

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

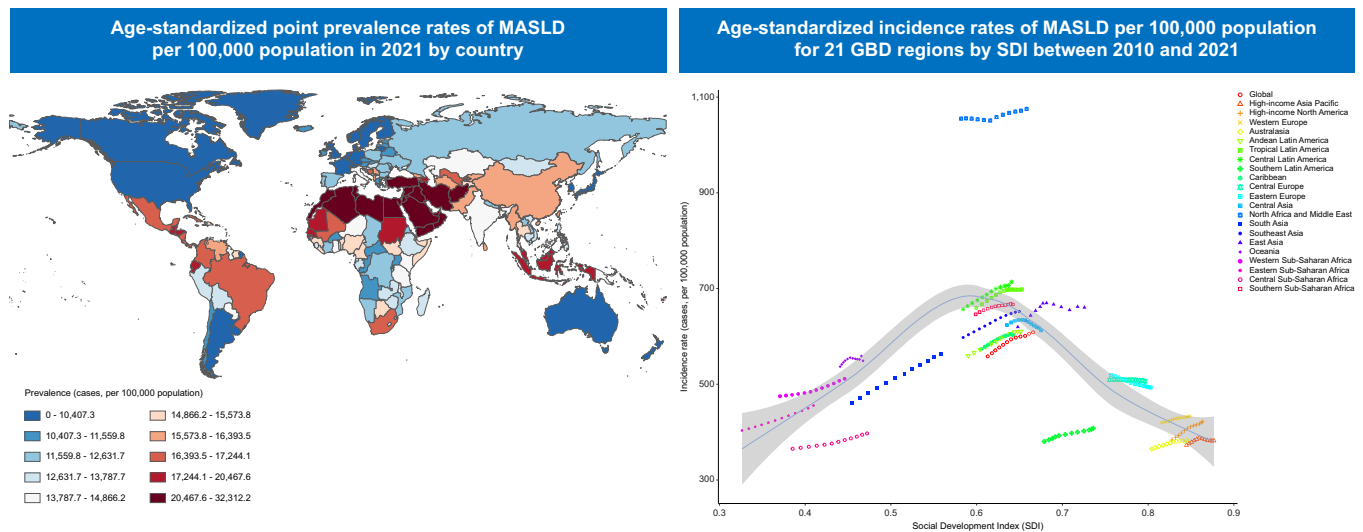
## Authors

Gong Feng, Giovanni Targher, Christopher D. Byrne, ..., Yu Jun Wong, Jacob George, Ming-Hua Zheng

## Correspondence

zhengmh@wmu.edu.cn (M.-H. Zheng).

## 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.

<https://doi.org/10.1016/j.jhepr.2024.101271>

# Global burden of metabolic dysfunction-associated steatotic liver disease, 2010 to 2021<sup>☆</sup>

Gong Feng<sup>1,2</sup>, Giovanni Targher<sup>3,4</sup>, Christopher D. Byrne<sup>5</sup>, Yusuf Yilmaz<sup>6,7</sup>, Vincent Wai-Sun Wong<sup>8</sup>, Cosmas Rinaldi Adithya Lesmana<sup>9,10,11</sup>, Leon A. Adams<sup>12,13</sup>, Jerome Boursier<sup>14,15</sup>, George Papatheodoridis<sup>16</sup>, Mohamed El-Kassas<sup>17,18</sup>, Nahum Méndez-Sánchez<sup>19,20</sup>, Silvia Sookoian<sup>21,22,23</sup>, Laurent Castera<sup>24</sup>, Wah-Kheong Chan<sup>25</sup>, Feng Ye<sup>2</sup>, Sombat Treeprasertsuk<sup>26</sup>, Helena Cortez-Pinto<sup>27</sup>, Hon Ho Yu<sup>28</sup>, Won Kim<sup>29,30</sup>, Manuel Romero-Gómez<sup>31</sup>, Atsushi Nakajima<sup>32</sup>, Khin Maung Win<sup>33</sup>, Seung Up Kim<sup>34</sup>, Adriaan G. Holleboom<sup>35</sup>, Giada Sebastiani<sup>36</sup>, Ponsiano Ocama<sup>37</sup>, John D. Ryan<sup>38</sup>, Monica Lupşor-Platon<sup>39</sup>, Hasmik Ghazinyan<sup>40</sup>, Mamun Al-Mahtab<sup>41</sup>, Saeed Hamid<sup>42</sup>, Nilanka Perera<sup>43</sup>, Khalid A. Alswat<sup>44</sup>, Qiuwei Pan<sup>45</sup>, Michelle T. Long<sup>46</sup>, Vasily Isakov<sup>47</sup>, Man Mi<sup>1</sup>, Marco Arrese<sup>48</sup>, Arun J. Sanyal<sup>49</sup>, Shiv Kumar Sarin<sup>50</sup>, Nathalie Carvalho Leite<sup>51</sup>, Luca Valenti<sup>52,53</sup>, Philip N. Newsome<sup>54</sup>, Hannes Hagström<sup>55,56</sup>, Salvatore Petta<sup>57</sup>, Hannele Yki-Järvinen<sup>58,59</sup>, Jörn M. Schattenberg<sup>60</sup>, Marlen I. Castellanos Fernández<sup>61</sup>, Isabelle A. Leclercq<sup>62</sup>, Gulnara Aghayeva<sup>63</sup>, Abdel-Naser Elzouki<sup>64,65,66</sup>, Ali Tumi<sup>67</sup>, Ala I. Sharara<sup>68</sup>, Asma Labidi<sup>69</sup>, Faisal M. Sanai<sup>70</sup>, Khaled Matar<sup>71</sup>, Maen Al-Mattooq<sup>72</sup>, Maisam Waid Akroush<sup>73</sup>, Mustapha Benazzouz<sup>74</sup>, Nabil Debzi<sup>75</sup>, Maryam Alkhatry<sup>76</sup>, Salma Barakat<sup>77</sup>, Said A. Al-Busafi<sup>78</sup>, John Rwegasha<sup>79</sup>, Wah Yang<sup>80</sup>, Agyei Adwoa<sup>81,82</sup>, Christopher Kenneth Opio<sup>83</sup>, Mohammadjavad Sotoudeheian<sup>84,85</sup>, Yu Jun Wong<sup>86,87</sup>, Jacob George<sup>88</sup>, Ming-Hua Zheng<sup>89,90,\*</sup>

