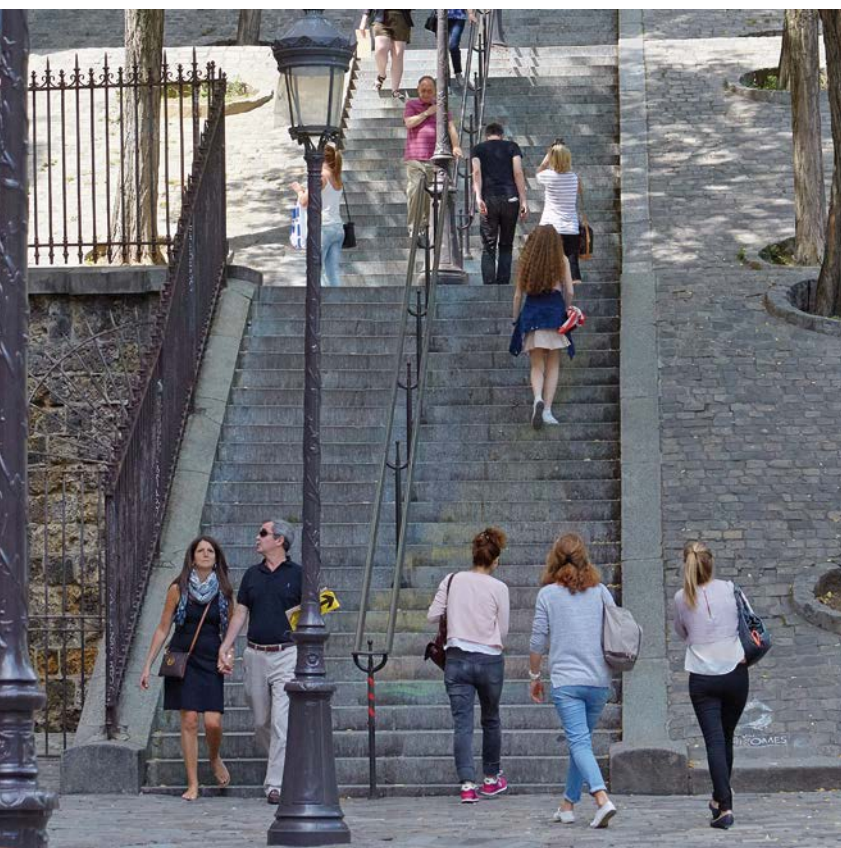


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How to implement a Comprehensive Plan For Hepatitis C in Spain

Identifying the key success factors





This report has been drafted in collaboration with Gilead.

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Prologue



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The recent appearance on the market of direct-acting antiviral drugs against hepatitis C which are more effective, safer and better tolerated than preceding therapies, warrant the need to draw up a Strategic Plan to tackle Hepatitis C nationwide.

The World Health Organisation had already recommended to the EU and its member states to develop and implement an action plan against hepatitis which would include raising awareness, prevention and treatment of the disease through all the relevant health policies.

In Spain in January 2015 the Ministry of Health, Social Services and Equality announced the creation of a National Plan which comes into force on April 1st. The present report is based on this framework for reflection. We intend to provide a vision of the key success factors for deploying and implementing the National Plan.



This report is split up into seven chapters. The first is of a general nature and identifies a series of specific areas on which to carry out a more in-depth reflection and the six subsequent chapters are focused on those specific areas in which the Plan is going to act to achieve successful implementation.

This has been an eminently participative approach. We have wished to involve a high number of multidisciplinary experts so that they could help to identify the key success factors from different perspectives.

Here at PwC we hope that the philosophy of this document, which is none other than to promote the development of political health debates to encourage the successful implementation of a National Plan, awakens interest and the debate amongst the various agents in the sector.



Executive summary

The Ministry of Health, Social Services and Equality drew up the Strategic Plan to tackle Hepatitis C in view of the health care problem presented by chronic hepatitis C in Spain (a prevalence of antibodies in adults of 1.7% is estimated) and the recent appearance on the market of new oral antivirals with cure rates exceeding 90%. The launch of this plan affords an extraordinary opportunity to reflect about the key success factors of appropriate implementation.

This Plan was published by the Ministry of Health, Social Services and Equality and is available at its website¹.






After reviewing the international experiences of France and Scotland, six

specific areas were identified to carry out a reflection so as to identify more tactical keys to success:

Epidemiology and mathematical models. Health records, goals and results in the medium-long term

In Spain today there is no homogeneous population register which is why there is not enough information about the scale of the disease nor about the impact does it generate. The data available shows the prevalence of antibodies in adults of 1.7% and it is estimated that only 40% have been diagnosed.

¿Cómo cuantificar la situación real de la infección por VHC en España?

-  Develop a population-based epidemiological study
 -  Designing a complete, transparent and audited record system
 -  Using, to a larger extent, mathematical prediction models for evidence informed policy & planning
 -  Using georeferencing systems to get to know the distribution of the disease
 -  Adopting policies to suit the epidemiological scale of each autonomous community
-

Monitoring implementation: importance of developing health information systems and key performance indicators to ensure health outcomes

Each AC (Spanish Autonomous Community) has developed, with different levels of progress, their own

health information systems for data collection causing a problem in terms of the heterogeneousness of the data. There is a lot of data available but it is dispersed amongst different sources and health information systems, making it difficult to obtain reliable, consolidated records.

¹ http://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/docs/plan_estrategico_hepatitis_C.pdf

How to develop health information systems which allow the investigation and monitoring of health outcomes and disseminate results socially with total transparency?

- Developing strategic planning centrally with a view to designing, constructing and managing an ongoing registration system from unique patient identification
 - Setting up coordination mechanisms with the assignment of responsibilities
 - Deploying evidence-based methodologies such as Real World Evidence
 - Boosting Big Data analysis
-

High-incidence population: prisons and injecting drug users

Despite having fallen in recent years, the rates of prevalence and reinfection are still very high in Spanish penitentiary institutions (21.3%) and

amongst injecting drug users (between 42 and 98%). Furthermore, access to treatment is not homogeneous in Spanish prisons and there are obstacles to accessing new, latest generation drugs as they require the transfer of the inmate to Madrid where treatment has been centralised.

How to treat high incidence collectives under the same principle of fairness as the general population?








- Integrating prison institutions into health services
 - Developing specific elimination programmes which include coordination protocols, training plans and educational courses
 - Fostering screening campaigns upon entering and leaving prison
 - Boosting prevention and damage reduction programmes in injecting drug users (IDUs)
-

Primary Care, prevention services and private health organisations

The field of primary care is part of a health system characterised by a high organisational complexity which may make it hard for GPs to take part in the strategies drawn up by specialist doctors.

On the other hand, political decisions based on short-term planning criteria do not allow the devising of prevention, diagnosis and treatment strategies which manage to achieve the elimination of the disease. Finally, it is worth mentioning that some segments of the population experience access barriers to diagnosis and/or to treatment.

How to achieve the systematic participation of Primary Care structures and coordination to ensure elimination?






-  Specifying the screening criteria and adjusting the risk groups to foster screening programmes
 -  Configuring warning systems in the electronic health records to contribute to early diagnosis
 -  Incorporating patient screening and patient access to care into the Primary care goals
 -  Drawing up protocols for practical, consensual action
 -  Involving private insurance companies in the strategy
 -  Llevando a cabo programas de formación continuada
 -  Realizando campañas de sensibilización
-

Health investment strategy

Despite the fall in the prevalence of HCV in recent years, health costs will keep growing as the population with HCV infection is growing old and the complications associated with the

advancement of the diseases (cirrhosis, transplants, hepatocellular carcinoma) have a high budget impact. Furthermore, the fragmentation of the financing system involves a distancing between the central and autonomous level.

How can we make the financing mechanisms more flexible?

-  Incorporating the return on the investment into decision-making process
 -  Rigorously incorporating economic evaluation into technical analyses
 -  Assuming multiannual, flexible budgets
 -  Setting up alternative financing mechanisms
 -  Establishing recommendations for health investment and disinvestment
-

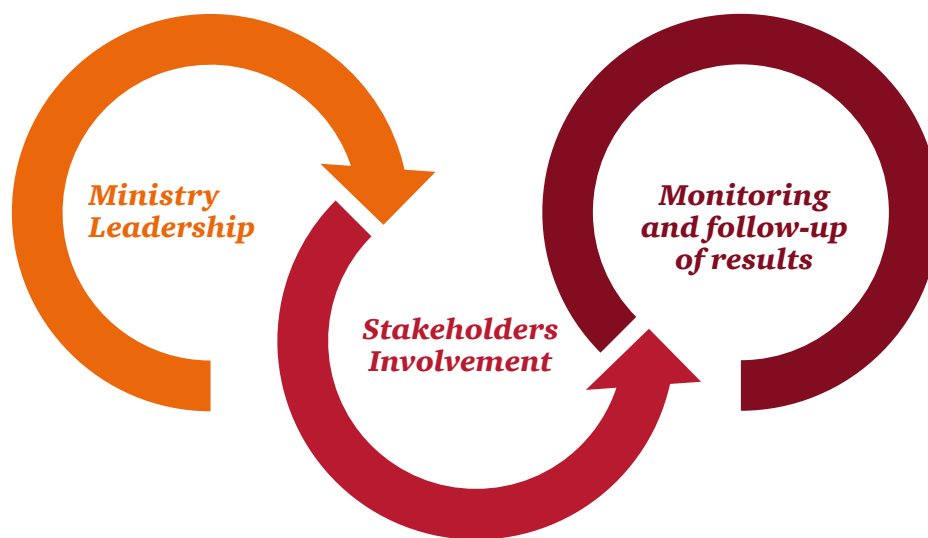
Policies for shared governance

In view of the autonomous decentralisation characteristics in Spain, our system faces the challenge of setting up governance which strikes a balance between ensuring national leadership – which guarantees that actions and resources are optimised and knowledge is shared – alongside maintaining autonomy which ensures that an appropriate response is given to the heterogeneity of each region.

