

POLICY APPROACHES TO TACKLING HEPATITIS C IN SPAIN



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About this research

Policy approaches to tackling Hepatitis C in Spain is a report by The Economist Intelligence Unit, sponsored by Gilead. The report focuses on various elements of the Spanish government's policy relating to fighting Hepatitis C, and the barriers still standing in the way of reaching the government's stated goal of eliminating the disease.

This report is based on several strands of research, as follows:

- A comprehensive **literature search** carried out by EIU Healthcare, a specialist research division of The Economist Group, focusing on the epidemiology and burden of HCV infection and milestones to eliminating the disease, among other topics.
- An **expert panel** meeting in Madrid on March 5th 2018 to discuss the epidemiologic situation and pathways toward elimination. The panel participants (listed alphabetically by surname) were:
 - Maria Buti, president, Spanish Society of Liver Diseases (Asociación Española para el Estudio del Hígado, AEEH); Hospital Universitat de Vall d'Hebron, Barcelona
 - José Luis Calleja, associate professor of medicine, Servicio de Gastroenterología y Hepatología, Hospital Universitario Puerta de Hierro, Universidad Autónoma, Madrid
 - Teresa Casanovas, president, Associació Catalana de Malalts d'Hepatitis, Barcelona
 - Javier Crespo, head of gastroenterology and hepatology department, University Hospital Marqués de Valdecilla; professor of medicine, University of Cantabria, Santander
 - Javier García-Samaniego Rey, co-ordinator, Alliance for the Elimination of Viral Hepatitis in Spain (Alianza para la Eliminación de las Hepatitis Víricas en España, AEHVE), and head of liver unit, Hospital Universitario La Paz, Madrid
 - Jeffrey Lazarus, associate professor, University of Barcelona, associate researcher, Instituto de Salud Global, Hospital Clínic, University of Barcelona
 - Enrique Ortega González, managing director, Consorcio Hospital General Universitario, Valencia
 - Eva Pérez Bech, president, National Federation of Liver Patients and Transplants (Federación Nacional de Enfermos y Trasplantados Hepáticos), Madrid
 - Carlos Roncero, director, psychiatric service, University of Salamanca Health Care Complex, Salamanca
 - Juan Turnes, head of service, department of digestive diseases, University Hospital Complex, Pontevedra

- A programme of **in-depth interviews** with 20 high-level experts in the topic. The interview programme participants (listed alphabetically by surname) were:
 - Agustín Albillos Martínez, head of gastroenterology, Hospital Universitario Ramón y Cajal, Madrid
 - Juan Berenguer, infectious disease service, Hospital Gregorio Marañón, Madrid
 - Sarah Blach, HCV group leader, and Dr Homie Razavi, managing director, CDA Foundation
 - Maria Buti, president, Spanish Society of Liver Diseases (Asociación Española para el Estudio del Hígado, AEEH); Hospital Universitat de Vall d'Hebron, Barcelona
 - Miguel Ángel Calleja Hernández, president, Spanish Society of Hospital Pharmacy (Sociedad Española de Farmacia Hospitalaria)
 - Miguel Ángel Casado, director-general, and Raquel Domínguez, Especialista en Evaluación Económica y Modelización, Pharmacoeconomics & Outcomes Research, Iberia (PORIB), Madrid
 - Joan Colom, deputy director, Sub-directorate General of Drug Dependencies, Barcelona
 - Jesús María Fernández Díaz, member of parliament, Partido Socialista Obrero Español (PSOE, Spanish Socialist Workers' Party)
 - Adolfo García Ortega, president, La Plataforma de Afectados por Hepatitis C de Madrid (PLAFHC)
 - Pablo Lazaro, epidemiologist, Hospital General Universitario Gregorio Marañón, Madrid
 - Jens Lundgren, Rigshospitalet, University of Copenhagen; director, Centre of Excellence for Health, Immunity and Infections
 - Juan Macías, infectious diseases and microbiology unit, Hospital Universitario Nuestra Señora de Valme, Seville
 - Juan Antonio Pineda, infectious diseases unit, Hospital Universitario Nuestra Señora de Valme, Seville
 - José Tomás Quiñonero Díaz, president, Spanish Society of Penitentiary Health (Sociedad Española de Sanidad Penitenciaria), Murcia
 - Bernardino Jimeno Resa, general practitioner, CatSalut, Barcelona
 - Pablo Ryan, internal medicine, Hospital Universitario Infanta Leonor, Madrid
 - Pablo Saiz de la Hoya Zamácola, Fontcalent prison, Alicante
 - Mark Sonderup, University of Cape Town Private Academic and Groote Schuur Hospital, and vice-chairman, South African Medical Association, South Africa
 - Jesús Troya García, Hospital Universitario Infanta Leonor, Madrid

- José Ignacio Torroba, head of hospital pharmacy, regional health ministry (Consejería Sanidad), La Rioja

The Economist Intelligence Unit would like to thank all participants in the expert panel and interview programme for their time and insights. The findings and views expressed in this report are those of The Economist Intelligence Unit and do not necessarily reflect the views of the sponsor.

June 2018

Executive summary

In 2015 the Spanish government set out a bold three-year programme to tackle Hepatitis C. It has made considerable progress, treating around 100,000 sufferers of the disease by early 2018, most of whom have cleared the virus from their blood.

Regional administrations have treated almost twice as many people as initially expected. Yet much work remains to be done before Spain can achieve its goal of eliminating the disease. Even as the per patient cost of administering new direct-acting antiviral (DAA) drugs falls, the country may have to commit further resources to detecting potentially thousands of as-yet unidentified Hepatitis C virus (HCV) patients. Doing so would bring relief for many more sufferers and their families, as well as delivering long-term benefits for the health system, as fewer would develop related fatal diseases or require a liver transplant.

Financial and structural barriers may impede further progress, however. Beyond the cost of mounting a campaign to detect remaining HCV cases is the challenge associated with a fragmented healthcare system. This fragmentation can lead to overlooking those most at risk, or losing them when their treatment pathways are too complex.

In particular, prison inmates, immigrants, people who inject drugs (PWIDs) and those who practice unsafe sex may not have regular, or any, contact with the health service, which could provide an opportunity for care. In the general population, thousands of people are estimated to carry the virus and remain undiagnosed. Many older patients may have been infected via blood products and hospital procedures, before the virus was discovered and tests for the virus made available.

The key findings of the research are:

- Spain has made substantial efforts, treating almost 100,000 HCV sufferers in three years, most of whom have cleared the virus from their blood.
- The goal of eliminating Hepatitis C in Spain is in sight, but may not be reached due to flagging efforts to detect and treat remaining patients.
- Hepatitis C could be eliminated relatively easily if resources were allocated and services within the health system harmonised.
- Focusing on the most long-standing, serious cases of HCV with advanced liver fibrosis, then widening access at a later stage was the strategy adopted in Spain.
- With the most urgent cases cleared, more must be done to reach those who present with signs of infection, as well as those who do not know they may be HCV-positive.
- Registers of who is being screened and the results of screening need to be created to ensure a more accurate picture of the task ahead.

- More outreach work and local service provision would improve detection and treatment among high-risk groups, such as PWIDs, those who practice unsafe sex and the prison population.
- A law change may be required to allow treatment in renal dialysis centres, drug dependency clinics and prisons.
- Public campaigns are needed to encourage individuals who may have been exposed to the virus to ask for a HCV test.
- Reaching a wider population will require significant spending—for education programmes, frontline screening, provision of diagnosis equipment and facilities, and provision of treatment and aftercare.

I. Introduction: a disease successfully targeted

1. Eliminating an elusive, “silent killer”

The Hepatitis C Virus (HCV) is often dubbed the “silent killer”. Sufferers may be unaware for decades that they harbour this blood-borne virus that attacks the liver. Indeed, until recently, Hepatitis C itself was unknown to medical science; the virus was only identified in 1989, with tests made available the following year. Previously, it was known as non-A, non-B hepatitis.

Prior to discovery of the virus, thousands of people in Spain and elsewhere developed liver diseases through blood transfusions and blood products in the 1970s, 1980s and into the early 1990s. Many others were—and still are—exposed to the virus through unsafe sexual practices, or the use of unsterilised needles when injecting drugs. Prisoners are also in the high-risk group, because of associated drug use and the high risk of transmitting the virus within the penitentiary population.

Early treatments of Hepatitis C in the 1990s were not always effective and had serious side effects. Treatment was long and cure rates were as low as 40% for certain genotypes of HCV. The introduction of direct-acting antivirals (DAAs) in 2013 boosted the effectiveness of treatment significantly. With DAAs, indicative success rates—with success determined by sustained virologic response (SVR) tests—are extremely high. The Ministry of Health reports a provisional SVR above 95% in Spain.¹

In 2015 the Spanish government set a goal of eliminating the disease and outlined a three-year programme to achieve this goal. The programme aimed to administer DAA therapies in cases where HCV infection had been detected. At the time, it was estimated that 467,000 people in Spain were HCV positive, but that only about 162,000 had been diagnosed—indicating a large gap between prevalence and diagnosis.²

Since the 2015 programme focused on priority, advanced level of fibrosis and high-risk groups, the size of the potential universe of cases remained unknown. Many HCV sufferers remained “hidden”—undiagnosed and unsuspecting that they may be harbouring the virus. A complicating factor is that often sufferers show few outward signs of infection. Early symptoms such as tiredness and aching joints can be easily misdiagnosed as simple flu.

The health implications of this detection gap are significant. In 10–40% of cases, HCV leads to cirrhosis of the liver. It can also lead to liver failure or hepatocellular cancer. In 2013 30% of all liver transplants were attributed to HCV. Systematic screening and treatment of HCV sufferers, therefore, could have large positive knock-on effects in the health system.

¹ Ministerio de Sanidad, Servicios Sociales e Igualdad, November 2016 [http://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/Plan_Estrategico_Abordaje_Hepatitis_C_\(PEAHC\).pdf](http://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/Plan_Estrategico_Abordaje_Hepatitis_C_(PEAHC).pdf)

² Healthcare in Europe, November 24th 2015 <https://healthcare-in-europe.com/en/story/15548-hepatitis-c-management-in-spain.html>

So far, however, the shortfall in detection and referrals to treatment and care is causing Spain to fall behind in the fight against HCV. Other countries are moving faster towards eliminating the disease by 2030³—a target set under the UN's Agenda for Sustainable Development, to which Spain is a signatory, and the goals of the World Health Organisation (WHO).

This report looks at the objectives of the Spanish HCV strategic plan and the results that have been achieved so far. It explores Spain's Hepatitis C policy and practices in detail, including: implementing the current programme; promoting public awareness; and carrying out screening, and access to, treatment and monitoring programmes. This report also looks at the equality of access to treatment across the Spanish health system, and at policies to prevent initial infections among high-risk groups. In addition, the research considers what more can be done and the barriers that stand in the way of eliminating Hepatitis C in Spain.

