Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

Title:
From recommendations to practice – Tracking the national rollout of comprehensive hepatitis diagnosis in Spain

Authors:
Joaquín Cabezas, Antonio Aguilera, Federico García García , Raquel Domínguez-Hernández, Araceli Casado Gómez, Nataly Espinoza-Cámac, Miguel Ángel Casado, Javier Crespo, María Jesús Alcaraz Soriano on behalf of Task Force Spanish Group for Comprehensive Hepatitis Diagnosis*

* Task Force Spanish Group for Comprehensive Hepatitis Diagnosis: María Jesús Alcaraz Soriano, Sonia Algarate Cajo, Roberto Alonso Fernández, Maitane Aranzamendi Zaldumbide, Marta Arias Temprano, Ricardo Manuel Arcay Barral, Ana Arribi Vilela, Teresa Arroyo Serrano, Raquel Baluja Pino, Berta Becerril Carral, Rafael Benito Ruesca, Samuel Bernal Martínez, Miriam Blasco Alberdi, Ana Blázquez Abellán, Teresa Cabezas Fernández, Rainer Campo Ramos, María Eliecer Cano García, Purificación Cantudo Muñoz, Laura Cardeñoso Domingo, Ángel Castaño Nuñez, Encarnación Clavijo Frutos, Rodolfo Copado Carretero, Sandra Cortizo Vidal, Alberto de la Iglesia Salgado, María Jesús del Amor Espín, Alberto Delgado Iribarren, Jose Luis Díaz de Tuesta del Arco, Felícitas Díaz-Flores Estévez, María del Carmen Domínguez Jiménez, Victoria Dominguez-Márquez, José María Eiros Bouza, Victoria Fernández Baca, Felipe Manuel Fernández Cuenca, Isabel Fernández Natal, Gema Fernández Rivas, Fernando Fernández Sánchez, Carolina Freyre Carrillo, Ignacio Gadea Gironés, Juan Carlos Galán Montemayor, Fernando García García, María Victoria García López, Sonsoles Garcinuño Pérez, Carmen Gómez González, Alejandro González Praetorius, María José Gude González, Maria Araceli Hernández Betancor, Juan Carlos Hurtado Negreiros, María Asunción Iborra Bendicho, María Magdalena Lara Pérez, María Josefa López de Goicoechea, María Fátima López Fabal, Jose Luis López Hontangas, María Dolores López Prieto, María del Carmen Lozano Domínguez, María Pilar Luzón García, María Dolores Maciá Romero, Yasmina Martín Martín, Olalla Martinez Macias, Ana Miqueleiz Zapatero, Luz Moldes Suárez, Laura Molina Esteban, Dolores Montero Vega, Natalia Montiel Quezel-Guerraz, Carmen Muñoz Almagro, María Navarro Aguirre, María Dolores Navarro Martínez, María Dolores Ocete Mochón, Valle Odero Bernal, Patricia Ordoñez Barrosa, Nieves Orta Mira, Diego Ortega Larrea, María Pilar Palacián Ruiz, María José Pena López, Ana Belén Pérez Jiménez, J. Alfredo Pérez Rivilla, Elisabeth Prieto Rodriguez, Andrés Quesada, Encarnación Ramirez de Arellano, Ariadna Rando Segura, Gabriel Reina González, Juan Carlos Rodríguez Díaz, Francisco Rodríguez Frías, Manuel Ángel Rodríguez Maresca, Luis Rodríguez Otero, Salud Rodríguez Pallares, María Mercedes Rodríguez Pérez, María Rodríguez Velasco, Susana Sabater Vidal, Ruth Sáez de la Maleta Úbeda, Maria Yolanda Salicio Bermejo, Mónica Sánchez Oñoro, Gemma María Sierra Dorado, Raquel Téllez Pérez, Luis Torres Sopena, Matilde Trigo Daporta, María Isabel Zamora Cintas

DOI: 10.17235/reed.2025.11496/2025
Link: PubMed (Epub ahead of print)

Please cite this article as:
Cabezas Joaquín, Aguilera Antonio, García García Federico, Domínguez-Hernández Raquel, Casado Gómez Araceli, Espinoza-Cámac Nataly, Casado Miguel Ángel, Crespo Javier, Task Force Spanish Group for Comprehensive Hepatitis Diagnosis. From recommendations to practice – Tracking the national rollout of comprehensive hepatitis diagnosis in Spain. Rev Esp Enferm Dig 2025. doi: 10.17235/reed.2025.11496/2025.

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Revista Española
de Enfermedades Digestivas
The Spanish Journal
of Gastroenterology

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

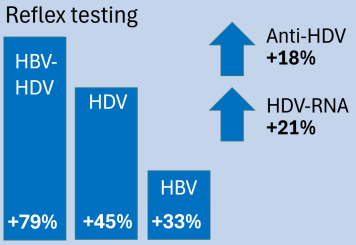
Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

COMPREHENSIVE DIAGNOSTICS IN SPANISH HOSPITALS: PROGRESS AFTER THE RECOMMENDATIONS DOCUMENT

METHODOLOGY

Re-examination of diagnostic progress among 79 hospitals between 2022 to 2024

RESULTS



IMPLEMENTATION INDICATORS

Alerts to specialist:
+24.1% (General)
+52.9% (HDV-specific)

Automated appointment scheduling:
Increased

Testing coverage:
HAV: **38**% of centres
HIV: **50**%
STI screening: **56**%

CONCLUSION

The implementation of comprehensive diagnostic protocols, particularly for hepatitis D, has improved. However, further efforts are required to achieve broader and more consistent coverage.

Author Last Name, et al.