In addition to the keys to success identified in the previous chapters for the implementation of the National Strategic Plan, we have identified three levers to success which are required

though are not sufficient, on which all the actions to be carried out should be based to successfully ensure the Plan's targets.

The successful implementation of the strategy will depend on the leadership & shared governance between the various stakeholders which is supported by an operating model which drives forward and monitors Plan follow-up. In this way, our health system can be adapted more flexibly and more speedily to the challenges of the hepatitis C epidemic, including the financing of new drugs which are in the pipeline of the laboratories and which foreseeably will come out onto the market in the short and medium term.



Presentation

We are presenting the document ***How to implement a Comprehensive Plan for HCV in Spain. Identification of the keys to success.***

The prime aim of this document is to provide a vision of those aspects which are critical for the deployment and start-up of the *Strategic Plan to tackle Hepatitis C in the National Health System.*

During the course of this document the main challenges and opportunities will be set out which face the National Health System to implement the National Strategic Plan

as well as the key success factors for implementing the Plan.

Metodology

Seeking a participative approach, the present document was drawn up in line with contributions from different experts and prominent personalities in the health sector. We have held personal interviews with them and working meetings and entered into seven debate forums around different themes. To promote an enriching debate, the venues have been made up of different, multidisciplinary experts so they could contribute to the aim of each event from different perspectives.



Participants

Here at PwC we would like to sincerely thank participants for their involvement and time in drawing up this document. The contributions they have made have been extremely enriching and have allowed a vision of the situation from different perspectives. We feel it is a privilege to have been able to rely on their vast experience and in-depth knowledge of health in Spain and of the Hepatitis C disease.

The data, opinions and comments gathered during the debate forums have been vital for the construction of this document whose final drafting was carried out by the PwC health and pharma team. Both the individual and group contributions have been included in the present document. However, the responsibility and author of the study is exclusively PwC.

The list of participants has been detailed below who have contributed to the drawing up of the report and their post or responsibility at the time they contributed to the document.

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- Martí Sansaloni. Conseller de Salut del Govern de les Illes Balears
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Study context

drugs (DAA) against hepatitis C which are more effective and safer; in January 2015, the Minister of Health, Social Services and Equality announced the creation of a *Strategic Plan to tackle Hepatitis C*. On March 26th 2015, the Plan was approved by the Plenary Session of the Interterritorial Council of the National Health System, being published in May 2015.

The Plan sets out to reduce the morbidity and mortality caused by the virus, improving prevention, diagnosis, treatment and the monitoring of patients in the National Health System.

The Plan has four strategic lines:

- To quantify the scale of the problem. To describe the epidemiological characteristics of patients infected by hepatitis C and establish prevention measures.
- To define the scientific-clinical criteria which allow the right therapeutic strategy to be established, considering the use of direct-acting antivirals for the treatment of hepatitis C in the National Health System.
- To set up coordination mechanisms to properly implement the strategy to tackle Hepatitis C in the National Health System.
- To promote the progress of knowledge of the prevention, diagnosis and treatment of hepatitis C in the National Health System by way of R&D&i actions.

By dint of the stipulations of the plan, as from April 1st all patients with fibrosis at grade F4, F3 and F2 will be treated with latest-generation drugs; though it has not yet proven possible to specify how many will be able to be treated this year with the new drugs. These new oral antivirals entail a revolution in the treatment of hepatitis viral C infection with curing rates exceeding 90% whilst at the same time allowing the treatment time to be reduced and lowering the side effects³.

In Spain the Health Ministry has, over the year, published different National Health Plans, including, inter alia, the Strategy to prevent and control HIV infection and other sexually transmitted infections, Cancer strategy, Strategy in ischemic cardiopathy, Strategy in diabetes, Strategy in rare diseases, Strategy in EPOC, Strategy in strokes, Strategy in mental health or the Strategy for tackling chronicity. The success of said national strategies largely depends on the political will and degree of collaboration between the different lobbies: the Ministry, Regional Health Services, care professionals, patient associations... both for definition and their subsequent deployment and evaluation of results.

The launch of a new nationwide Strategic Plan affords an extraordinary opportunity to reflect on the keys to success of an appropriate implementation. Although we will be focusing on the specific case of the Hepatitis C disease, many of the conclusions could be extrapolated to the case of other pathologies.

Today, hepatitis C is one of the most important causes of chronic liver disease worldwide and it is a serious public health problem. It is known as the “silent pandemic” owing to its high rates of prevalence and as it remains asymptomatic for decades before the disease develops into cirrhosis and liver cancer.

In view of the health problem entailed by chronic hepatitis C in Spain (it is the first cause of mortality from infectious diseases and it is estimated that there are 688,000 adults with antibodies and 472,000 adults with viremia², though the majority have not been diagnosed) combined with the recent appearance on the market of new direct-acting antiviral

² Estimates based on Gower, E. et al. Global epidemiology and genotype distribution of the hepatitis C virus infection *Journal of Hepatology* 2014 vol. 61 j S45–S57; and Bruggmann, P. et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. *Journal of Viral Hepatitis*, 2014, 21, (Suppl. 1), 5–33

³ Spanish Association for Liver Study. Document of II Spanish Consensus on the treatment of hepatitis C

Figure 1.
National-level policy recommendations

- To facilitate an open dialogue between patients and professionals.
- To obtain public financing for treatment.
- To offer unrestricted access to antiviral therapy.
- To treat infected children at specialised units.
- To facilitate access to new drugs.
- To offer treatment under the care of specialists.
- To require all professionals to follow the guides of the European Association for the Study of the Liver (EASL).

- To harmonise national systems in member states.
- To create centralised registers nationwide.
- To share results with stakeholders.

- To ensure that all those chronically infected by HCV are assessed for antiviral treatment.
- To ensure that the patients diagnosed are referred directly to specialists.
- To ensure that the patients have access to treatment options in line with latest clinical guides.
- To monitor patients to prevent cirrhosis and liver cancer
- To evaluate alcohol consumption and offer support.
- To ensure that access is free and integrated with other care services.
- To facilitate collaboration between health services and prison services.
- To ensure that the waiting list for an appointment with a specialist does not exceed six weeks.



- To obtain financing from governments for raising awareness campaigns.
- To provide information and support to stigmatised groups.
- To improve the raising of awareness of professionals.
- To increase raising awareness of the inmate population.
- To involve civil organisations nationwide.
- To involve society in the world hepatitis day.

- To implement local screening and patient access to care programmes
- To ensure the early identification of pregnant women with chronic hepatitis
- To implement routine tests amongst blood-donors with referral to a specialist for those who are positive.
- To provide anonymous tests to the whole population free-of-charge.
- To develop standardised protocols.
- To include a liver enzyme test in routine revisions

- To develop collaborative proposals with other diseases, including cancer.
- To involve society in prevention.
- To improve control of the infection in health environments.
- To implement differentiated strategies for injecting and non-injecting drug users.
- To prevent contagion in prisons.
- To promote screenings amongst donors.
- To implement prevention programmes amongst high-risk groups.
- To implement hepatitis B inoculation programmes.
- To promote safe sex practices.

Source: ELPA, EASL, VHPB, World Hepatitis Alliance, Correlation: European Network Social Inclusion & Health. Hepatitis B and C. An action plan for saving lives in Europe. The experts' recommendation summary

Debate forums

After reviewing international experiences, seven different themes were identified. The debate forums were developed during the first half of 2015:

1. The importance of a National Plan. The experience and key success factors of the Plans in Scotland and France.
2. Epidemiology and Mathematical Models. Database and records, goals and health outcomes in the medium-long term.
3. Monitoring Implementation: Importance of developing health information systems and key performance indicators to ensure health results.
4. National Strategy for eradication. High-incidence population: prisons and injecting drug users.
5. National Strategy for elimination: Recommendations to optimise diagnosis. Importance of primary care, prevention services and private health organisations.
6. Health investment strategy key in a Comprehensive Plan to tackle Hepatitis C in Spain.
7. Policies for leadership and shared governance. Importance of the effective implementation of a health plan.



1

The importance of a National Plan. Experience and key success factors in the Plans for Scotland and France



Spain is facing the challenge of implementing a national strategy to tackle Hepatitis C in an environment where disruptive drugs have appeared that entail a change in the disease management paradigm. Their appropriate implementation necessarily implies the transformation of some management aspects. It should be guaranteed that this is carried out in an aligned, efficient framework in which everybody's efforts are optimised. It is a complex process which requires an intense dialogue between the various system agents.

Concurrently, it is interesting to cast a glance beyond our borders to identify successful cases and learn from the experience of other countries. PwC invited Professor Daniel Dhumeaux, the coordinator of the French hepatitis C Plan, and Professor David Goldberg, his Scottish counterpart, to get to know the keys to the strategic plans developed in their countries and thereby find out the lessons learned. Both plans are quoted as leading examples of good practices⁴.