2. Spain's Hepatitis C programme: taking aim

As noted above, the Spanish Ministerio de Sanidad, Servicios Sociales e Igualdad (Ministry of Health, Social Services and Equality) launched a plan for reducing the burden from Hepatitis C in 2015.

The plan, called el Plan Estratégico para el Abordaje de la Hepatitis C en el Sistema Nacional de Salud (PEAHC, Strategic Plan for Tackling Hepatitis C in the Spanish National Health System), had four strategic aims:

- Quantifying the problem and determining measures for prevention;
- Defining the scientific-clinical criteria to determine when to use DAA drugs;
- Co-ordinating implementation throughout the healthcare system; and
- Advancing knowledge of prevention, diagnosis and treatment through research and development.

The plan envisioned an initial three-year programme of detection and treatment in collaboration with regional health services, prison institutions and other bodies. Using data from 2014, the Ministry of Health estimated that about 688,000 Spanish adults had the antibodies (known as anti-HCV Ac) to indicate they had been exposed to the virus at some point. Of these, 472,000 were estimated to have the HCV infection. (See Figure 1.)

Spain's HCV plan came around the time when the WHO was making noise in this area. The WHO global strategy for viral hepatitis (see boxout) was adopted at its annual assembly in 2016, when only 36 countries had already developed national strategic plans for viral hepatitis.

A 2016 report by the European Liver Patients Association found that only 13 out of 27 countries in Europe that responded to a survey have national plans for viral hepatitis. Nine out of the 13

³ *El Mundo*, November 1st 2017 <http://www.elmundo.es/ciencia-y-salud/salud/2017/11/01/59f8cc23268e3e27748b4576.html>

countries had strategies exclusively focused on viral hepatitis, while four countries' plans included other diseases as well. Three out of the 13 countries had plans specifically addressing Hepatitis C—Belgium, Spain and the UK.

Figure 1: The Hepatitis problem that Spain faced in 2015

Estimated prevalence of HCV in adult population in Spain and most frequent genotypes

Prevalence of anti-HCV Ac	1.7% (0.4-2.6%)
Adult population with anti-HCV Ac	688,000 (159,000-1,049,000)
Viraemia rate	68.6%
Prevalence of viraemia rate in adults	1.2% (0.3-1.8%)
Adult population with viraemia	472,000 (109,000-719,000)
Genotypes: Type and frequency	1a: 25.5% 1b: 43.8% 2: 3.1% 3: 19.6% 4: 8%

Note: The viraemia rate figure of 68.6% is the percentage of those with HCV antibodies who are actually still infected.

Source: Ministerio de Sanidad, Servicios Sociales e Igualdad⁴

Subsequent studies revised the number of outstanding cases down somewhat. One study estimated that 386,000 Spanish adults have the infection.⁵ Another study put the figure at 387,900.⁶

An important consideration, beyond the total number of estimated HCV-positive cases, is the severity of those cases, as measured by the level of cirrhosis damage to the liver. Grades of fibrosis (the thickening and scarring of liver tissue) range from F0 to F4, with F4 indicating the most severe damage.

From the outset, the government's plan targeted those with the most advanced liver fibrosis in stages F2, F3 and F4. Health ministry figures prior to the launch of the plan show that 54% of HCV patients had F2 to F4 level fibrosis (Figure 2).

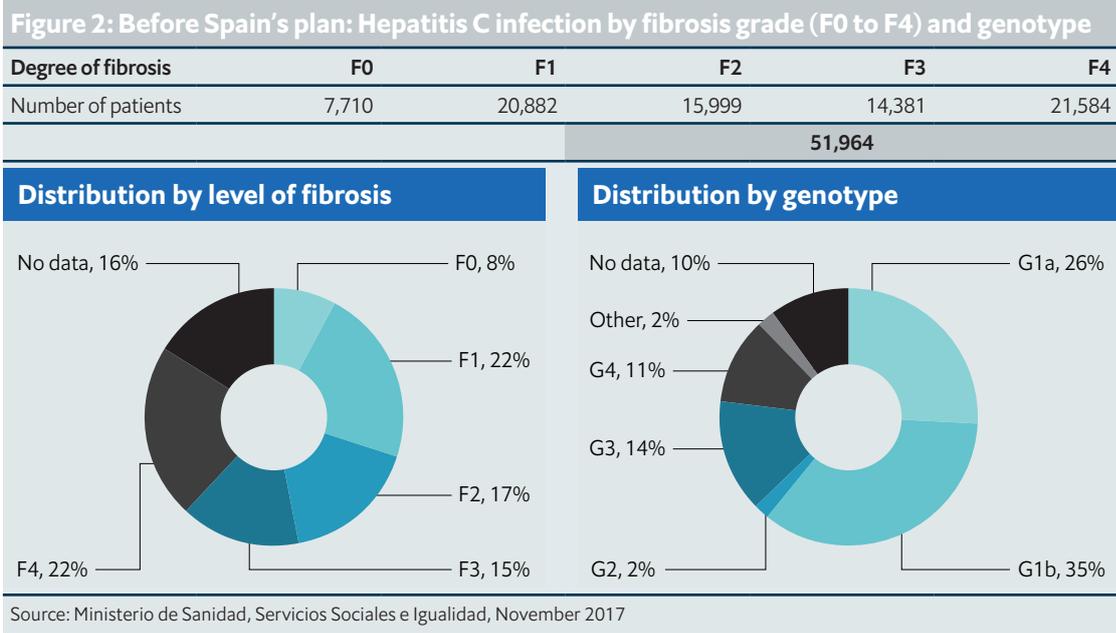
Patients waiting for liver transplants or who had been reinfected with HCV after a transplant were also given priority, along with other high-risk patients.

However, those with less serious levels of fibrosis (F0 and F1) had their DAA treatment deferred. From these groups, only those with a high risk of transmission to others or women wishing to become pregnant would receive treatment.

⁴ https://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/PEAHC_eng.pdf, page 22

⁵ "Global prevalence and genotype distribution of Hepatitis C virus infection in 2015: a modeling study", *Lancet Gastroenterol Hepatol.* 2017;2(3):161-76

⁶ Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modeling study. *Lancet Gastroenterol Hepatol.* 2017;2(5):325-36



Significantly, the health ministry had gaps in its data on the severity of HCV infections in 16% of diagnosed patients. This meant it had no data on the level of fibrosis for these patients, and this provided challenges around the precise budgeting and resourcing for diagnosis, treatment and long-term monitoring.

Extension time: Spain targets less severe cases

The plan has been a success in terms of the number of patients treated, according to recent top-line data, with over 95% of them cleared of the virus. The health ministry put the total number of patients treated at 99,031 at the end of January 2018.⁷

In a recent newspaper interview, the health minister, Dolors Montserrat, claimed that Spain was leading the treatment of HCV patients in Europe, calling it “an effort that nobody else has made”.⁸

In June 2017 the Ministry of Health extended eligibility to all patients, regardless of their level of fibrosis. The wait was too long for those diagnosed with F0 and F1 fibrosis, some patient groups think.

“With so many patients, the Spanish public system was not prepared,” says Adolfo García Ortega of Plataforma de los Afectados de Hepatitis C (Platform for Those Affected by Hepatitis C), a high-profile patients group in Madrid. “We found it insufficient. In short, the plan talked about treating the most serious in first, but did not talk about treating all patients and when.”

⁷ EFE Salud, March 15th 2018 <http://www.efesalud.com/100-000-enfermos-hepatitis-c-tratados-nuevos-farmacos/>

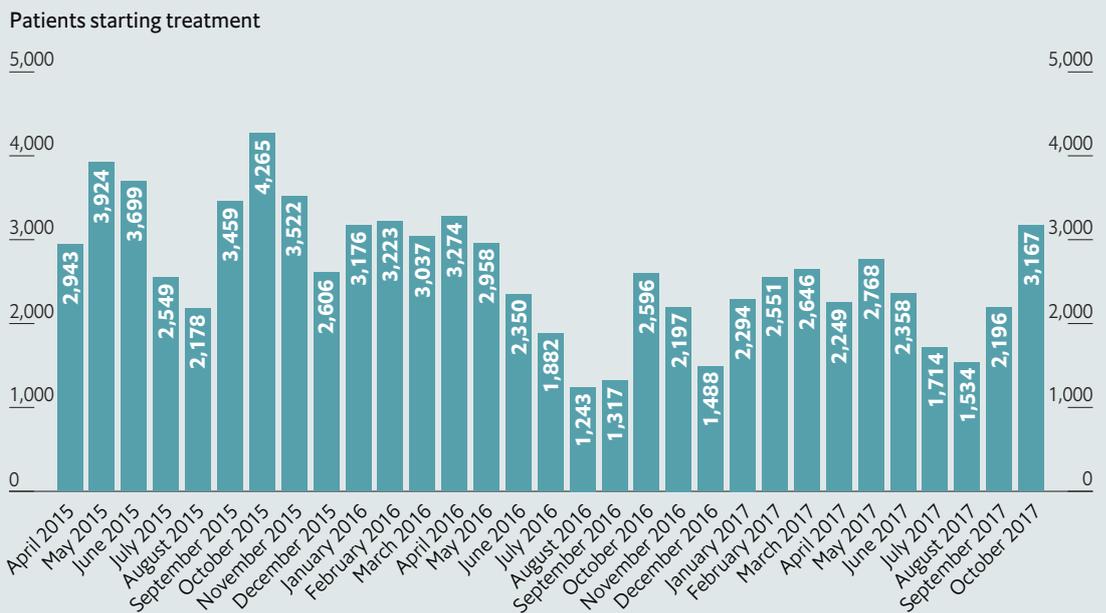
⁸ La Razon, March 4th 2018 <https://www.larazon.es/espana/dolors-montserrat-no-se-puede-decir-que-todas-las-mujeres-lo-tengan-mas-dificil-que-los-hombres-IP17819023>

Despite the extension of coverage to include those with F0 and F1 fibrosis, some interviewees report that patient numbers have begun to fall off recently, as the most urgent cases have now been dealt with. (Figure 3)

The shortfall worries patient groups and others, as it indicates that a large pool of people with active infections may remain undiagnosed and untreated. Many are concerned that the country’s elimination target will be missed unless more patients are detected and treated. The issue is to find and treat all patients who do not know they are ill, and how best to ensure the continuum of care. These issues have yet to be fully resolved.

“Mainly it is an issue of budgets. We have to treat all patients because there are no limitations by the degree of fibrosis. If we promote mass screening, we will have more patients than the budget can fund,” warns Juan Antonio Pineda of the infectious diseases unit of the Hospital Universitario Nuestra Señora de Valme in Seville. “But if we continue like we have done before, we will not hit the elimination target. We need a big commitment from the government.”