Revista Española de Enfermedades Digestivas (REED)
The Spanish Journal of Gastroenterology

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

From recommendations to practice – Tracking the national rollout of comprehensive hepatitis diagnosis in Spain

Joaquín Cabezas [1,2]; Antonio Aguilera [3.4]; Federico García [5-7]; Raquel Domínguez-Hernández [8]; Araceli Casado-Gómez [8]; Nataly Espinoza-Cámac [8]; Miguel Ángel Casado [8;] Javier Crespo [1,2,9]; Task Force Spanish Group for Comprehensive Hepatitis Diagnosis

1. Gastroenterology and Hepatology Service. Marqués de Valdecilla University Hospital. Santander, Spain.

2. Clinical and Translational Research Group in Digestive Diseases. Valdecilla Research Institute (IDIVAL). Santander, Spain.

3. Microbiology Service. University Clinical Hospital of Santiago de Compostela, Department of Microbiology and Parasitology, University of Santiago de Compostela, A Coruña, Spain.

4. Institute for Health Research of Santiago (IDIS). Santiago de Compostela Spain.

5. Microbiology Service, San Cecilio Clinical University Hospital. Granada, Spain

6. ibs.GRANADA Research Institute, Granada, Spain

7. Ciber de enfermedades infecciosas, CIBERINFEC, Madrid, Spain

8. Pharmacoeconomics & Outcomes Research Iberia. Madrid, Spain.

9. Faculty of Medicine, University of Cantabria. Santander, Spain.

Corresponding author:

Raquel Domínguez-Hernández

Pharmacoeconomics & Outcomes Research Iberia. Madrid, Spain

Email: rdominguez@porib.com

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

Authors names: Full name, mails and ORCID:

Joaquín Cabezas: joaquin.cabezas@scsalud.es; ORCID: 0000-0003-0012-484X

Antonio Aguilera: antonio.aguilera@usc.es; ORCID: 0000-0001-6940-241X

Federico García: fegarcia@ugr.es; ORCID: 0000-0001-7611-781X

Javier Crespo: javiercrespo1991@gmail.com; ORCID: 0000-0001-8248-0172

Raquel Domínguez-Hernández: rdominguez@porib.com; ORCID: 0000-0003-1083-7288

Araceli Casado-Gómez: acasado@porib.com; ORCID: 0000-0003-0201-7247

Nataly Espinoza-Cámac: nespinoza@porib.com; ORCID: 0000-0002-8116-6963

Miguel Ángel Casado: ma_casado@porib.com; ORCID: 0000-0002-8743-6653

Author Contributions: Conceptualization, Joaquin Cabezas, Antonio Aguilera, Federico García, Raquel Domínguez- Hernández, Araceli Casado-Gómez, Miguel Casado and Javier Crespo; Data curation, Raquel Domínguez-Hernández, Araceli Casado-Gómez and Nataly Espinoza-Camac; Formal analysis, Raquel Domínguez-Hernández, Araceli Casado-Gómez and Nataly Espinoza-Camac; Methodology, Joaquin Cabezas, Antonio Aguilera, Federico García, Raquel Domínguez- Hernández, Araceli Casado-Gómez, Miguel Casado and Javier Crespo; Resources, Raquel Domínguez-Hernández and Araceli Casado-Gómez; Software, Raquel Domínguez-Hernández and Araceli Casado-Gómez; Supervision, Joaquin Cabezas, Antonio Aguilera, Federico García and Javier Crespo; Validation, Joaquin Cabezas, Antonio Aguilera and Federico García; Writing original draft, Raquel Domínguez-Hernández, Araceli Casado-Gómez and Nataly Espinoza-Camac; Writing review & editing, Joaquin Cabezas, Antonio Aguilera, Federico García, Raquel Domínguez-Hernández, Nataly Espinoza-Cámac, Miguel Casado and Javier Crespo.

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

Abbreviations

HAV hepatitis A virus

HBV hepatitis B virus

HCV hepatitis C virus

HDV hepatitis D virus

HIV human immunodeficiency virus

PCR Polymerase chain reaction

POC Point-of-care

STI sexually transmitted infections

WHO World Health Organization

KEY POINT TABLE

What is already known about this topic?	**What this study contributes?**	**How will the results influence clinical practice?**
Prior to the publication of the recommendations, the status of their implementation in Spain was unknown.	Updated Spanish national data on the adoption of reflex testing and comprehensive diagnosis for hepatitis B, C and D, including delta hepatitis.	Highlights the need for standardised protocols and supports the implementation of automated alerts and follow-up systems to improve care linkage.

KEY POINTS

- Comprehensive diagnosis of viral hepatitis is key to achieving elimination.
- Its implementation in Spanish hospitals has improved following the publication of the guidelines.
- More awareness for comprehensive diagnosis of viral hepatitis is needed.

Declaration of data availability

Data supporting the study findings are available from the corresponding author upon request

Artificial intelligence (AI)

The authors declare that no artificial intelligence (AI) systems or AI-assisted methodologies were used during elaboration of the project. AI-based tool (ChatGPT Teams, Gemini) was employed exclusively for the purpose of refining the English language of the manuscript and generating the abstract as a graphical illustration.

Financing

This research was funded by Gilead [IN-ES-980-6538, IDIVAL 2022-8959]—Gilead did not take part in the design, data collection, results analysis, or manuscript preparation. Viral hepatitis surveillance in the Cantabria Cohort was funded by the FOCUS program (Gilead group). The funding sources were not involved in the research design or preparation of the article.

Ethical Considerations

This study involved a survey of healthcare professionals and did not collect any patient-level or identifiable personal data. In accordance with national regulations, formal ethical approval was not required. Nevertheless, the Cantabria Research Ethics Committee (CEIm Cantabria) was consulted, and ethical approval was granted (reference code CSI22/79, protocol 14/2022) on September 23, 2022.

Declaration of conflict of interest

J. Cabezas received research grants, advisory and/or lecture fees from Gilead, Abbvie and GSK (all outside the submitted work). J. Crespo received research grants, consultancy, speaker and clinical trials participation fees from Gilead Sciences, AbbVie, MSD, Shionogi, Intercept Pharmaceuticals, Janssen Pharmaceuticals Inc, Celgene, and Alexion (all outside the submitted work). A. Aguilera and F. García declare no conflicts of interest regarding this work. R. Domínguez-Hernández, A. Casado-Gómez, N. Espinoza-Cámac, and Miguel Ángel Casado are employees of PORIB and received fees for their consultancy services in

relation to the development of this work.