The route followed by France and Scotland in the implementation of the Plans enables them to take up an excellent, advantageous position to make the most of the benefits offered by the new direct-acting antivirals which afford high rates of Sustained Virological Response (SVR) in most patients.

Action plan against Hepatitis C: the case of France

France was pioneering in the implementation of the first Hepatitis C Plan in 1999. Almost a decade previously, in 1990, France had recognised that the hepatitis C data was insufficient to develop a public health plan. Consequently, it undertook a first initial estimate of the number of people infected and in 1996 it set up a network of 31 specialist reference centres spread all

around the country. These centres have prevention and diagnosis functions and they have been possible thanks to a public-private partnership model. Since that time, various national programmes have been undertaken to tackle hepatitis C.

The National Plan against hepatitis C (1999-2002) was pioneering in the world. It was possible thanks to the epidemiological studies which involved the taking of a political decision which was favourable to tackling the virus.

Subsequently, the National Hepatitis C and B Programme (2002 – 2005) was implemented. Strengthened and extended to hepatitis B, the programme was justified, inter alia, by the persistence of the transmission of the hepatitis C virus (HCV) amongst injecting drug users, insufficient medical care and deficient access to the treatment of patients.

The National Plan to combat hepatitis B and C (2009-2012) was based on 5 strategic mainstays: a reduction in transmission (primary prevention); improved detection; prison institutions; improvement in surveillance and epidemiological knowledge; and the development of evaluation and research.

Finally, in 2014 Recommendations were published for the treatment of patients suffering from Hepatitis B and C. This edition stands out for the creation of a specific national committee for the implementation and follow-up of the strategy, involving experts in 22 different themes. Despite wishing to represent all the actors in this process (hepatologist experts, epidemiologists, professional associations, Ministry of Employment, Finance Ministry, Ministry of Health, patients, prisons, drug addiction surveillance etc.), the size of the committee proved impractical and was finally reduced from 60 to 10 people.

⁴ Euro Hepatitis Index 2012 Report. Health Consumer Powerhouse AB, 2012

In 2004, France had a prevalence of antibodies from the hepatitis C virus of 0.84% and a prevalence of chronic infection of 0.53%⁵. At present it is estimated there are 200,000 people infected by HCV, whereof 70,000 had been treated by 2014 and 35,000 cured. There thus remain 165,000 infected patients, only 100,000 of whom have been diagnosed. If 15,000 new patients are treated every year, disease control would be achieved within the next 10 years⁶.

Key success factors in France

- **Governance model** powerful and supported by political leadership capable of taking decisions based on scientific evidence and an improvement in public health. An effort was made by the scientific community to inform politicians about the figures and health outcomes deriving from hepatitis C (cirrhosis, liver decompensation...) as well as the reduction in complications if the treatment is carried out (e.g. avoids transplants).

- **Coordination and involvement of all stakeholders.** En el último Plan (2009-2012), se propuso una comisión de expertos en el sector encargado de redactar las acciones del Plan y para evitar conflictos de interés se creó un comité independiente para avalar el informe final. Finalmente se estableció otra comisión para la implementación, controlada por el Ministerio.

- **Focus on prevention**, mainly with actions aimed at risk groups such as injecting drug users and the inmate population.

- **Screening focused on risk collectives.** Although it is initially very cost-effective, it did not allow the detection of a large quantity of infected people in the non-risk population.

- **Transparency and responsibility.** The plan had incorporated clear, measurable goals, though some of them did not achieve the proposed objective⁷.

Plan Key performance indicators

Indicator	Result (year)	Result (year)
Deaths from hepatitis C	670 (2001)	520 (2010)
% Population (20-59 years old) with HCV antibodies	1,05% (1994)	0,71% (2004)
% Population diagnosed	24% (1994)	57% (2004)

Source: The Economist Intelligence Unit Limited. French efforts to address the hepatitis C challenge. 2014

⁵ Prise en charge des personnes infectées par les virus de l'hépatite b ou de l'hépatite c. Rapport de recommandations 2014 sous la direction du Pr. Daniel Dhumeaux et sous l'égide de l'ANRS et de l'AFEF

⁶ Statements made by Profesor Daniel Dhumeaux, coordinator of the Hepatitis C Plan in France

⁷ French efforts to address the hepatitis C challenge. The Economist Intelligence Unit Limited 2014

Action plan against Hepatitis C: the case of Scotland

In 2004 it was recognised that the hepatitis C virus was one of the main public health problems in Scotland⁸. An Action plan was set in motion which comprised three stages: an initial stage developed during the period 2006-2008 to carry out the initial diagnosis and prepare the Business Case (it was backed up with aid of £4 million), a second stage during 2008-2011 to deploy 34 improvement actions aimed at policies for prevention, diagnosis, treatment and support services for the treatment of the hepatitis C virus (it was backed up with aid of £43 million) and a final stage which is still ongoing (2011-2015) to carry out maintenance and follow-up of the actions.

It is estimated that in 2009 there were 39,000 patients with chronic hepatitis C, entailing prevalence of 0.7%.

Key success factors in Scotland

- The mainstay of the Scottish plan lies in **comprehensive and collaborative approach**. A unique collaboration was sought between the public sector, the health institutions, the university environment and the patient associations. The support organisations for those affected were really active in raising the political awareness of the impact of the burden of the disease and of the existing inequalities. The influence exerted by some organisations was decisive to achieve the consensus required between the political forces and obtain the financing needed to develop the initiatives.
- In addition to setting up **overall coordination** nationwide, local networks were set up (local Managed Care Networks) formed by multidisciplinary teams responsible for local strategy. These networks were and still are responsible for the instrumentation of the policies.
- Since the outset of the Plan, an overall approach was adopted for **project management**. From this perspective, it was recognised that it was more effective to set and achieve reachable goals based on evidence. Project management controlled the costs as well as negotiation nationwide of the acquisition of drugs and equipment.
- Knowledge of the scale of the disease by **collecting epidemiological data** was crucial for setting individual strategies. Between 1995 and 2005 surveys were carried out on risk groups such as injecting drug users, the inmate population, pregnant women and hospital patients. A data base was set up with diagnose reporting carried out by 17 laboratories to the national centre. In addition, another clinical data base was set up which included the main specialist centres. Then, these data bases were connected to other national bases such as records of deaths and of diagnoses of patients who had been hospitalised.
- The Plan was attributed **sufficient financing**. Whilst the majority of the financing was used for prevention and treatment, a considerable proportion was assigned to the coordination and compilation of more information to provide greater data to the policy. Hence, around 40% of total financing was aimed at treatment, 30% to care support, including staffing costs and the 30% remaining was assigned to prevention policies and mechanisms to coordinate and monitor the plan itself.

⁸ Chisolm, M. Members' Debate on Hepatitis C, Scottish Parliament, Edinburgh, 30 June 2004

⁹ Wylie, L. et al. The successful implementation of Scotland's Hepatitis C Action Plan: what can other European stakeholders learn from the experience? A Scottish voluntary sector perspective. BMC Infectious Diseases 2014, 14(Suppl 6):S7

Plan Key performance indicators

Indicator	Result (2007)	Result (2013)
Prevention Transmissions/year	1.500	750
Diagnosis % population diagnosed	39%	55%
Treatment Treatments started/year	400	1.100
Coordination	-	Networks/holistic approach
Evaluation	-	Publicaciones

Source: Wylie, L. et al. BMC Infectious Diseases 2014, 14(Suppl 6):S7

Other Plans against Hepatitis C

Australia recently launched a national strategy for Hepatitis C. After the first plan which started in 1999, it launched the fourth strategy for the period 2014 – 2017. This strategy included two aims: a reduction in the incidence of new infections by 50% and an increase in the number of people who will receive antiviral treatment by 50% per year. The implementation and evaluation of the Strategy is backed up by an Implementation and Evaluation Plan and by a Surveillance and Monitoring Plan.

Canada, although it does not have a nationwide strategy, has set up provincial plans as is the case of Ontario and Prince Edward Island. In the former case, a strategy was proposed for the period 2009-2014 based on five focus areas: treatment, prevention, education, support and research and surveillance. In the latter case, a Budget item was assigned to treat infected patients with new direct-acting antivirals during the next three years.

On the other hand, England set in motion an Action plan against hepatitis

C in 2004. This Plan consisted of four lines of action: surveillance and research; raising awareness and the reduction of undiagnosed infections; high-quality health and social services; and prevention.

Key areas in the implementation of the Strategic Plan to tackle Hepatitis C

The international analysis carried out allowed the identification of a series of specific areas on which to reflect to identify more tactical keys to success:

- 1. Epidemiology and mathematic models.** Only if we know the true scale of the problem, can the necessary resources be adapted to fight against the disease and carry out suitable follow-up. In Spain, the lack of information about the real prevalence of virus C infection and the low percentage of patients diagnosed¹⁰ makes it vital to develop a population-based epidemiological study with the evaluation of hepatic fibrosis.
- 2. Health information system, key performance indicators**

¹⁰ Razavi, H. et al. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. Journal of Viral Hepatitis, 2014, 21, (Suppl. 1), 34-59



and health outcomes. Es necesario que el Plan se desarrolle bajo la base de una evidencia robusta, generada a través de sistemas de monitorización que cuantifiquen la gravedad del problema. Cada acción que se establezca en el Plan debiera tener un objetivo que tendría que ser medido para evaluar los progresos alcanzados. Por consiguiente, los indicadores deberán ser identificados en el propio Plan para poder realizar un seguimiento histórico. Para obtener esta información, los gobiernos deberán aunar esfuerzos para ofrecer sistemas diseñados para recibir y procesar en forma correcta registros normalizados. Por otro lado, el uso de metodologías basadas en Real World Evidence y Big Data contribuiría a un modelo de gestión basado en la medición de resultados y la transparencia.