JHEP Reports 2025. vol. 7 | 1–12



**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.

© 2024 The Author(s). Published by Elsevier B.V. on behalf of European Association for the Study of the Liver (EASL). This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 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.<sup>1,2</sup> 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.<sup>3</sup> 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).<sup>4</sup>

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

<sup>☆</sup> Given their roles as Co-Editor and Associate Editor respectively, Jacob George and Jörn Schattenberg had no involvement in the peer-review of this article and had no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to the Co-Editor Virginia Hernández-Gea.

\* Corresponding author: Address: MAFLD Research Center, Department of Hepatology, The First Affiliated Hospital of Wenzhou Medical University, Nanbaixiang Street, Ouhai District, Wenzhou 325000, Zhejiang Province, China. Tel: +86 577 5557 9611; fax: +86 577 5557 8522.

E-mail address: zhengmh@wmu.edu.cn (M.-H. Zheng).

<https://doi.org/10.1016/j.jhepr.2024.101271>



Metrics and Evaluation at the University of Washington, USA.<sup>5,6</sup> The GBD study is considered one of the most extensive burden of disease studies conducted to date.<sup>7</sup> While Paik *et al.*<sup>8</sup> 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.<sup>9-11</sup> 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.<sup>12</sup> 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.<sup>13</sup> 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.<sup>14</sup> 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.<sup>15</sup> 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.<sup>1</sup> 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  $\geq 15$  years), and economic prosperity (lag-distributed income per capita).<sup>16</sup> 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.<sup>16</sup>

### 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.<sup>16</sup> 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.<sup>16</sup> 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.**

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, %)
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

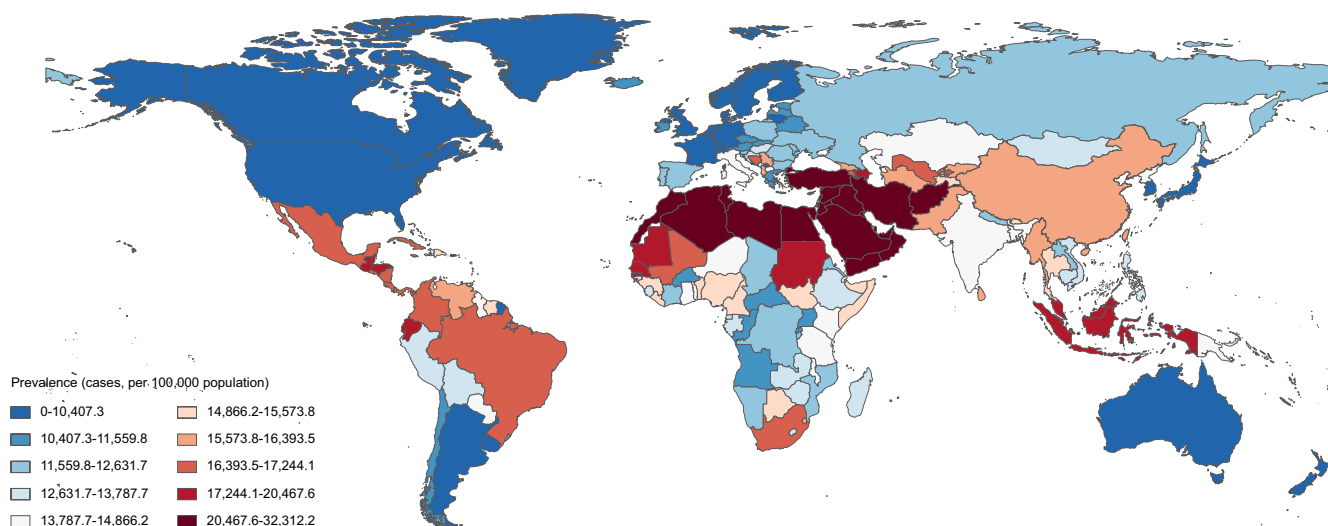


Fig. 1. Age-standardized point prevalence rates of MASLD per 100,000 population in 2021 by country.