LAY SUMMARY

Diagnosing viral hepatitis from a single blood sample is a key step towards its elimination. In 2022, Spain published a set of national recommendations to support this strategy. However, the extent to which these recommendations had been adopted by hospitals was unclear. To address this, a second survey was conducted in early 2024 among the 79 hospitals that had participated in the first evaluation. A total of 72 hospitals responded (91%), and several improvements were observed compared to the previous year. More hospitals reported using comprehensive diagnostic approaches for hepatitis B, C and D. The number of centres performing hepatitis D testing in-house increased, as did the use of reflex testing to detect hepatitis D in patients with hepatitis B. Importantly, more centres reported that positive test results for hepatitis B, C or D were being automatically communicated to specialist physicians. Some hospitals also implemented automated appointment systems for follow-up care. In cases of hepatitis B or C, testing for hepatitis A and HIV was more frequently performed. In patients suspected of having a sexually transmitted infection (STI), HIV testing and full viral hepatitis screening were also more common. These findings suggest that Spanish hospitals are increasingly aware of the importance of integrated diagnostic strategies for viral hepatitis, including hepatitis D. Continued efforts are needed to ensure wider adoption and to help achieve national and international goals for hepatitis elimination.

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

ABSTRACT

Introduction: The comprehensive diagnosis of viral hepatitis is an advance towards its elimination, but not all Spanish hospitals performed it in 2022. Our objective was to evaluate the situation of the comprehensive diagnosis after the publication of the guidelines and evaluate the degree of implementation in the centres that responded to both surveys.

Methods: A descriptive cross-sectional study was conducted among 79 hospitals that had participated in the initial survey. They were reinvited to respond via Google Forms (sent 23/12/2024).

Results: The response rate was 91% (72/79). Compared to the previous year, reflex testing increased by 3%, with notable increases for HBV (33%), HCV (2%), HDV (45%) and dual HBV-HDV (79%). Anti-HDV and HDV-RNA testing increased by 18% and 21%, respectively. Alerts to specialist physicians rose by 24.1% for HBV and 52.9% for HDV. Automated appointment systems and referral mechanisms also expanded. HAV testing was integrated in 38% of centres, HIV testing in 50%, and STI testing in 56%.

Conclusions: Awareness and implementation of integrated diagnostics, particularly for hepatitis D, have improved. Nonetheless, further progress is needed to ensure broader coverage and to contribute towards WHO elimination goals.

Keywords: Hepatitis B. Hepatitis C. Hepatitis D. Comprehensive diagnosis. Point-of-care testing.

INTRODUCTION

Viral hepatitis is a global health concern affecting millions of individuals and can progress to advanced liver disease, including hepatic decompensation, hepatocellular carcinoma, liver transplantation, or death(1). The asymptomatic course of the infection complicates early diagnosis, often resulting in identification at later stages and negatively impacting patient health and quality of life(1).

In 2022, there were approximately 2.2 million new cases of viral hepatitis worldwide, with an estimated 1.2 million attributable to hepatitis B virus (HBV) and 1.0 million to hepatitis

C virus (HCV). Additionally, around 5% of individuals with chronic HBV infection were co-infected with hepatitis D virus (HDV)(2). Co-infections, including human immunodeficiency virus (HIV) and sexually transmitted infections (STIs), are frequent and contribute to increased disease severity(1,3).

In response to these challenges, the World Health Organization (WHO) has proposed integrated strategies for the control, prevention, diagnosis, and treatment of viral hepatitis(4). Several countries, including Spain, have implemented national strategic plans to support these approaches, achieving notable progress in hepatitis C elimination through enhanced detection of undiagnosed cases and the involvement of multidisciplinary care teams(5–10).

An important contribution to the integration of diagnostic strategies was the publication, in 2023, of the national document titled *Recommendations for the comprehensive diagnosis of chronic viral hepatitis (B, C and D)*. This guideline also included recommendations for HIV screening and the assessment of immunity to hepatitis A virus (HAV). Moreover, it provided practical advice regarding reflex testing, point-of-care (POC) testing, targeted screening programmes, and structured communication of results, to promote implementation across Spanish hospitals(11,12).

In a previous study, a first national survey was conducted in 79 hospitals to assess the status of comprehensive diagnosis prior to the publication of the guideline(13). Therefore, the current study has two main objectives: (i) to evaluate the situation one year after the publication of the recommendation document; and (ii) to assess the degree of implementation among the centres that participated in both surveys.

METHODS AND MATERIALS

This was a descriptive cross-sectional study designed to assess the status of comprehensive viral hepatitis diagnosis one year after the publication of the national recommendations document(11). The 79 hospitals that had participated in the initial survey (13) were invited to respond to a second follow-up survey administered via Google Forms. The data collection period was from December 1, 2023, to January 29, 2024.

The follow-up questionnaire was based on the original survey, with adapted and updated questions, and included the following sections: details of the respondent and the participating hospital; diagnostic practices related to hepatitis B, C and D; availability and type of reflex testing; comprehensive diagnostic practices, including HAV and HIV testing; availability of point-of-care (POC) diagnostic testing; integration with hepatitis screening programmes; alert systems to notify specialist physicians and ensure continuity of care; assessment of programme dissemination and; sources of information about the implementation of diagnostic recommendations**.**

Survey responses were analysed independently and subsequently compared with those from the initial survey(13) in order to evaluate changes over time following the publication of the recommendations(11). Descriptive statistics were used, including absolute and relative frequencies expressed as percentages. To ensure consistency in the sampling frame and facilitate longitudinal comparability, the questionnaire was sent to the same hospitals that participated in the previous study. In addition, to mitigate non-response bias, follow-up reminders (emails and direct telephone contact) were issued to hospitals that did not respond within the initial timeframe. Quality assurance procedures included internal consistency checks, independent data analysis by multiple investigators, and cross-referencing with baseline survey data.