3. **High-incidence population.**

There is great diversity in the prevalence rates and the frequencies of the HCV genotypes in line with the geographic areas. However, there are two groups particularly vulnerable to contracting the virus: injecting drug addicts and inmates. Furthermore, as there is a high proportion of inmates who are injecting drug users, the prisons are a focus for contagion by HCV in the majority of countries. Although prevalence in Spain has more than halved in the last 15 years,

rates of 20% are still attained in the prison institutions¹¹. This is why it is necessary to define specific actions aimed at these collectives.

4. Primary Care, prevention services and private health organisations. Prevention is a key element for eradicating the disease. Campaigns to raise social awareness and measures aimed at population risk groups, essentially amongst injecting drug users, are necessary to avoid reinfections.

Furthermore, coordination between specialist doctors and general practitioners both in the public and in the private area is important to define consensual protocols. However, the overload of the health system prevents primary care professionals from playing a more active role in disease detection. In order to be able to optimise the cost, countries like Scotland and France have adapted the profile of the care provider. The Scottish example entails the training of nurses specialised in HCV, whilst the French case suggests that in addition to hepatologists, general practitioners may prescribe the treatment.

5. **Investment in Health Strategy.**

It is important to calculate the value of the new treatments based on health outcomes (reduction in the burden of the disease and release of the

¹¹ Home Office. Subdirectorate-General for Prison Health Coordination, 2015

resources required to deal with them) and comparing it with the treatment cost so as to thereby be able to develop an analysis of the investment. Furthermore, it is crucial to know the cost of the pathology and include the direct and indirect costs involved in an impact of the patient himself, on the health system and on society.

Furthermore, the Plan must have the financial support required and be sufficiently flexible to deploy the strategies defined.

The budgetary item established must be consistent with the deployment timeframes of the strategy and be broken down for each of the work lines, including specific financing for prevention, diagnosis, treatment, coordination, follow-up and evaluation actions.

As regards the financing of treatments, the appearance of disruptive innovations drives forward the need to negotiate new financing models.

6. Shared governance. Health coordination is a need which must be carried out by means of different mechanisms. In Spain, despite the decentralisation of the system, a cohesive National Health System is possible. On the one hand, the down-up coordination in which citizens exert pressure on their autonomous governments and on the other hand, the horizontal cooperation between autonomous governments constitutes the critical mechanism for coordination¹². In addition, central regulation is a key complementary tool for achieving the coordination required.

In this way, we could ensure fairness in terms of access to treatment between regions despite the budgetary differences that may exist between them.

Success levers in the deployment of the operating Plan

As we advanced in the context of this study, Spain already has a trajectory in the development of national health strategies. However, its development has not been tangible amongst the different agents of the sector. In order to be able to implement operating actions which contribute to the successful deployment of the strategy, it is recommended for three transversal actions to any action to be provided:

1. **Ministry Leadership.** Under the leadership and coordination of the Ministry, leading representatives must be assigned who are the implementers responsible for all key aspects to ensure the success of the strategy such as epidemiological, technological or financial aspects.
2. **Involvement of the stakeholders.** There must be collaboration between all the agents of interest, including the public administrations at a central and autonomous level, clinical professionals, patients, the pharmaceutical industry and society as a whole.
3. **Monitoring and follow-up of results.** Requirement to render accounts of the group responsible for the implementation of the strategy by means of shared tools which measure and evaluate the results and facilitate decision-making process with maximum transparency and communication.

The Strategic Plan must consider all the key areas mentioned here and it must be a living plan is updated and gets feedback from the results it produces over the years of its implementation.

¹² López-Casasnovas, G. y Rico, A. Decentralisation: part of the health problem or its solution? Gac Sanit, Barcelona, v. 17, n. 4, Jul. 2003

If we manage to put into practice the keys to success which are identified in the following chapters within the framework of shared governance, our health system can adapt more flexibly

and speedily to the challenges of the hepatitis C epidemic, including the financing of new drugs which are in the pipeline from other laboratories and which will foreseeably come onto the market in the short and medium-term.

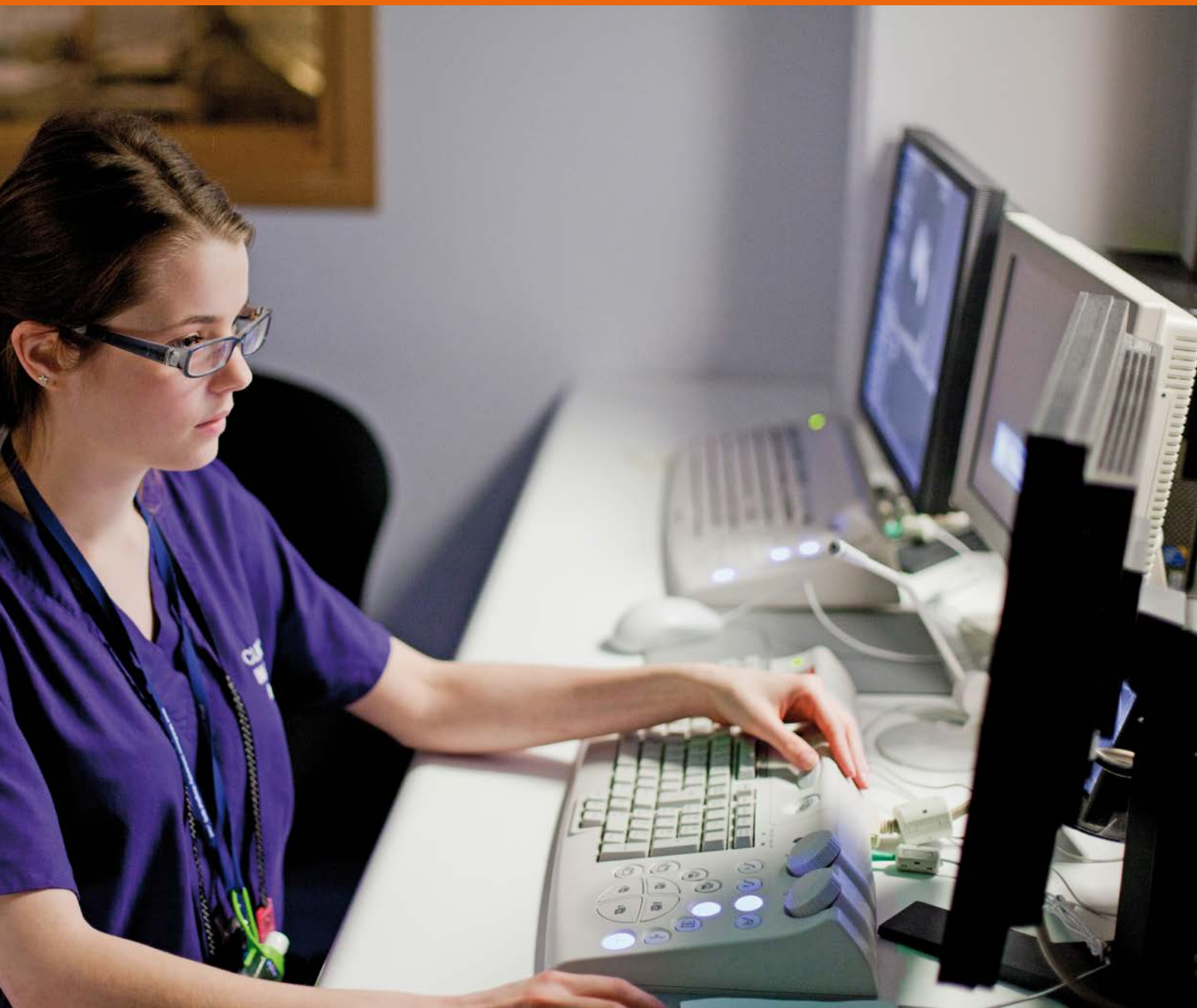
Figure 2.
Key Success Factors to implement the Plan



Source: In-house

2

Epidemiology and Mathematical models. Database and records, objectives and health outcomes in the medium-long term



Present situation

Hepatitis C is an infectious disease caused by the hepatitis C virus. It is a disease with high morbidity and mortality which may lead to liver cirrhosis, liver decompensation and the development of hepatocellular carcinoma (CHC).

The infection affects more than 185 million people worldwide though geographic distribution is not even¹³.

