Received: 19 September 2024 | Accepted: 22 January 2025

DOI: 10.1097/HC9.0000000000000689

ORIGINAL ARTICLE

OPEN

The global prevalence and impact of steatotic liver disease and viral infections: A systematic review and meta-analysis

Jiajing Li[1] | **Jiahua Zhou**[1] | **Pengfei Li**[1] | **Yining Wang**[1] | **Nathalie Ridderhof**[1] | **Jaffar A. Al-Tawfiq**[2,3,4] | **Willem Pieter Brouwer**[1] | **Kan Chen**[5] | **Robert J. de Knegt**[1] | **Maikel P. Peppelenbosch**[1] | **Bettina E. Hansen**[6] | **Maarten F.M. Engel**[7] | **Ming-Hua Zheng**[8,9] | **Ziad A. Memish**[10,11] | **Mohammed Eslam**[12] | **Harry L. A. Janssen**[1,13] | **Qiuwei Pan**[1] | **Ibrahim Ayada**[1]

[1]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

[2]Infectious Disease Unit, Specialty Internal Medicine, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

[3]Division of Infectious Diseases, Indiana University School of Medicine, Indianapolis, Indiana, USA

[4]Division of Infectious Diseases, Johns Hopkins University, Baltimore, Maryland, USA

[5]College of Life Sciences and Medicine, Zhejiang Sci-Tech University, Hangzhou, China

[6]Department of Epidemiology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

[7]Medical Library, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

[8]Department of Hepatology, MAFLD Research Center, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China

[9]Key Laboratory of Diagnosis and Treatment for the Development of Chronic Liver Disease in Zhejiang Province, Wenzhou, China

[10]College of Medicine, Al Faisal University, Riyadh, Saudi Arabia

[11]Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, USA

[12]Storr Liver Centre, Westmead Institute for Medical Research, Westmead Hospital and University of Sydney, NSW, Australia

[13]Toronto Center for Liver Disease, Toronto General Hospital, University of Toronto, Ontario, Canada

Correspondence
Qiuwei Pan, Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Wytemaweg 80, 3015 CN Rotterdam, The Netherlands.
Email: q.pan@erasmusmc.nl

Ibrahim Ayada, Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Wytemaweg 80, 3015 CN Rotterdam, The Netherlands.
Email: i.ayada@erasmusmc.nl

Abstract

Background: Steatotic liver disease (SLD) affects ~30% of adults worldwide. The global population is continuously threatened by epidemic and endemic viral diseases. This study aims to thoroughly examine the interaction between SLD and major viral diseases.

Methods: We systematically searched databases from inception to April 2, 2024, for observational studies recording viral-infected adult patients with eligible data on the presence of hepatic steatosis.

Results: Six hundred thirty-six eligible studies were included in the analysis of SLD prevalence. Among patients with monoinfections, the highest SLD

Abbreviations: CAP, controlled attenuation parameter; CMRF, cardiometabolic risk factor; MASLD, metabolic dysfunction–associated steatotic liver disease; SLD, steatotic liver disease; WHO, World Health Organization.

Qiuwei Pan and Ibrahim Ayada shared the senior authorship.

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.hepcommjournal.com.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.
Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Study of Liver Diseases.

prevalence was observed in those infected with HCV at 49% (95% CI: 47%–51%), followed by SARS-CoV-2 (39%, 95% CI [34%–44%]), HIV (39%, 95% CI [33%–44%]), and HBV (36%, 95% CI [32%–40%]). Additionally, co-infections, such as HCV-HIV and HBV-HCV, exhibit even higher SLD prevalence. The prevalence of steatohepatitis is particularly high in HIV-infected (24%, 95% CI: 17%–30%) and HCV-infected (18%, 95% CI: 13%–24%) populations. The co-existence of SLD with viral infections was associated not only with the progression of liver disease but also with more severe outcomes of the infections and poorer responses to antiviral treatment. The combination of cardiometabolic risk factors and viral-associated and host factors contributes to the higher risk of SLD in viral-infected populations.

Conclusions: SLD is highly prevalent in viral-infected populations, and the reciprocal interactions between SLD and viral diseases exacerbate both conditions, leading to poorer patient outcomes in general.

Keywords: cardiometabolic risk factors, MASLD, NAFLD, steatohepatitis, viral diseases

INTRODUCTION

Steatotic liver disease (SLD) is a newly adopted nomenclature encompassing a broad spectrum of hepatic steatosis conditions. Metabolic dysfunction–associated steatotic liver disease (MASLD) has replaced NAFLD to emphasize the cardiometabolic risk factors (CMRF) in its etiology. Metabolic dysfunction–associated steatohepatitis has replaced NASH to represent a subset of patients with MASLD with lobular inflammation and hepatocyte injuries.[1] Simple steatosis is the earliest stage of SLD, which can progress to fibrosis through increased inflammatory infiltration, eventually leading to progression to irreversible cirrhosis and HCC. SLD has attracted increasing attention due to the rapid growth of the affected population, resulting in massive health and economic burden.[2] MASLD alone afflicts approximately one third of the global population, and metabolic dysfunction–associated steatohepatitis affects about 5% of the general population. Despite regional variations in prevalence, the rising trend in MASLD cases continues to accelerate annually across all continents.[3,4]

In parallel, the global population is continuously threatened by epidemic and endemic viral diseases. The co-existence of viral infection and SLD is common in different patient populations. Considering hepatotropic viruses, chronic HCV infection is known to trigger hepatic steatosis, and steatosis may change the natural history of both HCV-related hepatic and extrahepatic diseases.[5] Although the association between chronic HBV infection and steatosis remains debatable,[6–8] the co-existence of HBV infection and MASLD may promote the progression of liver injury.[9] For systemic viral infections, liver disease is one of the major comorbidities in people living with HIV.[10] A higher prevalence of MASLD/metabolic dysfunction–associated steatohepatitis has been reported among HIV-infected individuals compared to the general population.[11,12] Liver dysfunction has been observed in many hospitalized patients with COVID-19 with moderate or severe SARS-CoV-2 infection, resulting in poorer prognosis.[13,14] Patients with MASLD are thought to be more susceptible to severe COVID-19 outcomes, as considerable evidence supports the association between COVID-19 and CMRF, including obesity, hypertension, impaired fasting glucose, and dyslipidemia.[15]

Given the complexity of viral disease and SLD co-existence, this study aims to comprehensively understand their mutual interactions with respect to epidemiology, clinical features, and outcomes through a large-scale systematic review, meta-analysis, and data synthesis.

METHODS

Search strategy

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (Supplemental Materials,

http://links.lww.com/HC9/B949).[16] The protocol for this study was registered on PROSPERO (International Prospective Register of Systematic Reviews, CRD42022345391). A comprehensive systematic search was conducted across 5 databases: Embase, Medline ALL, Web of Science Core Collection, Cochrane Central Register of Controlled Trials, and Google Scholar. We searched for published studies in English from inception to April 2, 2024, using an exhaustive set of search terms related to "fatty liver disease" and "viral infection." The full search strategies and selection criteria are detailed in the Supplemental Methods, http://links.lww.com/HC9/B949. Two investigators (Jiajing Li and Jiahua Zhou) independently screened the titles and abstracts of all identified citations and reviewed the full-text manuscripts of potentially relevant articles. Disagreements were resolved by consensus and a third reviewer (Ibrahim Ayada or Qiuwei Pan) if necessary. As our study utilized exclusively published data from existing studies, no additional ethical approval or participant consent was required.

Inclusion and exclusion criteria

Studies were included according to the following criteria: (1) cross-sectional and longitudinal observational studies and (2) adult patients (aged 18 y or above) with any viral infections; (3) availability of data on baseline hepatic steatosis with valid diagnostic methods; (4) clear definition for virally infected populations. Exclusion criteria included studies involving (1) liver transplant recipients because of their immunosuppressive status, (2) only individuals not representative of the entire population, (3) insufficient or incomplete data, or (4) fewer than 10 subjects. Diagnosis of steatosis based on both invasive and noninvasive methods is considered equal evidence validity. Steatohepatitis was confirmed by the presence of steatosis and inflammation. Liver fibrosis staging was based on histopathological features from biopsies by METAVIR or Ishak scoring system.[17,18] Viral infections were defined through biological specimens (eg, serological tests for HBV, HCV, and HIV infections and nasopharyngeal swabs for SARS-CoV-2 infections) with subsequent quantification of viral RNA and antigen. This study involved treatment-naive populations with chronic hepatitis B and chronic hepatitis C at baseline, while people living with HIV had typically undergone treatment with antiretroviral therapies.

Quality assessment and data extraction

Quality assessment of included articles was assessed independently in duplicate, using the Joanna Briggs Institute Critical Appraisal Checklist.[19] Two investigators (Jiajing Li and Jiahua Zhou) extracted data from each included study based on a standardized form. Study characteristics included first author, country, study period, and study design. Study population data contained the total sample size, the number of steatosis and steatohepatitis, and diagnostic methods. Baseline characteristics of patients included but were not limited to demographic data (age, sex, and BMI) and metabolic comorbidities, including overweight or obesity, hypertension, insulin resistance, type 2 diabetes mellitus, and dyslipidemia. Clinical information was collected on liver disease progression, treatment strategies such as antiretroviral therapy for HIV carriers, and outcomes of antiviral therapies. When duplicate data were identified, we excluded the duplicates with the smallest sample size or incomplete data. Details of data collection are provided in the Supplemental Methods, http://links.lww.com/HC9/B949.

