



Letter to the Editor



Acute Hepatitis E: A Global Problem, a European Vision

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Dear Editors,

We read with interest the article published in your journal by Huang *et al.*,¹ entitled *Global Trends and Cross-country Inequalities of Acute Hepatitis E in the Elderly, 1990–2021: A Comprehensive Analysis*. We found the age-adjusted incidence rates per 100,000 population of acute hepatitis E virus (HEV), presented for countries according to the socio-demographic index (SDI), very interesting, and we would like to make a comparison with the European Union (EU), as this is the region in which we live. In the Global Burden of Disease (GBD) study,² there is variation in SDI within the EU itself, with countries mainly falling into the high and medium-high SDI groups. Specifically, we analyzed the country with the highest GDP per capita — Luxembourg (€126,910), Spain, which is our country of origin and ranks 16th in the EU with a GDP per capita of €32,590 (placing it in the middle of the list and below the EU average), and the country with the lowest GDP per capita—Bulgaria (€16,110).³

Figure 1 shows the age-adjusted incidence rates per 100,000 population in the three EU countries. According to the GBD, Luxembourg belongs to the group of countries with a high SDI level, while Spain and Bulgaria fall into the medium-high SDI level. This classification is based not only on per capita income but also on average educational level and total fertility rate.² According to the observed data, it is striking that Bulgaria has an age-standardized incidence rate (ASIR) in both years above the world average and above countries with low SDI, whereas Spain, despite being in the same SDI group as Bulgaria, shows similar or even slightly better incidence rates than Luxembourg. Compared with the data reported by Huang *et al.*,¹ Spain and Luxembourg have better ASIRs than countries in the high SDI group, as shown in Figure 1. This difference may be because healthcare in Spain is comparable to that of high SDI countries, ensuring proper hygiene and access to safe drinking water, which could prevent the spread of HEV. Indeed, compared to Bulgaria, Spain has a higher life expectancy.⁴

Figure 2 shows that the age-standardized disability-adjusted life years rates per 100,000 population in the three

European countries analyzed remain below global rates and those of their respective SDI groups. This is despite Bulgaria's high ASIR, which has not affected this measure. Spain maintains the best rates, closely followed by Luxembourg. Further studies in Bulgaria would be valuable to investigate the reasons for this high ASIR and to determine whether factors beyond the known modes of HEV transmission are involved.

As GBD data indicate,² and as Huang *et al* report,¹ the number of HEV cases has been increasing considerably over the years, becoming a global problem, especially in areas with underdeveloped healthcare systems or infrastructure.⁵ This trend may also be driven by increasing population size and longevity.¹ There are different HEV genotypes; although the GBD does not distinguish between them,² types 1 and 2 are primarily associated with low- and middle-income countries,⁶ where proper sanitation, hygiene, and access to safe drinking water are crucial for prevention. A vaccine is licensed in China and Pakistan, which could be used for vulnerable populations, such as immunodeficient individuals, pregnant women, and people with liver disease, particularly in Africa and Asia, and its application in controlling the virus is of interest.⁷ Types 3 and 4 are increasing in incidence, especially in more developed countries, mainly through the consumption of undercooked meat or game.⁸ Despite World Health Organization recommendations for vaccination, it has not been incorporated into the vaccination campaigns of most countries.⁷

In conclusion, we believe it is essential to consider the use of the vaccine, especially in countries where incidence is rising, to help slow the spread of the disease.² This could also lead to savings in the costs associated with treating HEV, given the increasing number of cases reported in the data.