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.*<sup>17</sup> selected the period from 1990 to 2021, while Danpanichkul *et al.*<sup>18</sup> 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.*<sup>17</sup> 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.<sup>17</sup> Danpanichkul *et al.*<sup>18</sup> did not analyze incidence and YLDs. Allen *et al.*<sup>19</sup> 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

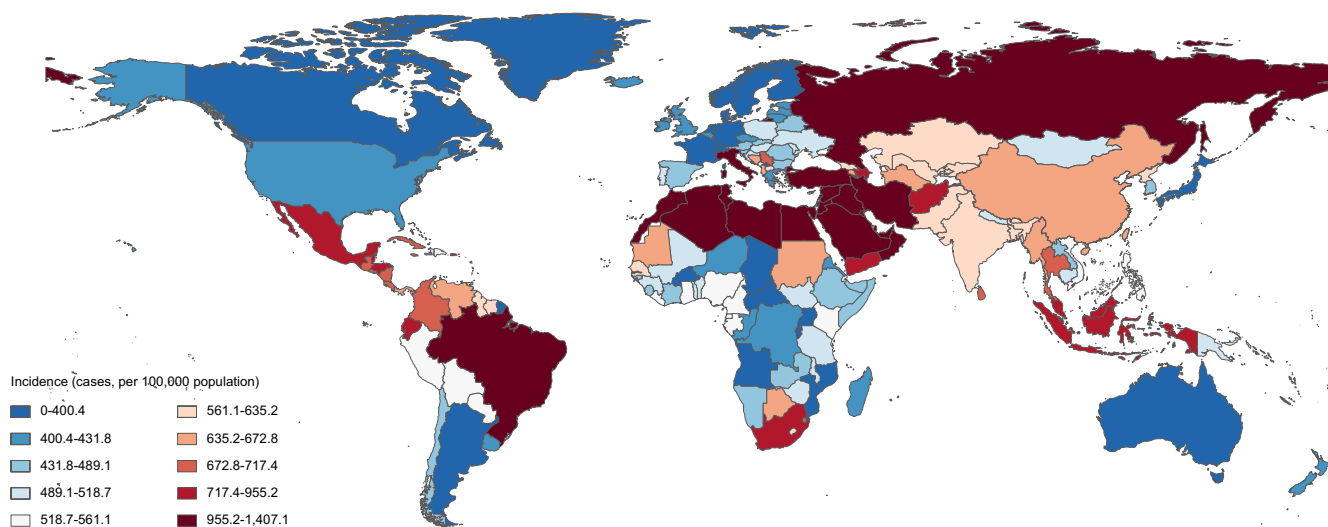
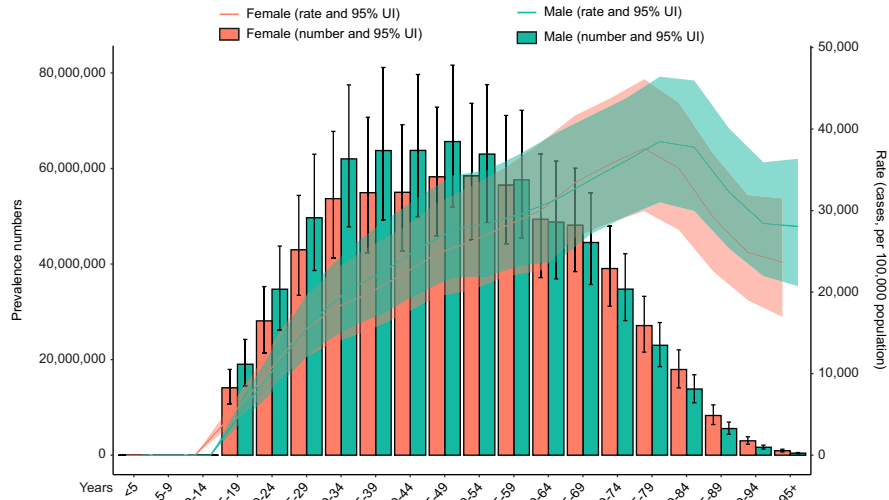
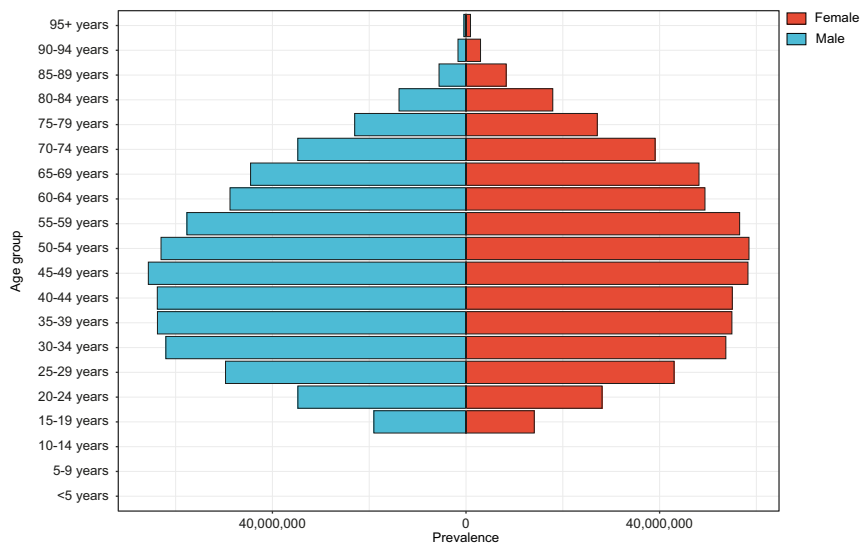