Statistical analysis

All statistical analyses were implemented by STATA 15.0, with a p value of 0.05 or less considered statistically significant. A random-effects (DerSimonian and Laird) meta-analysis model was used for all analyses to generate pooled estimates, reported as prevalence, OR, or weighted mean differences (WMD) with the corresponding 95% CI. Random-effects models were used due to the predictable heterogeneity from population diversity, and more robust effect estimates than fixed-effects models.[20] Pooled prevalence estimates in viral-infected populations were stratified by country, World Health Organization (WHO) regions, and diagnostic methods for hepatic steatosis. When analyzing potential risk factors for SLD, we pooled adjusted ORs and their 95% CIs as the estimated effect sizes when sufficient data were available. If sufficient data were not available, we separately pooled ORs and weighted mean differences from the original binary or continuous variable data provided in the studies. Continuous variables are converted or integrated into uniform units and formats (mean $\pm$ SD) using established formulas.[21–23] Heterogeneity between studies was assessed using Cochrane Q and I^2 statistic, with an I^2 of at least 50% considered to be significant heterogeneity.[24] Subgroup analyses and multivariate meta-regressions were performed to identify potential sources of heterogeneity and to determine the impact of specific moderator variables on prevalence estimates. Sensitivity analyses were performed as a "leave-one-out" approach to validate the robustness of pooled prevalence estimates by excluding one study or one subgroup at a time. Publication bias was assessed by Egger test and the funnel plots (only for >10 studies) of the study size against transformed outcome values (eg, log transformation for

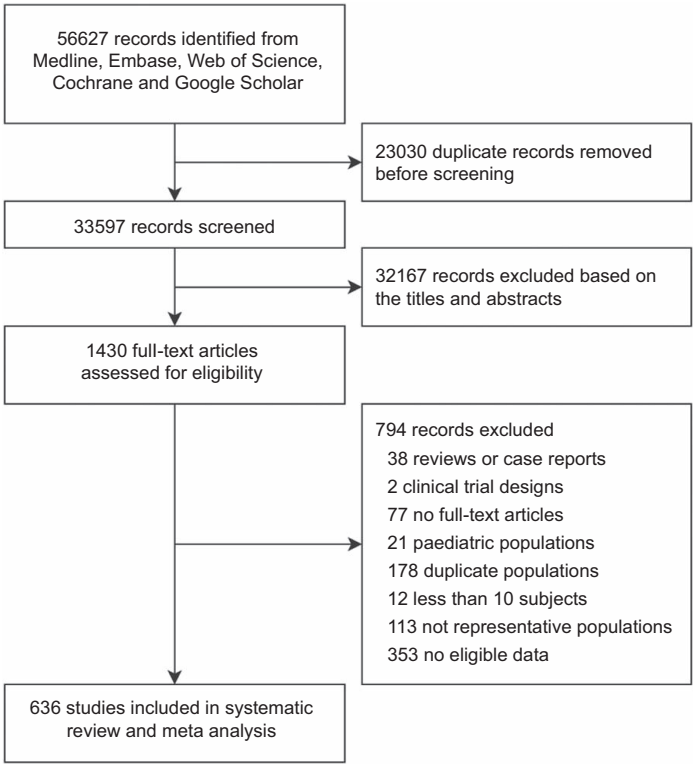


FIGURE 1 Flow diagram for study selection.

prevalence).[25] For binary variable analyses with <10 studies, publication bias was assessed using Harbord test. To illustrate the geographical differences in prevalence, a web-based interactive dashboard with maps and graphs was created using Tableau 2023.3.0.

RESULTS

Summary of included studies

The literature search identified 56,627 records. After removing 23,030 duplicates, 33,597 records were screened. Based on the titles and abstracts, 1,430 articles were selected for full-text review to assess eligibility. After excluding 794 articles, 636 studies were ultimately included in the meta-analysis (Figure 1). The main characteristics and quality assessment scores for all included studies are summarized in Supplemental Tables S1–S9, http://links.lww.com/HC9/B949.

Prevalence of SLD in different viral-infected populations

Overall, 636 studies involving 1,126,158 individuals from 59 countries were included in the analysis of SLD prevalence. The estimated prevalence of SLD in HBV monoinfected populations was 36% (95% CI [32%–40%]) pooled from 145 studies, with the highest SLD prevalence reported in the Western Pacific region (37%, 95% CI [35%–40%]) and the European region (37%, 95% CI [29%–46%]) (Figure 2). The highest estimated prevalence of SLD was observed in HCV monoinfected populations (49%, 95% CI [47%–51%]) from 321 studies, with pooled prevalences of 52% (95% CI [47%–56%]) in the Americas region (60 studies) and 50% (95% CI [44%–56%]) in the European region (143 studies) (Figure 3). In HIV monoinfected populations, the prevalence of SLD was 39% (95% CI [33%–44%]) pooled from 58 studies (Figure 4). In SARS-CoV-2 monoinfected populations, the prevalence of SLD was 39% (95% CI [34%–44%]) pooled from 58 studies (Figure 5). Only 3 studies documented SLD prevalence in HEV monoinfected populations, with a pooled prevalence of 21% (95% CI: 9%–33%) (Supplemental Figure S5, http://links.lww.com/HC9/B949). Populations with coinfection of HCV-HIV (44%, 95% CI [38%–49%]) (Supplemental Figure S6, http://links.lww.com/HC9/B949) or HBV-HIV (38%, 95% CI [18%–58%]) (Supplemental Figure S7, http://links.lww.com/HC9/B949) exhibited similar or even higher prevalence of SLD than those infected with HIV alone. The prevalence of SLD in HBV-HCV co-infected population (53%, 95% CI [38%–68%]) (Supplemental Figure S8, http://links.lww.com/HC9/B949) was higher than in those with only HCV or HBV monoinfection. SLD in other virus-infected populations from limited studies is reported in Supplemental Table S9, http://links.lww.com/HC9/B949. Detailed forest plots and publication bias assessment can be found in Supplemental Figures S1–S8, http://links.lww.com/HC9/B949.

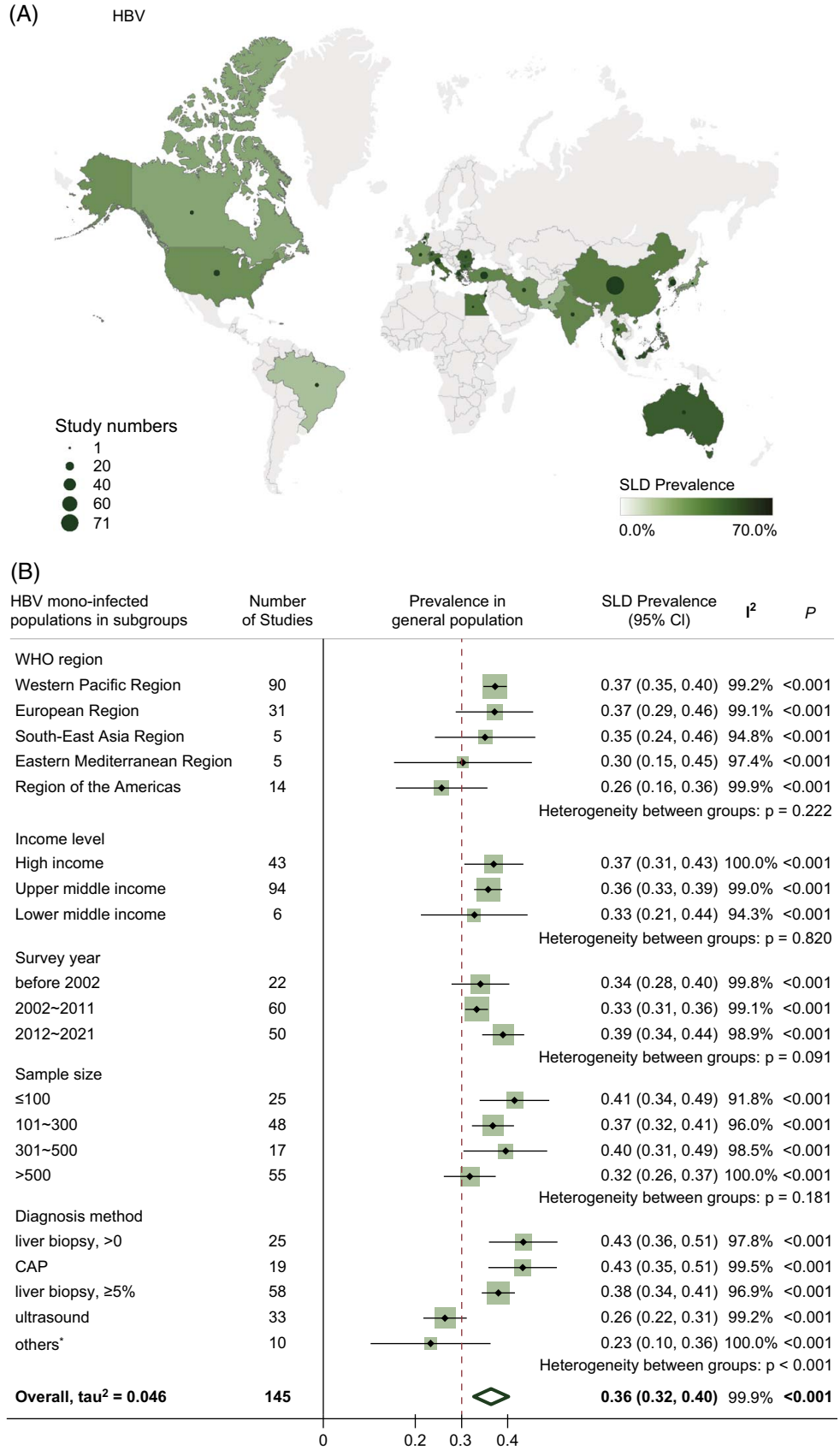


FIGURE 2 SLD prevalence in HBV monoinfected populations stratified by selected countries (A) and different subgroups (B). * MRS/MRI, ICD-10 codes, FLI ≥ 30, HSI ≥ 36, clinical records or multiple methods. Abbreviations: CAP, controlled attenuation parameter; FLI, fatty liver index; HSI, hepatic steatosis index; ICD-10, International Classification of Diseases 10th revision; MRS, magnetic resonance spectroscopy.

