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ASSOCIATIONS COLLABORATING ON HEPATITIS TO
IMMUNIZE AND ELIMINATE THE VIRUSES IN EUROPE

ACHIEVE contribution to the Cancer Inequalities Registry Inequalities in liver cancer prevention linked to viral hepatitis B (HBV) and C (HCV) services

The [ACHIEVE Coalition](#), advocating to end hepatitis by 2030 and comprising patient associations, academics, clinicians and industry, welcomes the European Commission's intention to build an EU Cancer Inequalities Registry and **calls for the inclusion of inequalities in liver cancer and its key determinant viral hepatitis**.

Making such inequalities visible should help in fighting them more effectively going forward. We hope that our collation of data on inequalities in viral hepatitis and liver cancer along the patient pathway will lead to constructive discussions at the EU level on how to emulate good practices. The EU collectively, i.e., all EU Member States, must take effective measures to fight viral hepatitis and meet the WHO 2030 elimination goal, which will significantly reduce the burden of liver cancer.

Viral hepatitis and Liver cancer

Viral hepatitis B and C are responsible for more than 70% of liver cancer cases and are recognised as cancer preventable risk factors in Europe's Beating Cancer Plan and by the WHO^{1,2,3}. Research also highlights a 'crucial need for resources directed towards cancer prevention programmes that target infection, including viral hepatitis, particularly in high-risk populations. Such interventions can markedly reduce the increasing cancer burden and associated mortality'³.

Hepatitis B infection can be prevented through childhood immunization, chronic hepatitis B can be controlled through effective treatments and hepatitis C cured⁴. However, the majority of people infected with hepatitis in the EU are unaware of their status, especially vulnerable populations.

According to the European Centre for Disease Prevention and Control (ECDC), 'many viral hepatitis infections do not show any symptoms, so the 'silent disease' is often not diagnosed'. Without being linked to care, chronic hepatitis infection can lead to liver cirrhosis and an increased risk of developing liver cancer⁵. This comes as no surprise as liver disease has for long been referred to as a neglected non-communicable disease (NCDs) in comparison to other NCDs, such as cardiovascular diseases and diabetes⁶.

Both the International Agency for Research on Cancer and the World Health Organization agree that 'linkages to risk factors and cancer-related outcomes can help to further explain transitions and

¹ Wild et al. (2020). World Cancer Report: Cancer Research for Cancer Prevention. Lyon, France: *International Agency for Research on Cancer*. Available from: <http://publications.iarc.fr/586>. Licence: CC BY-NC-ND 3.0 IGO.

² European Commission (2022). Europe's Beating Cancer Plan: Implementation Roadmap. Retrieved from https://ec.europa.eu/health/system/files/2022-01/2021-2025_cancer-roadmap1_en_o.pdf

³ de Martel et al. (2020). Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *The Lancet Global Health*, 8(2), e180–e190. [https://doi.org/10.1016/S2214-109X\(19\)30488-7](https://doi.org/10.1016/S2214-109X(19)30488-7)

⁴ Karlsen et al. (2022). The EASL–Lancet Liver Commission: protecting the next generation of Europeans against liver disease complications and premature mortality. *The Lancet*, 399(10319), 61–105. [https://doi.org/10.1016/S0140-6736\(21\)01701-3](https://doi.org/10.1016/S0140-6736(21)01701-3)

⁵ ECDC: around 9 million Europeans are affected by chronic hepatitis B or C. (2017, July 26). [Press release]. <https://www.ecdc.europa.eu/en/news-events/ecdc-around-9-million-europeans-are-affected-chronic-hepatitis-b-or-c>

⁶ Lopez et al. (2014). Remembering the forgotten non-communicable diseases. *BMC Medicine*, 12(1). <https://doi.org/10.1186/s12916-014-0200-8>



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inequalities in the cancer burden⁷. Modelling suggest that the elimination of viral hepatitis C alone would reduce the burden of liver cancer by more than 65%⁷.

However, data is still scarce, and significant gaps in the data on prevalence, diagnosis, treatment and treatment outcomes for HBV and HCV in the EU pose a significant challenge to not only monitoring progress towards the 2030 elimination goals, but also cancer prevention. According to the ECDC, countries should prioritise improving the availability and quality of their monitoring systems, as well as addressing methodological issues related to the WHO-defined indicators for the continuum of care for HBV and HCV⁸.

Inequalities in hepatitis B vaccination

People chronically infected with hepatitis B are up to 100 times more likely to develop liver cancer⁹. Hepatitis B vaccine has been instrumental in reducing the global incidence of hepatitis B amongst children under the age of 5. According to the WHO recommendations, effective vaccination of populations at risk as well as a cohesive policy with universal immunization throughout Europe should be encouraged^{10,11}.