RESULTS

Characteristics of respondents and participating centres

The response rate among the 79 hospitals previously contacted was 91% (n = 72) (Figure 1). Of these, 97% were university teaching hospitals, and 97% of the survey respondents were specialists in clinical microbiology. Regarding hospital size, 24 hospitals had between 200–500 beds, 33 had 501–1000 beds, and 15 had more than 1000 beds.

Reflex testing and comprehensive diagnostic approaches

Reflex testing for viral hepatitis was performed in 92% of participating centres (n = 66), regardless of hospital typology.

- HBV: Reflex testing for HBV was implemented in 92% (n = 61) of centres. Among patients with chronic HBV infection, 38% (n = 27) of centres assessed HAV immunity, with 78% (n = 21) performing this determination using the same blood sample. HIV serology was performed in 46% (n = 33) of HBV-infected patients, using the same sample in 73% (n = 24) of these cases.
- HCV: Reflex testing for HCV was available in 97% (n = 64) of centres. Complementary testing for HAV antibodies was performed in 32% (n = 23), with 78% (n = 21) using the same sample. HIV testing in patients with chronic HCV was reported in 47% (n = 34), of which 76% used the same sample.
- HDV: Anti-HDV serology was performed in 74% (n = 53) of centres, while only 32% (n = 23) carried out HDV-RNA testing in-house. Reflex testing for HDV was conducted in 68% (n = 45) of centres, and dual HBV-HDV reflex testing was reported in 76% (n = 50).

Point-of-care (POC) testing, screening programmes and continuity of care

Rapid POC diagnostic tests were available in 24% (n = 14) of centres. The most commonly used POC tests included dried blood samples (DBS; 50%, n = 7) and GeneXpert® HCV (43%, n = 6), followed by rapid capillary blood antibody tests (21%, n = 3) and Oraquick® HCV (7%, n = 1). All POC test results were supervised by central microbiology laboratories, and most were integrated into the patient's electronic medical record.

With regard to hepatitis C screening programmes, 81% (n = 58) of centres reported having a regional or community plan for hepatitis C management or elimination. Furthermore, 82% (n = 59) conducted systematic screening in addiction centres. Conventional venepuncture was the predominant method for detecting previously treated patients at risk of reinfection (88%, n = 63), followed by DBS (19%, n = 14) and GeneXpert® (7%, n = 5).

To ensure continuity of care in cases of active viral hepatitis, 78% (n = 56) of centres reported having an alert system to notify a specialist physician. These alerts were universally implemented for hepatitis C (100%, n = 56), while 64% (n = 36) and 46% (n = 26) included alerts for hepatitis B and D, respectively. Additionally, 22% (n = 16) of centres

had an automated system in place for scheduling follow-up appointments with specialist physicians. Of these, 94% (n = 15) also included automatic notification to the appointment management service.

Programme dissemination and information sources

Assessment of HAV immunity (natural or vaccine-induced) in HBV and/or HCV-positive patients was performed in 38% (n = 27) of centres. Among those not performing HAV screening, the most frequently cited reasons were testing upon specialist request, absence of a formal protocol, or non-standardised criteria.

HIV testing in patients with HBV and/or HCV seropositivity was reported in 50% (n = 36) of centres. Barriers to implementation included the need for patient consent, absence of systematic testing protocols, and reliance on clinician discretion.

In cases of suspected STI, 56% (n = 40) of centres conducted a comprehensive diagnosis of viral hepatitis, of which 55% (n = 22) used the same analytical sample. HIV testing in these patients was performed in 65% (n = 47) of centres.

Finally, 96% (n = 69) of hospitals reported implementing changes over the past year, such as the introduction of reflex testing, alerts to specialists, and/or the use of POC tests. The most common sources of information leading to these changes included congresses and conferences (70%, n = 48), scientific publications (54%, n = 37), and consensus documents (88%, n = 61).

The summary of results is available in Table 1.

Comparison with the first survey

Centres reported a 3% increase in reflex tests. HBV reflex testing increased by 33%, while complementary testing for HAV and HIV in patients with chronic hepatitis B increased by 42% and 32%, respectively. Use of the same sample for HAV and HIV diagnosis increased by 50% and 33%, respectively (Figure 2).

In hepatitis C diagnosis, reflex testing increased slightly (2%). Among patients with chronic hepatitis C, additional HAV and HIV testing increased by 53% and 21%, using the same sample in 73% and 44% of cases, respectively.

Regarding hepatitis D diagnosis, the second survey reported more anti-HDV and RNA-HDV tests than the previous year, with increases of 18% and 21%, respectively. Dual HBV-HDV reflex testing increased by 79%, and HDV reflex testing by 45%.

In the second survey, only 14 centres reported POC testing, an 18% drop from the previous year (17 centres). Use of the Capillary Rapid Blood Antibody test decreased by 50% (3/6), GeneXpert HCV by 33% (3/9), and DBS by 22% (2/9). All results were overseen by a microbiology laboratory.

The number of centres issuing alerts to specialists for active viral hepatitis was similar in both surveys (57 vs. 56). However, in the second survey, 56 centres reported increased alerts for HBV (24%) and HDV (53%). Implementation of automated appointment systems and related alerts increased slightly (by one centre).

In the first survey, 69% of centres (n=50/72) supported adding HAV testing to HBV, HCV, and HDV diagnostics; in the second, 38% (n=27) implemented it. For HIV, support was 90% (n=65) and implementation 50% (n=36). Comprehensive hepatitis testing in patients with suspected STIs, considered appropriate by 96% of centres in the first survey, had been implemented by 56% in the second (Figure 3).

DISCUSSION

This study provides valuable insight into the implementation of the national recommendations for the comprehensive diagnosis of viral hepatitis using a single blood sample and highlights the progress made by Spanish hospitals.

