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

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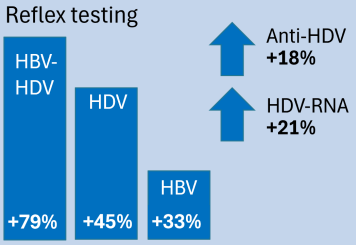
COMPREHENSIVE DIAGNOSTICS IN SPANISH HOSPITALS: PROGRESS AFTER THE RECOMMENDATIONS DOCUMENT

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.

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

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Authors´ contribution: Conceptualization: J. C., A. A., F. G., R. D.-H., A. C.-G., M. C., and J. C. Data curation: R. D.-H., A. C.-G., and N. E.-C. Formal analysis: R. D.-H., A. C.-G., and N. E.-C. Methodology: J. C., A. A., F. G., R. D.-H., A. C.-G., M. C., and J. C. Resources: R. D.-H., and A.

C.-G. Software: R. D.-H., and A. C.-G.. Supervision: J. C., A. A., F. G., and J. C. Validation: J. C., A. A., and F. G. Writing original draft: R. D.-H., A. C.-G., and N. E.-C. Writing review and editing: J. C., A. A., F. G., R. D.-H., N. E.-C., M. C., and J. C.

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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.

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Artificial intelligence: 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.

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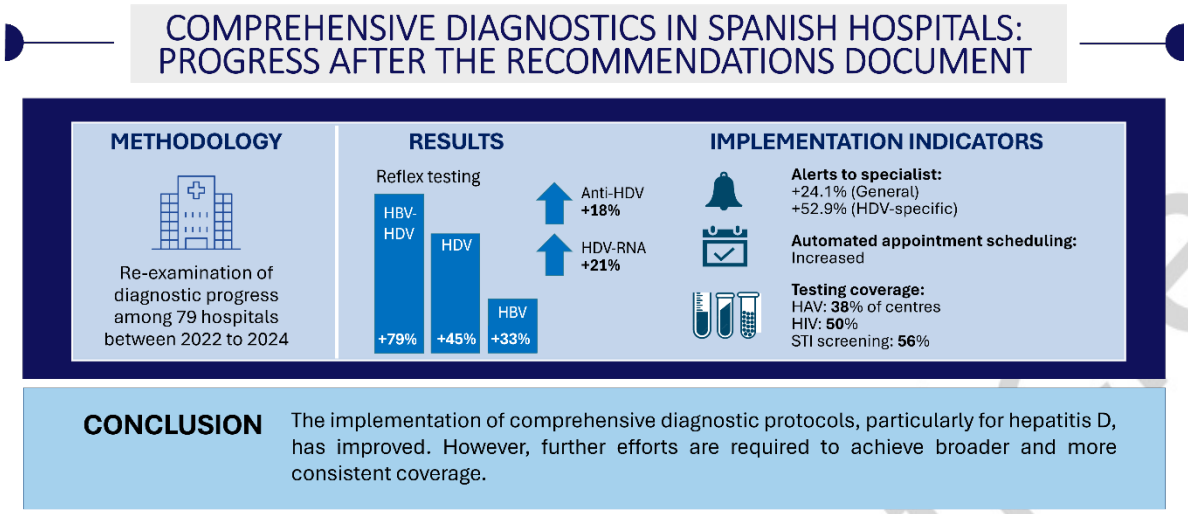

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LAY SUMMARY

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 centers 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 centers 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 human immunodeficiency virus (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.

ABSTRACT

Introduction: the comprehensive diagnosis of viral hepatitis is an advance towards its elimination, but not all Spanish hospitals performed this diagnosis 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 centers 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 hepatitis B virus (HBV) (33 %), hepatitis C virus (HCV) (2 %), hepatitis D virus (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. Hepatitis A virus (HAV) testing was integrated in 38 % of centers, human immunodeficiency virus (HIV) testing in 50 %, and sexually transmitted infections (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 World Health Organization (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).

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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 programs, 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: a) to evaluate the situation one year after the publication of the recommendation document; and b) to assess the degree of implementation among the centers that participated in both surveys.

MATERIALS AND METHODS

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 POC diagnostic testing; integration with hepatitis screening programs; alert systems to notify specialist physicians and ensure continuity of care; assessment of program dissemination; and sources of information about the implementation of diagnostic recommendations.