With the exception of Denmark, Finland and Iceland, all EU/EEA countries offer vaccination to children as part of national primary vaccination programmes¹². Although many of these programmes, have been in place for 20 to 30 years, coverage rates vary from under 90% to over 95%¹³. The 2020 target of 95% was met by 7 countries. Countries such as Bulgaria and Romania which are known to have the highest burden, have the lowest coverage. This exacerbates hepatitis related inequalities.

A successful prevention strategy includes also vaccination of high-risk groups such as people who inject drugs (PWID) and healthcare workers¹⁴. Eighteen countries have HBV vaccine programmes

⁷ European Union HCV Collaborators. (2017). Hepatitis C virus prevalence and level of intervention required to achieve WHO targets for elimination in the European Union by 2030: a modelling study. *Lancet Gastroenterol Hepatol*, 2(5), pp. 325-336.

⁸ European Centre for Disease Prevention and Control. (2020a). Monitoring of responses to the hepatitis B and C epidemics in EU/EEA countries – 2020 data. <https://www.ecdc.europa.eu/sites/default/files/documents/Monitoring-responses-to-hepatitis-B-and-C-epidemics-2020-data.pdf>

⁹ *Chronic Viral Hepatitis* » *Hepatitis B Foundation*. (2022). Hepatitis B Foundation. Retrieved June 7, 2022, from <https://www.hepb.org/research-and-programs/liver/risk-factors-for-liver-cancer/chronic-viral-hepatitis/>.

¹⁰ Yee et al. (2020). Gaps in Hepatitis B Vaccination Completion and Sero-Protection for People Who Inject Drugs in Hpakant, Myanmar, 2015–2018. *Tropical Medicine and Infectious Disease*, 5(2), 1–11. <https://doi.org/10.3390/tropicalmed5020077>

¹¹ Lernout, T., Hendrickx, G., Vorsters, A., Mosina, L., Emiroglu, N., & van Damme, P. (2014). A cohesive European policy for hepatitis B vaccination, are we there yet? *Clinical Microbiology and Infection*, 20, 19–24. <https://doi.org/10.1111/1469-0691.12535>

¹² *European Centre for Disease Prevention and Control*. (2022). Vaccine Scheduler | ECDC. Retrieved July 15, 2022, from <https://vaccine-schedule.ecdc.europa.eu/Scheduler/ByDisease?SelectedDiseaseId=6&SelectedCountryIdByDisease=-1>

¹³ *European Centre for Disease Prevention and Control*. (2020). Prevention of hepatitis B and C in the EU/EEA and the UK. https://www.ecdc.europa.eu/sites/default/files/documents/hepatitis-B-and-C-prevention_1.pdf

¹⁴ Falla AM, Hofstraat SHI, Duffell E, Hahné SJM, Tavošči L, Veldhuijzen IK. Hepatitis B/C in the countries of the EU/EEA: a systematic review of the prevalence among at-risk groups. *BMC Infectious Diseases*. 2018; 18: 79



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aimed at people who inject drugs in prisons and sixteen countries reported that they include PWID in their national hepatitis policies. However, there is limited data on vaccination coverage in this population, with only five countries reporting coverage rates ranging from 26% - 84%¹⁵.

Whilst four-fifths of EU/EEA reported that their HBV vaccination policies include healthcare workers, HBV vaccination is only mandatory for all healthcare workers in seven countries. In two other countries it is mandatory for healthcare workers who are “at risk” of contracting the virus. Additionally, only eight countries reported on coverage rates for eligible healthcare workers, with coverage varying from 15.1% to 100%.

HBV immunization is also sometimes **low among certain vulnerable groups**, including **adult migrants from endemic regions** (e.g., sub-Saharan Africa, the Middle East)⁴. A careful review of the full vaccine history is important among migrant populations to identify any gaps in coverage, including full vaccination against HBV¹⁶.

The COVID-19 pandemic has globally posed additional challenges by disrupting hepatitis B vaccination programmes, especially among infants, and increasing the need to expand vaccinations among vulnerable groups, including migrants, PWUD, prison inmates, among others¹⁷. In EU/EEA, some countries reported 1 to 3% decline in the coverage of the three doses of HBV vaccine since 2019¹⁸, which may be due to the COVID-19 pandemic and resultant public health measures¹⁹. While some countries were able to adapt services to continue vaccination coverage during the COVID-19 pandemic, other countries experienced interruptions to their vaccinations programmes and increased parental hesitancy towards vaccinations, negatively impacting vaccination rates^{19,20}.