Fig. 2. Age-standardized annual incidence rates of MASLD per 100,000 people in 2021 by country.

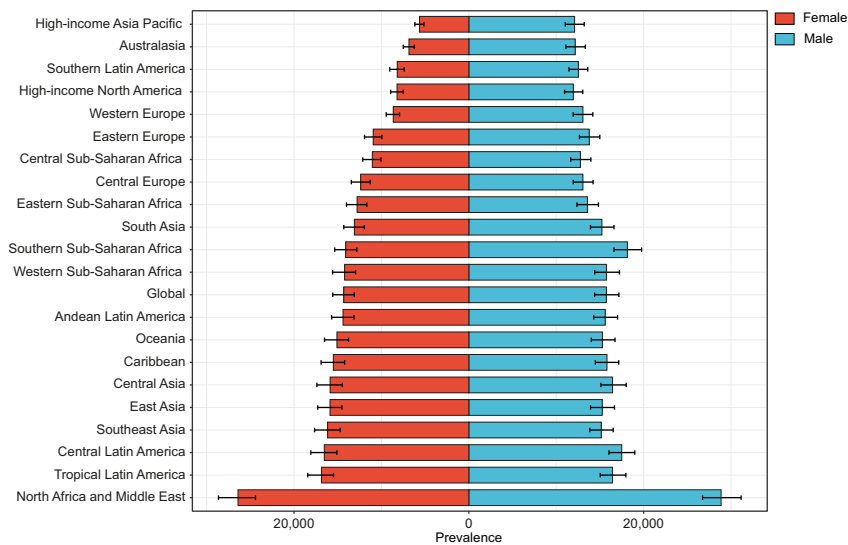
A



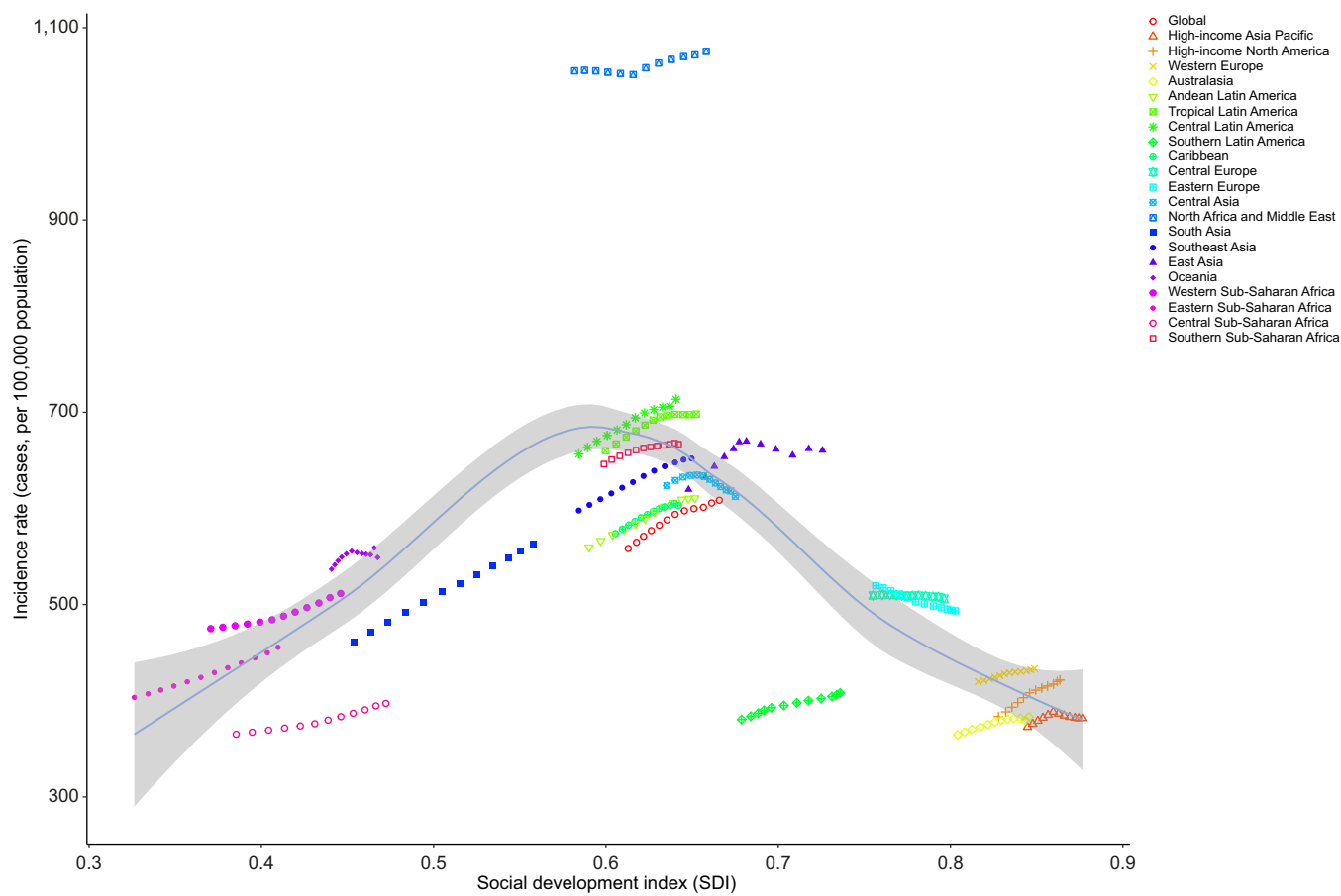
B



C



**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.<sup>20</sup> There is a notably higher incidence and prevalence of MASLD in men than women.<sup>20</sup> 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.<sup>21</sup> 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.<sup>22</sup> 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.<sup>23</sup> Women have greater amounts of visceral and subcutaneous fat depots, especially in the post-menopausal period, which may be associated with higher levels of inflammatory biomarkers related to MASLD, thereby exacerbating disease progression and quality of life impairment.<sup>24</sup>

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.*<sup>25</sup> suggested that the prevalence of MASLD exhibited varying trends worldwide from 1990 to 2019. MASLD prevalence was



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.<sup>30</sup> 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<sup>17</sup> 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.<sup>17</sup> 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.<sup>4</sup> 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.<sup>2</sup> 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 resmetrom, on the long-term outcomes of MASLD.<sup>28</sup> 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.

## Affiliations

<sup>1</sup>*Xi'an Medical University, Xi'an, China;* <sup>2</sup>*The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China;* <sup>3</sup>*Department of Medicine, University of Verona, Verona, Italy;* <sup>4</sup>*Metabolic Diseases Research Unit, IRCSS Sacro Cuore - Don Calabria Hospital, Negrar di Valpolicella, Italy;* <sup>5</sup>*Southampton National Institute for Health and Care Research Biomedical Research Centre, University Hospital Southampton and University of Southampton, Southampton General Hospital, Southampton, UK;* <sup>6</sup>*Department of Gastroenterology, School of Medicine, Recep Tayyip Erdoğan University, Rize, Turkey;* <sup>7</sup>*The Global NASH Council, Washington, DC, USA;* <sup>8</sup>*Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China;* <sup>9</sup>*Hepatobiliary Division, Department of Internal Medicine, Dr. Cipto Mangunkusumo National General Hospital, Medical Faculty Universitas Indonesia, Jakarta, Indonesia;* <sup>10</sup>*Digestive Disease & GI Oncology Center, Medistra Hospital, Jakarta, Indonesia;* <sup>11</sup>*Gastrointestinal Cancer Center, Mochtar Riyadi Comprehensive Cancer Center (MRCCC) Siloam Semanggi Hospital, Jakarta, Indonesia;* <sup>12</sup>*Department of Hepatology, Sir Charles Gairdner Hospital, Perth, Australia;* <sup>13</sup>*Medical School, The University of Western Australia, Perth, Australia;* <sup>14</sup>*HIFIH Laboratory, UPRES EA3859, Angers