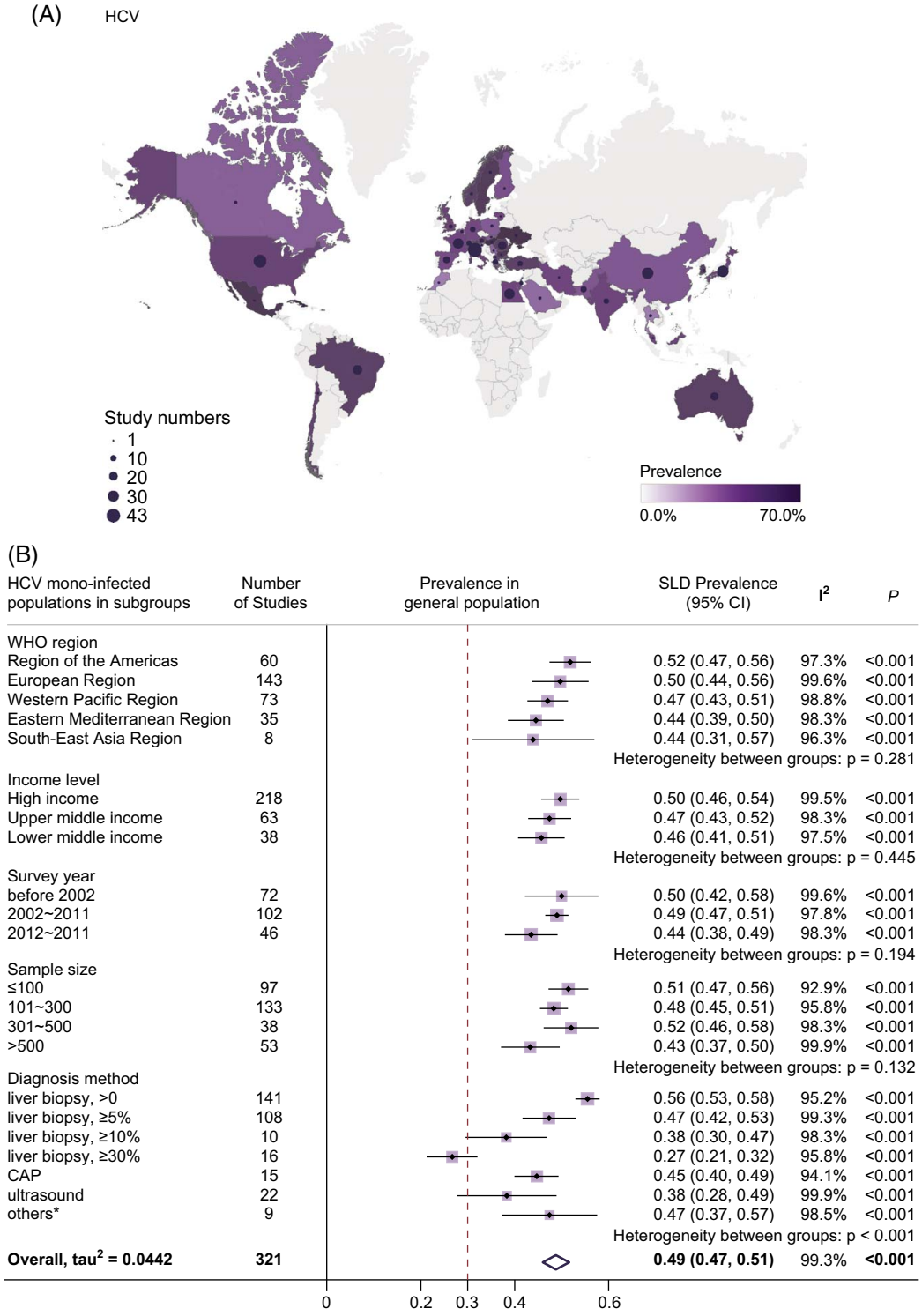


FIGURE 3 SLD prevalence in HCV monoinfected populations stratified by selected countries (A) and different subgroups (B). * MRS/MRI, FLI ≥ 30, SteatoTest score, or clinical records. Abbreviations: CAP, controlled attenuation parameter; FLI, fatty liver index; MRS, magnetic resonance spectroscopy.

Subgroup analyses of estimated SLD prevalence

Subgroup analyses stratified SLD prevalence in different viral-infected populations to explore potential sources of heterogeneity (Figures 2B–5B). SLD prevalence varies moderately according to geographical region and economic level. For instance, studies in the European region reported higher SLD prevalences across various populations. HIV monoinfected

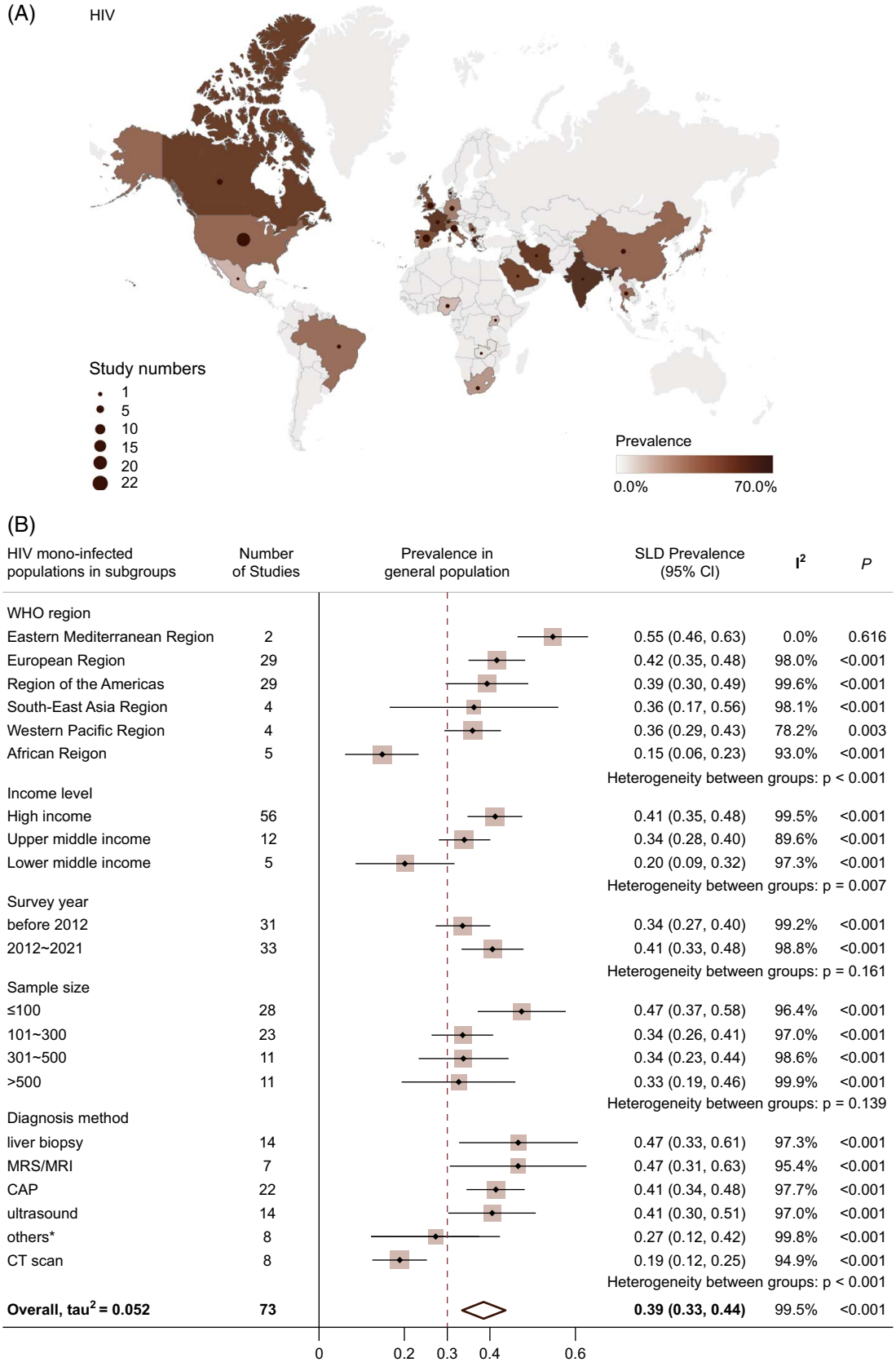
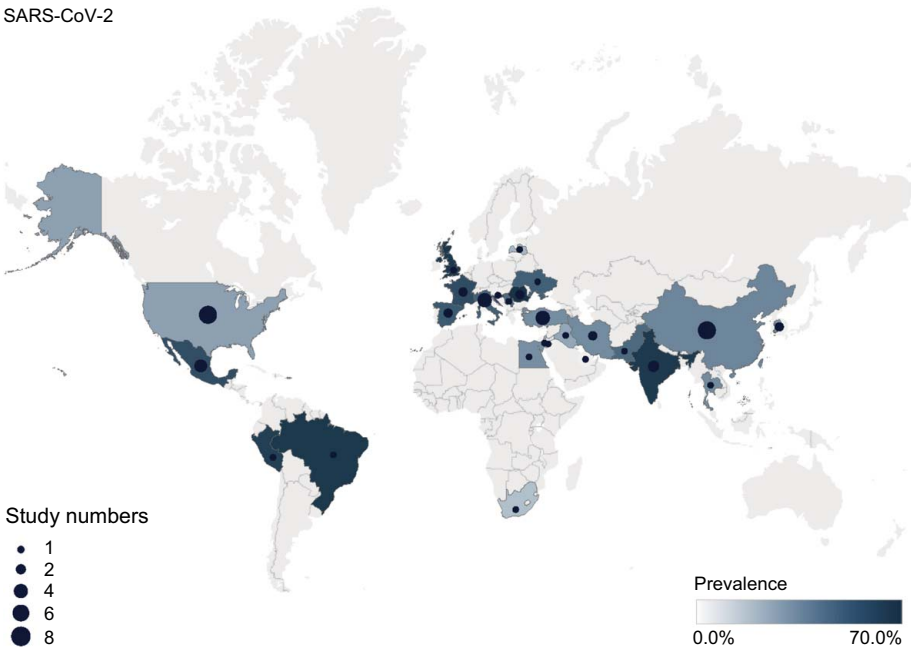