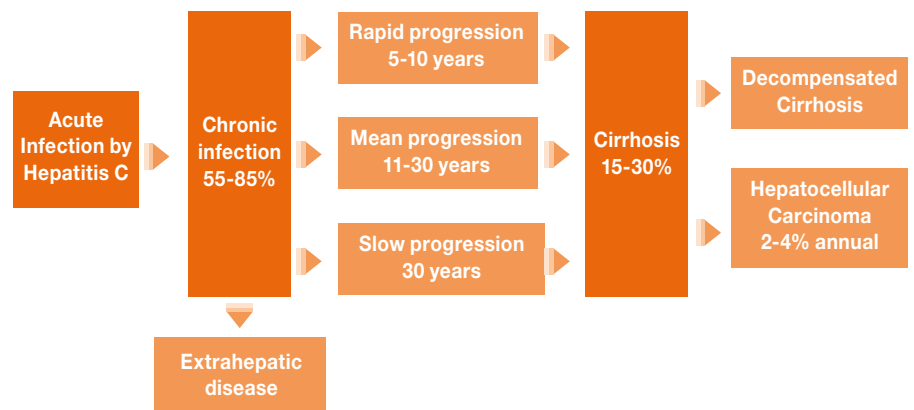
HCV may cause an acute or chronic infection. Acute infection is usually asymptomatic though 55-85% develop a chronic infection. Within a 20-year timeframe, 15-30% of chronic patients will develop liver cirrhosis. The risk of developing CHC in cirrhotic patients is around 2%-4% per annum.

The population groups with the highest risk of infection by HCV are¹⁴:

- Injecting drug users (IDUs): overall prevalence global of HCV of 67%.
- Receivers of blood products which are infected or submitted to invasive procedures at centres whose infection control practices are unsuitable.
- Children born from mothers infected by HCV.
- People whose sexual partners are infected by HCV.
- People infected by HIV.
- Intranasal drug users
- People who have had tattoos or piercings.

The prevalence of infection is unknown in Spain. Studies have been carried out on prevalence but they are outdated and biased towards certain population strata so they fail to represent the Spanish population as a whole.

Figura 3.
Natural history of Hepatitis C



Source: Strategic Plan to tackle Hepatitis C in the National Health System (May 21st 2015)

¹³ WHO. Guidelines for the screening, care and treatment of persons with hepatitis C infection. April 2014

¹⁴ Idem



Table 1.
Prevalence of serological markers for HCV in Spain

Region	No. cases	Anti-HCV (%)	Publication
Rioja	890	2	1996
Madrid	1.109	2,5	1997
Gijón	453	1,76	1997
Asturias*	1.170	1,6	2001
Catalonia	2.194	2,6	2002
Zamora	675	0,74	2002
Granada (pregnant)	381	0,5	2005
Madrid**	651	46	2006
Castile-Leon	364	1,1	2007
Andalusia**	1.468	16	2009
Madrid/ Murcia*	5.017	0,6	2013

* Healthy working population; ** HIV positive patients.

Source: Muñoz-Gámez, J.A. y Salmerón, J. Prevalence of hepatitis B and C in Spain: further data is required. Rev. esp. enferm. dig., Madrid, v. 105, n. 5, jun. 2013

At present, the data available in the publications reveal the prevalence of antibodies in adults of 1.7% (0.4%-2.6%) and a prevalence of viremia in adults of 1.2% (0.3%- 1.8%)¹⁵. This data would correspond to 688,000 adults with antibodies and 472,000 adults with viremia.

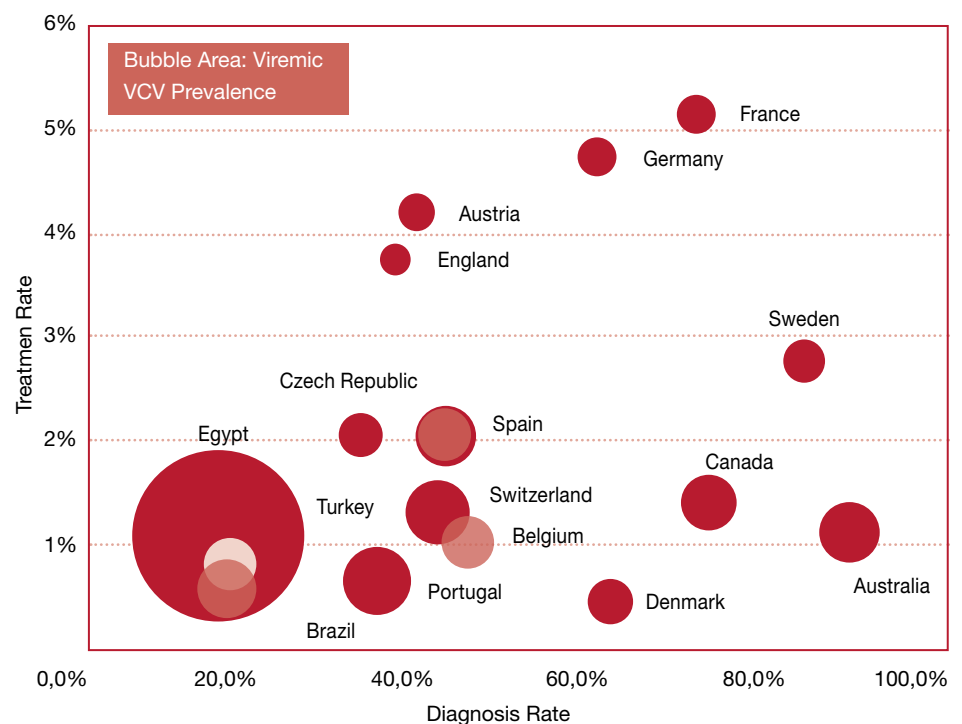
It is estimated that in Spain only 40% of cases¹⁶ have been diagnosed and that only around 9,800 patients with HCV are treated every year¹⁷. Hence, there is a high number of patients not diagnosed but it is also estimated that there is large

number of patients diagnosed who have not been evaluated as candidates for treatment by a specialist.

Compared with other countries, Spain has rates of diagnosis and treatment lower than those of France, Germany or Sweden. In actual fact, each territory has different epidemiological casuistic which will require policies to suit each situation¹⁸.

The incidence of new cases in Spain has fallen in recent years as a result of the prevention measures adopted¹⁹.

Figure 4.
Estimated prevalence of chronic hepatitis C, diagnosis rate and treatment rate 2013



Source: Dore, G. J. et al. Hepatitis C disease burden and strategies to manage the burden (Guest Editors Mark Thursz, Gregory Dore and John Ward). *Journal of Viral Hepatitis* 2014, 21: 1–4

¹⁵ Estimates based on Gower, E. et al. Global epidemiology and genotype distribution of the hepatitis C virus infection *Journal of Hepatology* 2014 vol. 61 j S45–S57; and Bruggmann, P. et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. *Journal of Viral Hepatitis*, 2014, 21, (Suppl. 1), 5–33

¹⁶ Dore, G. J. et al. Hepatitis C disease burden and strategies to manage the burden (Guest Editors Mark Thursz, Gregory Dore and John Ward). *Journal of Viral Hepatitis* 2014, 21: 1–4

¹⁷ González-García, J.J. et al. Prevalences of hepatitis virus coinfection and indications for chronic hepatitis C virus treatment and liver transplantation in Spanish HIV-infected patients. The GESIDA 29/02 and FIPSE 12185/01 Multicenter Study. *Enferm Infecc Microbiol Clin*. 2005;23:340-8

¹⁸ Deuffic-Burban, S. et al. Predicted effects of treatment for HCV infection vary among European countries. *Gastroenterology*. 2012 Oct;143(4):974-85.e14

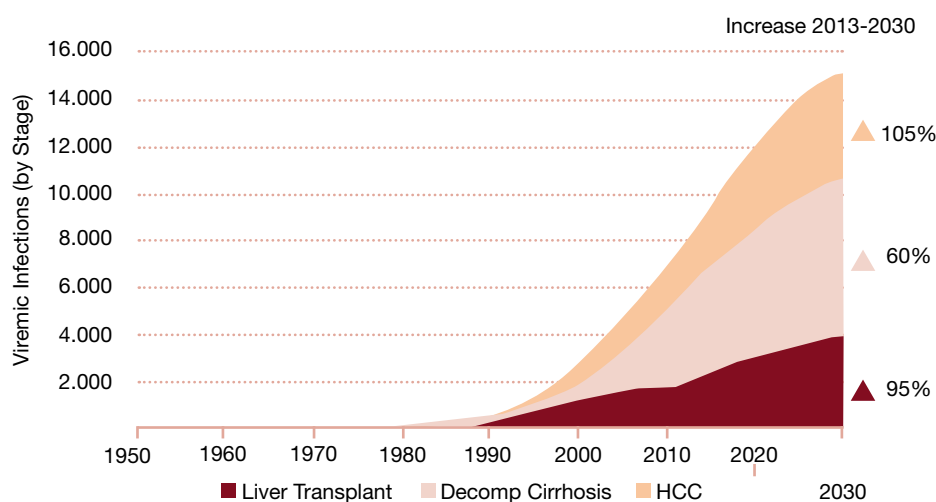
¹⁹ Calleja, J.L. y Crespo, J. Spanish Association for the Study of the Liver. White Paper on Hepatology in Spain, 1st ed. Madrid; 2015

Nevertheless, despite the fact that prevalence is falling, if measures are not taken, the future burden of the disease will increase as although at present patients are concentrated in fibrosis degrees 1 and 2, according to a study carried out at 48 hospitals in Spain, 44%

of patients with genotype 1 (with a predominant prevalence of 76,6%) have advanced fibrosis²⁰.

