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Original Article

National Epidemiological Trends in Hepatitis A–E Serologic and Virologic Markers in the United States, 2011–2023: A Population-Based Study

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Abstract

Background and Aims: Viral hepatitis caused by A to E imposes a substantial global burden of liver disease. Despite US control strategies, long-term national data covering serologic markers of all five hepatitis viruses remain limited. In this study, we analyzed epidemiologic trends from 2011 to 2023 and aimed to identify prevention gaps. ***Methods:*** We analyzed National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2023 using weighted logistic regression, with stratification by age, sex, and race/ethnicity. ***Results:*** Current hepatitis B virus (HBV) infection remained stable at 0.3%, while HBV susceptibility was 71.3%. Among individuals born in 1991 or later, HBV vaccination coverage declined from 90.0% to 83.6% during 2011–2020 (P for trend = 0.012); 57.0% of participants reporting vaccination were serologically susceptible. Anti-HDV positivity among participants with current HBV infection was 1.3%. Anti-hepatitis C virus (HCV) seroprevalence remained 1.6%, while active HCV viremia decreased from 0.8% to 0.4%, and viremia among anti-HCV-positive participants fell from 65.5% to 31.3% (P = 0.004). Hepatitis A virus antibody seroprevalence increased from 41.6% to 48.0% (P < 0.001) with stable vaccination coverage. Anti-HEV IgM positivity increased from 1.6% to 1.7% (P = 0.004). ***Conclusions:*** US viral hepatitis trends diverged from 2011 to 2023. The decrease in detectable HCV RNA was consistent with progress in HCV control, whereas persistent HBV susceptibility, declining vaccination coverage in younger birth cohorts, and increasing hepatitis A virus seroprevalence and hepatitis E virus IgM positivity indicate ongoing prevention and surveillance needs.

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Keywords: Viral hepatitis; Epidemiological trends; WHO 2030 goal; NHANES; Hepatitis B; Hepatitis C; Prevalence.

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Introduction

Viral hepatitis caused by hepatitis A to E viruses remains a leading global cause of acute liver failure, chronic hepatitis, cirrhosis, and hepatocellular carcinoma worldwide.[1] In 2016, the World Health Organization (WHO) formally launched the global strategy for viral hepatitis elimination, aiming to eliminate viral hepatitis as a major public health threat by 2030 by reducing new infections by 90% and virus-related mortality by 65% compared with the 2015 baseline.[2] Achieving these ambitious elimination targets requires continuous monitoring of population-level epidemiological trends, updated seroprevalence data, and identification of unmet public health needs.[3]

The United States (US) has implemented a series of viral hepatitis prevention and control policies over the past two decades, including universal childhood hepatitis B virus (HBV) vaccination, expanded hepatitis C virus (HCV) screening, and standardized antiviral treatment.[4] Nevertheless, comprehensive, long-term national data covering all five major hepatitis viruses (A–E) remain limited. Most previous US epidemiological studies focused on a single type of hepatitis infection or short-term surveillance data,[5–9] lacking continuous trend analyses from 2011 to 2023. In particular, contemporary changes in population susceptibility, vaccination coverage, and active infection burden across different age, sex, and racial/ethnic subgroups have not been systematically characterized.

The National Health and Nutrition Examination Survey (NHANES) provides nationally representative, cross-sectional serological data that enable robust assessment of population-level infectious disease epidemiology.[10] This study aimed to comprehensively evaluate temporal trends in the prevalence of hepatitis A virus (HAV), HBV, HCV, hepatitis D virus (HDV), and hepatitis E virus (HEV) among the US general population aged ≥6 years from 2011 to 2023, with stratified subgroup analyses and trend tests, to identify existing challenges and provide evidence relevant to future hepatitis elimination strategies.