University, Angers, France;* <sup>15</sup>*Hepato-Gastroenterology and Digestive Oncology Department, Angers University Hospital, Angers, France;* <sup>16</sup>*Department of Gastroenterology, Laiko General Hospital, Medical School of National and Kapodistrian University of Athens, Athens, Greece;* <sup>17</sup>*Endemic Medicine Department, Faculty of Medicine, Helwan University, Cairo, Egypt;* <sup>18</sup>*Steatotic Liver Disease Study Foundation in Middle East and North Africa (SLMENA), Cairo, Egypt;* <sup>19</sup>*Liver Research Unit, Medica Sur Clinic & Foundation, Mexico City, Mexico;* <sup>20</sup>*Faculty of Medicine, National Autonomous University of Mexico, Mexico City, Mexico;* <sup>21</sup>*Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina;* <sup>22</sup>*Faculty of Health Science, Maimónides University, Buenos Aires, Argentina;* <sup>23</sup>*Clinical and Molecular Hepatology, Translational Health Research Center (GENITRES), Maimónides University, Buenos Aires, Argentina;* <sup>24</sup>*Université Paris Cité, UMR1149 (CRI), INSERM, Paris, France, Service d'Hépatologie, Hôpital Beaujon, Assistance Publique-Hôpitaux de Paris (AP-HP), Clichy, France;* <sup>25</sup>*Gastroenterology and Hepatology Unit, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia;* <sup>26</sup>*Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand;* <sup>27</sup>*Clinica Universitaria de Gastroenterología, Laboratório de Nutrição, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal;* <sup>28</sup>*Department of Gastroenterology and Hepatology, Kiang Wu Hospital, Macau, China;* <sup>29</sup>*Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea;* <sup>30</sup>*Division of Gastroenterology and Hepatology, Department of Internal Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul, Korea;* <sup>31</sup>*UCM Digestive Diseases, University Hospital Virgen del Rocío, Institute of Biomedicine of Seville (CSIC/HUVR/US), Ciberehd, University of Seville, Sevilla, Spain;* <sup>32</sup>*Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan;* <sup>33</sup>*Department of Medical Research, Union of Myanmar, Naypyidaw, Myanmar;* <sup>34</sup>*Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul, South Korea;* <sup>35</sup>*Department of Vascular Medicine, Amsterdam University Medical Centers, Amsterdam, The Netherlands;* <sup>36</sup>*Division of Gastroenterology and Hepatology, Chronic Viral Illness Service, McGill University Health Centre, Royal Victoria Hospital, Montreal, Canada;* <sup>37</sup>*Department of Medicine, Makerere University of College of Health Sciences, Kampala, Uganda;* <sup>38</sup>*Department of Hepatology, RCSI School of Medicine and Medical Sciences, Dublin/Beaumont Hospital, Dublin, Ireland;* <sup>39</sup>*Department of Medical Imaging, "Prof. Dr. Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania;* <sup>40</sup>*Gastroenterology and Hepatology Service, Yerevan Scientific Medical Center, Yerevan, Armenia;* <sup>41</sup>*Department of Hepatology, Bangabandhu Sheikh*