FIGURE 4 SLD prevalence in HIV monoinfected populations stratified by selected countries (A) and different subgroups (B). * ICD-10 codes, FLI ≥ 30, HSI ≥ 36, LFS ≥ 1.257 or multiple methods. Abbreviations: CAP, controlled attenuation parameter; FLI, fatty liver index; HSI, hepatic steatosis index; ICD-10, International Classification of Diseases 10th revision; LFS, liver fat score; MRS, magnetic resonance spectroscopy.

(A)


SARS-CoV-2
Study numbers
1
2
4
6
8
Prevalence
0.0%
70.0%

(B)

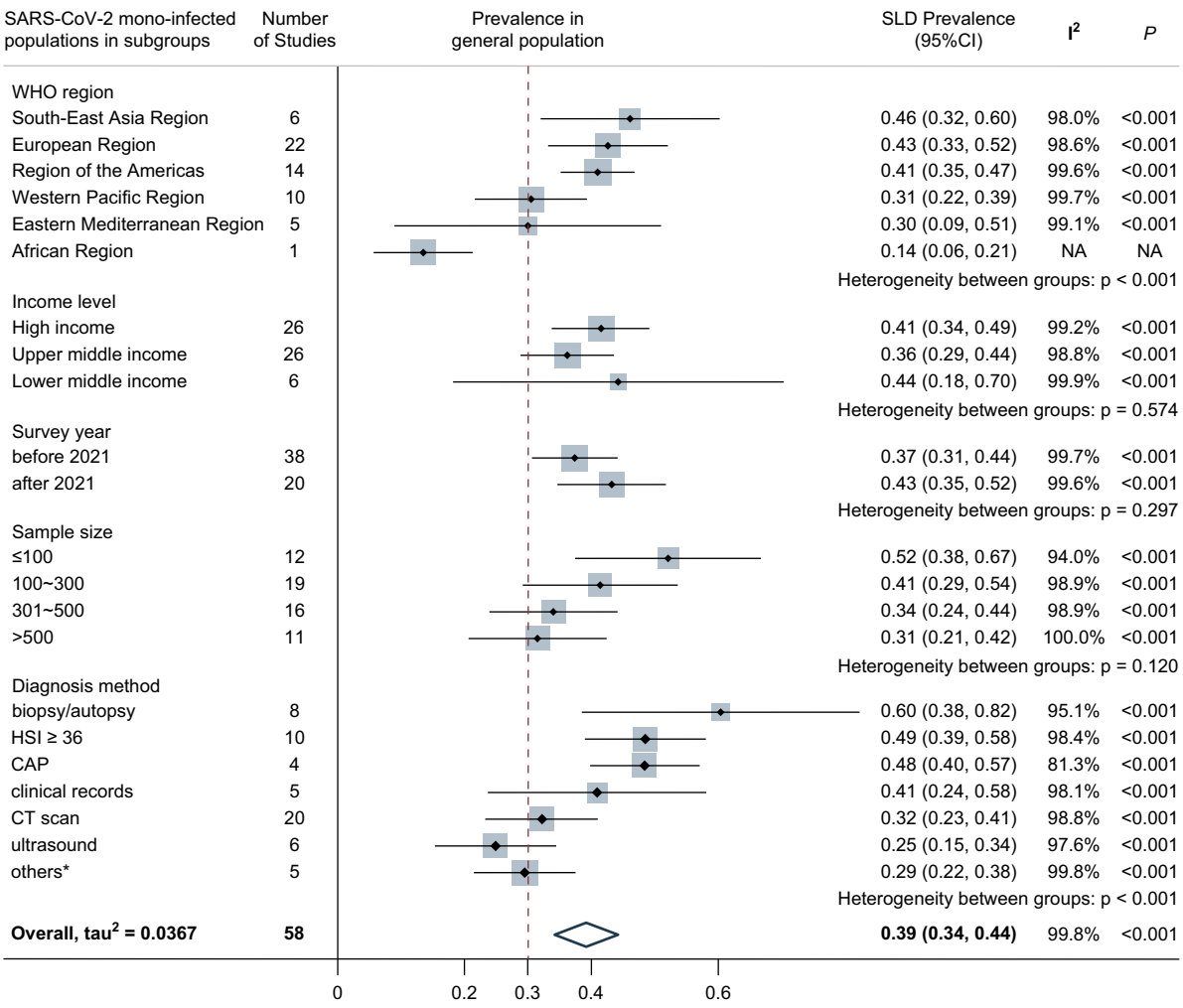

SARS-CoV-2 mono-infected populations in subgroups
Number of Studies
Prevalence in general population
SLD Prevalence (95%CI)
I²
P
WHO region
South-East Asia Region 6 0.46 (0.32, 0.60) 98.0% <0.001
European Region 22 0.43 (0.33, 0.52) 98.6% <0.001
Region of the Americas 14 0.41 (0.35, 0.47) 99.6% <0.001
Western Pacific Region 10 0.31 (0.22, 0.39) 99.7% <0.001
Eastern Mediterranean Region 5 0.30 (0.09, 0.51) 99.1% <0.001
African Region 1 0.14 (0.06, 0.21) NA NA
Heterogeneity between groups: p < 0.001
Income level
High income 26 0.41 (0.34, 0.49) 99.2% <0.001
Upper middle income 26 0.36 (0.29, 0.44) 98.8% <0.001
Lower middle income 6 0.44 (0.18, 0.70) 99.9% <0.001
Heterogeneity between groups: p = 0.574
Survey year
before 2021 38 0.37 (0.31, 0.44) 99.7% <0.001
after 2021 20 0.43 (0.35, 0.52) 99.6% <0.001
Heterogeneity between groups: p = 0.297
Sample size
≤100 12 0.52 (0.38, 0.67) 94.0% <0.001
100~300 19 0.41 (0.29, 0.54) 98.9% <0.001
301~500 16 0.34 (0.24, 0.44) 98.9% <0.001
>500 11 0.31 (0.21, 0.42) 100.0% <0.001
Heterogeneity between groups: p = 0.120
Diagnosis method
biopsy/autopsy 8 0.60 (0.38, 0.82) 95.1% <0.001
HSI ≥ 36 10 0.49 (0.39, 0.58) 98.4% <0.001
CAP 4 0.48 (0.40, 0.57) 81.3% <0.001
clinical records 5 0.41 (0.24, 0.58) 98.1% <0.001
CT scan 20 0.32 (0.23, 0.41) 98.8% <0.001
ultrasound 6 0.25 (0.15, 0.34) 97.6% <0.001
others* 5 0.29 (0.22, 0.38) 99.8% <0.001
Heterogeneity between groups: p < 0.001
Overall, tau² = 0.0367 58 0.39 (0.34, 0.44) 99.8% <0.001
0
0.2
0.3
0.4
0.6

FIGURE 5 SLD prevalence in SARS-CoV-2 monoinfected populations stratified by selected countries (A) and different subgroups (B). * ICD-10 codes, clinical records, DSI, or multiple methods. Abbreviations: CAP, controlled attenuation parameter; DSI, Dallas steatosis index; ICD-10, International Classification of Diseases 10th revision; MRS, magnetic resonance spectroscopy.

populations showed a higher prevalence in high-income countries (41%, 95% CI [35%–48%]) compared to lower-middle-income countries (20%, 95% CI [9%–32%]). Studies conducted after 2012 tended to report higher prevalence in both HBV- (39%, 95% CI [34%–44%]) and HIV-infected populations (41%, 95% CI [33%–48%]), whereas the trend was opposite in HCV-infected populations. Similarly, SARS-CoV-2–infected populations showed a higher prevalence (43%, 95% CI [35%–52%]) in studies after 2021. Smaller sample sizes were generally associated with higher prevalence of SLD compared to larger sample sizes. Diagnostic methods contribute significantly to heterogeneity and variance in estimated SLD prevalence. Liver biopsy was primarily used to assess steatosis in people with HCV or HBV-related infection, while noninvasive methods were more frequently used in populations with SARS-CoV-2 or HIV monoinfection. In HBV-infected populations, SLD detected by liver biopsy or controlled attenuation parameter (CAP) exceeded 40%, compared to $<30\%$ detected by ultrasound or other noninvasive methods. More than 40% of HCV-infected people had SLD, apart from those detected by ultrasound. SLD detected by biopsy, ultrasound, CAP, and MRI was found in more than 40% of HIV carriers. In patients with COVID-19, SLD detected by biopsy/autopsy, CAP, and hepatic steatosis index was found in $>40\%$, and $<40\%$ was detected by ultrasound, CT scan, and other noninvasive methods.