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Methods

Data source

NHANES is a nationally representative public health monitoring program managed by the United States Centers for Disease Control and Prevention (CDC), with data collected every two years.[10] A critical optimization of the survey sampling strategy in 2011 increased the recruitment of Asian participants, raising the sampling proportion from less than 2% to 13%. This methodological change addressed the limited sample size for Asian populations in earlier surveys and improved the feasibility of national estimates in this subgroup.[11] In addition, the COVID-19 pandemic led to the suspension of in-person NHANES data collection in March 2020. Incomplete recruitment for the 2019–2020 survey cycle rendered the data unrepresentative of the general US population; therefore, only the 2017–March 2020 prepandemic file was used.[12] Regular survey operations resumed in August 2021, initiating a new 2-year data collection phase. The 2021–2023 survey used updated sampling rules, questionnaires, and physical examination standards. Ultimately, this study incorporated data from five NHANES survey periods: 2011–2012, 2013–2014, 2015–2016, 2017–March 2020, and 2021–2023, with respective median time points of 2012, 2014, 2016, 2018.6, and 2022.7. Participants aged 18 years or older provided written informed consent before enrollment, whereas minors provided assent with permission from a parent or legal guardian. The CDC provides comprehensive documents detailing NHANES operational protocols, ethics review board approvals (Protocol #2021-05 and #2011-17), and public data-sharing specifications.[13] This observational epidemiological study was reported in accordance with the Declaration of Helsinki (as revised in 2024) and the Strengthening the Reporting of Observational Studies in Epidemiology statement.

Study population

This study used cross-sectional data from five NHANES survey periods covering 2011 to 2023. NHANES participants aged 6 years and older who completed standardized serological testing for viral hepatitis were included in the analysis. Participants with unavailable hepatitis serological measures or missing sampling weights were excluded from the final analytical cohort. The sample sizes included in analyses of HAV, HBV, HCV, and HEV were 39,753, 39,874, 39,644, and 39,879 participants, respectively. According to national demographic statistics, the civilian noninstitutionalized population of the United States was approximately 319 million during the study period, representing 98.4% of the overall national population (324 million). After further excluding children younger than 6 years (3.6% of the civilian noninstitutionalized population), the target population represented in this analysis was estimated at approximately 307 million individuals.[14–16]

Serological definitions

Uniform serological criteria were used to categorize hepatitis infection status and immune profiles. Current HBV infection was defined as positivity for both hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen (anti-HBc). Participants negative for HBsAg, anti-HBc, and antibody to hepatitis B surface antigen (anti-HBs) were classified as susceptible to HBV. HBV vaccination was defined as reported receipt of at least one dose of HBV vaccine. Active HCV viremia was defined as detectable HCV RNA among anti-HCV-positive participants. HAV seropositivity was defined by the presence of anti-HAV antibodies, whereas anti-HEV immunoglobulin M (IgM) positivity was defined by a positive anti-HEV IgM result. HAV vaccination was defined as reported receipt of at least one vaccine dose. Updated HDV testing protocols were released in August 2025 to address potential false-positive results generated by the original HDV assays used across the 2007–2008 to 2017–2018 survey cycles.[17] Accordingly, anti-HDV status in this study was reassessed using the revised testing algorithm among participants with current HBV infection.

Statistical analysis

Given the complex multistage sampling design of NHANES, all statistical analyses incorporated sampling weights, clustering, and stratification variables to ensure national representativeness. Categorical variables were summarized as weighted proportions, whereas continuous variables were summarized using medians and corresponding interquartile ranges.

Appropriate sampling weights were applied to generate nationally representative prevalence estimates and 95% confidence intervals (CIs). Weighted prevalence was extrapolated to the target population of 307 million US civilian noninstitutionalized residents aged ≥6 years to estimate the total number of infected or susceptible individuals. Temporal trends in seroprevalence and vaccination coverage across survey cycles were assessed using weighted logistic regression models, and *P* values for trend were used to evaluate statistical significance. Stratified analyses were conducted by sex, age group, and race/ethnicity. For HBV-related analyses, additional stratified comparisons were conducted by birthplace (US-born vs. non-US-born) and birth cohort (individuals born before 1991 vs. born in 1991 or later), in accordance with the universal childhood HBV vaccination guidelines issued by the Advisory Committee on Immunization Practices in 1991.[18] Because HBV vaccination records were unavailable for the 2021–2023 survey cycle, temporal trend analyses of HBV vaccination coverage were restricted to the 2011–2020 dataset.

All statistical analyses were performed using R software (version 4.6.0), and the NHANES design was accounted for using the survey package for R. A two-sided *P* value < 0.05 was considered statistically significant.

Results

Baseline demographic characteristics of participants

A total of 39,644 to 39,879 eligible participants were included in analyses of different viral hepatitis markers. As shown in Table 1, the median age of participants was 39 years, and 51.2% were female. Over two-thirds (74.1%) of participants were born in 1991 or later. Non-Hispanic White participants accounted for the largest proportion (61.8%), followed by Non-Hispanic Black and Mexican American participants, while Non-Hispanic Asian participants accounted for approximately 5.5%. Participant characteristics were similar across all hepatitis testing groups.