Mujib Medical University, Dhaka, Bangladesh; <sup>42</sup>Department of Medicine, Aga Khan University, Karachi, Pakistan; <sup>43</sup>Department of Medicine, University of Sri Jayawardenepura, Nugegoda, Sri Lanka; <sup>44</sup>Liver Disease Research Center, Department of Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia; <sup>45</sup>Department of Gastroenterology and Hepatology, Erasmus MC-University Medical Center, Rotterdam, The Netherlands; <sup>46</sup>Section of Gastroenterology, Boston Medical Center, Boston University School of Medicine, Boston, MA, USA; <sup>47</sup>Department of Gastroenterology and Hepatology, Federal Research Center for Nutrition, Biotechnology and Food Safety, Moscow, Russian Federation; <sup>48</sup>Departamento de Gastroenterología, Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile; <sup>49</sup>Stravitz-Sanyal Institute for Liver Disease and Metabolic Health, VCU School of Medicine, Richmond, VA, USA; <sup>50</sup>Department of Hepatology and Liver Transplant, Institute of Liver and Biliary Sciences, New Delhi, India; <sup>51</sup>Division of Hepatology, Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil; <sup>52</sup>Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy; <sup>53</sup>Precision Medicine and Biological Resource Center, Fondazione IRCCS Ca' Granda Ospedale Policlinico Milano, Milan, Italy; <sup>54</sup>Institute of Hepatology, Faculty of Life Sciences and Medicine, King's College London and King's College Hospital, London, UK; <sup>55</sup>Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden; <sup>56</sup>Division of Hepatology, Department of Upper GI Diseases, Karolinska University Hospital, Huddinge, Stockholm, Sweden; <sup>57</sup>Sezione di Gastroenterologia, PROMISE, University of Palermo, Palermo, Italy; <sup>58</sup>Department of Medicine, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; <sup>59</sup>Minerva Foundation Institute for Medical Research, Helsinki, Finland; <sup>60</sup>Department of Internal Medicine II, Saarland University Medical Center, Homburg, Germany; <sup>61</sup>Institute of Gastroenterology, University of Medical Sciences of Havana, Havana, Cuba; <sup>62</sup>UCLouvain, Université catholique de Louvain, Institute of Experimental and Clinical Research, Laboratory of Hepato-Gastroenterology, Brussels, Belgium; <sup>63</sup>Internal Diseases Department, Baku branch, Sechenov Medical University, Baku, Azerbaijan; <sup>64</sup>Department of Medicine, Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar; <sup>65</sup>Department of Medicine, College of Medicine, Qatar University, Doha, Qatar; <sup>66</sup>Department of Medicine, Weill Cornell Medical College, Doha, Qatar; <sup>67</sup>Department of Medicine, Tripoli University, Tripoli, Libya; <sup>68</sup>Division of Gastroenterology and Hepatology, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon; <sup>69</sup>Department of Gastroenterology and Hepatology, Rabta Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia; <sup>70</sup>Gastroenterology Section, Department of Medicine, King Abdulaziz Medical City, King Abdullah International Medical Research Center, Jeddah, Saudi Arabia; <sup>71</sup>Gastroenterology Department, European Gaza Hospital, Gaza, Palestine; <sup>72</sup>Department of Gastroenterology and Hepatology, Jaber AlAhmad & Farwaniya Hospital, Al Ahmadi, Kuwait; <sup>73</sup>Department of Gastroenterology and Hepatology, the Mediterranean Taskforce for Cancer Control (MTCC), Amman, Jordan; <sup>74</sup>Service of Medicine C, Centre Hospitalier Universitaire Ibn Sina, Rabat, Morocco; <sup>75</sup>Service d'Hépatologie, CHU Mustapha Bacha, Alger, Algeria; <sup>76</sup>Department of Gastroenterology, Obaidulla Hospital, Ras Al Khaimah, Emirates Health Services, Ministry of Health, Ras Al Khaimah, UAE; <sup>77</sup>National Center for Gastrointestinal and Liver Diseases, Ibn Sina Hospital, Ministry of Health, Khartoum, Sudan; <sup>78</sup>Department of Medicine, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman; <sup>79</sup>Department of Hepatology and Gastroenterology, Muhimbili National Hospital, Dar es Salaam, Tanzania; <sup>80</sup>Department of Metabolic and Bariatric Surgery, The First Affiliated Hospital of Jinan University, Guangzhou, China; <sup>81</sup>Department of Medicine, Korle Bu Teaching Hospital, Accra, Ghana; <sup>82</sup>Department of Medicine & Therapeutics, University of Ghana Medical School, Accra, Ghana; <sup>83</sup>Department of Medicine, Aga Khan University, Nairobi, Kenya; <sup>84</sup>Physiology Research Center, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran; <sup>85</sup>Department of General Medicine, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran; <sup>86</sup>Department of Gastroenterology & Hepatology, Changi General Hospital, Singapore, Singapore; <sup>87</sup>Liver Unit, Division of Gastroenterology & Hepatology, University of Alberta, Edmonton, Canada; <sup>88</sup>Storr Liver Centre, Westmead Institute for Medical Research, Westmead Hospital and University of Sydney, Sydney, NSW, Australia; <sup>89</sup>MAFLD Research Center, Department of Hepatology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China; <sup>90</sup>Key Laboratory of Diagnosis and Treatment for The Development of Chronic Liver Disease in Zhejiang Province, Wenzhou, China

