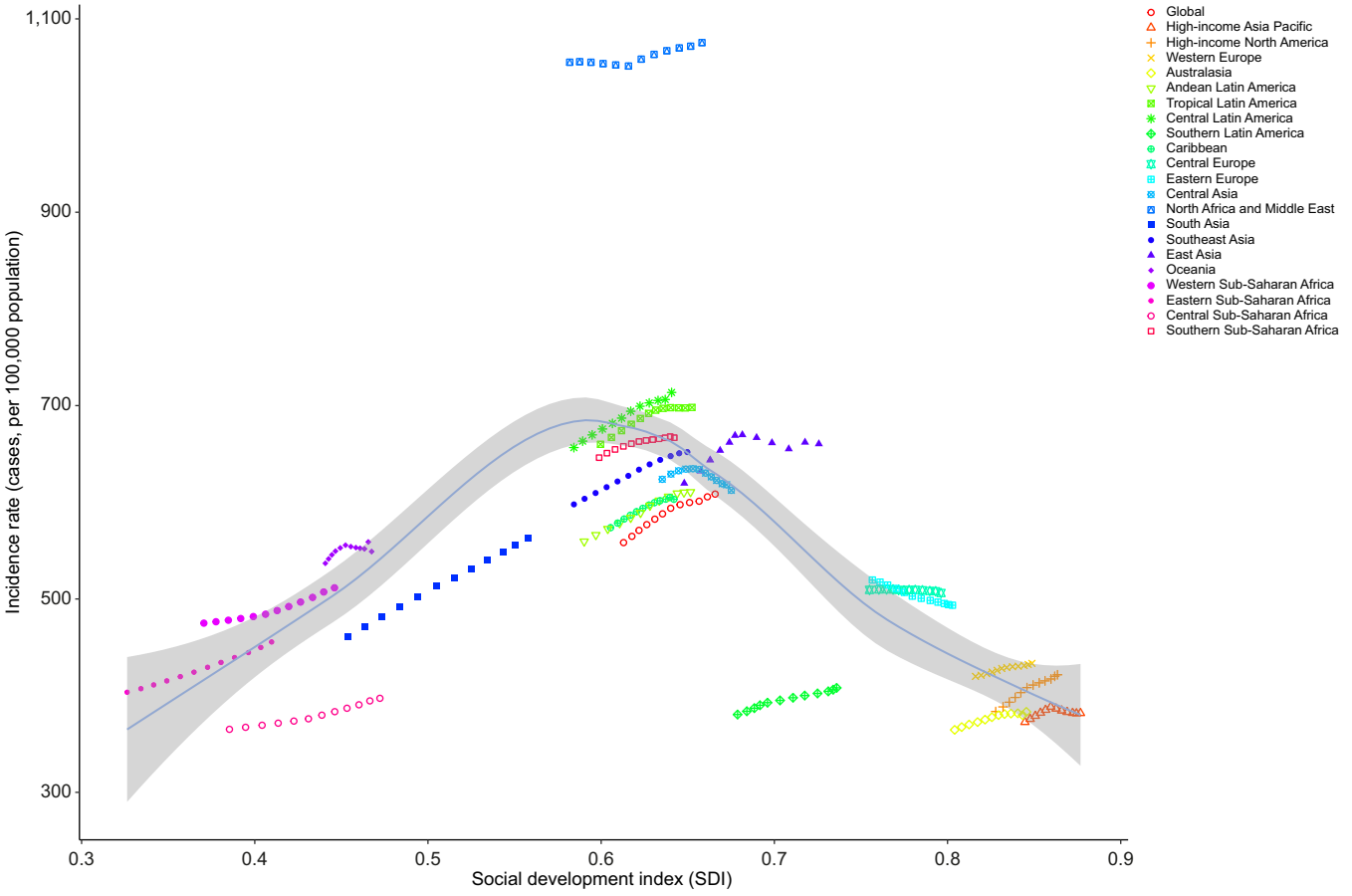

Fig. 4. Age-standardized incidence rates of MASLD per 100,000 population for 21 Global Burden of Disease regions by sociodemographic index (SDI) between 2010 and 2021. The purple line represents expected values based on the sociodemographic index and incidence rates in all locations. Twelve points are plotted for each Global Burden of Disease region and show the observed age-standardized incidence rates for that region from 2010 to 2021.

to specific dietary habits, lifestyle factors, and genetic susceptibility in these regions. Furthermore, China, India, and Sudan experienced the most significant increases in MASLD prevalence from 2010 to 2021. The rapid economic development and lifestyle changes in these countries might be the primary drivers for the rising prevalence of MASLD.