Progression of SLD in viral-infected populations

An important stage of SLD progression is the inflammatory infiltrate, leading to steatohepatitis. We included 17,199 individuals and estimated the prevalence of steatohepatitis in HBV, HCV, HIV, and SARS-CoV-2 monoinfected populations. The HIV-infected population showed the highest prevalence of steatohepatitis at 24% (95% CI: 17%–30%), followed by the HCV-infected population at 18% (95% CI: 13%–24%). The prevalence of steatohepatitis was lower than 10% in both HBV (8%, 95% CI [5%–11%]) and SARS-CoV-2 (4%, 95% CI [0%–9%]) monoinfected populations (Figure 6 and Supplemental Figure S9, http://links.lww.com/HC9/B949).

Patients with SLD have a high likelihood of developing irreversible or even malignant lesions. This risk appears to be more complex in patients with viral infections, as shown in Figure 7A (detailed forest plots in Supplemental Figure S10–S12, http://links.lww.com/HC9/B949). HIV carriers with hepatic steatosis were strongly associated with advanced fibrosis (OR 3.05, 95% CI [1.81, 5.13]) and cirrhosis (OR 3.07, 95% CI [1.55, 6.06]). Despite both being hepatitis viruses, HCV and HBV distinctly influence the progression from steatosis to irreversible liver damage in affected individuals. In the HCV-infected population, patients with SLD showed a positive association with advanced fibrosis (OR 1.80, 95% CI [1.54, 2.10]), cirrhosis (OR 1.43, 95% CI [1.14, 1.78]) and HCC (OR 2.43, 95% CI [1.51, 3.89]). This association was not found in HBV-infected patients with SLD (Figure 7A). In patients with HCV-HIV coinfection, SLD is also associated with advanced fibrosis (OR 1.77, 95% CI [1.21, 2.61]) and cirrhosis (OR 1.78, 95% CI [1.09, 2.89]). However, there is no significant association between SLD and liver cirrhosis in the limited SARS-CoV-2–infected populations we have included.

Prognosis of infected patients with SLD

The co-existence of SLD with viral infections is associated with a higher burden of liver disease but is also related to more severe outcomes of the infections and poorer responses to antiviral treatment (Figure 7B and Supplemental Figures S13–S19, http://links.lww.com/HC9/B949). SLD patients infected with SARS-CoV-2 are more likely to experience severe COVID-19 (OR 2.16, 95% CI [1.33, 3.53]). SLD in HIV carriers was positively associated with a CD4 cell count below 200 cells/mm^3 (OR 1.46, 95% CI [1.10, 1.93]) but not significantly associated with the detectable HIV RNA (OR 0.88, 95% CI [0.76, 1.01]). HCV-infected individuals with SLD were less likely to obtain sustained virological response after antiviral therapy (OR 0.60, 95% CI [0.46, 0.78]), and a similar trend was observed in the HBV-infected population, although our results did not show statistical significance.

Potential risk factors for SLD in viral-infected populations

Table 1 summarizes the potential risk factors for SLD in different viral-infected populations (detailed forest plots in Supplemental Figures S20–S23, http://links.lww.com/HC9/B949). A high risk of SLD in viral-infected populations was significantly associated with the CMRF, including overweight/obesity, type 2 diabetes mellitus, hypertension, and dyslipidemia, which is similar to the general population. Additionally, identified

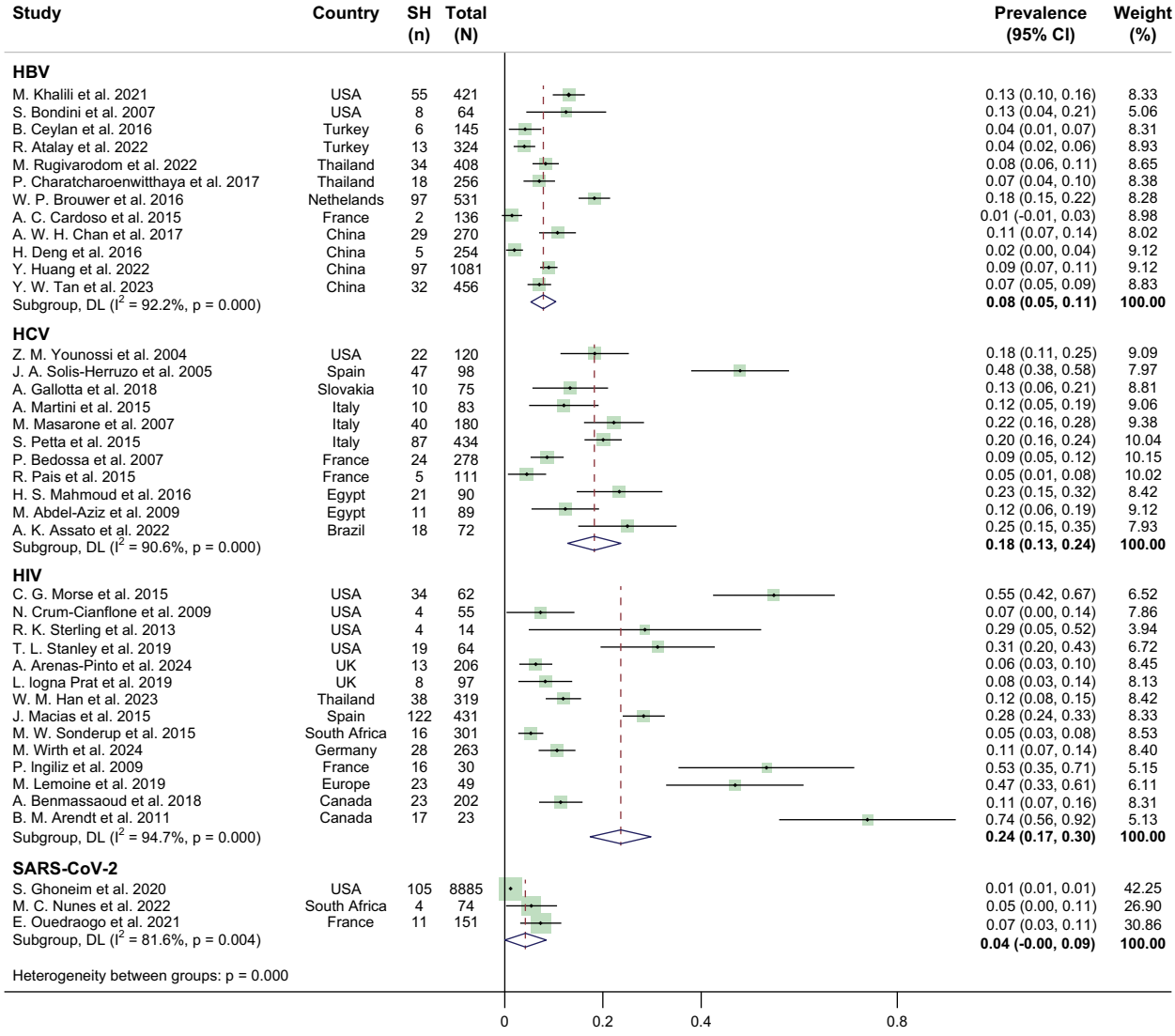


FIGURE 6 Prevalence of steatohepatitis in different types of viral-infected populations. Abbreviations: SH, steatohepatitis; DL, DerSimonian and Laird.

factors associated with SLD in various populations include age in patients infected with HBV, HCV, and HIV; male sex in patients infected with HBV, HIV, and SARS-CoV-2. *PNPLA3* rs738409 G allele and *TM6SF2* rs58542926 T allele in hepatitis virus-infected individuals; HCV RNA level and HCV genotype 3 in chronic hepatitis C patients; duration since diagnosis and nucleoside reverse transcriptase inhibitor treatment in HIV carriers; and the history of smoking in patients with COVID-19.

Publication bias, sensitivity analyses, and meta-regressions

Significant publication bias was observed in estimated prevalence pooled from all viral-infected populations except for the HCV monoinfected group ($p = 0.376$) shown by Egger test and the symmetry of funnel plots (Supplemental Figures S1G–S4G and S6G, http://links.lww.com/HC9/B949). Sensitivity analyses demonstrated the robustness of prevalence estimates for SLD in different viral-infected populations (Supplemental Figure S24, http://links.lww.com/HC9/B949). However, some studies with specific characteristics were found to contribute to the risk of bias. Higher prevalence estimates were more frequently reported in studies with smaller sample sizes in high-income countries in HIV-infected populations and in studies before 2021 in SARS-CoV-2–infected populations. Studies using non-invasive methods generally reported lower prevalence estimates in viral-infected populations. Meta-regression analyses identified potential factors contributing to the heterogeneity in SLD prevalence estimates. Diagnostic methods were consistently the most significant source of heterogeneity, while WHO region, survey year, and