The high response rate in this second survey likely reflects the selective invitation of hospitals that had already participated in the first survey. The strong participation of microbiology specialists reinforces the validity of the findings. Notably, there were significant increases in both anti-HDV and HDV-RNA testing, which indicate greater awareness of the importance of early diagnosis and improved test availability. In centres

without on-site HDV-RNA testing, outsourcing was adopted as a strategy to guarantee diagnostic completeness. Alongside reflex testing, there was a clear trend towards broader implementation across all forms of viral hepatitis, especially HDV reflex testing and dual HBV-HDV strategies. This positive trend may be explained by the publication of the recommendations document (11), the approval of bulevirtide for HDV treatment, and active awareness campaigns led by healthcare professionals, scientific societies and the pharmaceutical industry. Research has demonstrated that the implementation of reflex HDV testing increase diagnostic coverage and simplified the screening process as well as is cost-effectiveness (14,15).

Another relevant observation is the limited availability of POC testing, which hampers decentralised diagnosis, particularly in vulnerable populations. Only 20% of centres had adopted decentralised diagnostic strategies. This may relate to a noted decline in the use of DBS by microbiology services. Likewise, very few centres had implemented automated scheduling systems for follow-up of patients with positive serology, which hinders continuity of care and represents an area in need of improvement (16,17).

Although most centres in the first survey supported comprehensive viral hepatitis screening for patients living with HIV or those with suspected STIs, only about half reported implementing such testing one year later. The reasons for this low uptake were not formally investigated, but the need to obtain informed consent and the absence of unified protocols appear to be limiting factors. This is consistent with prior evidence of underdiagnosis of viral hepatitis in STI screening settings, particularly for HCV and HBV, in contrast with higher rates of HIV testing(18).

Despite these limitations, the results demonstrate meaningful progress. Still, important barriers must be addressed to achieve full integration of comprehensive diagnosis for viral hepatitis, HIV and STIs. These include the lack of established institutional protocols and the dependency on individual clinicians' requests. To overcome these, ongoing professional training should be prioritised, especially concerning the importance of early and integrated diagnosis and the use of updated diagnostic tools. Reflex testing and the expansion of POC strategies should be encouraged, particularly in underserved or geographically isolated populations.

Furthermore, the primary objective of the study was to provide an overview of the progress of comprehensive diagnostic implementation nationwide; it was not to assess diagnostic performance, patient outcomes, or linkage to care. Therefore, comparisons across regions or facility types were not included, nor were prevalence and patient linkage results shown. Furthermore, given the sample size, stratification by factors would significantly reduce the number of hospitals per factor, resulting in sample sizes too small to detect significant differences. Future studies are needed to assess the clinical and public health impact of the implementation initiatives described.

Artificial intelligence (AI)-based tools have shown considerable promise in identifying patients lost to follow-up or at high risk for chronic hepatitis C infection, by analysing healthcare data to prioritise testing and re-engagement (19,20). Integrating such tools may help streamline reflex testing and support public health objectives.

Finally, interdepartmental collaboration and harmonised workflows should be promoted through the systematic application of the recommendations. This includes reinforcing existing protocols, ensuring that reflex testing is automatically triggered upon identification of positive serology, and facilitating linkage to care. These measures are essential for Spain to meet the World Health Organization's hepatitis elimination targets (1,4).

Additionally, recent public-health and WHO frameworks for hepatitis elimination evidence underlines the importance of embedding our viral hepatitis diagnostic strategy within broader sexual-health pathways (3). Recently, a study that evaluated the simultaneous diagnosis of viral hepatitis in subjects suspected of having an STIs demonstrated a low diagnosis rate to include a complete diagnosis when a sexually transmitted disease is suspected(18). The Ministry of Health's review of community-based rapid testing legislation confirms that existing regulation already permits point-of-care screening for HIV and, potentially, other sexually transmitted infections (STIs), thereby providing an immediate framework for scaling reflex testing of viral hepatitis in primary care and community settings (21). Furthermore, the latest national epidemiological surveillance report documents sustained increases in bacterial STI incidence—particularly among young adults and men who have sex with men(22). These trends reinforce the urgency of

integrating comprehensive viral hepatitis, HIV, and STI screening programmes to maximise case-finding and linkage to care within Spain's public-health services(23).

In conclusion, one year after the publication of the national recommendations, the implementation of comprehensive viral hepatitis diagnostics has improved across Spanish hospitals, particularly in the context of hepatitis D. Nevertheless, significant gaps remain, especially in decentralised testing, linkage-to-care systems, and screening of high-risk populations such as individuals with suspected STIs or HIV infection. Continued efforts are required to overcome structural barriers, strengthen institutional protocols, and expand the use of reflex and point-of-care testing. Coordinated strategies involving training, policy alignment and the application of innovative tools, such as artificial intelligence, will be crucial to accelerate the elimination of viral hepatitis in line with WHO targets.

BIBLIOGRAPHY

1. World Health Organization. Global health sector strategy on viral hepatitis 2016-2021. Towards ending viral hepatitis. World Health Organization. 2016. Accessed July 5, 2024. https://iris.who.int/handle/10665/246177

2. World Health Organization. Global hepatitis report 2024: action for access in low- and middle-income countries. World Health Organization. 2024. Accessed July 10, 2024. https://www.who.int/publications/i/item/9789240091672

3. World Health Organization. Global health sector strategies on HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. 2022. Accessed April 8, 2024. https://www.who.int/publications-detail-redirect/9789240053779

4. World Health Organization. New report flags major increase in sexually transmitted infections, amidst challenges in HIV and hepatitis. May 21, 2024. Accessed July 11, 2024. https://www.who.int/es/news/item/21-05-2024-new-report-flags-major-increase-in-sexually-transmitted-infections---amidst-challenges-in-hiv-and-hepatitis

5. Spanish Ministry of Health. Hepatitis víricas. Accessed April 8, 2024. https://mirror.mscbs.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/hepatitis/ciudadanosMenu.htm

6. Spanish Ministry of Health. Plan Estratégico de Prevención y Control de VIH e ITS. Accessed July 11, 2024. https://mirror.mscbs.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/planNalSida/home.htm

7. Spanish Ministry of Health. Strategic Plan for tackling hepatitis C in the Spanish National Health System. Published online May 21, 2015. https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/PEAHC_eng.pdf

