

Oportunistic diagnosis based on age and hepatitis C virus clearance: an essential step to improve the overall health of the liver

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Back in January 2022, a The Lancet-European Association for the Study of the Liver (EASL) Commission on the impact of liver disorders in the European region commissioned by the World Health Organization (WHO) demonstrated that this condition is, actually, the second leading cause of loss of labor years in Europe after ischemic heart disease (1). This is a very relevant piece of information since this is something that is going to impact the new generations of Europeans unless a significant change is made in public health policies. Despite the advances made over the last few years in hepatitis C virus (HCV) clearance (understood as a significant reduction of morbidity and mortality associated with hepatitis B and C viruses), there are still challenges ahead to improve liver health due to the high use of alcohol, and the inseparable triad obesity/diabetes mellitus/metabolic associated fatty liver disease. Also, access to healthcare for several population groups at risk of presenting higher rates of liver disease has become a problem. The aforementioned commission established a series of recommendations. We should mention some of them here, like how important the early identification of liver fibrosis is by proactively looking for cases and, also, how significant the early management of liver conditions really is, both crucial to reduce the viral disease load in Europe. These recommendations try to shed light on the overall health of the liver, which will eventually contribute to individual health, a concept that should become our beacon for the coming years. And, in this context, hepatitis C is the paradigm of easily identifiable liver disease with healing rates close to 100 %. Treatment reduces hepatic and extra-hepatic morbidity and mortality significantly both in the short- and in the long-term.

Several countries have adopted national plans with the final objective of HCV clearance; among them, Iceland, Spain, and The Netherlands (Europe) are coming close to clearing this virus thanks to their health plans (2-4). Overall, these plans include HCV screening based on the existence of risk factors for acquiring the infection, the active search for patients previously diagnosed, and the development of micro-clearance strategies targeted at vulnerable populations (5). Some of these strategies are simplifying diagnosis and patient treatment (6), improving healthcare circuits, and the possibility of diagnosing and treating these patients in the community in an effort to bring down the barriers of access to the healthcare system of the most vulnerable populations. Since the induction of the National Strategic Plan for the Approach to Hepatitis C (PEAHC) in Spain (2), over 158,000 patients have received direct-acting antivirals (DAAD) with reported healing rates over 95 %. To give continuity to this line of action, the Spanish Ministry of Health published a set of guidelines for the screening of HCV infections (7). These guidelines summarize the indications given on the screening of HCV and the involvement of the people diagnosed at follow-up and regarding treatment compliance. Multiple individual and collective initiatives have joined the official healthcare plans envisioned by the government, but also with an academic and social approach. This has increased diagnosis substantially, as well as the relation between treatment and the overall population, especially, the most vulnerable groups, thus increasing HCV micro-clearance in many of these groups significantly. Some of the initiatives we should mention are multiple clearance projects scattered in different healthcare and community centers; micro-clearance projects in the prison system (8,9), population with psychotic disorders

(10) and the immigrant population (11); and recapture of patients lost in the system, including drug addicts (12,13). In all these population segments, the implementation of an overall HCV clearance strategy is not easy. Therefore, screening programs at the Emergency Department (ER) of different Spanish hospitals, the registries of patients treated from the Spanish Association for the Study of the Liver (AEEH), the challenge of multidisciplinary care at drug addict centers, the implementation of telemedicine programs (14), the creation of certification programs of excellence for the diagnosis and management of HCV in health centers of patients with chronic consumption of toxic drugs (15), the creation of the Alliance for the Clearance of Viral Hepatitis in Spain (AEHVE) (16) or the most recent creation of the decalogue for viral hepatitis clearance (17), the proposal for a comprehensive diagnosis of viral hepatitis (18), and the AEHVE program "Hepatitis C-free Cities" try to get local administrations involved in clearance politics. These initiatives mean qualitative advances and have reduced HCV-related hospitalizations significantly, and the need for liver transplantation, which is a double benefit for individual and collective health (19,20).