Figure 3: HCV patients starting treatment per month in Spain (April 2015-October 2017)



Source: Ministerio de Sanidad, Servicios Sociales e Igualdad, November 2017
[http://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/Plan_Estrategico_Abordaje_Hepatitis_C_\(PEAHC\).pdf](http://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/hepatitisC/PlanEstrategicoHEPATITISC/docs/Plan_Estrategico_Abordaje_Hepatitis_C_(PEAHC).pdf)

A global campaign: WHO's targets for 2030

Infection by Hepatitis A, B, C, D and E is a global issue. The Global hepatitis report, 2017 by the World Health Organisation (WHO) estimates that all hepatitis viruses cause 1.34m deaths worldwide each year, a number comparable to deaths caused by tuberculosis and HIV. However, although mortality from tuberculosis and HIV has been declining, deaths from hepatitis are on the rise.⁹

The WHO, under the aegis of the UN's Sustainable Development Goals, has set an objective of eliminating viral hepatitis by 2030.

To combat both Hepatitis B and C as public health threats, the WHO has developed ambitious targets. For Hepatitis C, it wants 90% of the infected population diagnosed and 80% treated by 2030. It wants to see an 80% reduction in new cases of chronic infection and a 65% reduction in deaths from Hepatitis C Virus (HCV).

The WHO's regional office in Europe has set tighter requirements in the short term to ensure these goals are reached. These include national surveillance programmes, communication and awareness campaigns, and specific targets for people who inject drugs and for people with chronic HCV infections or liver diseases, including cirrhosis and liver cancer. (Please see Appendix for details of the WHO's global and European targets.)

Conclusions:

- Spain's national plan has admirable intentions, and impressive results to date, as confirmed by Ms Montserrat.
- Around 100,000 patients have been treated, with over 95% of them cleared of the virus.⁷
- The Spanish government has stepped up its approach to HCV, by initially focusing on severe HCV cases with advanced fibrosis and then later widening access to treatment to early stages of fibrosis cases.
- Widening access to treatment could have come sooner, patient groups and some specialists believe.
- Specialists are also concerned that insufficient resources have been dedicated to detecting patients who may not be aware they have Hepatitis C.

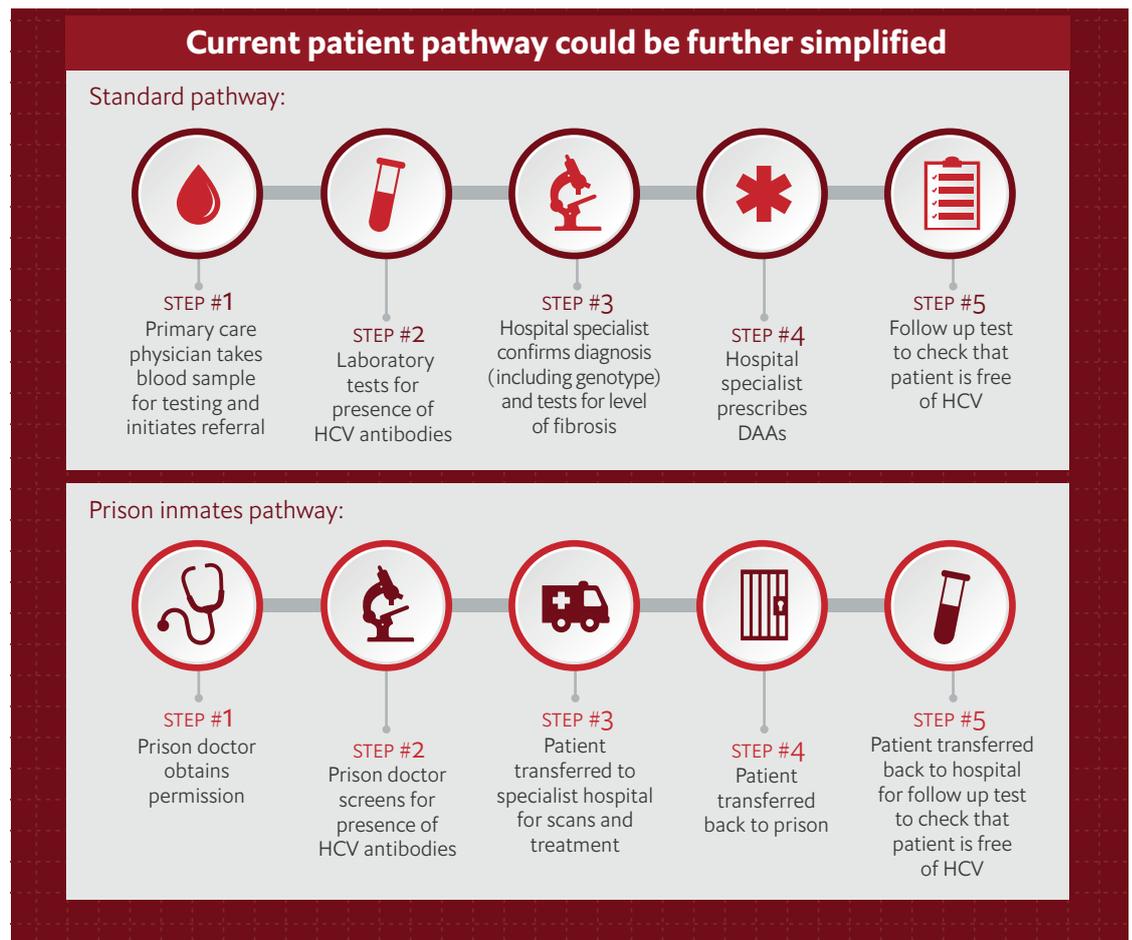
⁹ <http://www.who.int/mediacentre/news/releases/2017/global-hepatitis-report/en/>

3. The budget for fighting Hepatitis C: new focus on staff and facilities

The strategic plan for tackling Hepatitis C was created out of necessity and practicality. For the Ministry of Health, it was important to prioritise the rollout of DAA drugs to the patients who needed them first—and to do so quickly without damaging regional health budgets.

“The plan includes extending the treatment to all patients with Hepatitis C, as has been done at present, but was aware that not everyone could be treated simultaneously due to the limitations of the system’s resources,” notes Dr Agustín Albillos Martínez, head of gastroenterology, Hospital Universitario Ramón y Cajal, and a member of the scientific advisory committee for the national plan.

To reduce the total cost of treatment, the Ministry of Health negotiated volume-pricing agreements, the details of which remain confidential. The government also offered credit facilities so that the regions’ DAA HCV treatment spending would not affect their long-term financial stability—a mechanism similar to those deployed for other public health programmes.



The initial drug investment forecast for the plan was €786m to treat 51,900 patients over three years with fibrosis at stages F2, F3 and F4. That original patient target was exceeded, as access was widened to F0-F1 in a later agreement between the Ministry of Health and regional governments.¹⁰

A second concern of the regions has been the non-drug costs of the programme. For example, staff are needed to screen patients, a pathologist is needed for diagnoses, and specialists and nursing staff to look after them. Many experts think too little thought was put into paying these staffing and infrastructure costs. If local or regional budgets are already stretched, it is hard to pay upfront for the staff, resources or drugs, point out many interviewees.

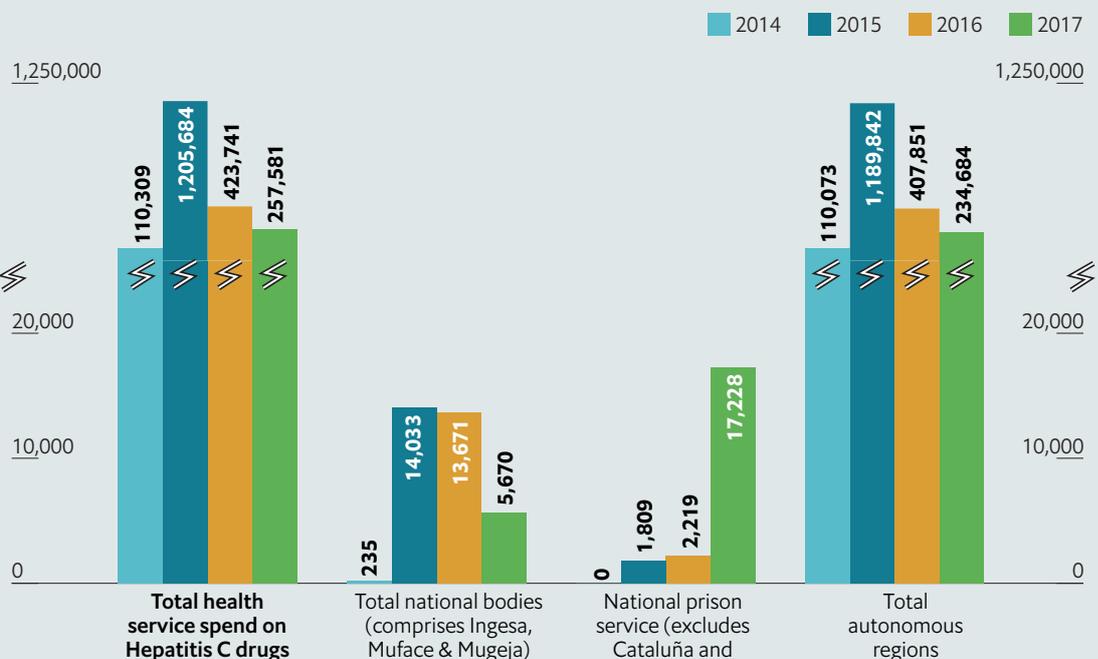
A patchwork of spending

A look at the amounts spent by each branch of the health system between 2014 and 2017 shows that the upfront drug costs for the regions have been significant. (Figure 4)

It also shows that although there has been a heavy frontloading of spending, aggregate annual spending has fallen considerably in the past two years as the most urgent cases were treated and before less severe patients were granted access to DAAs.

Figure 4: Hepatitis C drug spending by the total health service and national bodies

Hospital spending on Hepatitis C drugs, 2014-17, € '000, figures rounded



Source: EIU calculation based on Finance Ministry data (Ministerio de Hacienda y Función Pública)¹¹

¹⁰ *El País*, June 21st 2017
https://politica.elpais.com/politica/2017/06/21/actualidad/1498060903_372716.html

¹¹ Ministerio de Hacienda y Función Pública (finance ministry) <http://www.minhafp.gob.es/Documentacion/Publico/CDI/Gasto%20Sanitario/SERIE%20Gasto%20Farmac%C3%A9utico%20y%20Sanitario.xls>; Figures represent the difference between Table '1v' (total) and Table '1v sin Hep C'

Interviewees suggest that different branches of the health service follow different protocols, with varying levels of proactivity in finding and treating less severe HCV cases. Madrid and Valencia had begun treating all patients regardless of their level of fibrosis ahead of the agreement between the Ministry of Health and all of the regional governments. The regions with the best quality of data concerning patients were best placed to take advantage of new therapies using DAA drugs, suggest interviewees.