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Conflict of interest

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Author contributions

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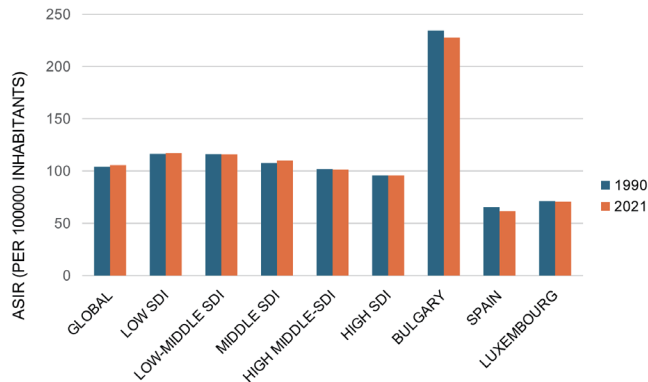


Fig. 1. ASIR per 100,000 inhabitants (95% CI) in 1990 and 2021. Blue bars correspond to the year 1990, and orange bars correspond to the year 2021. ASIR, age-standardized incidence rate; SDI, socio-demographic index; CI, confidence Interval.

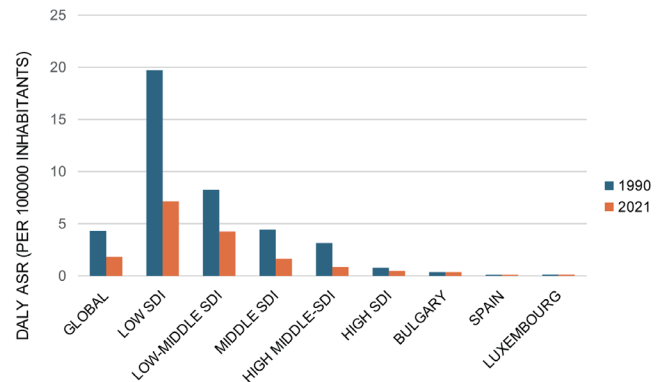


Fig. 2. ASR of disability-DALY per 100,000 inhabitants (95% CI) in 1990 and 2021. Blue bars correspond to the year 1990, and orange bars correspond to the year 2021. DALY, adjusted life years; ASR, age-standardized rate; SDI, socio-demographic index; CI, confidence Interval.

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References

- [1] Huang D, Jiang J, Peng J, Zhu Z, Chen Y, Zhang S, *et al*. Global Trends and Cross-country Inequalities of Acute Hepatitis E in the Elderly, 1990–2021: A Comprehensive Analysis. *J Clin Transl Hepatol* 2025;13(8):609–618. doi:10.14218/JCTH.2025.00101.
- [2] Institute for Health Metrics and Evaluation (IHME). GBD Results Tool. [Internet]. Seattle, WA: IHME, University of Washington; 2021. [cited 2025 July 2]. Available from: <https://vizhub.healthdata.org/gbd-re>.
- [3] Datosmacro. Países-Grupo Union Europea. [Internet]. Expansión. 2025. [cited 2025 July 2]. Available from: <https://countryeconomy.com/countries/groups/european-union>.
- [4] World Data. Country comparison: Bulgaria/Spain. [Internet]. 2025. [cited 2025 July 2]. Available from: <https://www.worlddata.info/country-comparison.php?country1=BGR&country2=ESP>.
- [5] World Health Organization. The global prevalence of hepatitis E virus infection and susceptibility: a systematic review. Geneva, Switzerland: World Health Organization; 2010.
- [6] WHO Library Cataloguing-in-Publication Data. Waterborne outbreaks of hepatitis E: recognition, investigation and control. Geneva, Switzerland: World Health Organization; 2014.
- [7] Dudman S, Zerja A, Hasanoğlu İ, Ruta S, van Welzen B, Nicolini LA, *et al*. Global vaccination against hepatitis E virus: position paper from the European Society of Clinical Microbiology and Infectious Diseases Viral Hepatitis Study Group. *Clin Microbiol Infect* 2025;31(2):201–210. doi:10.1016/j.cmi.2024.11.016, PMID:39550032.
- [8] Webb GW, Dalton HR. Hepatitis E: an expanding epidemic with a range of complications. *Clin Microbiol Infect* 2020;26(7):828–832. doi:10.1016/j.cmi.2020.03.039, PMID:32251845.