8. Spanish Ministry of Health. Guía de cribado de la infección por el VHC 2020. Accessed July 4, 2025. https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/docs/GUIA_DE_CRIBADO_DE_LA_INFECCION_POR_EL_VHC_2020.pdf

9. Crespo García J, Albillos A, Buti M, et al. Elimination of hepatitis C. Positioning document of the Spanish Association for the Study of the Liver (AEEH). *Rev Esp Enferm Dig*. Published online 2019. doi:10.17235/reed.2019.6700/2019

10. Crespo J, Albillos A, Buti M. The Spanish National Strategic Plan for Hepatitis C: A legacy of success. *Rev Esp Enferm Dig*. Published online 2025. doi:10.17235/reed.2025.11371/2025

11. Crespo J, Cabezas J, Aguilera A, et al. Recomendaciones para el diagnóstico integral de las hepatitis virales crónicas en una única extracción analítica. *Gastroenterología y Hepatología*. 2023;46(2):150-162. doi:10.1016/j.gastrohep.2022.09.009

12. Crespo J, Calleja JL, Cabezas J, et al. A call for the comprehensive diagnosis of viral hepatitis as a key step towards its elimination. *Liver International*. 2023;43(5):1145-1147. doi:10.1111/liv.15529

13. Cabezas J, Aguilera A, García F, et al. Comprehensive Diagnosis of Viral Hepatitis in Spain: Bases for Implementation. *Viruses*. 2025;17(5):667. doi:10.3390/v17050667

14. Ortega González E, Ocete Mochón MD, Martínez-Roma M, et al. Current prevalence of hepatitis delta diagnosis in Valencia, Spain. *Sci Rep*. 2025;15(1):7584. doi:10.1038/s41598-025-91765-8

15. Fuentes A, Estévez-Escobar M, De Salazar A, et al. Double reflex testing improves the efficacy and cost effectiveness of hepatitis delta diagnosis in southern Spain. *Sci Rep*. 2025;15(1):15413. doi:10.1038/s41598-025-00101-7

16. Vargas-Accarino E, Rando-Segura A, Palom A, et al. Enhancing linkage to care for hepatitis B, D, and C patients: A retrospective-prospective study. *Aliment Pharmacol Ther*. 2024;60(10):1308-1314. doi:10.1111/apt.18227

17. Lopes TB, Coelho FF, Roca TP, et al. A universal point-of-care immunochromatographic test for the serodiagnosis of hepatitis D. *J Clin Microbiol*. 2025;63(5):e0199924. doi:10.1128/jcm.01999-24

18. Cabezas J, Torres-Sangiao E, Llerena S, et al. The evaluation of people suspected of sexually transmitted diseases requires tools for the comprehensive diagnosis of viral hepatitis and HIV. *Journal of Hepatology*. 2023;78:S911-S912. doi:10.1016/S0168-8278(23)02934-3

19. Doyle OM, Leavitt N, Rigg JA. Finding undiagnosed patients with hepatitis C infection: an application of artificial intelligence to patient claims data. *Sci Rep*. 2020;10(1):10521. doi:10.1038/s41598-020-67013-6

20. Parada Vázquez P, Pérez-Cachafeiro S, Castiñeira Dominguez B, et al. Artificial intelligence-assisted identification and retrieval of chronic hepatitis C patients lost to follow-up in the health area of Pontevedra and O Salnés (Spain). *Gastroenterol Hepatol*. Published online June 29, 2024:502226. doi:10.1016/j.gastrohep.2024.502226

21. Spanish Ministry of Health. La realización de pruebas de diagnóstico rápido de VIH y otras ITS en el ámbito comunitario en España: marco normativo y situación actual. Accessed July 2, 2025. https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/ITS/Informe_LegislaciOn_Pruebas_Rapidas_VIH_e_ITS_en_Espana_2021.pdf

22. Spanish Ministry of Health, Surveillance Unit for HIV, Sexually Transmitted Infections (STIs), and Hepatitis B and C. Vigilancia epidemiológica de las infecciones de transmisión sexual en España, 2023. Centro Nacional de Epidemiología, Instituto de Salud Carlos III/División de Control de VIH, ITS, Hepatitis virales y Tuberculosis, Dirección General de Salud Pública y Equidad en Salud; 2024. Published online October 2024. Accessed July 2, 2025. https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/ITS/Vigilancia_ITS_1995_2023.pdf

23. Akıllı FM, Özbay Haliloğlu EN, Güncü MM, Turan Gökçe D. Investigation of Hepatitis C, D, and HIV Seroprevalence and Evaluation of APRI and FIB-4 Scores in HbsAg-Positive Patients. *Viruses*. 2025;17(4):568. doi:10.3390/v17040568