Survey responses were analyzed 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 (e-mails 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 centers

The response rate among the 79 hospitals previously contacted was 91 % (*n* = 72) (Fig. 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 501-1,000 beds, and 15 had more than 1,000 beds.

Reflex testing and comprehensive diagnostic approaches

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

— HBV: reflex testing for HBV was implemented in 92 % (*n* = 61) of centers. Among patients with chronic HBV infection, 38 % (*n* = 27) of centers 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 centers. 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 centers, while only 32 % (*n* = 23) carried out HDV-RNA testing in-house. Reflex testing for HDV was conducted in 68 % (*n* = 45) of centers, and dual HBV-HDV reflex testing was reported in 76 % (*n* = 50).

Point-of-care testing, screening programs and continuity of care

Rapid POC diagnostic tests were available in 24 % (*n* = 14) of centers. 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 programs, 81 % (*n* = 58) of centers reported having a regional or community plan for hepatitis C management or elimination. Furthermore, 82 % (*n* = 59) conducted systematic screening in addiction centers. Conventional venipuncture 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 centers 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 centers 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.

Program 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 centers. Among those not performing HAV screening, the most frequently cited reasons were testing upon specialist request, absence of a formal protocol, or non-standardized criteria.

HIV testing in patients with HBV and/or HCV seropositivity was reported in 50 % (*n* = 36) of centers. 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 centers 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 centers.

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

Centers 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 (Fig. 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 centers reported POC testing, an 18 % drop from the previous year (17 centers). 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 centers issuing alerts to specialists for active viral hepatitis was similar in both surveys (57 *vs* 56). However, in the second survey, 56 centers reported increased alerts for HBV (24 %) and HDV (53 %). Implementation of automated appointment systems and related alerts increased slightly (by one center).

In the first survey, 69 % of centers (*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 centers in the first survey, had been implemented by 56 % in the second (Fig. 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 centers 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 its cost-effectiveness (14,15).

Another relevant observation is the limited availability of POC testing, which hampers decentralized diagnosis, particularly in vulnerable populations. Only 20 % of centers had adopted decentralized diagnostic strategies. This may relate to a noted decline in the use of DBS by microbiology services. Likewise, very few centers 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 centers 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 sexually transmitted infections (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 prioritized, 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 analyzing healthcare data to prioritize testing and re-engagement (19,20). Integrating such tools may help streamline reflex testing and support public health objectives.

Finally, interdepartmental collaboration and harmonized 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 WHO'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 POC screening for HIV and, potentially, other 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 programs to maximize 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 decentralized 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 POC 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.

TASK FORCE SPANISH GROUP FOR COMPREHENSIVE HEPATITIS DIAGNOSIS

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Table 1. Summary of the results

Question variables	Response alternatives	*n*	%
Consent to participate in the project (*n* = 79)			
Guest centers	Total	79	100 %
Consent	No	7	9 %
	Yes	72	91 %
Respondent and center data (*n* = 72)			
Specialty	Microbiology	71	99 %
	Infectious diseases	1	1 %
Diagnosis of hepatitis D (*n* = 72)			
Determinations of anti-HDV in the center	No	19	26 %
	Yes	53	74 %
HDV-RNA determination in the center	No, it is outsourced to another center	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	No	49	68 %

Question variables	Response alternatives	*n*	%
hepatitis C, anti-HAV IgG or total IgG was determined	Yes	23	32 %
	→ In the same sample	*19*	*83 %*
	→ In another sample	*4*	*17 %*
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: POC (*n* = 72)			
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 %

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Question variables	Response alternatives	*n*	%
Systematic screening in addiction centers	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 center'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 %
	→ HBV	36	64 %
	→ HDV	26	46 %
	→ HCV	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 viral hepatitis is performed	No	32	44 %
	Yes	40	56 %
	→ In the same sample	*22*	*55 %*
	→ In another sample	*18*	*45 %*
If STI is suspected, an HIV	No	25	35 %

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Question variables	Response alternatives	*n*	%
evaluation is performed	Yes	47	65 %

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Question variables	Response alternatives	*n*	%