Hepatitis B and hepatitis D epidemiological trends

From 2011 to 2023, the national weighted prevalence of current HBV infection remained stable at 0.3% (95% CI: 0.2%–0.4%) (Table 2), corresponding to an estimated 0.92 million (95% CI: 0.61–1.23 million) individuals nationwide. Prevalence changed only slightly from 0.3% in 2011 to 0.4% in 2023 (Fig. 1A). The overall prevalence of HBV susceptibility remained high at 71.3% (95% CI: 70.4%–72.2%) across the study period, corresponding to an estimated 219.48 mil-

Table 1. Baseline characteristics of participants tested for hepatitis A, B, C, and E viruses in the US population, 2011–2023

Variable	HAV	HBV	HCV	HEV
Total participants	39,753	39,874	39,644	39,879
Age, years	39 (18, 60)	39 (18, 60)	39 (18, 60)	39 (18, 60)
Age group (years)				
6–24	13,043 (25.1%)	13,087 (25.1%)	13,031 (25.1%)	13,087 (25.1%)
25–49	11,529 (36.4%)	11,559 (36.4%)	11,501 (36.4%)	11,562 (36.4%)
≥50	15,181 (38.5%)	15,228 (38.5%)	15,112 (38.5%)	15,230 (38.5%)
Sex				
Male	19,327 (48.8%)	19,382 (48.8%)	19,266 (48.8%)	19,386 (48.8%)
Female	20,426 (51.2%)	20,492 (51.2%)	20,378 (51.2%)	20,493 (51.2%)
Race/ethnicity				
Mexican American	5,615 (9.6%)	5,642 (9.6%)	5,611 (9.6%)	5,641 (9.6%)
Other Hispanic	4,325 (7.6%)	4,336 (7.6%)	4,314 (7.6%)	4,337 (7.6%)
Non-Hispanic White	15,080 (61.8%)	15,121 (61.8%)	15,065 (61.9%)	15,119 (61.8%)
Non-Hispanic Black	8,628 (11.3%)	8,644 (11.2%)	8,578 (11.2%)	8,649 (11.3%)
Non-Hispanic Asian	4,112 (5.5%)	4,125 (5.5%)	4,079 (5.5%)	4,125 (5.5%)
Other race	1,993 (4.2%)	2,006 (4.2%)	1,997 (4.2%)	2,008 (4.2%)
Birth cohort				
Born before 1991	13,094 (25.9%)	13,141 (25.9%)	13,083 (25.9%)	13,143 (25.9%)
Born in 1991 or later	26,659 (74.1%)	26,733 (74.1%)	26,561 (74.1%)	26,736 (74.1%)
Birthplace				
US-born	30,474 (83.5%)	30,559 (83.5%)	30,390 (83.5%)	30,563 (83.4%)
Non-US-born	9,265 (16.5%)	9,301 (16.5%)	9,240 (16.5%)	9,302 (16.6%)

Note: Data are shown as the median (interquartile range) or unweighted frequency counts (weighted percentage) as appropriate. HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus; US, United States.

Table 2. Overall prevalence of hepatitis A to E viruses in the US population, 2011–2023

Etiology	Characteristics	N	*n*	Overall prevalence, % (95% CI)
HBV	Current HBV infection	39,874	184	0.3 (0.2–0.4)
	Susceptibility to HBV	39,848	27,808	71.3 (70.4–72.2)
	HBV vaccination coverage[#]	31,858	16,766	48.8 (47.7–49.9)
	HBV susceptibility among HBV-vaccinated participants	14,683	8,561	57.0 (55.6–58.4)
HDV	Anti-HDV positive among participants with current HBV infection	135	2	1.3 (0.3–6.1)
HCV	Anti-HCV positivity	39,644	644	1.6 (1.4–1.8)
	HCV RNA positivity	39,675	297	0.7 (0.6–0.9)
	HCV RNA positivity among anti-HCV-positive individuals	633	297	45.5 (40.6–50.4)
HAV	Anti-HAV positivity	39,753	22,271	44.7 (43.4–46.0)
	HAV vaccination coverage	37,526	17,040	40.9 (39.7–42.0)
HEV	Anti-HEV IgG positivity	39,879	2,990	7.4 (6.8–8.1)
	Anti-HEV IgM positivity	39,879	603	1.6 (1.4–1.8)