The present study reported a higher prevalence of MASLD in men than in women. In 2021, the global age-standardized point prevalence rate of MASLD for men was 15,731.4 cases per 100,000 individuals, whereas for women, it was 14,310.6 cases per 100,000 individuals. A recent meta-analysis revealed that the global prevalence of MASLD is higher than previously estimated and continues to rise at an alarming rate.[20] There is a notably higher incidence and prevalence of MASLD in men than women.[20] Sex-related differences in MASLD prevalence and incidence could be attributed to various factors, such as different plasma hormone levels, menopausal status, body fat distribution, and coexisting metabolic traits.[21] This study also shows that MASLD prevalence peaked at different ages for men and women. In men, the prevalence of the disease peaked in the 45–49 age group and gradually decreased. For women, the prevalence of MASLD reached its highest value in the 50–54 age group. This age disparity might indicate distinct physiological changes in metabolic function and hepatic lipid accumulation between men and women. Moreover, the disparity observed between affected ages in men and women might also be attributable to the menopausal status, as menopause is associated with an increased risk for many metabolic diseases.[22] In our study, women had higher MASLD-related YLDs than men. Studies have shown that compared with men, women tend to report a more pronounced decline in the quality of life and a greater symptom perception when facing chronic diseases.[23] Women have greater amounts of visceral and subcutaneous fat depots, especially in the postmenopausal period, which may be associated with higher levels of inflammatory biomarkers related to MASLD, thereby exacerbating disease progression and quality of life impairment.[24]

SDI is a composite indicator that assesses the socioeconomic development level of a country or region, considering factors such as *per capita* income, education level, and fertility rate. The GBD study indicates that SDI levels may significantly influence the incidence rates of MASLD. Generally, MASLD is most prevalent in countries with intermediate SDI levels, likely a result of the impact of economic growth and lifestyle changes. Conversely, in countries with high SDI levels, the incidence of MASLD tends to be lower, possibly because of improved health education and preventive strategies. The study by Wu *et al.*[25] suggested that the prevalence of MASLD exhibited varying trends worldwide from 1990 to 2019. MASLD prevalence was