## 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.

## Financial support

This work was supported by grants from the National Natural Science Foundation of China (82070588, 82370577), the National Key R&D Program of China (2023YFA1800801), Science and Technology project of Shaanxi Province (2023-YBSF-385), Natural Science Basic Research Program of Shaanxi Province (2020JM-399 and 2023-JC-YB-699), and Scientific Research Plan Project of Shaanxi Provincial Department of Education (23JK0646).

## 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 KOBIO LABS; consulting fees from Boehringer Ingelheim, Novo Nordisk, Standigm, Daewoong, TSD Life Sciences Ildong, Olix Pharma, HK Inoen, and KOBIO LABS; honoraria for lectures from Ildong, Samil, and Novo Nordisk, and owns stocks in KOBIO LABS and Lepidyne and he is the founder of Remedygen. GS reports honoraria from Merck, Gilead, AbbVie, Novonordisk, and Pfizer, and unrestricted research funding from Theratechnologies Inc. VV-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, Viatrix 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, Diotech Pharmacogenetics, IONIS, and Viatrix; 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, VV-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

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhepr.2024.101271>.

#### References

*Author names in bold designate shared co-first authorship*

- [1] Rinella ME, Lazarus JV, Ratzliff V, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology* 2023;78:1966–1986.
- [2] **Wong VW, Ekstedt M**, Wong GL, et al. Changing epidemiology, global trends and implications for outcomes of NAFLD. *J Hepatol* 2023;79:842–852. <https://doi.org/10.1016/j.jhep.2023.04.036>.
- [3] **Li Q-Q, Xiong Y-T, Wang D**, et al. Metabolic syndrome is associated with significant hepatic fibrosis and steatosis in patients with nonalcoholic steatohepatitis. *iLIVER* 2024;3:100094.
- [4] Feng G, Fan Y-F, Li R-X, et al. Unraveling the epidemiology of metabolic dysfunction-associated liver cancer: insights from mixed etiologies, regional variations, and gender disparities. *iLIVER* 2024:100113. <https://doi.org/10.1016/j.iliver.2024.100113>.
- [5] Huang H, Liu Z, Xu M, et al. Global burden trends of MAFLD-related liver cancer from 1990 to 2019. *Portal Hypertens Cirrhosis* 2023;2:157–164.
- [6] **Cen J, Wang Q**, Cheng L, et al. Global, regional, and national burden and trends of migraine among women of childbearing age from 1990 to 2021: insights from the Global Burden of Disease Study 2021. *J Headache Pain* 2024;25:96.
- [7] **Tuo Y, Li Y**, Li Y, et al. Global, regional, and national burden of thalassemia, 1990-2021: a systematic analysis for the global burden of disease study 2021. *EClinicalMedicine* 2024;72:102619.
- [8] Paik JM, Henry L, Younossi Y, et al. The burden of nonalcoholic fatty liver disease (NAFLD) is rapidly growing in every region of the world from 1990 to 2019. *Hepatol Commun* 2023;7:e0251.
- [9] Zhou XD, Cai J, Targher G, et al. Metabolic dysfunction-associated fatty liver disease and implications for cardiovascular risk and disease prevention. *Cardiovasc Diabetol* 2022;21:270.
- [10] **Sun DQ, Targher G, Byrne CD**, et al. An international Delphi consensus statement on metabolic dysfunction-associated fatty liver disease and risk of chronic kidney disease. *Hepatobiliary Surg Nutr* 2023;12:386–403.
- [11] Zhang L, El-Shabrawi M, Baur LA, et al. An international multidisciplinary consensus on pediatric metabolic dysfunction-associated fatty liver disease. *Med* 2024;5:797–815.