Note: Current HBV infection was defined as positive HBsAg and anti-HBc; susceptibility to HBV was defined as negative HBsAg, anti-HBc, and anti-HBs; vaccination coverage was defined as receipt of at least 1 vaccine dose. [#]HBV vaccination data were unavailable for the 2021–2023 cycle, so HBV vaccination trend analyses were restricted to the 2011–2020 period. anti-HAV, antibody to hepatitis A virus; anti-HBc, antibody to hepatitis B core antigen; anti-HBs, antibody to hepatitis B surface antigen; anti-HCV, antibody to hepatitis C virus; anti-HDV, antibody to hepatitis D virus; anti-HEV, antibody to hepatitis E virus; CI, confidence interval; HAV, hepatitis A virus; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis D virus; HEV, hepatitis E virus; IgG, immunoglobulin G; IgM, immunoglobulin M; N, number tested; *n*, number positive; RNA, ribonucleic acid.

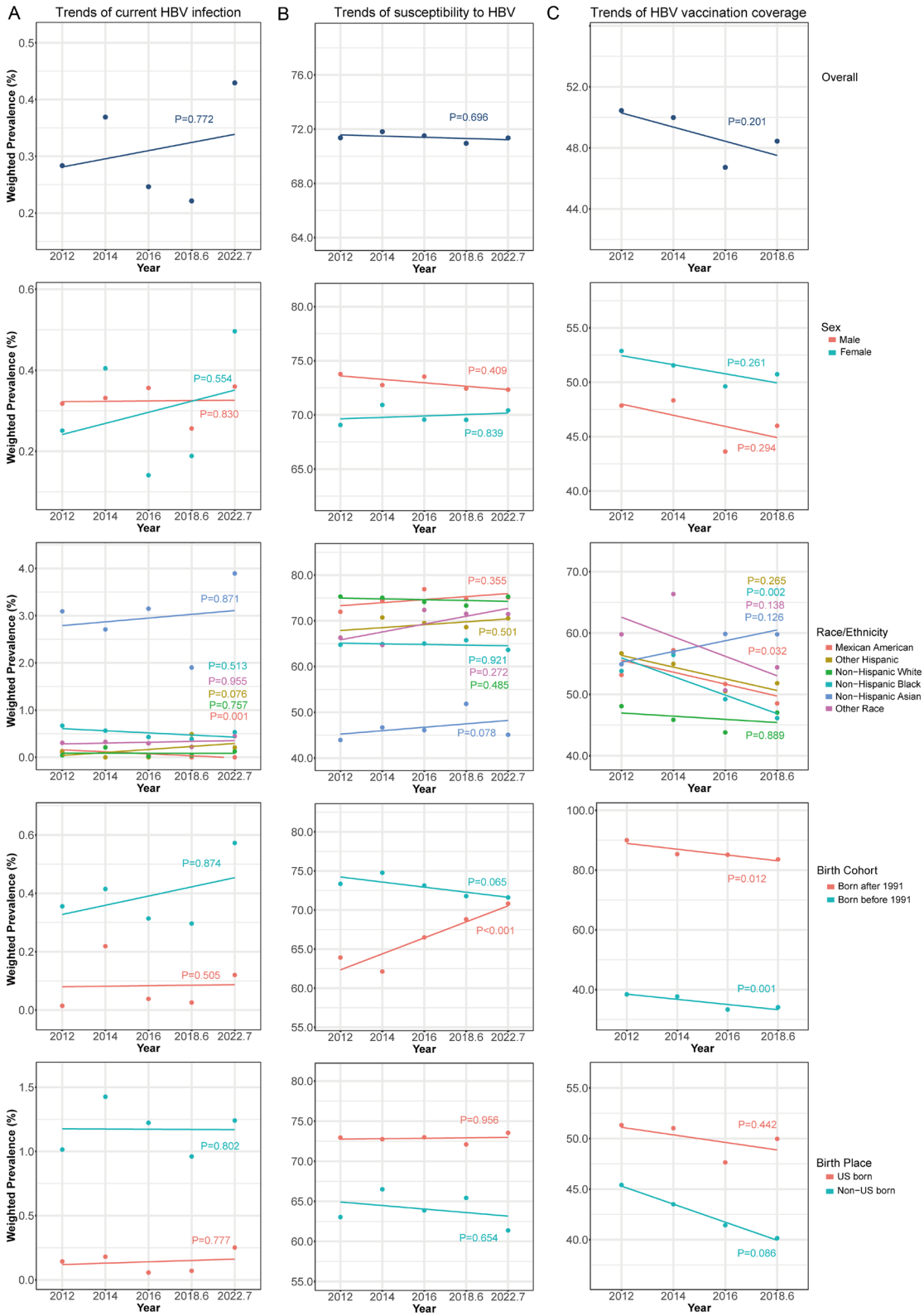


Fig. 1. Trends in HBV infection, susceptibility, and vaccination coverage in the US general population, 2011–2023. (A) Trends in current HBV infection (defined as positive HBsAg and anti-HBc). (B) Trends in susceptibility to HBV (defined as negative HBsAg, anti-HBc, and anti-HBs). (C) Trends in HBV vaccination coverage (at least one dose), 2011–2020. All panels show weighted prevalence overall and stratified by sex, race/ethnicity, birth cohort, and birthplace. anti-HBc, antibody to hepatitis B core antigen; anti-HBs, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus.

lion (95% CI: 216.41–221.94 million) individuals classified as susceptible to HBV (Table 2; Fig. 1B).

HBV vaccination coverage (at least 1 dose) decreased from 50.4% (95% CI: 47.8%–53.1%) in 2011 to 48.4% (95% CI: 46.2%–50.7%) in 2020, although the overall trend was not statistically significant (*P* for trend = 0.201). The decline was significant among individuals born in 1991 or later, with coverage decreasing from 90.0% to 83.6% (*P* for trend = 0.012). Significant declines were also observed among Mexican American and Non-Hispanic Black participants, whereas the Non-Hispanic Asian subgroup showed a nonsignificant increase from 54.9% to 59.8% (*P* for trend = 0.126) (Fig. 1C). Notably, 57.0% (95% CI: 55.6%–58.4%) of participants reporting at least one HBV vaccine dose met the study's serological definition of HBV susceptibility. Anti-HDV seroprevalence among participants with current HBV infection was 1.3% (95% CI: 0.3%–6.1%; *n* = 2) (Table 2).