Despite all the plans and multiple successful individual initiatives implemented and/or coming from scientific societies and/or patient associations, the lack of an effective vaccine complicates our goal of eradicating hepatitis C virus from our lives. Still, our road ahead looks much clearer compared to that of some of our neighboring countries (21). Seroprevalence studies in the general population treated in Spanish health centers in 2018 say we are a low prevalence country, since 0.22 % of the overall population between 20 and 80 years old had an active infection due to HCV in 2018 and 0.34 % back in 2016. However, we should mention that prevalence is much higher in men between the ages of 45 and 70, reaching rates close to 1 %. We should mention that these prevalence studies only take into consideration the general population admitted to Primary Care centers. Also, these studies are the result of people being called upon who eventually accept to take a serological test (22). We recently saw how opportunistic screenings among ER and hospital populations showed significantly higher prevalence rates (up to three times higher in some subgroups), which suggests that studies conducted among the general population could have underestimated the actual prevalence, especially among the most vulnerable patients who rarely visit conventional healthcare centers (23,24). Also, these studies demonstrate that a relatively high number of patients know about their disease, but just will not go to the hospital seeking healthcare, which tells us that these patients with hepatitis C need to be addressed. We know that diagnosis comes late in more than 25 % of the cases, with the corresponding loss of opportunity for these patients and the corresponding increased healthcare and social spending that could have been avoided with timely diagnoses and earlier commitments being made (25,26). Therefore, the significant impact liver diseases have in Europe is already known leading to discrimination, avoiding medical attention in Primary Care centers, and fewer resource allocation, something of paramount importance in viral hepatitis (1). Finally, we cannot obviate the consequences of the COVID-19 pandemic on the comprehensive approach of viral hepatitis that, added to inducing delays in all conventional diagnostic systems, brought all HCV screening programs to an end. Therefore, it has been

demonstrated that all the steps that are part of the cascade of healthcare provided in the management of viral hepatitis have been affected by the COVID-19 pandemic, which confirms the negative effect it has had on worldwide clearance programs. In addition, it suggests that the actions needed to meet the WHO targets for 2030 should be reassessed and reviewed while taking into consideration the progress made by every country in relation to the existing values prior to the COVID-19 pandemic (27).

We are pretty sure that to achieve this goal of complete hepatitis C clearance a more proactive approach should be adopted in the diagnosis of this infection. Diagnosis based on symptoms and/or risk of infection acquisition has proven insufficient and difficult to implement in the real-world routine clinical practice. Therefore, HCV screening should fall within a framework of population screening programs or through opportunistic activities upon petition from the patient that be or when seeking medical attention for other reasons. In our humble opinion, there is robust clinical evidence from both national and international clinical trials on the efficacy and cost-effectiveness ratio of general population screening programs of a certain age (in general, people born between 1950 and 1980). Therefore: a) different international organisms recommend screening in priority populations like age cohorts with higher hepatitis C viral loads (28-33); b) most studies already published on this issue conclude that a universal screening strategy is efficient compared to other strategies (non-screening, routine clinical practice or compared to other strategies); and c) several studies conducted on this issue in our country (20,34-36) conclude that the implementation of screening programs is clearly cost-effective in the age cohorts studied, and higher to the screening of just the risk factors. However, the Spanish Ministry of Health does not support population or age screenings based on a systematic review of the clinical effectiveness, safety, and financial assessment of population management of HCV commissioned to the Spanish Network of Agencies for Assessing National Health System Technologies and Performance (37), whose non-definitive conclusions suggest that the screening of higher-risk groups would be the most effective strategy of all. In our own opinion, this report has some serious evidence and methodological issues, the main of which is the inclusion of old studies on the management of hepatitis C. Also, it was based on the administration of interferon, drugs with a high number of adverse events, contraindications, and a response < 45 %, which clearly overestimates costs vs benefits compared to the results obtained in studies that apply the current DAAD-based therapies, safe drugs without contraindications that heal over 95 % of the cases. All of it obviously compromises the conclusions reached in the aforementioned report.

Although scientific evidence justifies universal population screening, especially in certain age groups, we believe that a pragmatic and viable approach could be more efficient: opportunistic diagnosis in people born between 1950 and 1980. This approach should include, by default, a serological test of hepatitis C virus in everybody seeking medical attention for whatever reasons as established in some clearance plans recently approved by some Spanish autonomous communities (38-40), which demonstrates not only its convenience but also its viability. This opportunistic diagnosis has some clear advantages: it is feasible in the en-

tire Spanish national territory, it is not conditioned by the rigidity of screening programs, and epidemiological interrogation is not needed. As a matter of fact, there are times when these questionnaires are not answered with sincerity by some patients (being stigma the main reason) or are not properly questioned by the health personnel, unmotivated, in most cases, when it comes to viral hepatitis. Also, it does not depend on the existence of a many times inexistent symptomatology. In addition, this type of screening can be performed on a biological sample obtained through venopuncture as in a drop of dry blood (41) or saliva (42) (which facilitates access to most vulnerable populations [43]). Today's computing systems allow us to avoid duplicities in its determination, can be adapted to the epidemiological peculiarities of this infection in a certain region and, also, it is the only way to diagnose vulnerable people. Besides, we would be avoiding the potential increase of social gradient that the acceptance of screening can cause and reducing the impact of the existing inequality in such a stigmatizing disease. Also, if this opportunistic diagnosis is achieved by adopting the comprehensive diagnosis we recently proposed (18) with just one single sample of blood, we can diagnose other viral diseases like hepatitis B virus and the human immunodeficiency virus. Although from an operative point of view, we recommend age-based opportunistic diagnosis as a big step forward since there are infected patients that spend years without running any blood tests or seeking medical attention.