In conclusion, well-implemented childhood programmes with good coverage and vaccination programmes targeting key risk groups can further reduce transmission and prevent the disease burden from growing further. However, one must not forget the 2021 statement of EASL–Lancet Liver Commission: ‘although vaccination has reduced the prevalence of HBV in children, **vaccination programmes will not alleviate the large existing burden of chronic HBV infection in older generations**⁴. Greater efforts to screen people at risk and link those who are chronically infected to the appropriate care are thus indispensable. The same is true for viral hepatitis C.

Inequalities in hepatitis screening and diagnosis

¹⁵ European Monitoring Centre for Drugs and Drug Addiction. *Elimination barometer on viral hepatitis among people who inject drugs in Europe*. Luxembourg: EMCDDA; 2021 [12 August 2022]. Available at: https://www.emcdda.europa.eu/publications/html/viral-hepatitis-elimination-barometer_en

¹⁶ Socha, A., & Klein, J. (2020). What are the challenges in the vaccination of migrants in Norway from healthcare provider perspectives? A qualitative, phenomenological study. *BMJ Open*, 10(11), e040974. <https://doi.org/10.1136/bmjopen-2020-040974>

¹⁷ Pley et al. The global impact of the COVID-19 pandemic on the prevention, diagnosis and treatment of hepatitis B virus (HBV) infection. *BMJ Global Health* 2021;6:e004275. doi:10.1136/bmjgh-2020-004275

¹⁸ World Health Organization. (n.d.). *Hepatitis B vaccination coverage*. Retrieved August 25, 2022, from <https://immunizationdata.who.int/pages/coverage/HEPB.html?CODE=Global&ANTIGEN=HEPB3&YEAR=>

¹⁹ Chiappini et al. (2021, June 2). Impact that the COVID-19 pandemic on routine childhood vaccinations and challenges ahead: A narrative review. *Acta Paediatrica*, 110(9), 2529–2535. <https://doi.org/10.1111/apa.15949>.

²⁰ Huss et al. Implications of the COVID-19 pandemic for pediatric primary care practice in Europe. *European Paediatric Association*. 2021; 233: 290 – 291.



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Often, liver cancer prevention services fail to reach those in need. **Poor testing and screening uptake for viral hepatitis among the most vulnerable restricts prevention opportunities for liver cancer and sets the ground for inequalities in access to life-saving treatment.**

In the EU, large proportion of cases are undiagnosed, with rates varying by country; undiagnosed HCV rates range from around 1100 (per 100 000 population) in Romania to less than 50 (per 100 000 population) in France. For HBV, it is still not possible to estimate the number of remaining undiagnosed people⁸. It is estimated that **most of those undiagnosed belong to vulnerable groups** as infection rates are higher among this population (e.g., people who inject drugs (PWID), prison inmates, etc.)²¹. Particularly, PWID are disproportionately affected by HBV and HCV infections due to shared injection equipment and drug paraphernalia. In Europe, there is a high prevalence of infection and ongoing transmission in this population, especially for HCV²³. Out of 14 countries in the EU/EEA region that provided data, only three (21%) met or exceeded the 2020 target of 200 syringes distributed per PWID per year and nine countries (64%) reported met or exceeded the 40% coverage target of more of opioid substitution treatment (OST). However, only two (14%) met both the OST coverage target and the syringe distribution target¹⁵. Additionally, only nine countries reported achieving the 2020 target of more than 50 % of people injecting drugs entering drug treatment had been tested for HCV in the last 12 months¹⁵.

PWID and prison inmates have the highest prevalence for hepatitis B and C; in particular, viral hepatitis is 15–50 times higher in PWID than in the general population⁴, causing a **15 to 20-fold increase in the risk of liver cancer**²². Marginalised, stigmatised and with low resources, they face **many access barriers to primary care services**²³ and have restricted access to liver cancer prevention services despite being in greater need than the general population.

However, inequalities do not only exist with regards to vulnerable populations. Geographically, inequalities between countries are also significant. It is estimated that the number of people living with chronic HBV infection ranges with a difference of 18-fold between Romania, with the highest number, and Denmark, with the lowest (per 100 000 population)⁸. Regarding HCV, the estimated number of people living with the chronic infection (per 100 000 population) varies even more from 88 people in Iceland to 410 775 people in Italy, disclosing a larger gap between countries than for chronic HBV⁸. Overall, only few countries were able to report data on the number of people diagnosed with viral hepatitis.