Hepatitis C epidemiological trends

The overall anti-HCV seroprevalence remained stable at 1.6% (95% CI: 1.4%–1.8%) in the US population from 2011 to 2023 (Fig. 2A; Table 2), corresponding to an estimated 4.92 million (95% CI: 4.30–5.53 million) individuals with evidence of prior HCV exposure. In contrast, the prevalence of active HCV viremia decreased from 0.8% in 2011 to 0.4% in 2023, corresponding to a decrease from 2.46 million to 1.23 million individuals. The decline was most apparent among Mexican American and Non-Hispanic Black participants (Fig. 2B).

Furthermore, the proportion with active viremia among anti-HCV-positive individuals decreased from 65.5% in 2011 to 31.3% in 2023, with a significant linear downward trend (*P* for trend = 0.004). The decline was most apparent among women, Non-Hispanic Black participants, and those aged ≥50 years and was consistent with improved HCV treatment uptake and cure rates over the study period (Fig. 2C).

Hepatitis A and hepatitis E trends

Anti-HAV seroprevalence showed a significant upward trend, increasing from 41.6% (127.88 million individuals) in 2011 to 48.0% (147.55 million individuals) in 2023 (*P* for trend < 0.001). The increase was most apparent among Non-Hispanic White participants and those aged <50 years (Fig. 3A). In contrast, national HAV vaccination coverage (at least 1 dose) remained relatively stable throughout the study period, with no significant temporal trend (Fig. 3B). Anti-HEV IgM positivity also increased slightly, from 1.6% in 2011 to 1.7% in 2023 (*P* for trend = 0.004), with the increase most apparent among men, Non-Hispanic White participants, and those aged ≥50 years (Fig. 3C).

Discussion

Using nationally representative NHANES data, this study provides a comprehensive epidemiological analysis of hepatitis A–E markers in the United States from 2011 to 2023. The findings show divergent patterns across hepatitis viruses, including progress in some areas and continuing challenges in others. These findings have important implications for long-term liver disease prevention, clinical practice, and progress toward the WHO 2030 viral hepatitis elimination goals.