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Question variables	Response alternatives	*n*	%
If STI is suspected, an HIV evaluation is performed			
Sources of the dissemination of the program (*n* = 72)			
DUSP, alerts, POC tests, etc., have been implemented in the hospital in the last year	Not applicable	3	4 %
	Yes	69	96 %
The information has been obtained from the following sources	→ Congresses, conferences	*48*	*70 %*
	→ Scientific publications	*37*	*54 %*
	→ Consensus documents	*61*	*88 %*
	→ Others	*2*	*3 %*

HDV: hepatitis D virus; HCV: hepatitis C virus; HBV: hepatitis B virus; HAV: hepatitis A virus; HIV: human immunodeficiency virus; PCR: Polymerase chain reaction; POC: point-of-care; STI: sexually transmitted infection; DUSP: one-step diagnosis document.

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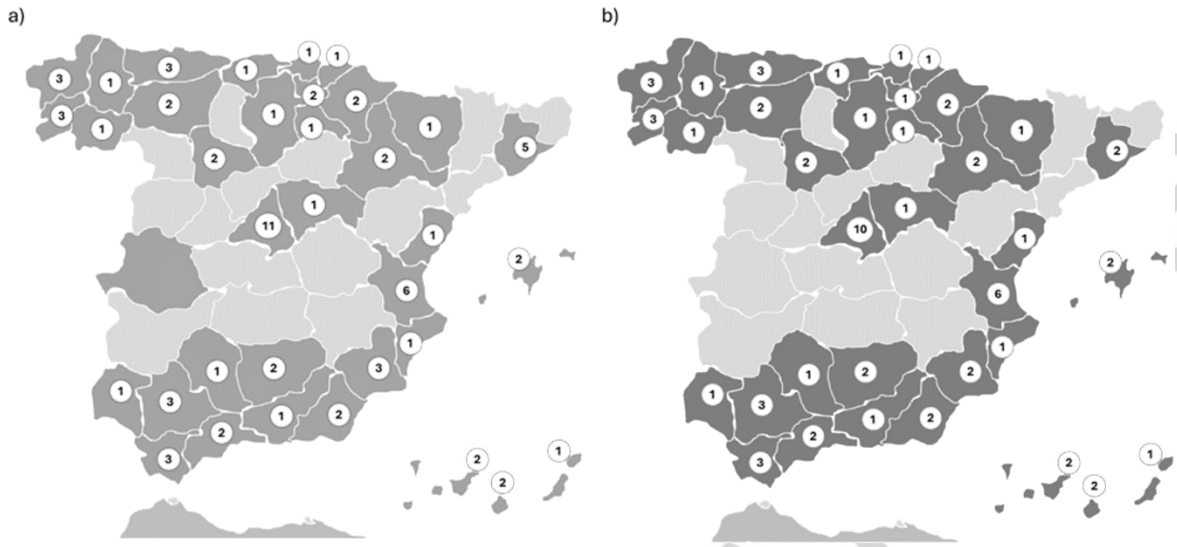

Fig. 1. Distribution of participating hospitals in both surveys by province, Spain. A. Regional location of the hospitals that responded to the first survey (79 participating hospitals). B. Regional location of the hospitals that responded to the second survey (72 hospitals).

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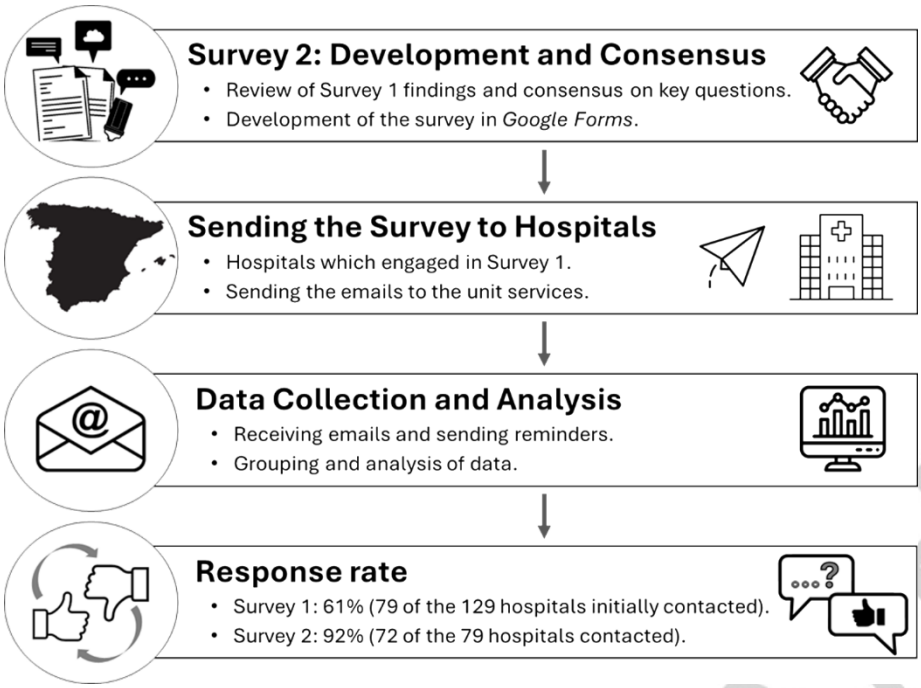