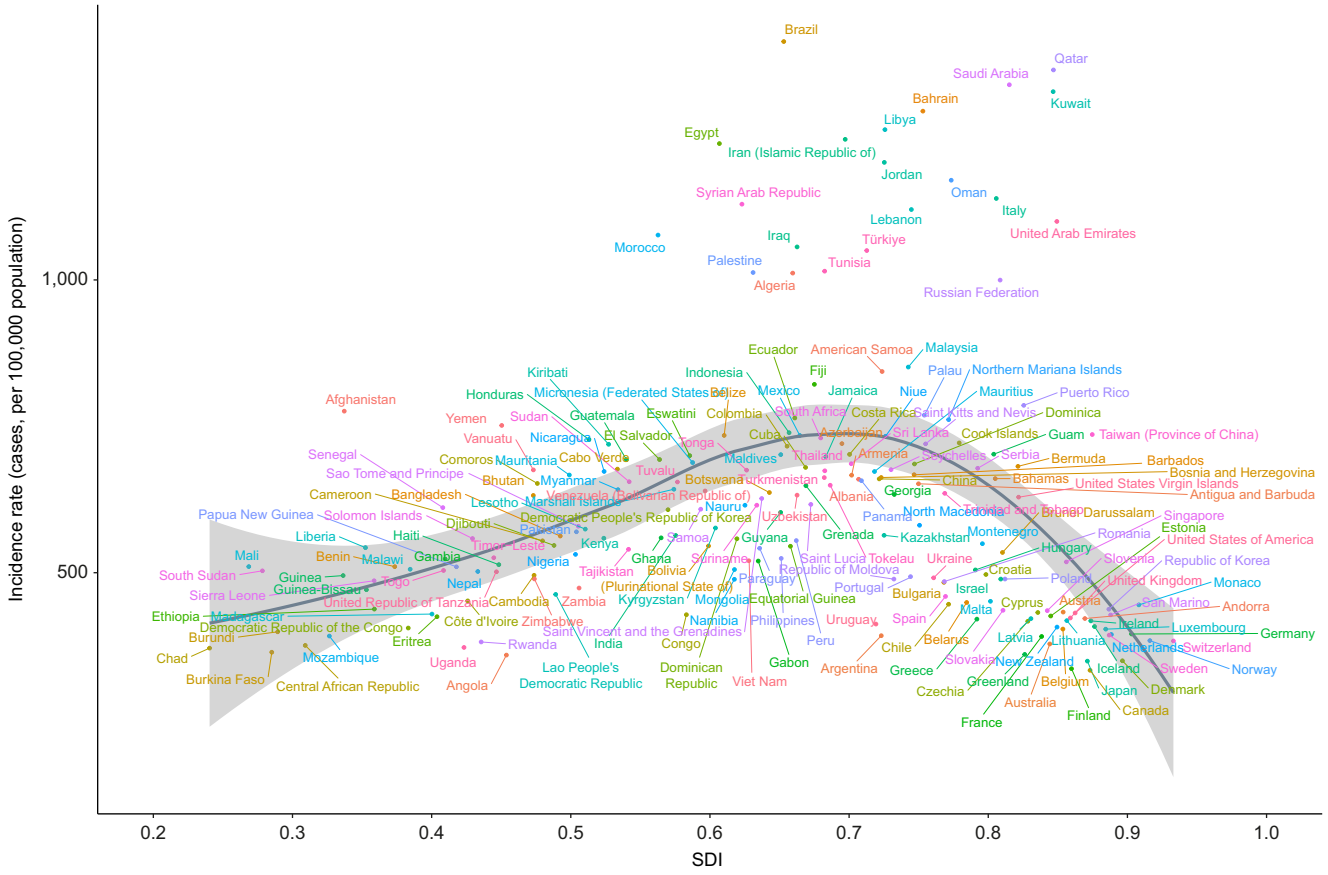

Fig. 5. Age-standardized incidence rates of MASLD per 100,000 population by 204 countries and sociodemographic index (SDI) in 2021. The black line represents expected values based on the sociodemographic index and incidence rates in 204 countries. Each point shows observed age-standardized incidence rates for a specified country in 2021.

the highest in the moderate SDI group and the lowest in the low SDI group.

The analysis of GBD 2021 data in our study can substantially support policymakers and public health experts. Firstly, it is essential to enhance health education to increase public awareness about MASLD and its major cardiometabolic risk factors. Encouraging a healthy diet, promoting physical activity, and reducing obesity rates may effectively lower the incidence rates of MASLD from common sense. However, further research is needed to confirm this relationship. Secondly, the healthcare system should focus on early screening and diagnosis of MASLD. Thirdly, we must pay attention to the clinical complications related to MASLD.[26] This condition is not only associated with severe liver-related outcomes, such as cirrhosis and HCC, but it is also closely linked to the development of cardiovascular disease.[27] Therefore, management of MASLD should focus on maintaining and restoring liver health and including a comprehensive assessment and intervention of the patient's cardiovascular health status to reduce overall health risks. Furthermore, advocating for and implementing effective treatments, such as lifestyle intervention and pharmacotherapies, may represent a reasonable approach to potentially reduce symptoms and risk of long-term complications in people with MASLD. The recent FDA approval of resmetirom, a liver-targeted thyroid hormone receptor-β selective drug, offers hope for the treatment of adults with non-cirrhotic MASH and moderate to advanced fibrosis.[28] Resmetirom has shown efficacy in reducing hepatic fat content, improving liver histology, and ameliorating liver damage biomarkers while favorably affecting plasma lipid profile. Implementing resmetirom treatment will require careful patient selection and reliance on non-invasive liver fibrosis tests, marking a significant advancement in MASLD/MASH treatment and highlighting the need for ongoing research and therapeutic development.[29] While the data in the present study illustrate the magnitude of the problem and the increasing trends of MASLD over time, these findings could also inform policy decisions. With appropriate actions, it is possible that the observed global, regional and national trends of MASLD could be reversed, improving the individual's quality of life and reducing the overall health burden. However, it is essential to acknowledge that these outcomes remain hypothetical at this stage, as further evidence is needed to support these conclusions.