A notable finding was the substantial reduction in active HCV infection over the study period, from an estimated 2.46 million to 1.23 million individuals nationwide. The stable overall anti-HCV seroprevalence accompanied by a decline in the viremic proportion is consistent with the nationwide scale-up of direct-acting antiviral therapy and improved population-level cure rates in the US.[19] The marked decrease in the proportion of viremic individuals among anti-HCV-positive participants is also consistent with improvements in HCV screening and treatment, particularly among older populations. These trends are consistent with progress toward reducing HCV-related liver disease and mortality.

Conversely, the analysis identified continuing challenges in HBV prevention and control. First, the persistently high serological susceptibility rate (71.3%) indicates that more than 219 million US residents aged 6 years and older met the study definition of susceptibility to HBV. Second, overall HBV vaccination coverage decreased slightly, and the decline was statistically significant among individuals born in 1991 or later, the target population for universal childhood vaccination. Declining vaccination coverage in younger birth cohorts could hinder progress toward long-term HBV elimination and increase the future burden of HBV-related disease. The different vaccination pattern observed among Non-Hispanic Asian participants may reflect population-specific health education, screening, or other factors and warrants further investigation.

Notably, 57.0% of participants reporting at least one HBV vaccine dose met the study's serological definition of HBV susceptibility. This finding may reflect incomplete vaccination, waning detectable anti-HBs levels over time, or individual variation in immune response and should not be interpreted as direct evidence of suboptimal vaccine immunogenicity. Further evaluation of vaccination completion and time since vaccination may help clarify this finding.

For HAV, increasing seroprevalence despite stable reported vaccination coverage may reflect natural exposure in addition to vaccination; however, the cross-sectional data do not establish the source of seropositivity. This pattern is consistent with the continued occurrence of community HAV transmission and outbreaks in the United States.[20] Although anti-HEV IgM positivity remained low and increased only slightly, the finding suggests continued low-level HEV circulation. Acute HEV infection is usually self-limiting in healthy individuals but may cause severe acute liver injury, acute liver failure, and high mortality in older adults, pregnant women, and individuals with underlying chronic liver disease.[8,21,22] Using the updated testing method, we observed a low anti-HDV seroprevalence among participants with current HBV infection, consistent with previous studies.[17,23]

This study has several strengths. First, the use of multiple NHANES cycles enabled assessment of temporal patterns in a nationally representative survey. Second, the analysis considered all five major hepatitis viruses within a common framework. Third, stratified subgroup analyses and formal trend tests helped identify population patterns relevant to prevention efforts. Several limitations should also be considered. First, NHANES excludes institutionalized populations and people experiencing homelessness, which may underestimate viral hepatitis prevalence in some high-risk groups. Second, because NHANES is a population survey rather than a formal national epidemiological surveillance system, its sampling framework may not capture all groups at highest risk of viral hepatitis. Third, some serological definitions used in this study do not correspond directly to standard clinical diagnoses, which may limit interpretation of the prevalence estimates. Fourth, the small number of HDV-positive cases limited further statistical analyses of HDV epidemiology. Fifth, relevant behavioral risk factors, including food-related exposures, injection drug use, high-risk sexual exposure, and travel to endemic areas, were missing in several NHANES cycles, precluding additional stratified analyses.