These predictions are based on mathematical models. They are a very robust methodological alternative to

Figure 5.
Evolution in the burden of the Hepatitis C disease in Spain



Source: Razavi, H. et al. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. *Journal of Viral Hepatitis*, 2014, 21, (Suppl. 1), 34-59



²⁰ Buti, M. et al. Profiles and clinical management of hepatitis C patients in Spain: disHCovery study. *Rev Esp Quimioter.* 2015 Jun;28(3):145-53

carry out predictions, though its weakness is the quality of the data entered.

Challenges

At present in Spain there is no **homogenous population register**. Each AC, each hospital and even each individual practice carry out their registers in a different way which is why at present there is not enough information about the scale of the disease nor its impact. In early 2015, with a view to setting in motion the drafting of the Strategic Plan to tackle Hepatitis C, the Ministry of Health asked the AC to notify it of cases of hepatitis C. The data reported was very varied with rates, for example, of 0.18 for every 100,000 inhabitants in the Basque country or 4.05 in Castile- León.

On the other hand, the scarce screening and the delay in diagnosis is one of the aspects which limits the access of patients to their therapies and implies greater potential contagion to other patients during such time as elapses from the infection until the appearance of signs or symptoms which lead to the final diagnosis²¹.

Opportunities

To quantify the real situation of HCV infection in Spain as well as the characterisation of the disease is one of the priority actions set out in the Strategic Plan to tackle Hepatitis C. The option considered by the Ministry to evaluate the scale of the problem is to carry out a survey on hepatitis C seroprevalence in the adult population but the question we should answer is: Who should we aim it at? With this in mind, some criteria need to be set to select the highest risk population. Transmission via injecting drugs, and in particular the consumption of endovenous drugs, has represented the

main cause of contagion for HCV in developed countries. nosocomial transmission represents between 15-25% of cases²² and, in the majority of cases, can be put down to a failure to comply with the standard regulations on hygiene and risk factors related with, more and more frequently, surgery and invasive diagnosis procedures.

In cases of clinical suspicion, a virological and narrow serological follow-up should be carried out to detect new cases of hepatitis C.

The keys to success

1. **Developing a population-based epidemiological study**, which allow the scale of the problem to be ascertained. We are talking about a holistic dimension to the problem which allows us not only to know the current and real situation of the rate of patients diagnosed in all AC, but also to establish the rate of patients not diagnosed and the rate of patients who are with the primary care doctor and have not been referred to a specialist for their evaluation. Each AC may evaluate its own needs or priorities to carry out studies in higher risk groups and/or studies by age groups.

Furthermore, it is not only necessary to ascertain how many patients there are but also to characterise them in line with the degree of advancement of the disease. The elastography of hepatic transition provides instantaneous information about the degree of rigidity of the liver and allows a differentiation between patients with a high or low probability of advanced fibrosis or cirrhosis.

2. **Designing a complete, transparent and audited registration system** which seeks to measure the health indicators established previously.

²¹ Calleja, J.L. y Crespo, J. Spanish Association for the Study of the Liver. White Paper on Hepatology in Spain, 1st ed. Madrid; 2015.

²² Martínez-Rebollar, M. et al. Current State of Acute hepatitis C. *Enferm Infecc Microbiol Clin*. 2011; 29(3):210-215.

The current design of the survey of RENAVE (National Epidemiological Surveillance Network) includes more than 25 fields related with patient data, laboratory data, genotype type, risk factors etc. However, it does not include data related with the degree of fibrosis developed. The latter is data which should be gathered in standardised fashion with a view to being able to analyse the disease burden and make future projections using quality data. The data gathered in the epidemiological surveys and other data bases should be consolidated periodically so that the information can be shared by all the AC.

Completion of the registrations must be carried out by the AC but it must be the Ministry of Health which lays the foundations for establishing homogeneity between them and disseminating the results in a format which allows data exploration.

3. Using, to a greater extent, mathematic prediction models for evidence informed policy & planning.

These models, if they are based on a good structure and calculations and are transparent and flexible in their hypotheses, are extremely useful as they bring up predictions which allow the facilitation of political decision-making.

4. Using georeferencing systems to ascertain the distribution of the disease.

These geographic health information systems are defined as an organised set of

computer technology, methods and procedures designed for capture, storage, recovery, handling, deployment and analysis of geographically referenced data with a view to backing up decision-making process when solving problems that occur in a given geographic space²³. In the Valencian Community there are already some initiatives in this regard. It has the georeferenced health card and there is a research project which commenced three years ago for diagnosed cases of HIV in which practically all the public hospitals in the region take part.

The implementation of these systems for the case of hepatitis C would allow epidemiological monitoring to be carried out, the identification of genotype distribution and the setting up of relations between the cases to anticipate public health decision-making process.

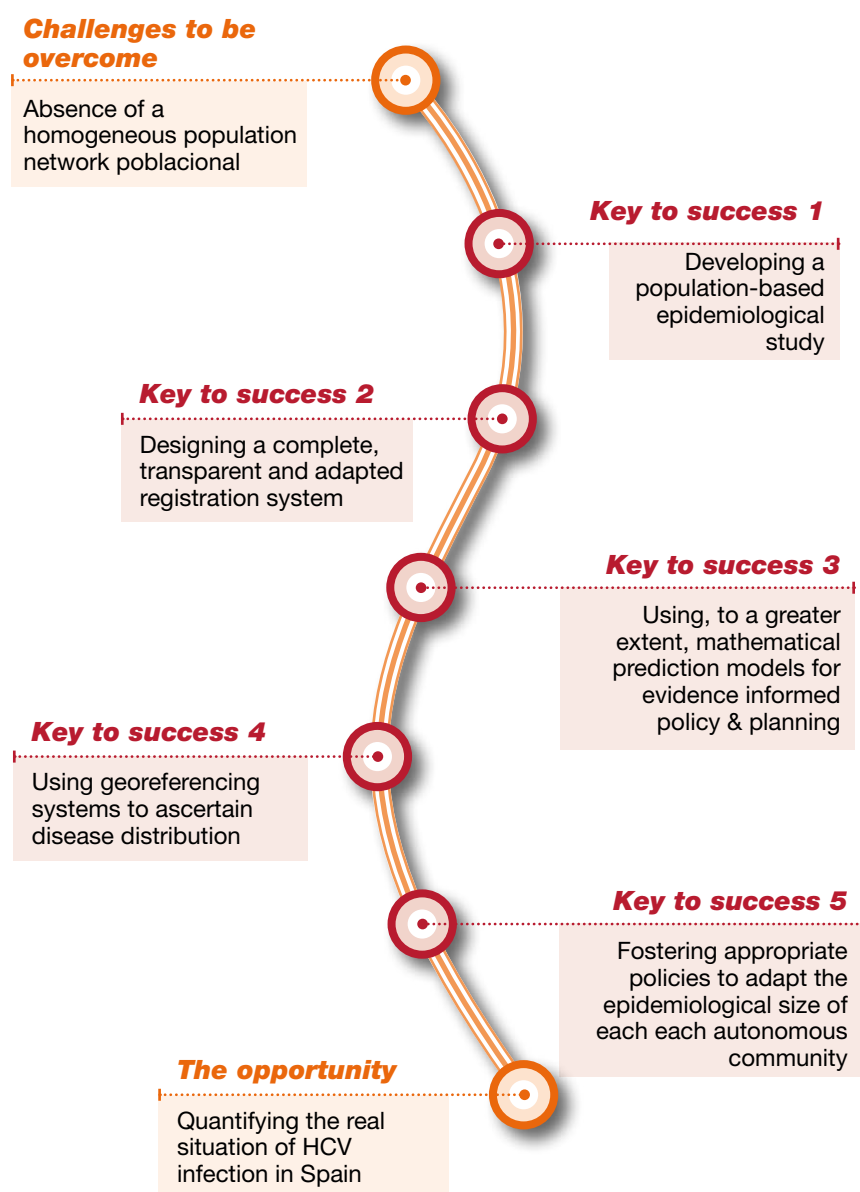
The use of molecular epidemiology tools based on phylogeography and phylodynamics studies could contribute to the georeferencing of the disease.

5. Implementing policies suitable for the epidemiological size of each autonomous community.

Each region faces a different reality in line with its socioeconomic context, immigration, whether it has a larger urban or rural population etc. It is necessary to size the problem in each autonomous community to adapt policies in terms of prevention, diagnosis, treatment and follow-up.

²³ Castillo-Salgado, C. et al. Geographic Information Systems in Health: Basic Concepts. Washington, DC.: PAHO, 2003

Figure 6.
Diagram of the keys to success in Epidemiology and mathematical models



Source: In-house

3

***Monitoring implementation:
the importance of developing
Health information systems and
Key performance indicators to
ensure health outcomes***



Present situation

The Strategic Plan to tackle Hepatitis C in the National Health System is making its priority action “To quantify the scale of the problem and describe the epidemiological characteristics of patients with infection by the hepatitis C virus”. To achieve this objective, it is proposed to implement “health information systems which are valid, reliable, and assessable and endowed with broad territorial coverage”. The Plan sets out to implement health information systems for new RENAVE diagnosis. This system is insufficient as it serves to detect outbreaks and new diagnoses but not for carrying out clinical follow-up nor evaluating the impact of the plan or the results obtained on health.

As regards new diagnoses, since March 2015, there has been specific incorporation of the requirement to include in Spain the hepatitis C disease on the list of notifiable diseases²⁴.