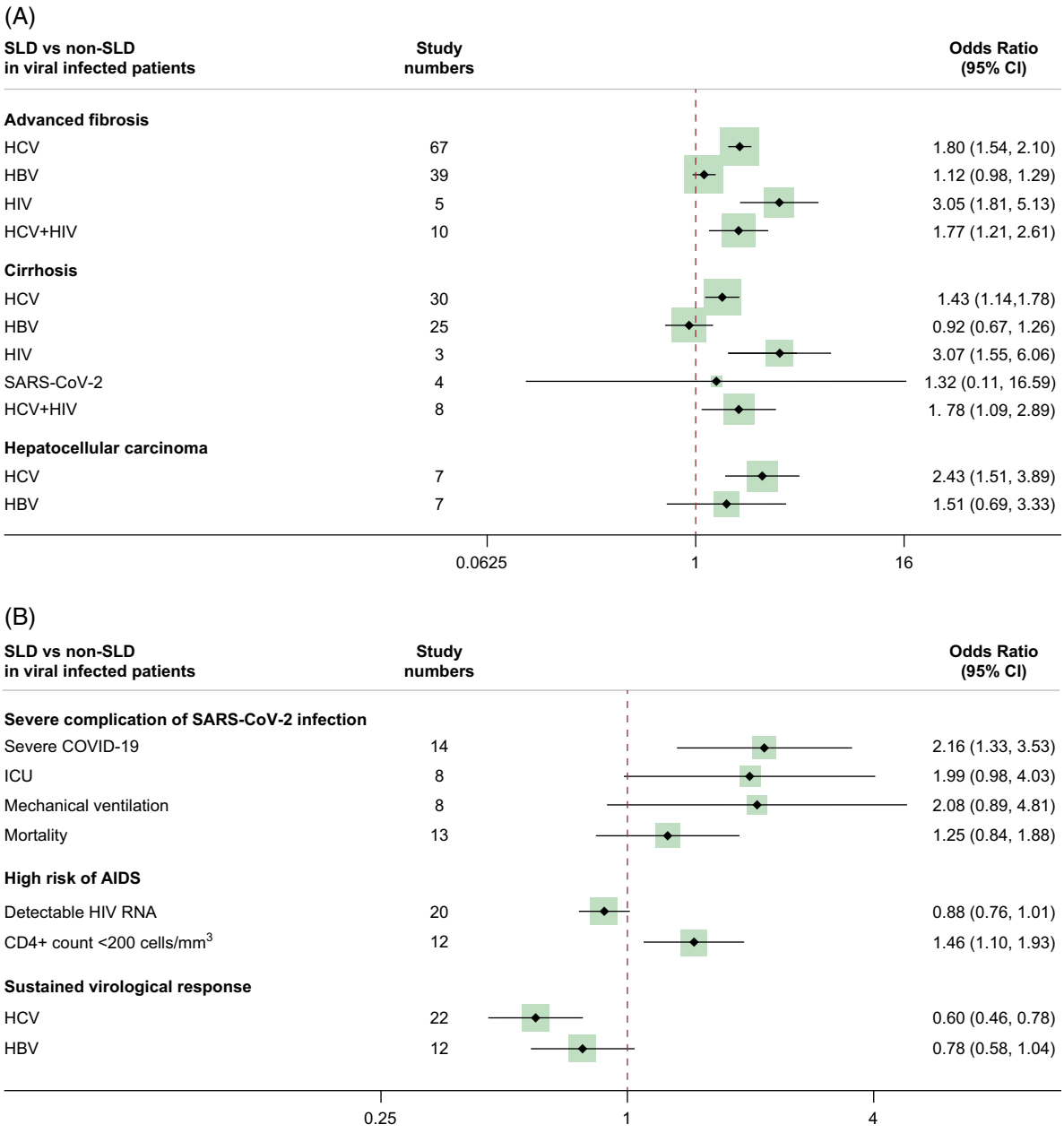


FIGURE 7 The association between SLD and the progression of liver disease (A) or the clinical outcomes of viral infection (B) in different viral-infected populations. Abbreviations: SLD, steatotic liver disease; ICU, intensive care unit.

sample characteristics, such as sample size and age distribution, also have an impact (Supplemental Table S10, http://links.lww.com/HC9/B949).

DISCUSSION

This systematic review and meta-analysis performed a comprehensive examination of the prevalence and clinical features of SLD in populations infected with various types of viruses. Notable regional differences exist in the distribution of viral-infected populations. For instance, HBV infection is more prevalent in the African and Western Pacific regions than in the American and European region,[26,27] while HCV is most common in the Eastern Mediterranean and Central Asia.[28,29]. The HIV epidemic is most severe in East and Southern Africa.[30] In the general population, the global prevalence of NAFLD is estimated at 30%, with Latin America having the highest prevalence.[31]

Our study showed that the geographical distribution of SLD varies in different virus-infected populations, and does not always align with the regions having high viral disease burden. For instance, the estimated SLD prevalence among HCV-infected patients is highest in the European and American regions, exceeding 50%.

TABLE 1 Risk factors of SLD in different viral-infected populations

Risk factors	No. studies	Participants included	Effect size (95% CI)			Heterogeneity	Publication bias
			OR	Lower limit	Upper limit	I^2 (%)	*p*
Risk factors of SLD in HBV-infected or HCV-infected population							
HBV-infected population							
Age (y)	15	8077	1.07	1.03	1.11	90.00	0.009
Sex (male vs. female)	12	7130	1.76	1.48	2.09	7.30	0.515
BMI (kg/m^2)	14	12,342	1.40	1.23	1.58	92.50	0.044
Overweight or obesity	10	3759	3.26	1.76	6.03	94.50	< 0.001
T2DM	11	6579	1.66	1.09	2.53	84.00	0.902
Hypertension	7	6092	1.20	1.03	1.38	93.70	—
Dyslipidemia	6	4239	1.97	1.22	3.18	94.30	—
Triglyceride (mg/dL)	8	9669	1.67	1.22	2.29	93.10	—
Viral load (HBV DNA level)	3	2146	0.94	0.80	1.09	65.40	—
PNPLA3 rs738409 G allele	4	949	2.91	1.77	4.79	19.30	—
HCV-infected population							
Age (y)	23	13,818	1.02	1.01	1.03	50.40	0.797
Sex (male vs female)	24	10,946	0.97	0.82	1.15	63.70	0.116
BMI (kg/m^2)	32	17,535	1.12	1.09	1.14	73.70	0.071
Overweight or obesity	20	5604	2.47	2.11	2.90	0	0.017
T2DM	21	10,315	1.86	1.51	2.29	44.70	0.018
IR	20	7558	1.37	1.22	1.53	80.10	< 0.001
Hypertension	4	2027	1.57	1.12	2.21	50.10	—
Dyslipidaemia	10	1595	1.67	1.18	2.37	42.10	0.013
Triglyceride (mg/dL)	14	5490	1.01	1.01	1.01	77.80	0.001
Viral load (HCV RNA level)	9	4673	1.66	1.13	2.45	90.80	—
Genotype 3 vs non-3	37	16,405	3.81	3.23	4.50	50.30	0.117
PNPLA3 rs738409 G allele	15	9182	1.86	1.60	2.17	45.40	0.244
TM6SF2 rs58542926 T allele	6	3813	1.16	1.04	1.29	0	—
Risk factors of SLD in HIV or SARS-CoV-2–infected population							
HIV-infected population							
Age (y)*	28	19,731	2.17	1.12	3.22	88.70	0.611
Sex (male vs female)	24	20,577	1.30	1.09	1.56	71.10	0.006
Overweight or obesity	13	4426	3.51	1.98	6.25	92.20	0.981
T2DM	18	17,141	2.28	1.49	3.51	84.50	0.012
Hypertension	17	17,951	1.49	1.18	1.89	77.10	0.221
Dyslipidaemia	12	16,923	2.08	1.51	2.87	88.40	0.277
Metabolic syndrome	11	1604	4.19	2.28	7.71	76.80	0.365
Smoking	10	7981	0.85	0.71	1.01	40.70	0.183
Duration since diagnosis*	14	8209	1.13	0.58	1.68	56.80	0.291
ART duration*	9	1960	0.29	−0.17	0.75	70.90	—
ART drugs							
NRTIs	17	18,515	1.28	1.05	1.57	69.30	0.129
Pis	17	18,230	1.04	0.90	1.20	54.60	0.535
NNRTIs	14	17,687	1.03	0.85	1.24	73.90	0.646
INSTIs	12	17,630	1.00	0.94	1.07	0	0.624
SARS-CoV-2–infected population							
Age (y)*	24	70,566	−1.04	−3.00	0.91	95.50	0.362
Sex (male vs. female)	25	144,826	1.27	1.11	1.45	90.20	0.382
Overweight or obesity	15	140,240	3.60	2.77	4.67	97.20	0.001

TABLE 1. (*continued*)

Risk factors	No. studies	Participants included	Effect size (95% CI)			Heterogeneity	Publication bias
			OR	Lower limit	Upper limit	I^2 (%)	*p*
T2DM	23	120,018	2.32	1.81	2.98	96.20	0.029
Hypertension	19	119,109	1.68	1.32	2.14	97.00	0.77
Dyslipidemia	5	75,079	1.87	1.07	3.25	83.00	0.987
Smoking	7	108,745	1.47	1.21	1.77	93.00	0.666

Note: Potential risk factors for SLD in HCV- and HBV-infected populations are evaluated by pooling adjusted ORs and 95% CIs from multivariate logistic regression. Publication bias was assessed by Egger test. Potential risk factors for SLD in HIV-infected and SARS-CoV-2–infected populations are evaluated by pooling effect sizes based on original data; ORs for binary variables and WMDs for continuous variables (marked by *). Publication bias was assessed by Egger test for studies > 10, otherwise Harbord test. Specific forest plots for all potential risk factors can be found in Supplemental Figures S20–S23, http://links.lww.com/HC9/B949.
Abbreviations: ART, antiretroviral therapy; BMI, body mass index; INSTIs, integrase strand transfer inhibitors; IR, insulin resistance; NNRTIs, non-nucleoside reverse transcriptase inhibitors; NRTIs, nucleoside reverse transcriptase inhibitors; PIs, protease inhibitors; PNPLA3, patatin-like phospholipase domain-containing protein 3; T2DM, type 2 diabetes mellitus; TM6SF2, transmembrane 6 superfamily member 2.