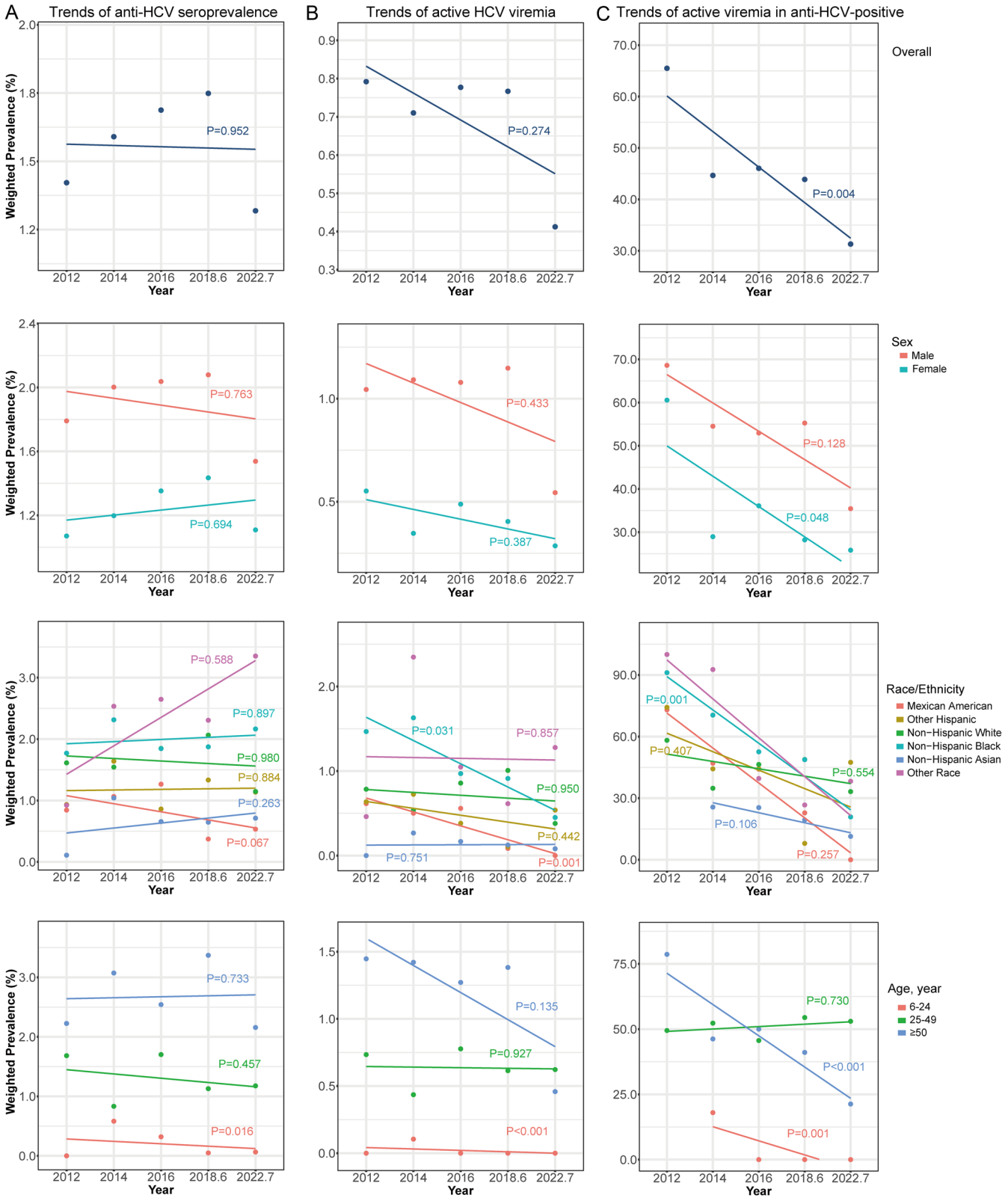


Fig. 2. Trends in HCV infection in the US general population, 2011–2023. (A) Trends in anti-HCV seroprevalence. (B) Trends in active HCV viremia (defined as positive HCV RNA). (C) Trends in active viremia among anti-HCV-positive individuals. All panels show weighted prevalence overall and stratified by sex, race/ethnicity, and age. anti-HCV, antibody to hepatitis C virus; HCV, hepatitis C virus; RNA, ribonucleic acid.