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

455

456

457

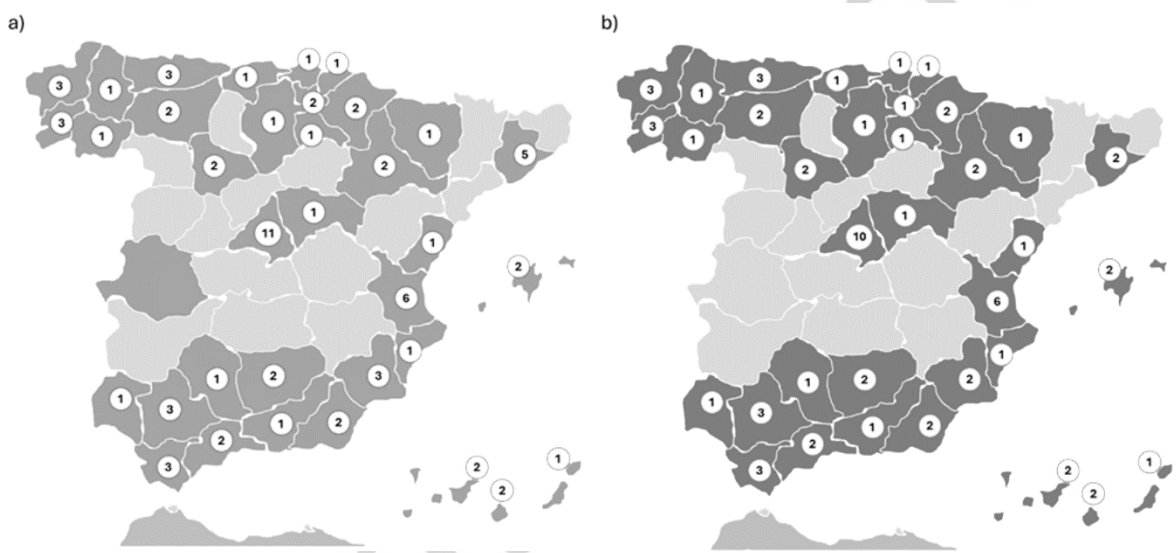
458

459

460

461 **FIGURES and TABLES**

462



463

464 Figure 1. Distribution of participating hospitals in both surveys by province, Spain

465 Map (a) shows the regional location of the hospitals that responded to the first survey (79
466 participating hospitals).

467 Map (b) shows the regional location of the hospitals that responded to the second survey
468 (72 hospitals).

469

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

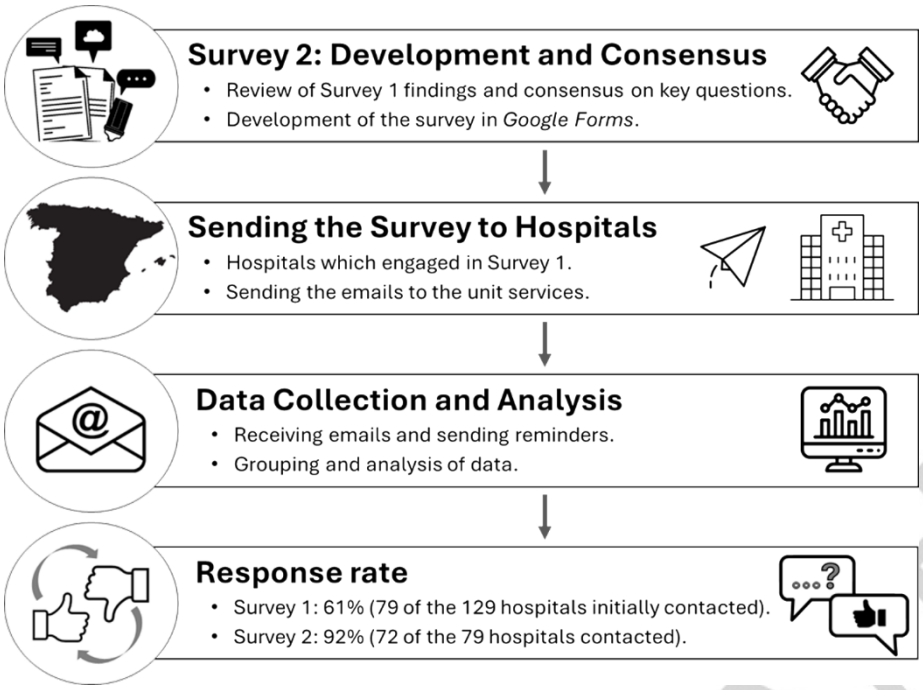


Figure 2. Process Workflow

It shows the steps taken in the study from the development of the second survey to the receipt of the hospitals' responses, showing the response rates for both surveys.

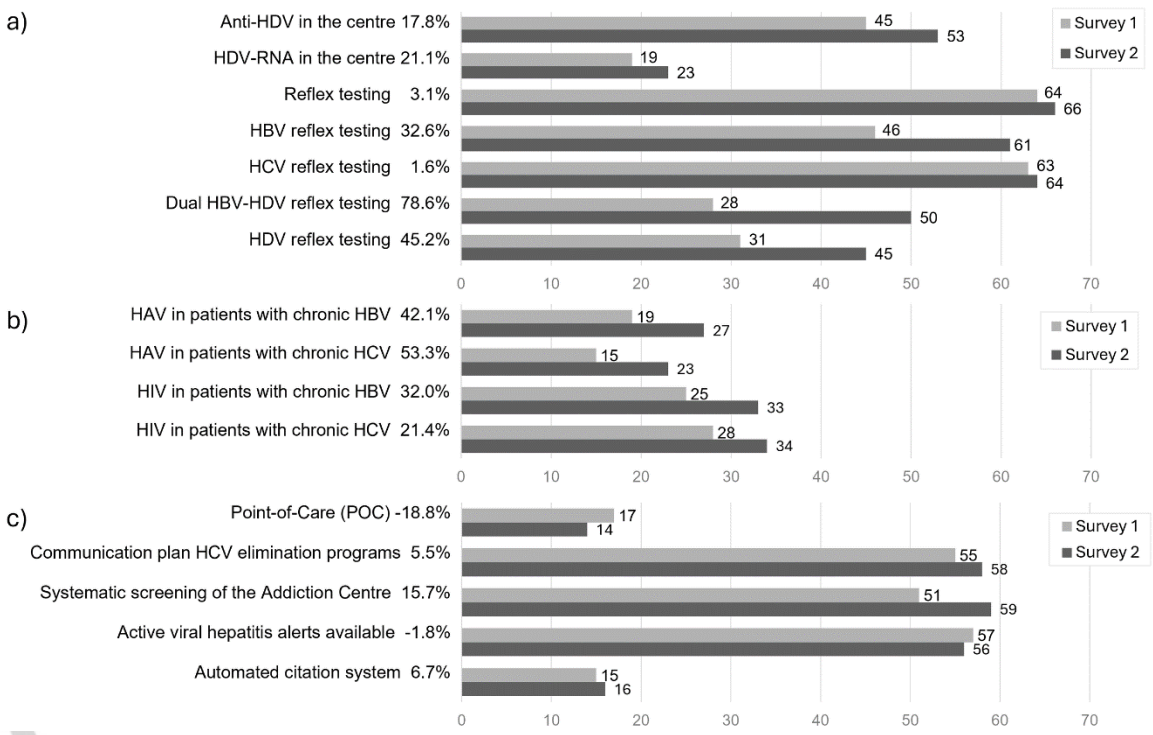


Figure 3. Comparison of the results obtained in the first and second surveys

a) Diagnosis and reflex testing capabilities. b) Comprehensive diagnosis testing. c) Integrated linkage to care tools.