Patient numbers: US and European trends

Interestingly, the CDA Foundation, which studies Hepatitis B and C epidemiological data collected under its Polaris Observatory initiative, has noticed a fall in the total number of treated patients in developed countries recently.

Data from the EU and the US show a fall since 2015 in the numbers of newly diagnosed patients or diagnosed patients awaiting treatment.

Dr Homie Razavi, managing director of the CDA Foundation, suggests that numbers fall when efforts to locate less chronic cases do not include high-profile, wide-ranging screening programmes, like those undertaken in countries such as Egypt and Brazil.

“The WHO says we need to get to 90% of the population screened by 2030. Most European countries are far behind. There is a level of conservatism. They say it cannot be done, that it is not cost effective,” he says.

Conclusions:

- In the fight against HCV, as in many other areas of public policy, the budget allocated to the effort is a key factor.
- Financial assistance from the national government has been positive for the rapid deployment of DAA drugs.
- Further co-operation between the Ministry of Health, the regions and other branches of the health service will be necessary to maintain momentum.

II. Implementing the programme: progress so far

1. A worthy destination

The health ministry is responsible for setting which services and treatments must be offered across the country. However, it does not control implementation. And it does not allocate budgets at the regional level to pay for the services and resources required. That has posed a challenge around investment in HCV management.

Spain's 17 Comunidades Autónomas (Autonomous Communities) are responsible for the health of the general population within each region. There are also separate branches of the Spanish National Health System for most of the prison population, for certain civil servants, the army and for the judiciary. That can lead to different policy priorities and different pathways for the identification of HCV sufferers and the speed at which they are treated.

Care is provided within each region by Primary Care Centres (Centros de Atención Primaria) and by hospitals and their various specialist departments. In the case of HCV, only hospitals are entitled to prescribe and dispense DAAs. Primary care doctors do not prescribe or administer these drugs, but they may take blood samples to be tested for antibodies to the HCV virus.

If a test result is positive, patients are usually directed to hospital infectious and/or digestive diseases departments for the RNA (ribonucleic acid) test, which confirms the diagnosis. These specialist departments also administer further tests to ascertain whether other diseases are present and to determine the level of liver damage (fibrosis) they have already suffered.

Only hospitals can prescribe the HCV treatment itself. Hospital departments also administer the later SVR test, usually 12 weeks after treatment, to check that patients are free of HCV.

With the exception of Cataluña and País Vasco, patients in the prison system are not the responsibility of the regional healthcare system. As we explore later, in the rest of the country, that division causes its own set of issues.

Autonomous registers in autonomous regions

Madrid, Valencia and La Rioja were among the first to dedicate resources to identifying chronic Hepatitis C patients. Others held back, not due to any unwillingness, but rather because their registers were incomplete. That made it difficult to reach out to those in need of treatment.

Dr Maria Buti, president of the Spanish Society of Liver Diseases, believes an immediate change in reporting procedures would help to make implementation easier. At present, only chronic cases

of HCV must be reported. A requirement to report acute cases, in addition to the chronic ones, would provide a clearer picture of the job that remains.

“In Spain, only the chronic infection registry is mandatory. To reduce the incidences of new cases, we would have to have a register of both chronic and acute hepatitis,” she says.

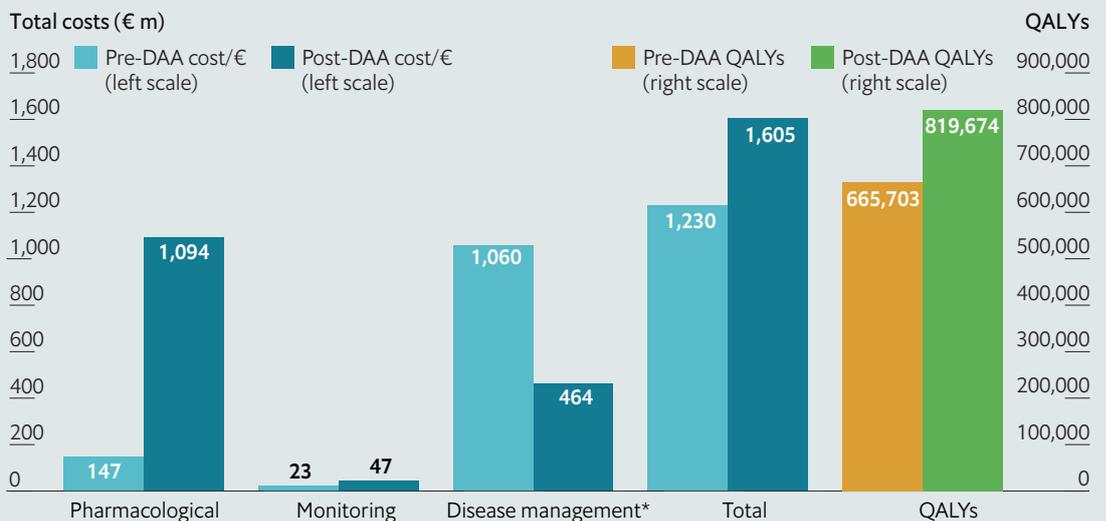
Dr Miguel Ángel Calleja Hernández of the Spanish Society of Hospital Pharmacy also believes that some regions are doing better than others. Andalucía is widening the net to identify more cases of Hepatitis C, but may not be moving quickly enough to meet targets. “In Andalucía, we now have the budget, but we have not detected all the patients,” he says. “We have more control over who we can treat now with the new drugs, but we are seeing fewer patients.”

Measuring costs and outcomes

Despite that unevenness in implementation, a growing body of data is pointing towards successful outcomes—in both health and economic terms—from the efforts made so far.

A widely quoted 2017 study of 51,900 patients showed the benefits—in terms of both individual health and national economics—obtained from HCV treatment as well as costs incurred by the introduction of DAAs.

Figure 5: Costs and benefits before and after the introduction of DAAs



Results of the analysis of the 51,900 patient cohort with the post-DAA strategy compared with the pre-DAA strategy, applying a discount rate of 3% to health costs and outcomes (costs* of disease management-fibrosis, cirrhosis, SVR, regression of liver cirrhosis, decompensated cirrhosis, hepatocellular carcinoma and liver transplantation. Incremental cost post-DAA v. pre-DAA: €375m. Incremental QALYs post-DAA v. DAA: 153,970 QALYs. DAA: Direct-acting antiviral; QALYs: quality-adjusted life year).

Source: Turnes J, et al. Value and innovation of direct-acting antivirals: long-term health outcomes of the strategic plan for the management of Hepatitis C in Spain. REV ESP ENFERM DIG 2017. Vol.109, No12

Dr Miguel Ángel Casado and Raquel Domínguez-Hernández of Pharmacoeconomics & Outcomes Research Iberia (PORIB), a consultancy, co-authored the study with Juan Turnes of the Complejo Hospitalario Universitario de Pontevedra.¹² (Figure 5)

The Gilead-funded study compared the cost of pre-DAA treatments and costs after DAA drugs were introduced, and also assessed the health benefits of DAAs for patients with F2 fibrosis or higher. The health benefits were measured in quality-adjusted life years (QALYs) and in terms of liver complications and deaths avoided after DAA treatment.

From a welfare economics perspective, the study concluded that long-term morbidity and mortality were reduced in patients treated during the first year after the introduction of DAAs under the Spanish plan. The number of QALYs also increased. The authors believed their analysis demonstrated the plan is “an efficient use of public health resources”.

That case is even stronger now that the cost of drugs has fallen, says Dr Casado. “The gain in the number of QALYs of life is spectacular in function of the investment,” he thinks.

An important consideration is also the economic impacts of effective treatment, says Dr Casado. For example, a 45-year old could expect to keep contributing to the economy for another 20 years, but only if they are not chronically ill.

A poster-update¹³ of the study, based on 66,777 patients and including F0-F1 patients concluded that the incidence of liver-related death fell by 82% and that of decompensated cirrhosis by 87%. There was also an 84% reduction in patients needing a liver transplant, which would lead to lower costs associated with the management of these complications.

For Dr Casado, the “events avoided” data represent both a cost saving and an opportunity for healthcare providers. “Reducing the number of liver transplants has an additional benefit. Those organs that were previously destined for patients with Hepatitis C can go to other patients,” he says.

In addition to hepatic conditions, nearly three-quarters of HCV patients can suffer extrahepatic manifestations, with related illnesses and medical events, according to a 2018 Gilead-funded study looking at five European countries.¹⁴ (Figure 6)

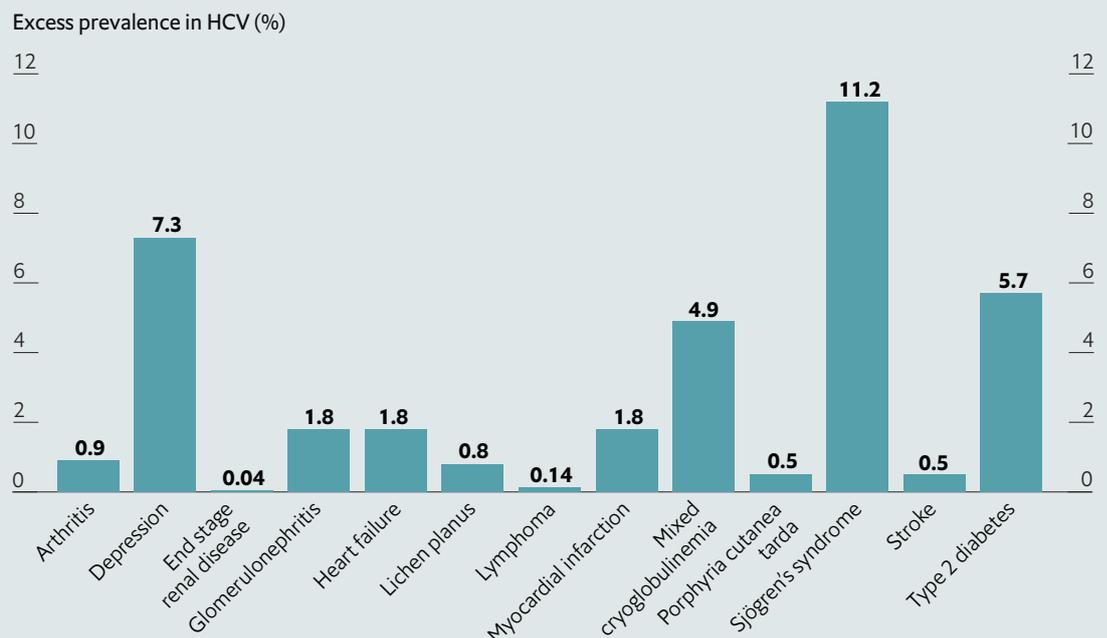
The study shows that HCV sufferers were more likely to develop Sjögren’s Syndrome and Type 2 diabetes, and are more susceptible to depression.