- [12] Clayton-Chubb D, Kemp WW, Majeed A, et al. Late-life metabolic dysfunction-associated steatotic liver disease and its association with physical disability and dementia. *J Gerontol A Biol Sci Med Sci* 2024;79:glae011.
- [13] Guzman CB, Duvvuru S, Akkari A, et al. Coding variants in PNPLA3 and TM6SF2 are risk factors for hepatic steatosis and elevated serum alanine aminotransferases caused by a glucagon receptor antagonist. *Hepatol Commun* 2018;2:561–570.
- [14] Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* 2023;402:203–234.
- [15] Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. *J Hepatol* 2020;73:202–209.
- [16] **Fu L, Tian T, Wang B**, et al. Global, regional, and national burden of HIV and other sexually transmitted infections in older adults aged 60–89 years from 1990 to 2019: results from the Global Burden of Disease Study 2019. *Lancet Healthy Longev* 2024;5:e17–e30.
- [17] Zhang H, Zhou XD, Shapiro MD, et al. Global burden of metabolic diseases, 1990-2021. *Metabolism* 2024;160:155999.
- [18] Danpanichkul P, Suparan K, Dutta P, et al. Disparities in metabolic dysfunction-associated steatotic liver disease and cardiometabolic conditions in low and lower middle-income countries: a systematic analysis from the global burden of disease study 2019. *Metabolism* 2024;158:155958.
- [19] Allen AM, Lazarus JV, Younossi ZM. Healthcare and socioeconomic costs of NAFLD: a global framework to navigate the uncertainties. *J Hepatol* 2023;79:209–217.
- [20] Riazhi K, Azhari H, Charette JH, et al. The prevalence and incidence of NAFLD worldwide: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2022;7:851–861.
- [21] Rinaldi R, De Nucci S, Donghia R, et al. Gender differences in liver steatosis and fibrosis in overweight and obese patients with metabolic dysfunction-associated steatotic liver disease before and after 8 weeks of very low-calorie ketogenic diet. *Nutrients* 2024;16:1408.
- [22] Gutierrez-Grobe Y, Ponciano-Rodríguez G, Ramos MH, et al. Prevalence of non alcoholic fatty liver disease in premenopausal, postmenopausal and polycystic ovary syndrome women. The role of estrogens. *Ann Hepatol* 2010;9:402–409.
- [23] Vlassoff C. Gender differences in determinants and consequences of health and illness. *J Health Popul Nutr* 2007;25:47–61.
- [24] Gavin KM, Bessesen DH. Sex differences in adipose tissue function. *Endocrinol Metab Clin N A* 2020;49:215–228.
- [25] Wu W, Feng A, Ma W, et al. Worldwide long-term trends in the incidence of nonalcoholic fatty liver disease during 1990-2019: a jointpoint and age-period-cohort analysis. *Front Cardiovasc Med* 2022;9:891963.
- [26] EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). *J Hepatol* 2024;81:492–542.
- [27] Targher G, Byrne CD, Tilg H. MASLD: a systemic metabolic disorder with cardiovascular and malignant complications. *Gut* 2024;73:691–702.
- [28] Feng G, Hernandez-Gea V, Zheng MH. Resmetirom for MASH-related cirrhosis. *Lancet Gastroenterol Hepatol* 2024;9:594.
- [29] Lazarus JV, Ivancovsky Wajcman D, Mark HE, et al. Opportunities and challenges following approval of resmetirom for MASH liver disease. *Nat Med* 2024. <https://doi.org/10.1038/s41591-024-02958-z>.
- [30] Paik JM, Henry L, Younossi ZM. Nonalcoholic fatty liver disease mortality may not be decreasing: a need for careful interpretation of GBD 2019 estimates of liver deaths. *Cell Metab* 2023;35:1087–1088.

**Keywords:** Metabolic dysfunction-associated fatty liver disease; Non-alcoholic fatty liver disease; Metabolic dysfunction-associated steatotic liver disease; Epidemiology.

*Received 11 July 2024; received in revised form 30 October 2024; accepted 3 November 2024; Available online 14 November 2024*