Despite the severe HIV burden in Africa, the prevalence of SLD among HIV-infected populations in this region is relatively low (14%), although this estimate is based on limited studies. These discrepancies likely result from multiple factors, including the high burden of metabolic syndrome in developed regions, underdiagnosis due to insufficient medical resources, and a limited number of studies from some regions. Therefore, region-specific surveillance and screening strategies are essential to improve the management of SLD in virus-infected patients. Study characteristics, such as survey year and sample size, also influenced the pooled prevalence estimates. SLD prevalence in HCV-infected populations declined over the past decade compared to previous years, probably due to the widespread use of effective antiviral therapies and improved noninvasive diagnosis. In contrast, the lower estimated prevalence among patients with COVID-19 during the first year of the outbreak appears more complex and calls for further research. Smaller sample sizes tended to represent specialized sample populations, such as hospital-based populations and more severe patients, contributing to higher reported prevalence.

The diagnostic methods employed in the analyzed studies also affect the estimated prevalence of SLD. Studies using liver biopsies reported higher SLD prevalence, likely due to the selection of more severe cases for biopsy. In contrast, noninvasive methods generally yield lower prevalence estimates. For instance, noninvasive assessments consistently report lower steatosis prevalence in chronic HBV populations compared to the general population.[32] We indicate that chronic hepatitis B populations evaluated with ultrasound or other noninvasive tests showed lower SLD prevalence, whereas those assessed with liver biopsy and CAP showed higher prevalence. These differences were also observed among HIV carriers and COVID-19 patients. An even higher prevalence of steatosis was observed in autopsy samples from the COVID-19 population. Importantly, CAP provided prevalence estimates comparable to liver biopsy. Given its accessibility and noninvasive nature, CAP is suited for the monitoring and diagnosis of SLD in viral-infected populations.

Our findings highlight the potential interaction between certain viral infections and an elevated risk of SLD, which in turn leads to poorer clinical outcomes. Approximately 30% of SLD prevalence in the general population, diagnosed by noninvasive methods (mostly ultrasound), has been cited as a reference, but we do not intend to directly compare this rate with our results. HCV is currently the virus most closely associated with hepatic steatosis. Although different HCV genotypes induce steatosis through different mechanisms, the HCV-induced imbalance of host lipid metabolism does not appear to be entirely genotype specific.[33] Fibrosis progression is strongly associated with worsening steatosis in patients with untreated CHC.[34] Our analysis revealed that nearly 50% of individuals had comorbid SLD and 18% of individuals had steatohepatitis in the HCV-infected population, which also imposes high risks of irreversible liver injury. In addition, HCV-infected patients with comorbid SLD are more difficult to achieve a sustained virological response after antiviral treatment. In HBV-infected individuals, while SLD does not appear to have as severe consequences, its prevalence still exceeded 35%. Co-infections such as HCV-HIV, HBV-HIV, and HCV-HBV co-infections are potentially related to a higher risk of SLD compared to monoinfections. Similarly, higher SLD prevalence was observed in populations infected with nonhepatitis viruses such as HIV and SARS-CoV-2. Up to 24% of people infected with HIV develop steatohepatitis. Consistent with existing evidence,[35] HIV carriers with comorbid SLD have an increased risk of steatohepatitis and fibrosis, particularly in those with persistently elevated liver enzymes under combination antiretroviral therapy.[36] Our results also demonstrated that SLD was likely associated with the development of more severe AIDS in people living with HIV, as evidenced by higher

CD4 cell counts and HIV RNA levels in individuals with SLD.[37,38] In COVID-19 patients, pre-existing SLD does not necessarily increase the risk of liver damage but is associated with more severe infection outcomes. This vulnerability is closely related to the increased availability of angiotensin-converting enzyme 2, a key receptor for SARS-CoV-2 entry, in the context of lipid overload.[39] Meanwhile, the essential roles of host metabolism, especially the glucose and lipid metabolism, in SARS-CoV-2 infection suggested the considerable connection between SLD and COVID-19.[40]

The necessary element of defining MASLD is the presence of hepatic steatosis in conjunction with at least one CMRF.[1] We found that SLD in viral-infected populations was influenced by a combination of CMRF and viral-associated factors as well as other host factors. In HBV-infected individuals, SLD is primarily driven by age, male sex, and CMRF. Evidence suggests that serological levels of HBV infection are negatively correlated with hepatic steatosis.[6–8] In our analysis, HCV-infected populations exhibited the highest prevalence of SLD, influenced by HCV RNA level and genotype 3. HCV genotype 3 is directly linked to hepatic steatosis due to the interactions between core protein and lipid metabolic pathways. For non-genotype 3 HCV infections, liver steatosis mainly stems from obesity, insulin resistance, and metabolic syndrome.[41,42] Host genetic factors, such as *PNPLA3* rs738409 and *TM6SF2* rs58542926, also play a significant role in the development of SLD in HCV- and HBV-infected populations. These genetic variants are robustly associated with steatosis, hepatic fibrosis, cirrhosis, and NAFLD-related HCC.[43,44] Additionally, certain antiviral treatments could also be “poisons” that trigger SLD. For instance, several nucleoside reverse transcriptase inhibitors, such as zidovudine, didanosine, and stavudine, have been implicated in hepatic steatosis and liver failure.[45,46] General COVID-19 treatment metabolized in the liver may also lead to abnormal liver function.[47,48]

Of note, this study has several limitations. First, we only pooled the estimated prevalence based on existing SLD cases in viral-infected populations at baseline. The incidence rate of SLD was not analyzed as a primary outcome because the order in which the patients acquired viral infections and SLD was not available. Our analysis consequently lacked evidence to confirm a causal association between viral infection and SLD. Second, substantial heterogeneity and significant publication bias may have a negative impact on the evidence strength of this meta-analysis. However, meta-regression analyses partially explained the key sources of heterogeneity, and sensitivity analyses confirmed the robustness of the estimated effect sizes. Finally, but importantly, when analyzing risk factors for SLD in viral-infected populations, we could not fully adjust for the interactions between different factors. For instance, the direct induction of insulin resistance by HCV through a virus-associated inflammatory response,[49] potential interactions between various metabolic syndromes, and the impact of the treatment duration on HIV carriers having different therapeutic strategies were not fully accounted for.

In summary, SLD is highly prevalent in populations affected by viral diseases, and the reciprocal interactions between SLD and viral diseases exacerbate both conditions, leading to poorer patient outcomes. However, there are discrepancies in the interactions of SLD with different types of viral disease, requiring further research to better clarify. We strongly recommend tailoring surveillance and treatment strategies to the unique characteristics and challenges of each viral-infected population. For individuals with hepatitis virus infection, routine monitoring of SLD progression is crucial to prevent long-term complications. In populations with a rising risk of SLD, such as HIV carriers, broader SLD screening programs are essential to enable early intervention. We, therefore, call for enhanced awareness and more comprehensive research to explore the correlation between SLD and viral infections.

DATA AVAILABILITY STATEMENT

Data collected for the study will be made available upon publication and reasonable request to the corresponding author.

AUTHOR CONTRIBUTIONS

Conceptualization: Jiajing Li, Ibrahim Ayada, and Qiuwei Pan. Data curation: Jiajing Li, Jiahua Zhou, Nathalie Ridderhof, Ibrahim Ayada, Qiuwei Pan. Analysis and visualization: Jiajing Li, Ibrahim Ayada, BH, Qiuwei Pan. Drafting of the manuscript: Jiajing Li, Ibrahim Ayada, and Qiuwei Pan. Critical revision of the manuscript for important intellectual content: all.

FUNDING INFORMATION

This study was supported by the ZonMw COVID-19 Programme (No. 50-56300-98-2201) and a VIDI grant (No. 91719300) from the Dutch Research Council to Qiuwei Pan.

CONFLICTS OF INTEREST

Ming-Hua Zheng has received honoraria for lectures from AstraZeneca, Hisky Medical Technologies, and Novo Nordisk consulting fees from Boehringer Ingelheim. Harry L. A. Janssen has received grants from Gilead Sciences, GlaxoSmithKline, Janssen, Roche, Vir Biotechnology Inc. Prof. Dr. Harry L. A. Janssen is consultant for Aligos, Gilead Sciences, GlaxoSmithKline, Grifols, Roche, Vir Biotechnology Inc., Precision Biosciences. Robert J. de Knegt is consultant for Bracco. Robert J. de Knegt has received honoraria for consulting or speaking from AbbVie, Echosens, Gilead, Schallware,

and grants from Echosens, Gilead, GSK, Inventiva, Janssen-Cilag. Bettina E. Hansen consults, is on the speakers' bureau, and received grants from Ipsen. She consults and is on the speaker's bureau for Advanz. She consults and received grants from Mirum and Gilead. She consults for Intercept. She advises Pilant. The remaining authors have no conflicts to report.