Hepatitis C virus could be cleared within the next few years. However, it all depends on diagnosing all or, at least, most infected patients. We hereby recommend age-related opportunistic screening and diagnosis that should be offered to the Spanish population born between 1950 and 1980, at least, once in a lifetime, or annually in the case of patients who still have risk factors for acquiring the infection, as it has already been the case with some Spanish autonomous communities where every visit to a health center serves as an excuse for HCV screening. We are talking about a procedure that can easily be taken over by our National Health Service and, also, automatized. This is the only way to take a qualitative leap in the process of clearing HCV, meet the requirements set forth by the WHO as one of the very first countries capable of reaching the target HCV clearance indicators proposed, reduce the equity breach in the diagnosis and management of hepatitis C virus in the most vulnerable patients, and eventually, move forward in the challenge of improving liver health, a type of health we should considered holistically.

REFERENCES

1. Karlsen TH, Sheron N, Zelber-Sagi S, et al. The EASL-Lancet Liver Commission: protecting the next generation of Europeans against liver disease complications and premature mortality. *Lancet* 2022;399(10319):61-116. DOI: 10.1016/S0140-6736(21)01701-3
2. Secretaría General de Sanidad y Consumo. Plan estratégico para el abordaje de la hepatitis C en el Sistema Nacional de Salud 2015. Madrid: Ministerio de Sanidad, Servicios Sociales e Igualdad; 2015. Available from: https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/plan_estrategico_hepatitis_C.pdf.
3. Olafsson S, Tyrfinngsson T, Runarsdottir V, et al. Treatment as prevention for hepatitis C (TraP Hep C) - A nationwide elimination programme in Iceland using direct-acting antiviral agents. *N Intern Med* 2018;283(5):500-7. DOI: 10.1111/joim.12740