Fig. 2. Process workflow. It shows the steps taken in the study from the development of the second survey to the receipt of the hospitals' responses, showing the response rates for both surveys.

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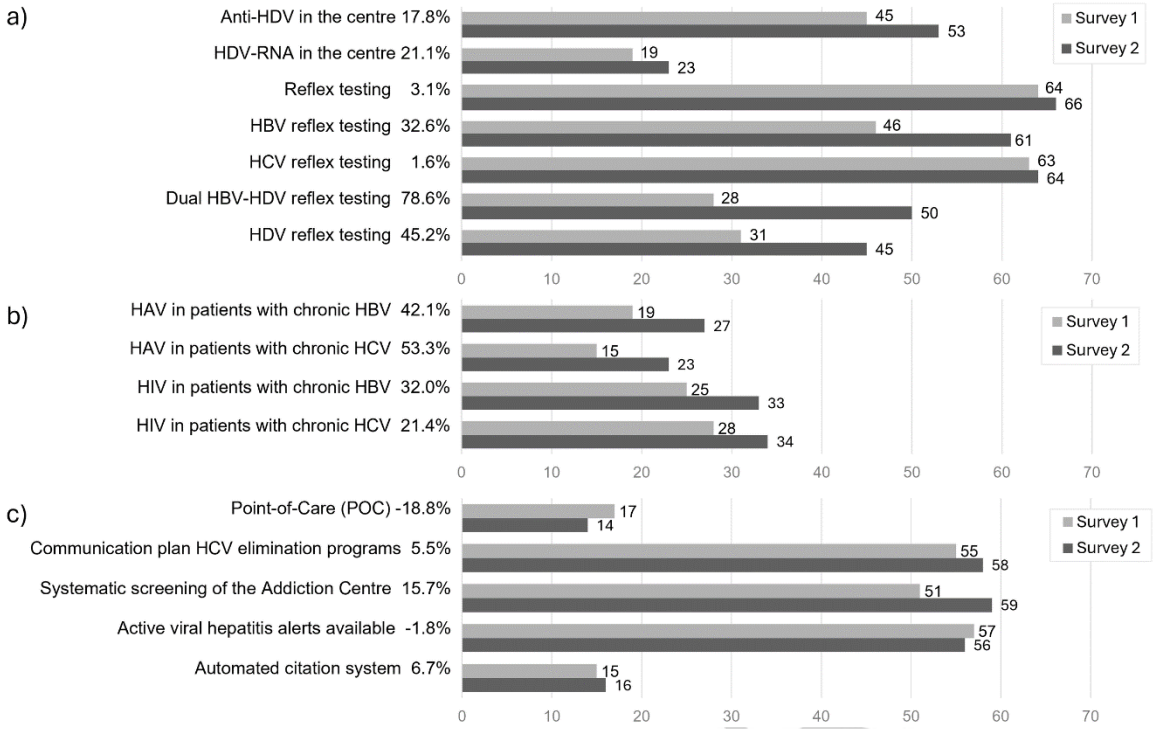

Fig. 3. Comparison of the results obtained in the first and second surveys. A. Diagnosis and reflex testing capabilities. B. Comprehensive diagnosis testing. C. Integrated linkage to care tools. Anti-HDV: antibodies against HDV; HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; HDV: hepatitis D virus; HDV-RNA: hepatitis delta virus ribonucleic acid; HIV: human immunodeficiency virus.