ORCID

Qiuwei Pan https://orcid.org/0000–0001–9982–6184

REFERENCES

1. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol. 2023;79:1542–56.
2. Miao L, Targher G, Byrne CD, Cao YY, Zheng MH. Current status and future trends of the global burden of MASLD. Trends Endocrinol Metab. 2024;35:697–707
3. Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): A systematic review. Hepatology. 2023;77:1335–47.
4. Le MH, Yeo YH, Li X, Li J, Zou B, Wu Y, et al. 2019 Global NAFLD Prevalence: A systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20:2809–817 e2828.
5. Adinolfi LE, Rinaldi L, Guerrera B, Restivo L, Marrone A, Giordano M, et al. NAFLD and NASH in HCV infection: Prevalence and significance in hepatic and extrahepatic manifestations. Int J Mol Sci. 2016;17:803.
6. Machado MV, Oliveira AG, Cortez-Pinto H. Hepatic steatosis in hepatitis B virus infected patients: Meta-analysis of risk factors and comparison with hepatitis C infected patients. J Gastroenterol Hepatol. 2011;26:1361–7.
7. Zheng Q, Zou B, Wu Y, Yeo Y, Wu H, Stave CD, et al. Systematic review with meta-analysis: prevalence of hepatic steatosis, fibrosis and associated factors in chronic hepatitis B. Aliment Pharmacol Ther. 2021;54:1100–9.
8. Jiang D, Chen C, Liu X, Huang C, Yan D, Zhang X, et al. Concurrence and impact of hepatic steatosis on chronic hepatitis B patients: A systematic review and meta-analysis. Ann Transl Med. 2021;9:1718.
9. Fernandez CJ, Alkhalifah M, Afsar H, Pappachan JM. Metabolic dysfunction-associated fatty liver disease and chronic viral hepatitis: The interlink. Pathogens. 2024;13:68.
10. Price JC, Thio CL. Liver disease in the HIV-infected individual. Clin Gastroenterol Hepatol. 2010;8:1002–12.
11. Kalligeros M, Vassilopoulos A, Shehadeh F, Vassilopoulos S, Lazaridou I, Mylonakis E, et al. Prevalence and characteristics of nonalcoholic fatty liver disease and fibrosis in people living with HIV monoinfection: A systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2023;21:1708–22.
12. Maurice JB, Patel A, Scott AJ, Patel K, Thursz M, Lemoine M. Prevalence and risk factors of nonalcoholic fatty liver disease in HIV-monoinfection. AIDS. 2017;31:1621–32.
13. Luxenburger H, Thimme R. SARS-CoV-2 and the liver: Clinical and immunological features in chronic liver disease. Gut. 2023;72:1783–94.
14. Mengual-Moreno E, Nava M, Manzano A, Ariza D, D'Marco L, Castro A, et al. Pancreatic and hepatic injury in COVID-19: A worse prognosis in NAFLD patients? Biomedicines. 2024;12:283.
15. Buchynskyi M, Kamyshna I, Oksenych V, Zavidniuk N, Kamyshnyi A. The intersection of COVID-19 and metabolic-associated fatty liver disease: An overview of the current Evidence. Viruses. 2023;15:1072.
16. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
17. Chowdhury AB, Mehta KJ. Liver biopsy for assessment of chronic liver diseases: A synopsis. Clin Exp Med. 2023;23:273–85.
18. Everhart JE, Wright EC, Goodman ZD, Dienstag JL, Hoefs JC, Kleiner DE, et al. Prognostic value of Ishak fibrosis stage: Findings from the hepatitis C antiviral long-term treatment against cirrhosis trial. Hepatology. 2010;51:585–94.
19. Moola SMZ, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, et al. Chapter 7: Systematic reviews of etiology and risk. Aromataris E MZ, ed. JBI Manual for Evidence Synthesis: JBI. JBI Global Wiki; 2020.
20. Bell A, Fairbrother M, Jones K. Fixed and random effects models: making an informed choice. Quality & Quantity. 2019;53:1051–74.
21. Shi J, Luo D, Wan X, Liu Y, Liu J, Bian Z, et al. Detecting the skewness of data from the five-number summary and its application in meta-analysis. Stat Methods Med Res. 2023;32:1338–60.
22. Shi J, Luo D, Weng H, Zeng XT, Lin L, Chu H, et al. Optimally estimating the sample standard deviation from the five-number summary. Res Synth Methods. 2020;11:641–54.
23. Higgins, JPT, Li, T, Deeks, JJ. Choosing effect measures and computing estimates of effect. In: Cochrane Handbook for Systematic Reviews of Interventions. Chapter 6. Publisher; Wiley. 2019:143–76.
24. Melsen WG, Bootsma MC, Rovers MM, Bonten MJ. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. Clin Microbiol Infect. 2014;20:123–9.
25. Hunter JP, Saratzis A, Sutton AJ, Boucher RH, Sayers RD, Bown MJ. In meta-analyses of proportion studies, funnel plots were found to be an inaccurate method of assessing publication bias. J Clin Epidemiol. 2014;67:897–903.
26. Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: A systematic review of data published between 1965 and 2013. Lancet. 2015;386:1546–55.
27. Polaris Observatory C. Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study. Lancet Gastroenterol Hepatol. 2023;8:879–907.
28. Petruzziello A, Marigliano S, Loquercio G, Cozzolino A, Cacciapuoti C. Global epidemiology of hepatitis C virus infection: An up-date of the distribution and circulation of hepatitis C virus genotypes. World J Gastroenterol. 2016;22:7824–40.
29. Salari N, Kazeminia M, Hemati N, Ammari-Allahyari M, Mohammadi M, Shohaimi S. Global prevalence of hepatitis C in general population: A systematic review and meta-analysis. Travel Med Infect Dis. 2022;46:102255.
30. HIV/AIDS in Africa. In: World Health Organization; 2022.
31. Teng ML, Ng CH, Huang DQ, Chan KE, Tan DJ, Lim WH, et al. Global incidence and prevalence of nonalcoholic fatty liver disease. Clin Mol Hepatol. 2023;29:S32–42.
32. Huang J, Jing M, Wang C, Wang M, You S, Lin S, et al. The impact of hepatitis B virus infection status on the prevalence of nonalcoholic fatty liver disease: A population-based study. J Med Virol. 2020;92:1191–7.
33. Syed GH, Amako Y, Siddiqui A. Hepatitis C virus hijacks host lipid metabolism. Trends Endocrinol Metab. 2010;21:33–40.
34. Castera L, Hezode C, Roudot-Thoraval F, Bastie A, Zafrani ES, Pawlotsky JM, et al. Worsening of steatosis is an independent factor of fibrosis progression in untreated patients with chronic hepatitis C and paired liver biopsies. Gut. 2003;52:288–92.

35. Fourman LT, Stanley TL, Zheng I, Pan CS, Feldpausch MN, Purdy J, et al. Clinical predictors of liver fibrosis presence and progression in human immunodeficiency virus-associated non-alcoholic fatty liver disease. Clin Infect Dis. 2021;72:2087–94.
36. Rockstroh JK. Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) in HIV. Curr HIV/AIDS Rep. 2017;14:47–53.
37. Doyle T, Smith C, Vitiello P, Cambiano V, Johnson M, Owen A, et al. Plasma HIV-1 RNA detection below 50 copies/ml and risk of virologic rebound in patients receiving highly active antiretroviral therapy. Clin Infect Dis. 2012;54:724–32.
38. Battistini Garcia SA, Guzman N Acquired Immune Deficiency Syndrome CD4+ Count. 2024.
39. Cano L, Desquilles L, Ghukasyan G, Angenard G, Landreau C, Corlu A, et al. SARS-CoV-2 receptor ACE2 is upregulated by fatty acids in human MASH. JHEP Rep. 2024;6:100936.
40. Chen P, Wu M, He Y, Jiang B, He ML. Metabolic alterations upon SARS-CoV-2 infection and potential therapeutic targets against coronavirus infection. Signal Transduct Target Ther. 2023;8:237.
41. Adinolfi LE, Gambardella M, Andreana A, Tripodi MF, Utili R, Ruggiero G. Steatosis accelerates the progression of liver damage of chronic hepatitis C patients and correlates with specific HCV genotype and visceral obesity. Hepatology. 2001;33:1358–64.
42. Dempsey JL, Ioannou GN, Carr RM. Mechanisms of lipid droplet accumulation in steatotic liver diseases. Semin Liver Dis. 2023; 43:367–82.
43. Liu YL, Patman GL, Leathart JB, Piguet AC, Burt AD, Dufour JF, et al. Carriage of the PNPLA3 rs738409 C > G polymorphism confers an increased risk of non-alcoholic fatty liver disease associated hepatocellular carcinoma. J Hepatol. 2014;61:75–81.
44. Li XY, Liu Z, Li L, Wang HJ, Wang H. TM6SF2 rs58542926 is related to hepatic steatosis, fibrosis and serum lipids both in adults and children: A meta-analysis. Front Endocrinol (Lausanne). 2022;13:1026901.
45. Bleeker-Rovers CP, Kadir SW, van Leusen R, Richter C. Hepatic steatosis and lactic acidosis caused by stavudine in an HIV-infected patient. Neth J Med. 2000;57:190–3.
46. Neff GW, Jayaweera D, Sherman KE. Drug-induced liver injury in HIV patients. Gastroenterol Hepatol (NY). 2006;2:430–7.
47. Qi RB, Wu ZH. Association between COVID-19 and chronic liver disease: Mechanism, diagnosis, damage, and treatment. World J Virol. 2023;12:22–9.
48. Li P, Liu Y, Cheng Z, Yu X, Li Y. COVID-19-associated liver injury: Clinical characteristics, pathophysiological mechanisms and treatment management. Biomed Pharmacother. 2022;154:113568.
49. Cheung O, Sanyal AJ. Hepatitis C infection and nonalcoholic fatty liver disease. Clin Liver Dis. 2008;12:573–85; viii-ix.

How to cite this article: Li J, Zhou J, Li P, Wang Y, Ridderhof N, Al-Tawfiq JA, et al. The global prevalence and impact of steatotic liver disease and viral infections: A systematic review and meta-analysis. Hepatol Commun. 2025;9:e0689. https://doi.org/10.1097/HC9.0000000000000689