4. Isfordink CJ, Brakenhoff SM, van Dijk M, et al. Hepatitis C elimination in the Netherlands (CELINE): study protocol for nationwide retrieval of lost to follow-up patients with chronic hepatitis C. *BMJ Open Gastroenterol* 2020;7(1):e000396. DOI: 10.1136/bmjgast-2020-000396
5. Lazarus JV, Picchio CA, Byrne CJ, et al. A global systematic review of hepatitis C elimination efforts through micro-elimination. *Semin Liver Dis* 2022;42(2):159-72. DOI: 10.1055/a-1777-6112
6. Pawlotsky JM, Ramers CB, Dillon JF, et al. Simplification of care for chronic hepatitis C virus infection. *Semin Liver Dis* 2020;40(4):392-402. DOI: 10.1055/s-0040-1713657
7. Secretaría General de Sanidad; Dirección General de Salud Pública, Calidad e Innovación. Guía de cribado de la infección por el VHC 2020. Madrid: Ministerio de Sanidad, Servicios Sociales e Igualdad; 2020. Available from: https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/docs/GUIA_DE_CRIBADO_DE_LA_INFECION_POR_EL_VHC_2020.pdf
8. Cuadrado A, Llerena S, Cobo C, et al. Microenvironment eradication of hepatitis C: a novel treatment paradigm. *Am J Gastroenterol* 2018;113(11):1639-48. DOI: 10.1038/s41395-018-0157-x
9. Cabezas J, Llerena S, Mateo M, et al. Hepatitis C micro-elimination beyond prison walls: navigator-assisted test-and-treat strategy for subjects serving non-custodial sentences. *Diagnostics (Basel)* 2021;11(5). DOI: 10.3390/diagnostics11050877
10. Cuadrado A, Cabezas J, Llerena S, et al. Prevalence of hepatitis C in patients with non-affective psychotic disorders. *Rev Esp Enferm Dig* 2020;112(7):550-4. DOI: 10.17235/reed.2020.7278/2020
11. Estévez Escobar M, Casado Martín M, Moreno Moraleda I, et al. Experience in the treatment of hepatitis C with direct-acting antivirals in a foreign population at a high-immigration area. *Rev Esp Enferm Dig* 2021;113(10):704-8. DOI: 10.17235/reed.2021.7830/2021
12. Burgui C, Martín C, Aguinaga A, et al. Prevalence and detection of undiagnosed active hepatitis C virus infections in Navarre, Spain, 2017-2019. *Rev Esp Enferm Dig* 2021;113(1):28-34. DOI: 10.17235/reed.2020.7000/2020
13. Pérez Castano Y, Chouza Pérez JM, Sanz Largo V, et al. Linkage to care strategy for the micro-elimination of hepatitis C among parenteral drug users on methadone replacement therapy in Gipuzkoa. *Rev Esp Enferm Dig* 2020;112(7):545-9. DOI: 10.17235/reed.2020.7194/2020
14. Morales-Arráez D, Hernández-Bustabad A, Medina-Alonso MJ, et al. Telemedicine and decentralized hepatitis C treatment as a strategy to enhance retention in care among people attending drug treatment centres. *Int J Drug Policy* 2021;94:103235. DOI: 10.1016/j.drugpo.2021.103235
15. Colom J, Torrens M, Rodríguez-Cejas A, et al. Certification program of addiction centres for hepatitis C virus elimination in Spain. *HepCelentes Project. Adicciones* 2022;0(0):1743. DOI: 10.20882/adicciones.1743
16. Alianza para la eliminación de las hepatitis virales (AEHVE). Accessed: October 28th, 2022. Available from: <https://aehve.org>
17. Calleja JL, Aguilera A, Buti M, et al. Ten steps to eliminating hepatitis C in hospitals. *Nat Rev Gastroenterol Hepatol* 2022;19(8):481-3. DOI: 10.1038/s41575-022-00647-1
18. Crespo J, Cabezas J, Aguilera A, et al. Recommendations for the integral diagnosis of chronic viral hepatitis in a single analytical extraction. *Gastroenterol Hepatol* 2022;S0210-5705(22)00235-7. E-pub: October 19th, 2022. DOI: 10.1016/j.gastrohep.2022.09.009
19. Vegas JJ, Flores-Herrera J, Latasa P, et al. Reduction in hepatitis C-related hospitalizations after the implementation of the Strategic Plan for Tackling Hepatitis C in the Spanish National Health System: regional level differences. *J Viral Hepat* 2021;28(6):859-69. DOI: 10.1111/jvh.13491
20. Rodríguez-Tajes S, Domínguez A, Carrión JA, et al. Significant decrease in the prevalence of hepatitis C infection after the introduction of direct acting antivirals. *J Gastroenterol Hepatol* 2020;35(9):1570-8. DOI: 10.1111/jgh.14984
21. Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. *Lancet Gastroenterol Hepatol* 2022;7(5):396-415. DOI: 10.1016/S2468-1253(21)00472-6
22. Grupo de Trabajo del Estudio de Prevalencia de la Infección por Hepatitis C en Población General en España; 2017-2018. Resultados del 2.º Estudio de Seroprevalencia en España (2017-2018). Madrid: Ministerio de Sanidad, Consumo y Bienestar Social; 2019. Available from: https://www.msccbs.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/docs/INFORME_INFEC-CION_VHC_ESPANA2019.pdf
23. Llaneras J, Barreira A, Rando-Segura A, et al. Clinical impact and cost-effectiveness of hepatitis C testing in an emergency department in Barcelona, Spain. *J Hepatol* 2022;77:S44. DOI: 10.1016/S0168-8278(22)00498-6
24. Rosato V, Kondili LA, Nevola R, et al. Elimination of hepatitis C in Southern Italy: a model of HCV screening and linkage to care among hospitalized patients at different hospital divisions. *Viruses* 2022;14(5). DOI: 10.3390/v14051096
25. Picchio CA, Lens S, Hernández-Guerra M, et al. Late presentation of chronic HBV and HCV patients seeking first time specialist care in Spain: a 2-year registry review. *Sci* 2021;11(1):24133. DOI: 10.1038/s41598-021-01885-0
26. Santos M, Protopopescu C, Delarocque-Astagneau E, et al. Late presentation for HCV care: time to target people with diabetes and/or hazardous alcohol use (ANRS CO22 HEPATHER cohort). *Liver Int* 2022;42(1):38-49. DOI: 10.1111/liv.15056
27. Kondili LA, Buti M, Riveiro-Barciela M, et al. Impact of the COVID-19 pandemic on hepatitis B and C elimination: an EASL survey. *JHEP Rep* 2022;4(9):100531. DOI: 10.1016/j.jhepr.2022.100531
28. US Preventive Services Task Force (USPSTF). Draft Recommendation Statement. Hepatitis C Virus Infection in Adolescents and Adults: Screening. USPSTF Recommendations; 2019. Available from: <https://www.uspreventiveservicestaskforce.org/uspstf/document/draft-recommendation-statement/hepatitis-c-screening>.
29. Action Hepatitis Canada (AHC). Progress towards viral hepatitis elimination by 2030 in Canada: 2021 Report. AHC; 2021.
30. Canadian Network on Hepatitis C (CanHepC); Blueprint Writing Committee and Working Groups. Blueprint to inform hepatitis C elimination efforts in Canada 2019. Accessed: October 28th, 2022. Available from: https://www.canhepc.ca/sites/default/files/media/documents/blueprint_hcv_2019_05.pdf
31. AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: recommendations for testing, managing, and treating hepatitis C. *Clin Liver Dis* 2018;12(5):117. DOI: 10.1002/cld.791
32. Kondili L, Quaranta M, Ferrigno L, et al. Eliminazione dell'epatite C cronica in Italia: strategie di screening gratuito. *Not Ist Super Sanità* 2021;34(5):6.
33. Crespo J, Albillos A, Buti M, et al. Elimination of hepatitis C. Positioning document of the Spanish Association for the Study of the Liver (AEEL). *Rev Esp Enferm Dig* 2019;111(11):862-73. DOI: 10.17235/reed.2019.6700/2019
34. Buti M, Domínguez-Hernández R, Casado M, et al. El cribado y tratamiento del virus de la hepatitis C en población general española entre 20 y 79 años de edad es coste-efectivo. *Gastroenterol Hepatol* 2018;41(SE1).
35. Crespo J, Cuadrado A, Perello C, et al. Epidemiology of hepatitis C virus infection in a country with universal access to direct-acting antiviral agents: data for designing a cost-effective elimination policy in Spain. *J Viral Hepat* 2020;27(4):360-70. DOI: 10.1111/jvh.13238
36. Nicolás Pérez D, Morales Arráez DE, Castilla Rodríguez I, et al. Hepatitis C virus infection screening reduces mortality and is cost-effective independently of the intervention test. *Rev Esp Enferm Dig* 114(12):731-7. DOI: 10.17235/reed.2022.8609/2022
37. Llanos-Méndez A, Molina-Linde J, Cerezo-Hidalgo C, et al. Efectividad clínica, seguridad y evaluación económica del cribado poblacional de hepatitis C. Revisión sistemática. AETSA Evaluación de Tecnologías Sanitarias de Anda-