This study has certain limitations that are strictly inherent to the GBD database and need to be acknowledged. Firstly, the accuracy and completeness of GBD database could be hindered by variations in data collection and reporting standards across different countries and regions. This variability might impact the comparability and interpretability of the data. Secondly, while the SDI utilized in the study is a composite measure, it may not entirely capture the socioeconomic status of diverse regions and its implications on MASLD. Thirdly, the

GBD study, which estimates etiology-specific liver deaths through proportion models, has been criticized for its potential inaccuracies in measuring the trends of MASLD mortality.[30] Low-income countries may underreport the incidence and prevalence rates of MASLD, which could underestimate the exact rates in this group. That said, we chose to use the GBD model because of its comprehensive global scope and the ability to provide standardized comparisons across different regions and periods, which are essential for analyzing broad epidemiological patterns and informing public health strategies. In the future, we plan to conduct more detailed analyses considering these risk factors to provide a more comprehensive explanation of the epidemiological characteristics of MASLD. Fourthly, although the data used in this study primarily originate from the NAFLD era, it is important to acknowledge the highly consistent overlap between NAFLD and MASLD nomenclatures. NAFLD and MASLD are not two terms entirely identical, as MASLD always incorporates metabolic dysfunction in its definition, but because of the consistent overlap between the two conditions, using MASLD as the primary term for this study is justified. Fifthly, no stratification considering cardiovascular risk factors has been made throughout the study. While Zhang *et al.*'s[17] study does mention cardiovascular risk factors, their analysis of these factors is not specific to the MASLD population. Instead, it encompasses the general population as a whole. This broad approach lacks specificity and may fail to elucidate the unique characteristics of cardiovascular risk factors within the MAFLD cohort.[17] We recognize that cardiovascular risk factors may provide additional insights into the observed differences. In future studies, we plan to explicitly integrate these cardiovascular risk factors to better clarify their specific role in the differences in the rates of MASLD observed between countries and regions. Additionally, our data presentation format is aligned with the style used in most current GBD studies. Although the GBD database contains relevant data on type 2 diabetes and obesity, these data cannot be correlated or matched with MASLD, meaning that a subgroup analysis of MASLD epidemiological data based on diabetes and obesity is not feasible.

Future research should leverage the granular data provided by this study to delve deeper into the regional disparities in MASLD prevalence and incidence.[4] Understanding the underlying causes of these differences, particularly the socioeconomic factors driving MASLD prevalence in countries with varying SDI levels, could reveal more about the U-shaped relationship between economic development and MASLD burden. Moreover, identifying region-specific risk factors, such as genetic predispositions, dietary habits, or healthcare access, could help design more targeted public health interventions.[2] Additional research should also evaluate the effectiveness of socioeconomic policies to reduce MASLD risk in intermediate SDI regions, where the disease burden is most pronounced. Additionally, future studies should uncover the impact of lifestyle interventions and new pharmacological therapies, such as resmetirom, on the long-term outcomes of MASLD.[28] Understanding how these metabolic disorders may influence MASLD onset and progression will be key to refining treatment and prevention strategies.

In conclusion, this updated analysis of the GBD study examines the global burden of MASLD from 2010 to 2021, revealing a significant increase in the prevalence and incidence and YDL rates of this metabolic liver disease. Countries with intermediate SDI levels show the highest burden, likely a result of rapid economic and lifestyle changes. China, India, and Sudan also showed substantial increases. Men exhibit a higher prevalence of MASLD than women, although women are more affected in terms of YLDs, with the peak age of prevalence of MASLD differing between sexes. Despite limitations like data variability, we believe that the study can offer important insights into MASLD's global trends, guiding public health strategies and early intervention efforts in high-burden regions.

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Abbreviations

ASR, age-standardized rate; GBD, Global Burden of Diseases; HCC, hepatocellular carcinoma; MAFLD, metabolic dysfunction-associated fatty liver disease; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; NAFLD, non-alcoholic fatty liver disease; SDI, sociodemographic index; SLD, steatotic liver disease; UI, uncertainty interval; YLDs, years lived with disability.