The study estimates that the total annual economic cost of these non-liver complaints in Spain is around €400m. Assuming that treated HCV patients are cured, avoiding type 2 diabetes, arthritis, strokes, heart attacks and kidney failure, this could save Spain €70m on its overall health bill, the study estimates.

¹² Turnes J, et al. Value and innovation of direct-acting antivirals: long-term health outcomes of the strategic plan for the management of hepatitis C in Spain. *Rev esp Enferm Dig* 2017. Vol.109, N°12; The study received funding from Gilead

¹³ Turnes J, et al. AASLD 2017 poster. Health outcomes and costs associated with the implementation of a national treatment plan for Hepatitis C in Spain. The Liver meeting 2017, Washington (Poster 764)

¹⁴ Cacoub P et al; Direct Medical Costs Associated with the Extrahepatic Manifestations of Hepatitis C Infection in Europe, Study funded by Gilead

Figure 6: HCV infection is associated with other conditions

Source: Cacoub, P, et al. Direct Medical Costs Associated with the Extrahepatic Manifestations of Hepatitis C Infection in Europe, J Viral Hepat. February 24th 2018. DOI: 10.1111/jvh.12881

A special fund for special needs

Competing priorities and a multi-layer system can hinder efficient implementation of major health programmes. Several politicians, including Dr Jesús María Fernández Díaz of the Partido Socialista Obrero Español (PSOE, Spanish Socialist Workers Party), suggest a solution: a special fund for researching, developing and delivering new Hepatitis C Virus (HCV) drugs nationally.

A dedicated HCV fund could include the associated costs of public education and deploying medical and outreach staff throughout the system. It could also help to deal with the diseases that often accompany HCV infection, he says.

“Therapeutic innovation requires a specific fund that helps the autonomous regions to incorporate new medicines on an equitable basis,” says Dr Fernández Díaz. “The Spanish economy is growing, now this growth must be translated into a new health financing agreement with the autonomous regions.”

England’s Cancer Drugs Fund offers an example. The fund allocated specific budgets to cancer treatments that had been rejected on cost grounds by the National Institute for Health and Care Excellence. The fund had its flaws: it overspent its budget, and access to new treatments was eventually narrowed.

Done well, a national fund and broader strategy may help to produce a holistic approach to funding and setting priorities. But agreeing the details could be politically charged. Any formula for dividing up money could cause political infighting. It may encourage some regions or nationally controlled branches of the health service to seek a first-mover advantage. Those with the resources to implement a broader detection, diagnosis and treatment plan might squeeze out those unable to move as quickly.

Conclusions:

- A body of research shows significant health and economic benefits from treatment of Hepatitis C with DAAs, which compensates for the investment Spain has committed.
- Among those benefits are an elimination of the virus from patients, increased economic productivity and avoided medical costs.
- A politician has proposed that a special fund be set up for HCV treatments that could speed up delivery of care, and improve pathways and treatment, particularly if related costs of detection and care are included.

2. A complex journey

The introduction of DAA drugs has been a success for approximately 100,000 HCV patients in Spain. But interviewees for this report question whether enough HCV sufferers have been or will be detected to enable Spain to reach the 2030 elimination target.

The rate of progress is uneven across Spain's regions, and the number of newly diagnosed HCV sufferers is unclear. Moreover, the flow of new patients has slowed because detection systems are not identifying those who remain. Specialists simply do not know where their next patients might be.

R&D: finding the remaining patients

One part of the national Hepatitis C programme dealing with research and development, is often overlooked. Yet nearly €1m of the original budget (over €700m) was dedicated to research on prevalence rates.

Scientists tested over 7,000 patients scheduled for non-HCV related surgery in the Navarra region of Spain.¹⁵ HCV antibodies were detected in 42 patients, indicating a confirmed viraemic prevalence of 0.51%, with more men affected than women. Many had a previous positive result. The authors concluded that previous estimates of HCV infection should be revised down. They also said that only a small proportion of HCV-positive patients remain undiagnosed.

There are more poster studies looking at Spanish prevalence rates, and the national picture will become clearer as results are published in peer-reviewed journals. Using the different prevalence rates of these studies, there might be 150,000, possibly over 200,000, infected people in Spain, between 35% and 65% of whom remain undiagnosed.

Regional discrepancies in policy

The differences partly reflect the composition of local populations and concentrations of those groups most at risk from Hepatitis C infection. Yet interviewees also say the quality of regional registries of known patients has hampered efforts to ensure patients get the care they need.

¹⁵ Aguinaga A et al. The prevalence of diagnosed and undiagnosed hepatitis C virus infection in Navarra, Spain, 2014–2016. *Enfermedades Infecciosas y Microbiología Clínica*, April 2018 <https://doi.org/10.1016/j.eimce.2018.03.001>

The Sistema de información de monitorización terapéutica de pacientes con Hepatitis C crónica (the national register of chronic Hepatitis C patients, known as SITHepaC) was the first step in quantifying and monitoring the HCV population at a national level. But more data are needed. As regions are not obliged to report how many people they are testing for HCV, it is difficult to see how registers will have complete data on the population. (Figure 7)

“There are two lines to follow. One is prevention, the other is the search for undiagnosed patients. Madrid is the most advanced on the diagnosis, treatment and information of patients in their registry,” says Mr Ortega of the Plataforma de los Afectados de Hepatitis C.

“The health ministry has to lead the process with all the autonomous communities in the search for the undetected,” he adds.

Figure 7: HCV testing policies in Spain

HCV testing policies in Spain

Testing policies	Availability
Dedicated HCV testing guidance	✓
Policy on frequency of testing for those at continued risk	✗
Testing in prison setting (opt in or opt out at reception)	✓
Funding of testing (free at point of use)	✓
Monitoring of testing, diagnosis and treatment (positive cases and number treated)	✓
Monitoring the number of tests performed	✗
Estimates of proportion of cases undiagnosed	✗

Source: European Centre for Disease Prevention and Control

“Nudge” initiatives: bringing patients into clinics

If you know more patients are out there, how do you get them to come to you? Nudging the public to step forward is one solution. A new public awareness campaign in La Rioja aims to do just that, based on a simple questionnaire that takes one minute to complete. (Figure 8)

The campaign asks a simple question: “¿Sabes si puedes tener la hepatitis C?” (Do you know whether you could have Hepatitis C?). It then offers a simple eight-point questionnaire. If anyone responds in the positive to any question, they are urged to seek a test from a local doctor or pharmacist, or to call a central number.

La Rioja has been one of the most successful in treating its known HCV cases.¹⁶ But Dr José Ignacio Torroba, head of pharmacy services at the Hospital San Pedro in Logroño, knows there are more patients that could be treated, if only he knew who and where they were.

¹⁶ Rioja Salud, November 2nd 2017 <https://www.riojasalud.es/noticias/5921-salud-inicia-una-campana-informativa-de-busqueda-activa-de-pacientes-con-hepatitis-c-para-erradicar-la-enfermedad-antes-de-2020>

Figure 8: What might a public awareness campaign look like?

¿Sabes si puedes tener la hepatitis C?

SÓLO NECESITAS MINUTO PARA RESPONDER ESTE CUESTIONARIO

He recibido una transfusión de sangre o plasma antes de 1991.

He tenido una operación quirúrgica antes de 1986.

He donado sangre en centros, a cambio de dinero.

He utilizado drogas inyectadas o inhaladas, compartiendo agujas u otro material de administración.

Me he hecho un tatuaje o un piercing en un centro sin las debidas precauciones de seguridad.

Mi madre tiene o ha tenido hepatitis C.

Mi pareja tiene o ha tenido hepatitis C.

Tengo o he tenido relaciones sexuales con múltiples parejas.

Si has seleccionado al menos una de las opciones, deberías realizarte la prueba de la hepatitis C

Consulta con tu médico de familia, farmacéutico o llama a Salud Responde: 941 298 333



The region has launched a publicity campaign, including leaflets, web materials and bus stop posters, to get people to come forward if they think they may be at risk. It aims to eliminate all HCV infections by 2020.

It is early days yet. Dr Torroba says primary care practitioners have referred around 275 new patients in the few months since the initiative started. The awareness campaign has helped maintain a similar level of new treatment starts as experienced in 2017. He thinks raising general awareness is vital if the disease is to be eliminated.

“In Spain, there is no national education plan. In all autonomous regions, including La Rioja, we have information on our websites, but we need more national action,” he says.

He warns that national targets will be missed if proactive steps are not taken elsewhere. More resources will be necessary, he thinks. “Research and staff are a big part of the cost of treating patients.”

Target 2021

While the World Health Organisation has set a 2030 target for the elimination of Hepatitis C, in Spain, the Alianza para la Eliminación de las Hepatitis Víricas en España (The Alliance for the Elimination of Viral Hepatitis in Spain) has set a target date of 2021 for eliminating Hepatitis B and C.

The alliance, which encompasses leading medical associations and patient groups, has set a 21-point action plan that includes a call for short treatment periods and single-step diagnosis. Under the single-step procedure, a healthcare professional can test for the presence of antibodies (indicating past infection) and active infection at the same time.

The 2021 target might not be reached. Gearing up the Spanish national health service to find all remaining infected cases over the next three years would be a considerable political and logistical task.

A new call to action in France

France introduced its Hepatitis C Virus (HCV) elimination programme in 2016. L'Association Française pour l'Étude du Foie (The French Association for Liver Studies) recently issued new recommendations to boost the country's efforts to tackle HCV.

Around 75,000 carriers of the virus are believed to remain undetected in the country.

The association believes the country can hit the World Health Organisation objectives before 2025, by reducing new infections by 90% and Hepatitis C-linked mortality by 65%. To do so, it is calling for universal screening for every adult at least once in their lifetime.

It also wants the government to allow all doctors to treat patients, not just those in hospitals, and for non-hospital pharmacies to be able to dispense direct-acting antiviral drugs.