Anti-HDV, antibodies against HDV; HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis D virus; HDV-RNA, hepatitis delta virus ribonucleic acid; HIV, human immunodeficiency virus.

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

482 **Table 1. Summary of the results**

QUESTION VARIABLES	RESPONSE ALTERNATIVES	n	%
CONSENT TO PARTICIPATE IN THE PROJECT (n = 79)			
Guest centres	Total	79	100%
Consent	No	7	9%
	Yes	72	91%
RESPONDENT AND CENTRE DATA (n = 72)			
Specialty	Microbiology	71	99%
	Infectious Diseases	1	1%
DIAGNOSIS OF HEPATITIS D (n = 72)			
Determinations of anti-VHD in the centre	No	19	26%
	Yes	53	74%
HDV-RNA determination in the centre	No, it is outsourced to another centre	49	68%
	Yes	23	32%
→ PCR type (n = 23)	→ Commercial PCR	*20*	*87%*
	→ PCR in house	*3*	*13%*
INTEGRATION OF REFLEX TESTING OF VIRAL HEPATITIS (n = 72)			
Reflex testing is performed	No	6	8%
	Yes	66	92%
→ Type of reflex testing (n = 66)	→ HBV	*61*	*92%*
	→ HCV	*64*	*97%*
	→ HDV	*45*	*68%*
	→ Dual HBV-HDV	*50*	*76%*
OTHER DIAGNOSTIC RECOMMENDATIONS (n = 72)			
HEPATITIS A			
In patients with chronic hepatitis B, the level of anti-HAV IgG or total IgG was determined.	No	45	63%
	Yes	27	38%
	→ In the same sample	*21*	*78%*
	→ In another sample	*6*	*22%*
In patients with chronic hepatitis C, anti-HAV IgG or total IgG was determined	No	49	68%
	Yes	23	32%
	→ In the same sample	*19*	*83%*
	→ In another sample	*4*	*17%*
Human Immunodeficiency Virus (HIV)			
Anti-HIV status is determined in patients with chronic hepatitis B	No	39	54%
	Yes	33	46%
	→ In the same sample	*24*	*53%*
	→ In another sample	*9*	*27%*
Anti-HIV status is determined in patients with chronic hepatitis C	No	38	53%
	Yes	34	47%
	→ In the same sample	*26*	*76%*
	→ In another sample	*8*	*24%*
GENERAL MEASURES: POINT-OF-CARE (n = 72)			

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

QUESTION VARIABLES	RESPONSE ALTERNATIVES	n	%
Point-of-Care (POC) tests	No	58	81%
	Yes	14	19%
→ Type of tests in the POC (n = 14)	→ GeneXpert® HCV	*6*	*43%*
	→ Dried Blood Samples	*7*	*50%*
	→ Rapid capillary blood antibody test	*3*	*21%*
	→ Oraquick® HCV (capillary blood or saliva)	*1*	*7%*
→ Central Microbiology laboratories monitor POC results (n=14)	→ No	*0*	*0 %*
	→ Yes	*14*	*100%*
→ POC results integrated in the clinical history (n=14)	→ No	*1*	*7%*
	→ Yes	*13*	*93%*
INTEGRATION OF SCREENING PROGRAMS (IMPLEMENTATION OF HEPATITIS C ELIMINATION PROGRAMS) (n = 72)			
Community or regional plan	No	14	19%
	Yes	58	81%
Systematic screening in addiction centres	No	13	18%
	Yes	59	82%
Screening in previously treated patients at risk of reinfection	Conventional extraction	63	88%
	Dried Blood Samples	14	19%
	GeneXpert®	5	7%
COMMUNICATION STRATEGIES OF THE CENTRE'S RESULTS (n = 72)			
The treating physician is alerted on the existence of active viral hepatitis (alerts for the following types: HBV, HDV or HCV)	No	16	22%
	Yes	56	78%
	→VHB	36	64%
	→VHD	26	46%
	→VHC	56	100%
Automated appointment with the specialist physician for cases of positive serology	No	56	78%
	Yes	16	22%
	→ Yes, alert to appointment management	*15*	*94%*
	→ No, alert to appointment management	*1*	*6%*
EVALUATION OF THE DIFFUSION OF THE PROGRAM (n = 72)			
If HBV or HCV positive, HAV is diagnosed using the same sample.	No	45	63%
	Yes	27	38%
If HBV or HCV positive, HIV is diagnosed using the same sample.	No	36	50%
	Yes	36	50%
If STIs is suspected, a comprehensive diagnosis of	No	32	44%
	Yes	40	56%

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

QUESTION VARIABLES	RESPONSE ALTERNATIVES	n	%
viral hepatitis is performed.	→ In the same sample	*22*	*55%*
	→ In another sample	*18*	*45%*

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

QUESTION VARIABLES	RESPONSE ALTERNATIVES	n	%

Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

QUESTION VARIABLES	RESPONSE ALTERNATIVES	n	%
If STIs is suspected, a comprehensive diagnosis of viral hepatitis is performed.			
If STI is suspected, an HIV evaluation is performed	No	25	35%
	Yes	47	65%
SOURCES OF THE DISSEMINATION OF THE PROGRAM (n = 72)			
DUSP, alerts, POC tests, etc., have been implemented in the hospital in the last year. The information has been obtained from the following sources.	Not applicable	3	4%
	Yes	69	96%
	→ Congresses, conferences	*48*	*70%*
	→ Scientific publications	*37*	*54%*
	→ Consensus documents	*61*	*88%*
	→ Others	*2*	*3%*

483