- lucía, Ministerio de Sanidad; 2022. Available from: https://www.aetsa.org/download/AETSA_Cribado_VHC_DEF_WEB.pdf
38. Crespo J, Tejerina Puente A, Cuadrado A, et al.; Grupo de Trabajo para la Eliminación de la Hepatitis C. Strategy for the elimination of hepatitis C in Cantabria. *Rev Esp Enferm Dig* 2020;112(7):565-70. DOI: 10.17235/reed.2020.7108/2020
39. Dirección Xeral de Saúde Pública, Consellería de Sanidade. Estratexia para a eliminación da hepatite C como problema de saúde pública en Galicia. Consellería de Sanidade; 2022. Available from: https://www.sergas.es/Saude-publica/Documents/6927/Estratexia_eliminacion_hepatite_C_en_Galicia.pdf
40. Consejería de Salud y Consumo de la Junta de Andalucía. Boletín Oficial de la Junta de Andalucía. Número 201, miércoles 19 de octubre de 2022. Plan para la eliminación de la hepatitis C en Andalucía. Consejería de Sa-
- lud y Consumo; 2022. Available from: https://www.juntadeandalucia.es/boja/2022/201/BOJA22-201-00048-16280-01_00269544.pdf
41. Catlett B, Hajarizadeh B, Cunningham E, et al. Diagnostic accuracy of assays using point-of-care testing or dried blood spot samples for the determination of hepatitis C virus RNA: a systematic review. *J Infect Dis* 2022;226(6):1005-21. DOI: 10.1093/infdis/jiac049
42. Forn X, Colom J, García-Retortillo M, et al. Point-of-care hepatitis C testing and treatment strategy for people attending harm reduction and addiction centres for hepatitis C elimination. *J Viral Hepat* 2022;29(3):227-30. DOI: 10.1111/jvh.13634
43. Saludes V, Antuori A, Lazarus JV, et al. Evaluation of the Xpert HCV VL Fingerstick point-of-care assay and dried blood spot HCV-RNA testing as simplified diagnostic strategies among people who inject drugs in Catalonia, Spain. *Int J Drug Policy* 2020;80:102734. DOI: 10.1016/j.drugpo.2020.102734