Conclusions:

- A significant number of specialists doubt that the country will eliminate Hepatitis C over the next three years, although the WHO's 2030 goal is more achievable if resources are dedicated to improving reporting systems and detecting the remaining cases of infection.
- Interviewees emphasise the significant variations in access, detection, diagnosis and treatment across Spain's autonomous regions. Mr Ortega of the Plataforma de los Afectados de Hepatitis C says: "The health ministry has to lead the process with all the autonomous communities in the search for the undetected."
- Variations in policy and implementation practices occur within regions, from hospital to hospital, and within different branches of the Spanish Health Service.
- More needs to be done at both national and regional level to encourage potential patients to come forward and accurately monitor screening and diagnosis.

III. Remaining challenges: screening patients and improving access

1. Screening patients

The need for screening to find remaining cases of HCV was a recurrent theme in the interviews conducted for this report. With no current national plan to educate the population and deliver national screening programmes for HCV, Spain might not hit its elimination targets.

As with all viral illnesses, HCV needs a sufficient number of hosts who interact with other people to continue its process of replication. For viruses where vaccines are available, a high proportion of children—but not necessarily all—must be vaccinated to reduce the infection pool and break the cycle of transmission.

There is no HCV vaccine yet, so specialists and policymakers need to ensure that sufficient numbers of sufferers are identified and treated to halt new infections. If too many infected patients remain at large, the overall number of sufferers, complications and deaths could rise again. Many think that would undo the successes of the past three years.

“Screening the general adult population is cost-effective,” says Maria Buti of the Vall d’Hebron hospital in Barcelona and head of the Spanish Society of Liver Diseases.

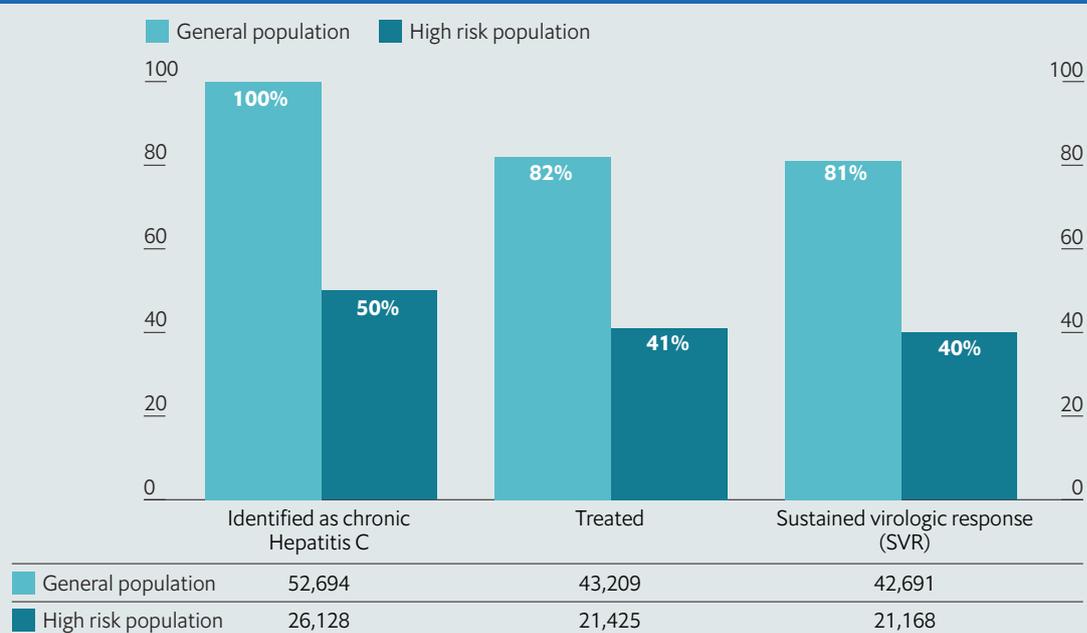
According to a study she participated in, titled *Screening and treatment of the Hepatitis C virus*,¹⁷ of the 34.5m people in Spain born between 1938 and 1997, around 35% (numbering 12m) have never been tested for HCV antibodies.

Of those 12m, 52,694 individuals are believed likely to have an active infection. Of these, 43,209 would probably have received treatment, and the majority of those—42,691—are likely to be cured. That is, 81% of new cases found in the general population could expect to be cured. (Figure 9)

The authors’ corresponding calculation for high-risk groups—a subset of the general population—is less encouraging. Here, screening can be expected to uncover 26,128 new HCV cases in the targeted age group (20 to 79 years old), of whom 21,168 are expected to be cured. That figure represents 40% of the total number of new HCV cases (52,694)—a considerably lower cure rate than that of the general population.

Moreover, according to their calculations, screening the general population would reveal twice as many chronic HCV patients in the wider population (52,694) than there are likely to be in high-risk groups alone (26,128). Focusing purely on high-risk groups, as is now the case, would clear just 40% of the whole infection pool and leave many cases in the general population undetected.

¹⁷ Buti et al. The screening and treatment of the Hepatitis C virus in the general Spanish population aged 20 to 79 years is cost effective. Presented as a poster (funded by Gilead) at the 43rd Annual Congress of the Spanish Association for Liver Studies, Madrid, 21-23 February 2018.

Figure 9: The value of screening the general population

Source: Buti et al. The screening and treatment of the Hepatitis C virus in the general Spanish population aged 20 to 79 years is cost effective. *Journal of Hepatology* April 2018, Vol 68, Supplement 1, p S190 (poster).
DOI: [https://doi.org/10.1016/S0168-8278\(18\)30593-2](https://doi.org/10.1016/S0168-8278(18)30593-2)

General-population screening may save a significant number of lives and dramatically reduce the demands on Spain's health resources in the next few decades. But this will involve costs: someone has to organise and pay for the screening first, and for the diagnosis and treatment that follow. As Dr Jesús Troya García of the Hospital Universitario Infanta Leonor Vallecas points out, resources and medical staff are not evenly spread.

"We now have the possibility of treating all patients, but there are some limitations due to the lack of equality in the resources available in some autonomous communities: some have limitations to certain drugs, a need for more doctors and more time for the professionals to dedicate to caring for the patients," he says.

Implementing a population screening and treatment plan can involve setting up multi-step patient pathways, as well as offering a range of services. (Figure 10)

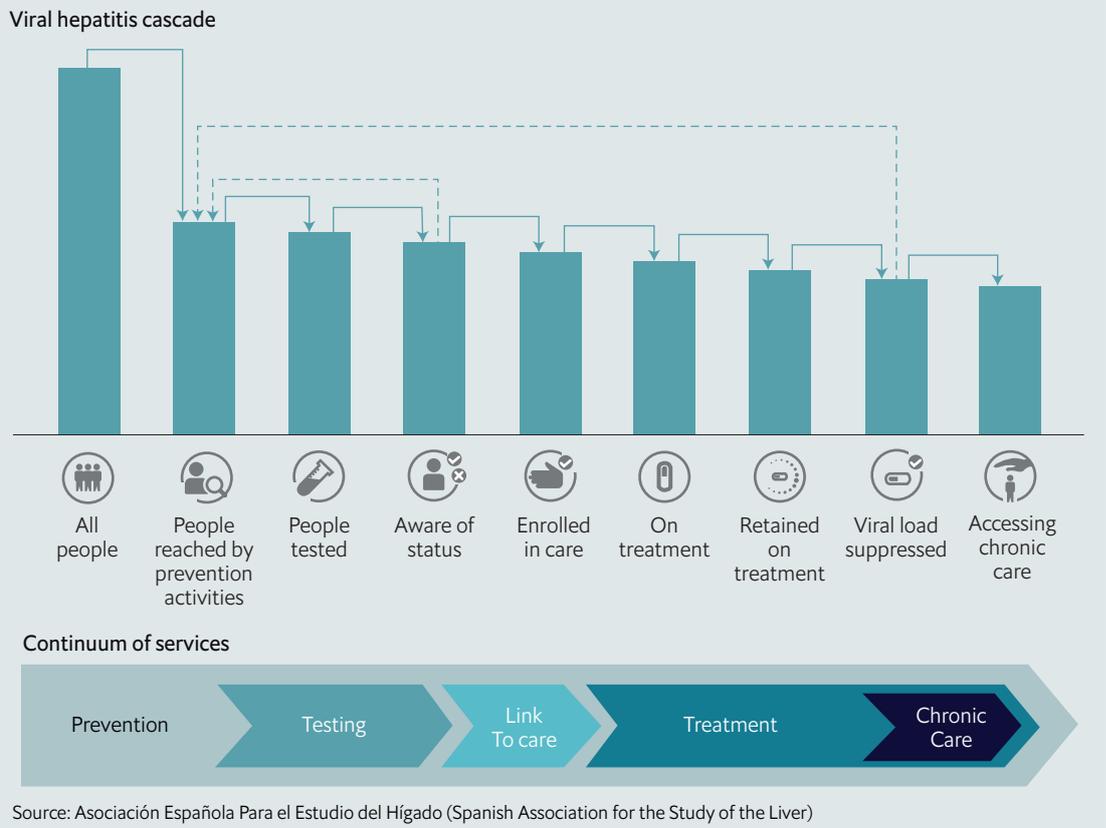
New screening technologies might help. A recent study by the Spanish Society of Liver Diseases found that 81% of hospitals already have the means to conduct one-stop diagnoses, in which the presence of antibodies and the presence of an active virus can be determined at the same time, but only 38% of them do so.¹⁸ The measures may not even cost that much; an antibody blood test may cost no more than €2 or €3.¹⁹

¹⁸ *Diario Medico* <http://www.diariomedico.com/2018/02/22/area-profesional/gestion/el-diagnostico-de-la-hepatitis-c-en-un-paso-solo-en-4-de-cada-10-hospitales>

¹⁹ *La Vanguardia* <http://www.lavanguardia.com/vida/20171204/433418695135/piden-un-cribado-de-hepatitis-c-para-que-afloren-los-casos-sin-diagnosticar.html>

Plataforma de Afectados por Hepatitis C de Madrid <http://plataformadeafectadoshepatitiscmadrid.org/propuesta-plan-cribado>

Figure 10: The logistics of HCV elimination



2. Improving access to diagnosis and care

Other controversial issues remain to be resolved. One is whether local practitioners should take on some of the additional treatment burden.

Sarah Blach of the CDA Foundation, a research organisation focusing on Hepatitis B and C, thinks Spain should consider devolving some treatment to primary care doctors. She notes that primary care physicians treat around 60% of HCV patients in Australia, and 35% of patients in New Zealand are treated by local health centres.

Policymakers should not worry about allowing general practitioners to prescribe such treatments, she thinks. With clear protocols, they can ensure similar levels of successful treatment as seen in hospitals. Deploying general practice doctors could also save funds compared with using specialists for all HCV cases. "SVR rates were the same; they do not oversubscribe," Ms Blach says. "In fact, the system costs less because primary care physician staffs are cheaper and more readily available."