As regards clinical follow-up, the Plan puts forward some initial key performance indicators, pending definition, which include the following: By contrast, the Plan puts forward the

protocolized collection of follow-up therapeutic data of patients treated with the new direct-acting antivirals by means of the “Therapy monitoring Health information system for patients with chronic Hepatitis C” (SITHepaC) with a view to carrying out a monitored follow-up of all hepatitis C patients submitted to treatment.

At present, each AC has developed, with a different degree of advancement, its own health information systems for data collection. We can differentiate two major sources of information which serve to feed the knowledge generation system in public health²⁵.

- The health sources include the registration of clinical activity through clinical history, the microbiological results, the hospitalisation diagnoses, outpatient appointments, emergencies, minimum basic data sets (MBDS), pharmaceutical consumption records or bibliographic data bases.
- Non-health sources provide the characteristics of the population and its resources which determine the living conditions and health of society. Civil registration, mortality

Tabla 2.
Key performance indicators' proposal

Indicadores
Annual incidence of Hepatitis C
Injecting drug users on syringe Exchange programmes
Estimation of prevalence of infection
Estimation of proportion of people not diagnosed
No. of people in treatment according to drug type
Therapeutic effectiveness according to prescription guideline
No. of patients transplanted
Annual mortality attributable to Hepatitis C

Source: Strategic Plan to tackle Hepatitis C in the National Health System (May 21st 2015).

²⁴ Order SSI/ 445/ 2015 of March 9th.

²⁵ United Nations. e-Health Guidebook for managers of healthcare systems and services. 2012

records (death certificates), the municipal register of inhabitants and health surveys are examples of this type of sources of information.

Technology allows the technical and functional integration of health information systems generated by different organisations provided that this involves a real wish to collaborate that allows agreements to be reached and generates strategic alliances to the benefit of the population's health. Hence, in Spain it is feasible to gather both technical and functional information. What is missing is for the system to be structured and evolved from traditional data models which are independent and merely descriptive to a homogenous system which allows the integration of information individually, explore it and analyse it in integrated fashion, thus facilitating the generation of knowledge and decision-making process.

International experiences, such as Scotland, make it clear that the knowledge of the scale of the disease through epidemiological data collection was vital for decision-making process and being able to set individual strategies. Basically, it is not enough just to collect data and measure, it is essential to agree on and define the minimum basic data to be gathered as well as agreeing on and setting the necessary key performance indicators (including survival data, adjusted by quality of life and geared towards endpoints in health) in order to be able to make evidence-based decisions.

Challenges

There is a **problem with heterogeneity** in Spain as it depends on data from such varied information sources (from each clinical practice, each centre, hospital... and care up to each AC). At present, there is already a

lot of data but it is very dispersed at different sources and health information systems, making it hard to have reliable, consolidated records. The setting of recommendations with homogeneousness criteria must follow from the highest levels (from European level then State and Autonomous level until finally reaching each centre and care point).

Opportunities

Having health information systems would allow information of interest to be integrated which is currently dispersed at different sources and developing reliable, secure, powerful and flexible analyses so that the management of knowledge attains the public health intelligence level. When faced by a curable disease with a very great economic impact, health information systems must be the instrument **not only to provide a proper patient care but also to foster health outcomes studies to publish transparently the Plan achievements**, as well as being able to adjust the strategy in line with the progress in the implementation of the Plan itself. In this way, we will have the opportunity to generate knowledge and learning during the process.

The keys to success

- 1. Developing strategic planning centrally, endowed with an overall vision with a view to designing, constructing and managing a continuous registration system from the unique patient identification.**

The registration must be overall and start at such time as antibodies of the virus are detected in the blood. It must go through all the stages of the disease, including treatment and its subsequent follow-up as well as achieving a sustained viral response.



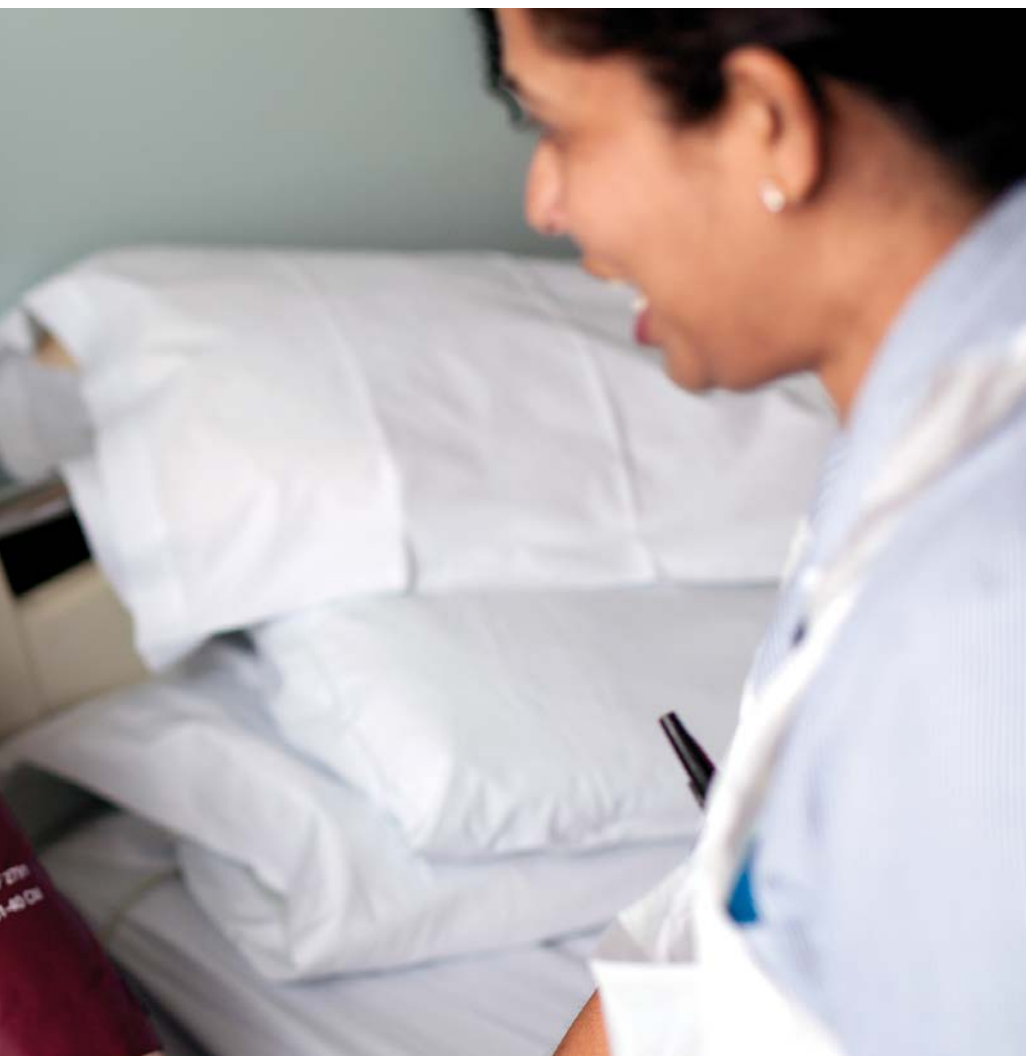
The construction of this population system should be supported by primary care for data validation and integrate the clinical, epidemiological, economic and results' information. The ultimate aim will be to ascertain, at any time, the scale, situation and characteristics of the population affected as well as being able to evaluate results and carry out research, generating evidence and new knowledge.

The results of the periodic analyses gradually carried out must be communicated to all the agents involved with maximum transparency. In line with the metrics obtained over time, including adverse reactions and resistances to the virus, therapeutic

actions may be designed, differentiated by population segments.

2. Putting into place coordination mechanisms with the assignment of responsibilities.

The autonomous levels should be responsible for gathering and facilitating data centrally as well as controlling the systems implemented at their centres. In turn, the central level should be responsible for establishing the homogeneous conditions based on consensus and consolidating data, assuming the leadership of management and coordination. With this in mind, the Ministry will need to set prior data homogenization criteria which put



into place guidelines about how to collect information. This coordination task must include and will facilitate the carrying out of systematic analyses.

3. Making use of evidence-based methodologies such as Real World Evidence (RWE) to obtain real life data, outside a clinical trial environment. The use of RWE generates a disruptive model with regard to the current research model²⁶ as it allows the health system to ascertain the impact on its population of a given treatment in real time, the trustworthiness of existing treatment protocols, the decision models followed by doctors in the event of certain groups of

patients or the care cost. In this way, the safety and efficacy evaluations are extended when prescribing treatments.