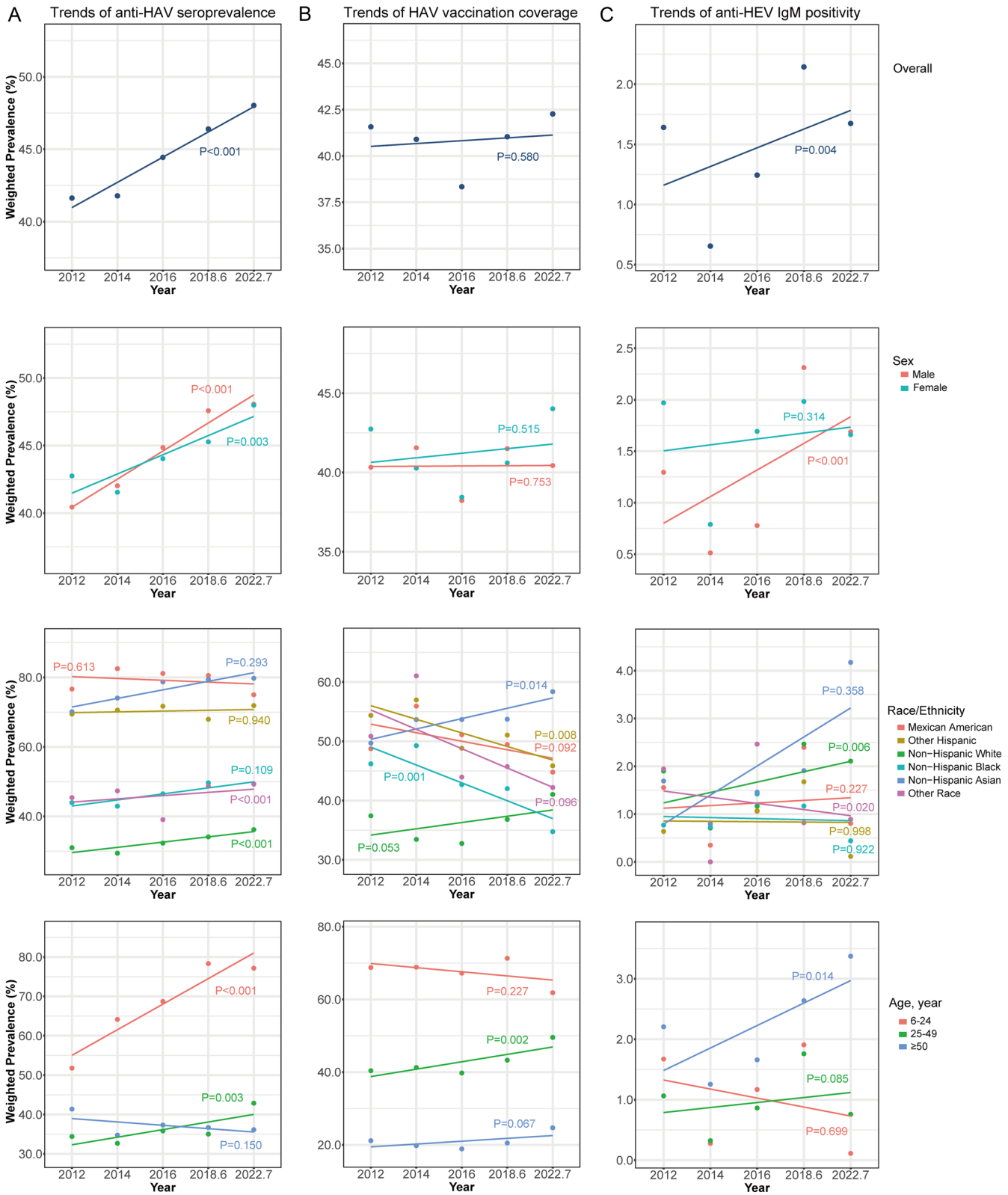


Fig. 3. Trends in HAV and HEV infection in the US general population, 2011–2023. (A) Trends in anti-HAV seroprevalence. (B) Trends in HAV vaccination coverage (at least one dose). (C) Trends in anti-HEV IgM positivity. All panels show weighted prevalence overall and stratified by sex, race/ethnicity, and age. HAV, hepatitis A virus; HEV, hepatitis E virus; IgM, immunoglobulin M.

Conclusions

This population-based analysis showed divergent epidemiological trends in hepatitis A–E markers in the United States from 2011 to 2023. Active HCV infection decreased, a pattern consistent with progress in national HCV control. However, persistent HBV susceptibility and declining HBV vaccination coverage among younger populations remain important public health challenges. Changes in HAV seroprevalence and a slight increase in anti-HEV IgM positivity warrant continued surveillance and further investigation. Targeted vaccination efforts, continued assessment of population immunity, and sustained nationwide viral hepatitis surveillance may support further progress toward the WHO 2030 viral hepatitis elimination goals in the United States.

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Conflict of interest

PH has been an Editor-in-Chief of *Journal of Clinical and Translational Hepatology* since 2026. The other authors have no conflict of interests related to this publication.

Author contributions

Study concept and design (ZC, PH), acquisition of data (ZL, ZC), analysis and interpretation of data (ZL, YC, YZ), drafting of the manuscript (ZL), critical revision of the manuscript for important intellectual content (ZC, PH), administrative, technical, or material support (ZC), and study supervision (ZC). All authors made significant contributions to this study and approved the final manuscript.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2024). NHANES was approved by the NCHS Research Ethics Review Board (Protocol #2021-05 and #2011-17). Adult participants provided written informed consent, and minors provided assent with permission from a parent or legal guardian.

Data sharing statement

All data used in this study are publicly available in the NHANES database (https://wwwn.cdc.gov/nchs/nhanes/Default.aspx).

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