Spanish healthcare specialists interviewed for this report tended to argue that local treatment is most effective in the simplest cases, where there is no co-infection and no cirrhosis. But many expressed doubts that Spain could implement a national screening programme and simultaneously devolve treatment duties to general practitioners quickly and effectively.

A view from the frontline

Dr Bernardino Jimeno Resa, a general practitioner in Cataluña, is not convinced that local doctors should administer Hepatitis C treatments. He notes that such cases can involve special needs; his latest referral for diagnosis and treatment, for example, was an 80 year old patient.

Treatment is not necessarily straightforward. The Hepatitis C Virus can mutate and other complications may be involved.

“The current system works well, particularly for asymptomatic patients,” Dr Jimeno says. He notes, though, that even asymptomatic patients may have other conditions that should be considered when doctors decide on the correct treatment.

Conclusions:

- Specialists, policymakers and regional health authorities agree that tens of thousands of HCV cases remain undetected.
- However, opinion is divided on the next steps in screening and diagnosis. A debate is a good way to reach an agreement on what strategy could be implemented.
- An agreement between the national government and the regions related to public outreach, detection and diagnosis could improve the chances that regions will invest people and resources in a general-population screening programme.

IV. Remaining challenges: managing high-risk groups

Spain's fragmented health system does not always serve high-risk groups effectively. The fragmentation can complicate access to care for some of the highest-risk patient groups, such as prison inmates. Fine-tuning protocols and patient care pathways for such patient groups can simplify the continuum of care from screening to diagnosis and treatment.

The government identified the highest-risk groups to be targeted in its 2015 programme. It listed 11 groups, beginning with users of drugs that are injected or sniffed, and patients who were treated with blood products prior to 1990. (Figure 11)

However, health policymakers have not yet developed the protocols to ensure effective, across-the-board outreach to these groups.

Figure 11: Micro-elimination: which are the high-risk patient groups to be treated first ?

- Injecting and sniffing drug users
- Patients treated with blood products prior to 1990
- Patients exposed to nosocomial Hepatitis C infection
- Persons living with chronic Hepatitis C patients
- Persons with tattoos or piercings and exposed to procedures using sharp-pointed instruments without suitable hygienic-sanitary control
- Children of mothers with HCV infection
- Healthcare professionals exposed to procedures involving biological risks
- Haemodialysis patients
- Men who have risk-involved sexual relation with men
- Patients infected with HIV, Hepatitis B Virus or Tuberculosis
- Prison institution inmates.

Source: Ministerio de Sanidad, Servicios Sociales e Igualdad

1. Prison populations: too many barriers

The Administración Penitenciaria (prison service), part of the Ministry of the Interior, is responsible for the healthcare of some 50,000 prisoners across most of the autonomous regions.²⁰ There are two exceptions. Cataluña and País Vasco are responsible for prison care within their regions. Between them, they have direct control of the health of almost 10,000 inmates.

Whether outreach is nationally or regionally controlled, the process of finding and treating prisoners infected by HCV should be straightforward, for the simple reason that the target

²⁰ Secretaría General de Instituciones Penitenciarias, data as at February 28th 2018 <http://www.institucionpenitenciaria.es/web/portal/documentos/estadisticas.html?r=s&asem=2018&msem=3&dsem=1&ts=CCAA>

population is held in one place. Nonetheless, patient and lobby groups contend that too many inmates are not given access to treatment, even after diagnosis.

Dr José Tomás Quiñonero Díaz, head of the Sociedad Española de Sanidad Penitenciaria (the Spanish prison health society), says HCV infections are rife in the prison population. He says prevalence in 2017 was around 13%, due to the high number of drug takers who come into the prison system. Untreated, they represent a risk, not only to their own long-term health, but also to others through transmission, either in prison or on release. Further studies are needed to determine the exact level of inmate infection.

“Screening is fundamental. A single diagnosis is very important in order to offer treatment quickly in the short term,” says Dr Quiñonero Díaz.

Screening is only the first step, however. Although prison populations are, by nature, captive, and most prisoners are willing to be tested, the wait for test results can be long. Few prisons have new digital equipment that allows for rapid identification of antibodies and active HCV infections on site. “Perhaps it is more expensive, but it certainly is more effective,” says Dr Quiñonero Díaz.

Things might be easier—and diagnosis costs avoided in some cases—if hospital staff had direct access to prisoners’ medical records. But the prison medical system is separate from those of the comunidades (except in Cataluña and País Vasco). A prison doctor must obtain the patient’s permission, then write to their primary care doctor for details. Again, prisoners tend to agree, but bureaucracy delays the process.

Integrating prison and regional healthcare was promised more than a decade ago. Dr Quiñonero Díaz says his members and the regions mostly agree that it would benefit all stakeholders, but progress is stalled.

A further prison wall to scale is access to treatment. Dr Quiñonero Díaz says that some 5,000 inmates are infected, but less than half have been treated. The prison service has few liver specialists of its own who can prescribe DAAs. Legally, treatment must be given in hospital settings, so patients must be transferred to specialist hospital units for scans and treatment. That is a security risk and can take three to four months to arrange.

An easier solution would be to allow prison medical teams to diagnose and treat, without the need to move patients to hospitals. That would require a change to the law. But as Dr Quiñonero Díaz points out, many prison medical units are understaffed already and may not be able to take on a bigger workload. Working in a prison medical facility is not the most attractive job, he says.

Dr Pablo Saiz de la Hoya Zamácola, an infectious diseases specialist working at the Fontcalent prison in Alicante, agrees that more frontline resources would help ease the situation. He believes that adopting elements of the prison system’s approach to HIV would help eliminate HCV among the incarcerated population.

“The HIV and Hepatitis C programmes in Spanish institutions were excellent, with egalitarian levels of coverage, diagnosis and therapy. With the emergence of direct action antivirals, the prison administration broke the protocols and the hepatitis programme,” he says.

Prison doctors receive HIV drugs in bulk, allowing them to prescribe as and when needed directly to inmates. In 2011 the prison service prohibited a similar system for HCV treatments on cost grounds.

This can have health consequences. Fontcalent prison hosts short-term prisoners, often facing sentences of just six months, or awaiting a place in higher-security facilities. Quick diagnosis and treatment are therefore vital. “In the next six months, more than 15 infected people will be imprisoned. They need a quick treatment before they go back to the street or go to another institution,” says Dr Saiz de la Hoya Zamácola.

Despite the political lethargy, change is happening slowly at a local level. Dr Saiz de la Hoya Zamácola says Valencia’s health authority is conducting a test with one local prison and allowing it direct access to DAA drugs. And at least now, prisoners cannot be moved to other sites once they begin treatment. Fortunately, he adds, the prison system management recognise that patients are far too easily lost, even behind prison walls.

2. Intravenous drug users

In an ideal world, every drug user who is diagnosed as HCV positive in a drug clinic would turn up for their appointment with a hospital specialist. Real life does not work like that, explains Dr Juan Macías of Hospital Universitario Valme.

Dr Macías’s catchment area is largely rural; the nearest addiction clinic is 10 km away, and the furthest 75 km. Getting his patients to specialist treatment is difficult. “They won’t get on the bus,” he says simply.

In his experience, around 25% of those diagnosed don’t turn up for hospital appointments. As treatment continues, even more drop out. “The only way to get to reduce the number of lost patients would be to take treatment out of hospitals into the addiction centres, like we do for methadone,” he says.

But delivering in different locations is not enough. Patients need pre-treatment evaluation and a supervised follow-up. Those with cirrhosis need additional management to prevent complications from advanced liver disease, he adds.

Dr Macías and other doctors and nurses regularly travel to local addiction centres to screen drug users. They are also part of the Hepcheck programme, a study on the effective use of onsite, rapid testing equipment that uses mouth swabs to test for HCV antibodies in 20 minutes. “It is quick, like testing for HIV,” he says.

Of around 500 drug users screened, he calculates that 25% have HCV antibodies. Blood samples are taken at the same time for further RNA testing for active infections. In over half of all HCV positive diagnoses, active infections are found.

Dr Macías says most sexual health, drug and other services operate almost as a “parallel health service”. They are allowed to perform certain functions, but not others. Moreover, what can be done locally differs depending on where people live and where they have contact with the system.

When the system is so fragmented, too many people fall between the cracks. Those who suffer from mental health issues are at further risk, as they must see yet another specialist for their needs. Dr Macías says integrated addiction clinics and healthcare may depend on the region, provincial authorities, town halls or even the non-governmental organisations involved.

“They have tried to integrate for 30 years. It has not been resolved at a national level,” he says. “If it is not integrated, it won’t help the elimination plan.”

Dr Pablo Ryan from the Hospital Universitario Infanta Leonor agrees that services for PWIDs must be more joined up—and more local. That is particularly true as the drug-taking population profile changes. Dr Ryan says Spain made good progress after an increase in drug taking in the 1980s. Even so, as habitual Spanish drug takers age, they become more susceptible to chronic infections.

A younger group of PWIDs has also emerged. They are most likely to be immigrants, often from Eastern Europe or North Africa. Across the two groups, Dr Ryan estimates one in five carries the HCV virus.

The younger immigrant population is far less likely to have contact with the health system. Dr Ryan says a more proactive approach is required to reach this population. That effort needs to include colleagues from other specialisations, including psychiatric care, social services and housing.

“These patients are at risk from HIV, tuberculosis, depression, Hepatitis B as well as Hepatitis C,” says Dr Ryan.

In addition to encouraging a multidisciplinary approach, Dr Ryan is trying out new equipment and testing procedures to ensure that diagnosis is quick when PWIDs are finally contacted. Collecting dry blood samples, rather than vials, makes the process easier. But, says Dr Ryan, it still takes two weeks for the results to be returned. Any delays in the continuum of care will deter some patients from taking the next steps to treatment.

“For many people, Hepatitis C is a tiny problem. A percentage of them never come to the hospital,” he says.