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Conflicts of interest

CDB has received grant support from Echosens. YY is a consultant to Zydus and Novo Nordisk. WK reports grants from Glaxo-SmithKline, Gilead, Novartis, Pfizer, Roche, Springbank, Ildong, Galmed, Dicerna, Enyo, Hanmi, Novo Nordisk, and KOBIOLABS; consulting fees from Boehringer Ingelheim, Novo Nordisk, Standigm, Daewoong, TSD Life Sciences Ildong, Olix Pharma, HK Inoen, and KOBIOLABS; honoraria for lectures from Ildong, Samil, and Novo Nordisk, and owns stocks in KOBIOLABS and Lepidyne and he is the founder of Remedygen. GS reports honoraria from Merck, Gilead, AbbVie, Novonordisk, and Pfizer, and unrestricted research funding from Theratecnologies Inc. VW-SW reports grants from Gilead Sciences; consulting fees from AbbVie, Boehringer Ingelheim, Echosens, Gilead Sciences, Intercept, Inventiva, Novo Nordisk, Pfizer, TARGET PharmaSolutions; honoraria for lectures from Abbott, AbbVie, Gilead Sciences, Novo Nordisk and he is Chairman of Subspecialty Board of Gastroenterology and Hepatology, Hong Kong College of Physicians and Co-founder of Illuminatio Medical Technology Limited. JB reported receiving grants and personal fees from Echosens. W-KC is a consultant or advisory board member for Abbott, Roche, AbbVie, Boehringer Ingelheim and Novo Nordisk; and a speaker for Abbott, Novo Nordisk, Echosens, Viatris and Hisky Medical. JDR received consultancy fees from Falk, Gilead, Pfizer and a speaker honorarium from Takeda. LV reports consulting fees from Gilead, Pfizer, Astra Zeneca, Novo Nordisk, Intercept pharmaceuticals, Diatech Pharmacogenetics, IONIS, and Viatris; honoraria from MSD, Gilead, AlfaSigma, AbbVie, and Resalis, and grants from Gilead. JMS serves as a consultant for Akero, Alentis Therapeutics, Astra Zeneca, Apollo Endosurgery, Boehringer Ingelheim, GSK, Ipsen, Inventiva Pharma, Madrigal, MSD, Northsea Therapeutics, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi, and Siemens Healthineers. He has received research funding from Gilead Sciences, Boehringer Ingelheim, and Siemens Healthcare GmbH. He holds stock options in AGED diagnostics and Hepta Bio. He has also received speaker honorarium from Gilead Sciences, Advanz, Echosens, MedPublico GmbH. MR-G reported receiving personal fees from Echosens. SUK reported personal fees from Gilead Sciences, GSK, Bayer, Eisai, AbbVie, Echosens, MSD, Bristol-Myers Squibb, AstraZeneca, and grants from AbbVie, Bristol-Myers Squibb, and Gilead Sciences. PNN reported receiving grants from Novo Nordisk, advisory board and personal consulting fees, honoraria for lectures and travel expenses from Novo Nordisk, personal consulting and advisory board fees from Boehringer Ingelheim, Gilead, Intercept, Poxel Pharmaceuticals, Bristol-Myers Squibb, Pfizer, MSD, Sun Pharma, Eli Lilly, Madrigal, GSK, and nonfinancial support for educational events from AiCME. AS reported receiving grants from Intercept, Merck, personal consulting fees from Gilead, Pfizer, Genentech, ALnylam, Regeneron, Zydus, LG chem, Hanmi, Madrigal, Path AI, and 89 Bio, grants and personal consulting fees from Eli Lilly, Novo Nordisk, Boehringer Ingelheim, Novartis, and Histoindex, and stock options from Genfit, Tiziana, Durect, Inversago, and Galmed. LAA reports consulting fees from Novo Nordisk, Pfizer, Gilead, and CSL Behring. HH reported personal fees from AstraZeneca, Bristol-Myers Squibb, MSD, Novo Nordisk, Boehringer Ingelheim, KOWA, and GW Phara outside the submitted work, and grants from AstraZeneca, Echosens, Gilead Sciences, Intercept, MSD, Novo Nordisk, and Pfizer outside the submitted work. JG serves on Advisory Boards and receives honoraria for talks from Novo Nordisk, Astra Zeneca, Roche, BMS, Pfizer, Cincera, Pharmaxis, Gilead, AbbVie, and Boehringer Ingelheim. M-HZ has received honoraria for lectures from AstraZeneca, Hisky Medical Technologies, and Novo Nordisk, and consulting fees from Boehringer Ingelheim. No other disclosures were reported.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Conceptualization: GF, M-HZ, FY, MM. **Data curation and formal analysis:** GF, M-HZ, FY. **Writing, review, and editing:** GF, GT, CDB, YY, VW-SW, CRAL, LAA, JB, GP, ME-K, NM-S, SS, LC, W-KC, FY, ST, HC-P, HHY, WK, MR-G, AN, KMW, SUK, AGH, GS, PO, JDR, ML-P, HG, MA-M, SH, NP, KA, QP, MTL, VI, MM, MA, AS, SKS, NCL, LV, PNN, HH, SP, HY-J, JMS, MICF, IL, GA, A-NE, AT, AIS, AL,

FMS, KM, MA-M, MWA, MB, ND, MA, SB, SA A-B, JR, WY, AA, CKO, MS, YJW, JG, M-HZ. All authors approve the final version of the manuscript, including the authorship list and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability statement

Data are available upon reasonable request.

Supplementary data

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Author names in bold designate shared co-first authorship

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