Worryingly, even fewer countries were able to report estimates of the proportion of individuals with chronic hepatitis infection who had end-stage liver disease, including decompensated cirrhosis or hepatocellular carcinoma, at the time of diagnosis. Of those, as many as 27.2% of diagnosed chronic HCV cases presented with end-stage liver disease, while for HBV estimates range from 1.5-40%⁸.

Inequalities in access to treatment

²¹ European Centre for Disease Prevention and Control. (2018). *Hepatitis B and C epidemiology in selected population groups in the EU/EEA*. ECDC. <https://www.ecdc.europa.eu/sites/default/files/documents/Hepatitis-B-C-epidemiology-in-selected-populations-in-the-EU.pdf>

²² Thylur et al. (2020). Assessment of risk factors, and racial and ethnic differences in hepatocellular carcinoma. *JGH Open*, 4(3), 351–359. <https://doi.org/10.1002/jgh3.12336>

²³ Hopwood, M., & Treloar, C. (2015). *Barriers to viral hepatitis treatment in primary care settings*. Sydney: Centre for Social Research in Health, UNSW Australia. https://www.arts.unsw.edu.au/sites/default/files/documents/Viral_hepatitis_in_primary_care_settings_FINAL.pdf



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Every year, thousands of individuals from the most vulnerable groups **develop and die from liver cancer due to late hepatitis treatment initiation or loss of follow-up**. For a timely treatment initiation and for liver cancer to be avoided, **people must be linked to care** following the diagnosis²⁴. According to Mauss et al., for patients with advanced liver disease, or late presenters, 'there is indisputable evidence that earlier initiation of treatment would have provided significant benefit. This can 'help quantify the proportion of cases missing timely diagnosis and treatment'²⁴.

Liver diseases are linked to social and health inequalities. Socially disadvantaged groups and vulnerable populations are disproportionately affected by liver disease for a several of reasons, including a higher risk of viral hepatitis infection⁴. Barriers to primary care associated with social and economic inequalities also translate into **poor treatment adherence** and **poor monitoring along the care pathway**^{4,23}. In recent years, there have been great advances in the treatment of hepatitis, with **therapeutical options not reaching those from the most vulnerable groups systematically**, as compared to the general population^{4,23}. ECDC has reported that at least 11 countries have reported restrictions on access to treatment with the most affected population being undocumented migrants and PWID⁸.

Inequalities in liver cancer monitoring

While marginalised groups with chronic hepatitis are at the highest risk of liver cancer, they have disproportionately **low access to cancer monitoring through health checks, resulting in more advanced cancer stage at diagnosis, restricted treatment options, and, ultimately, lower cancer survival** than the general population^{25,26}.

However, even in the general population access for people with chronic hepatitis to monitoring for follow on diseases can be difficult. Across the EU, the use of liver cancer screening is often inconsistent and frequently done late. Even though cancer surveillance in Europe is higher than in other regions of the world, the implementation is heterogeneous highly contributing to inequalities between countries⁴.

Despite the urgency and widespread support from healthcare professionals and patients themselves, there is still lack of attention and political will in the European Union²⁷. Health systems amplify increasing sociodemographic burdens, and early detection of preventable and treatable liver disease is hindered by shortcomings in effective screening mechanisms, associated stigma and social inequities⁴. Barriers are easily identified and can serve as important targets to overcome, increasing HCC surveillance.²⁸

²⁴ Mauss et al. (2017). Late presentation of chronic viral hepatitis for medical care: a consensus definition. *BMC Medicine*, 15(1). <https://doi.org/10.1186/s12916-017-0856-y>

²⁵ Kim et al. (2018). Liver Disease Monitoring Practices After Hepatitis C Cure in the Underserved Population. *Hepatology Communications*, 2(10), 1274–1283. <https://doi.org/10.1002/hep4.1246>

²⁶ Kim, A. K., & Singal, A. G. (2014). Health disparities in diagnosis and treatment of hepatocellular carcinoma. *Clinical Liver Disease*, 4(6), 143–145. <https://doi.org/10.1002/cld.427>

²⁷ EASL Policy and Public Health Committee & EASL Task Force on Liver Cancer. (2022, May 22). EASL Policy Statement on Liver Cancer Screening. In https://easl.eu/wp-content/uploads/2022/05/policy-statement-on-liver-cancer-screening_25May2022.pdf. *European Association for the Study of the Liver*. Retrieved September 5, 2022, from https://easl.eu/wp-content/uploads/2022/05/policy-statement-on-liver-cancer-screening_25May2022.pdf

²⁸ Farvardin et al. (2016). Patient-reported barriers are associated with lower hepatocellular carcinoma surveillance rates in patients with cirrhosis. *Hepatology*, 65(3), 875–884. <https://doi.org/10.1002/hep.28770>