3. People with HIV: applying the lessons learnt

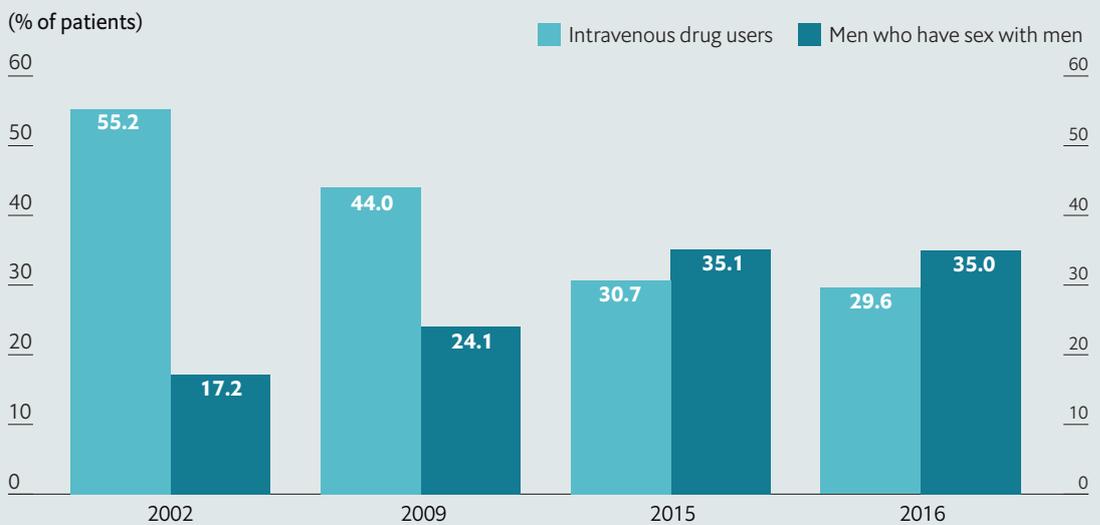
HCV is the number one cause of death among Spaniards living with HIV. But it doesn’t need to be. There are 130,000-160,000 people living with HIV in Spain. Between 2015 and 2016, DAAs helped reduce the number of those who are also infected with HCV by 47%, according to a recent study.²¹ Yet HIV patients have to take medication for the rest of their lives; Hepatitis C patients do not—they could be clear of HCV in as little as 2-3 months.

Dr Juan Berenguer of the Hospital General Universitario Gregorio Marañón, thinks Spain is “just a stone’s throw away” from eliminating HCV in HIV patients. That has led to a fall in HIV patients developing serious liver conditions. Yet he also thinks that the burden of liver disease may remain significant despite the elimination of HCV infection. These patients will need long-term screening with an ultrasound every six months for hepatocellular carcinoma.

“According to our studies, 7-8% of HIV infected patients living in Spain have or have had HCV related cirrhosis,” he says.

Unsafe sexual practices, on the other hand, could lead people who have been cured of HCV to be reinfected. There has been a noticeable change in the profile of co-infected patients. Men who have sex with men have overtaken intravenous drug users as the biggest risk group. Failure to track the health of men who have sex with men could lead to more cases of cirrhosis and death in the decades ahead. (Figure 12)

Figure 12: Sex: a riskier source of new HCV infections



Source: Juan Berenguer et al²²

²¹ Juan Berenguer et al, “Human Immunodeficiency Virus/Hepatitis C Virus Coinfection in Spain: Elimination Is Feasible, but the Burden of Residual Cirrhosis Will be Significant.” January 2018. *Open Forum Infect Dis.* 2018;5(1):ofx258

²² Ibid

Dr Berenguer believes that many men may become reinfected and then transmit the disease to others through unsafe practices, including “chemsex”—the taking of drugs to enhance the sexual experience. He also believes that preventive measures should not be abandoned, particularly among men who have sex with men, for which reinfection rates after an HCV cure in Spain are 5.93 per 100 person-years. This is significantly higher than the reinfection rates in people who acknowledge acquisition of HCV by injection drug use, which sees reinfection rates of 0.21 per 100 person-years.

He suggests changes to follow-up procedures to ensure that men remain clear of the virus. “They need six-monthly screening and ultrasound. The cirrhosis and decompensation risk has dropped but has not been eliminated,” he says.

Beyond monitoring reinfection through unsafe sex or drug injection, doctors and clinics may also need to revisit patients who were treated with older interferon or other legacy drugs, as they may still be at risk of liver cancer. In general, more vigilance is needed to prevent further outbreaks of HCV, says Dr Berenguer: “We need better micro-elimination because one size does not fit all.”

The Editorial Advisory Board discussions also noted elimination procedures may need to be extended to haemophiliacs who were infected by HCV through unscreened blood prior to 1990, and to renal dialysis centres.

Working together in Cataluña

Cataluña’s current efforts to integrate its health programmes for drug addicts, HIV sufferers and those with sexually transmitted diseases should also help in the battle against Hepatitis C, says Dr Joan Colom, deputy director for drug-dependency in Barcelona.

According to Dr Colom, some 7,500 people are receiving methadone treatment at dozens of centres across the region. They will be early targets for local HCV testing, as health officials know they will turn up for their methadone fix.

Dr Colom is also looking at how to reach other high-risk groups, especially immigrants from HCV high endemic countries who have no contact with health providers or outreach centres. His department is also collaborating with community centres serving men who have sex with men.

Linked-up in Copenhagen

For an example of a community that is adapting lessons learned from treating HIV patients to treating those with Hepatitis C Virus (HCV), consider Copenhagen. Jens Lundgren, professor at Rigshospitalet, University of Copenhagen, and director of its Centre of Excellence for Health, Immunity and Infections, says officials are adopting “shared care” practices to detect more HCV cases among various high-risk groups.

For example, his team is working with local halfway houses where drug-injectors receive methadone. Such individuals, he says, “should not be taken out of their safe environment, and they have an incentive to come because that is where they get their methadone.”

It has taken three years to establish the procedures and build links with other care providers. “Is it more costly? Yes, but not much. It is not the money for care that is the bottleneck, it is the price of the drugs,” says Professor Lundgren.

Conclusions:

- Separating prisoner healthcare from general healthcare causes delays in screening and leaves thousands of diagnosed inmates without treatment.
- The prison system’s approach to HIV provides a positive example of conducting screening and treatment onsite and should be adopted for HCV.
- But the prison health system lacks resources—staff, equipment, money—to eliminate HCV from a captive population.
- The populations of intravenous drug users and those engaging in unprotected sex are subject to high risks of reinfection and transmission of HCV, and require special attention.
- A rise in chemsex-related infections could indicate an emerging problem among a younger population of men who have sex with men.
- Accessing high-risk populations via outreach clinics has proven effective, and has shortened diagnosis times and the wait for treatment.
- A significant lesson from programmes to fight HIV is that they work best at a local level. The same applies to HCV programmes.

Conclusion

Based on the success of its Hepatitis C initiative in 2015, Spain could be close to eliminating the disease. No other European country has come so far so fast. But with new case numbers dwindling, indicating the possibility of a large group of undetected cases, there are urgent decisions to take.

Policymakers are targeting high-risk groups and in future may have to debate the resources that may be needed to detect possible sufferers among the wider general population.

If high-risk groups remain the priority, then the prison service—in charge of one of the main high-risk groups—should increase its efforts. It has a captive pool of infected patients that it could treat quickly if prison staff were given more resources and allowed to administer DAA drugs, just as they administer HIV drugs.

On the high-risk front, more can be done to encourage integration between outreach centres, charitable groups and specialists targeting PWIDs and men who have sex with men. Providing for more onsite testing where such high-risk groups congregate and delivering treatment locally could improve detection and successful treatment.

As for the general population, there may be a case for increased screening if resources can be found for education and efforts made to smooth the path to treatment. New screening technologies may also be able to help.

Even when an active infection is spotted, communication channels are not always clear. Eradicating such barriers to detection and treatment should be a priority.

Other changes need not be radical, or even new. Spain's approach to HIV sets a good example by allowing detection and some treatment close to where patients are.

To continue on the present course could jeopardise Spain's chances of achieving its targets in the short term, and could result in more Hepatitis C infections in the long term. Calls by patient groups and others for general screening should not be overlooked. But Spain should also not rush into a massive programme without careful planning and budget review.

That review should consider how the full programme of screening, diagnosis, treatment and care is organised and funded. It should also include how the rationale for an expanded effort should be explained to the wider population. Setting ambitious screening and diagnosis targets could detect more patients infected with HCV, but the costs of doing this would need to be carefully assessed.

Appendix

WHO global targets for HCV elimination²³

Target area	Baseline 2015	2020 targets	2030 targets
Impact			
Incidence: new cases of chronic HCV infections (reduction %)	6-10m infections are reduced to 900,000 by 2030 (Hepatitis B and C)	30%	80%
Mortality (reduction %)	1.46m deaths reduced to less than 500,000 by 2030 (Hepatitis B and C)	10%	65%
Service provision targets			
Blood safety (% of donations screened in a quality-assured manner)	89%	95%	100%
Safe injections (% of injections administered with safety-engineered devices in all settings)	5%	50%	90%
Harm reduction (number of sterile needles and syringes provided per person who injects drugs per year)	20	200	300
HCV diagnosis (coverage %)	<5%	30%	90%
HCV treatment (coverage %)	<1% (Hepatitis B and C)	3m people have received HCV treatment	80% of eligible people treated

²³ Adapted from WHO. Global health sector strategy for viral hepatitis 2016–21. Geneva: World Health Organization, 2016. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_32.

WHO European region targets for HCV elimination²⁴

Target area	Milestones 2018	2020 targets
Surveillance and data	<ul style="list-style-type: none"> • Adoption of harmonised surveillance objectives and case definitions aligned with WHO technical considerations • National disease burden estimate & investment case 	<ul style="list-style-type: none"> • National hepatitis infection surveillance programme in place to provide real time data on viral hepatitis diagnosis, treatment and care cascade
Evidence-based policy	<ul style="list-style-type: none"> • Costed and funded national hepatitis plan with clear targets 	
Awareness	<ul style="list-style-type: none"> • World Hepatitis Day marked in all countries 	<ul style="list-style-type: none"> • National viral hepatitis communications and awareness strategy adopted in most countries
Blood safety	<ul style="list-style-type: none"> • Effective haemovigilance system in place • All donations tested a least with serological methods 	<ul style="list-style-type: none"> • All donated blood tested with nucleic acid testing-screening methods • All donated blood from non-remunerated donors
Infection prevention & control in and out of healthcare settings	<ul style="list-style-type: none"> • Safe injections policies and intrahepatic cholestasis of pregnancy rules for preventing transmission in health sector (including prisons) implemented • National disinfections & sterilisation protocols for non-healthcare settings 	<ul style="list-style-type: none"> • 50% of injections administered with safety engineered devices in all settings
Prevention among PWIDs	<ul style="list-style-type: none"> • Policies implemented to support comprehensive package for prevention & harm reduction 	<ul style="list-style-type: none"> • Comprehensive package for prevention & harm reduction: including at least 200 syringes per person per year; at least 40% of opioid-dependent PWID receive substitution therapy; 90% of PWIDs receive targeted information, education and communication provided by needle and syringe programmes, drug treatment services, and other services targeting PWIDs

Source: World Health Organisation

²⁴ Adapted from WHO Regional Office for Europe. Action plan for the health sector response to viral hepatitis in the WHO European Region. Copenhagen: WHO Regional Office for Europe, 2016. Available from: http://www.euro.who.int/__data/assets/pdf_file/0008/315917/66wd10e_HepatitisActionPlan_160555.pdf?ua=1.

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