4. Boosting the analysis of Big Data to offer new possibilities in terms of the drawing up of predictive models, behavioural standards, the discovery of new requirements, risk reduction, as well as providing more personalised services, all in real time and bearing in mind all relevant information²⁷. The great availability of data to be found today and the capacity offered by new technologies to evaluate them, facilitate a management model based on the measurement of results and transparency. However, the specific

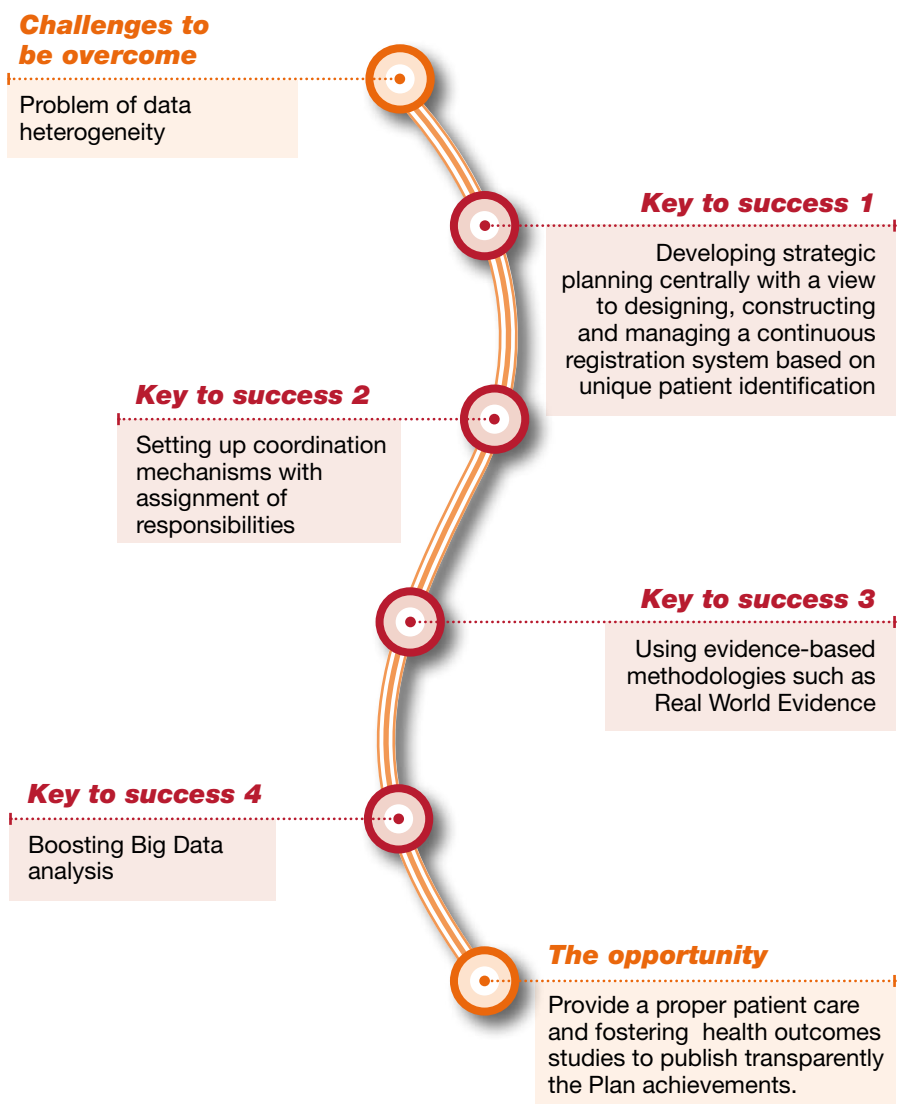
²⁶ Strategy &. Revitalizing pharmaceutical R&D. The value of real world evidence. 2015

²⁷ Martínez Sesmero, JM. "Big Data"; application and usefulness for the health system. Hospital Pharmacy, 2015; 39(2):69-70

benefits which may derive from the release of data largely depends on the quality of the data released and, first and foremost, the capacity of using it to generate value²⁸.

It would be recommendable to publish a comparative analysis by AC to create situation benchmarking.

Figura 7.
Esquema de las claves de éxito en la importancia de desarrollar sistemas de información e indicadores para asegurar resultados en salud



Source: In-house

²⁸ PwC. Ten hot topics regarding Spanish Health for 2013. So that the economic crisis does not become a public health crisis. 2013

4

National Strategy for elimination. High-incidence population: prisons and injecting drug users



Present situation

Hepatitis C is the most common infectious disease amongst injecting drug users. Overall, around 90% of new infections can be put down to the use of injected drugs²⁹. On the other hand, many users of this type of drugs are inmates at prison institutions meaning it would make sense to put forward some specific actions both for the inmate population as well as for drugs' users owing to the high rates of prevalence and reinfection they have.

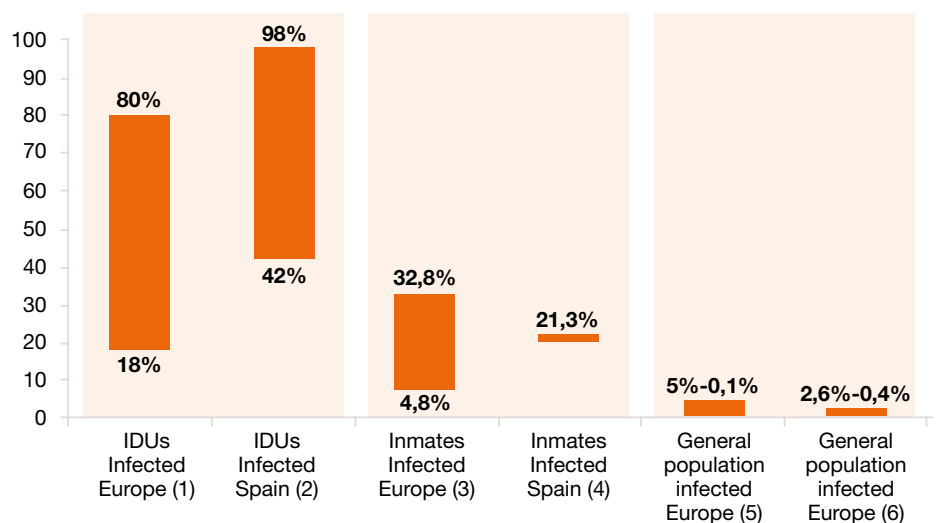
In actual fact, the *Strategic Plan to tackle Hepatitis C* is being carried out bearing in mind the collaboration of Prison institutions. Its priority actions include maintaining and boosting damage reduction programmes, to increase

access availability and the use of sterile material amongst injecting drug users (IDUs), particularly at prison institutions" and "setting up a collaboration programme with prison institutions for improving HCV prevention and diagnosis".

In Spain HCV prevalence attains 20% of the inmate population³⁰, equivalent to around 11,000 of inmates infected by HCV.

As regards injecting drug users, this is the collective which presents the highest rates of infection (between 42 and 98%). Non-injecting drug users have lower rates of prevalence than the former, but between 10 and 30 times greater than those of the general population³¹.

Figure 8.
Comparison of HCV infection prevalence rates by population groups



Source: (1) European Monitoring Centre for Drugs and Drug Addictions. Perspectives on Drugs. Hepatitis C treatment for injecting drug users. Updated 20.05.2014; (2) Bruguera, M. and Forn, X. Hepatitis C in Spain. Med Clin (Barc). 2006 Jun 17;127(3):113-7; (3) Health Without Barriers (HWB). Board of Directors Meeting. Barcelona, October 2014 (range of maximum and minimum rate between Italy (2012), Spain (2013), France (2010) and the UK (2013)); (4) Health Without Barriers (HWB). Board of Directors Meeting. Barcelona, October 2014; (5) Calleja, J.L. et al. Prevalence of viral hepatitis (B and C) serological markers in healthy working population. Rev Esp Enferm Dig 2013;105:249-54; (6) Estimates based on Gower, E. et al. Global epidemiology and genotype distribution of the hepatitis C virus infection Journal of Hepatology 2014 vol. 61 j S45-S57; and Bruggmann, P. et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. Journal of Viral Hepatitis, 2014, 21, (Suppl. 1), 5-33

²⁹ European Monitoring Centre for Drugs and Drug Addictions. Perspectives on Drugs. Hepatitis C treatment for injecting drug users. Updated 20.05.2014

³⁰ Spanish Prison Health Society

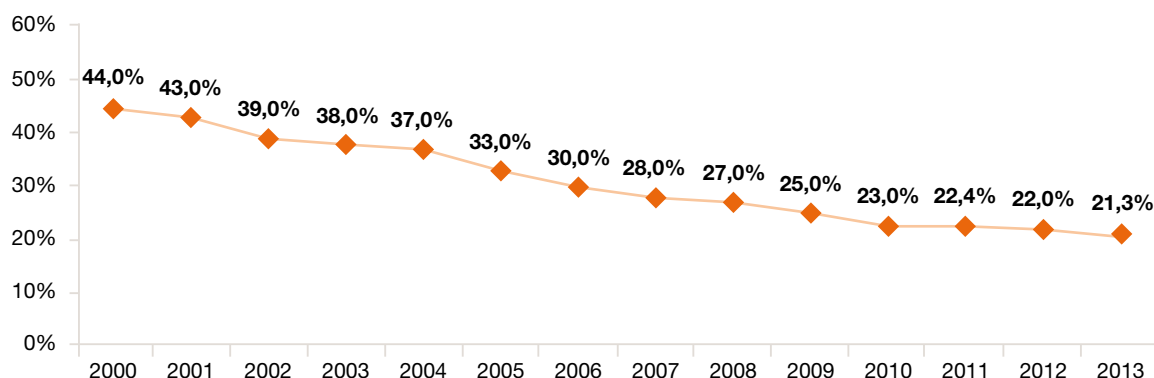
³¹ Bruguera, M. and Forn, X. Hepatitis C in Spain. Med Clin (Barc). 2006 Jun 17;127(3):113-7

The implementation of prevention and control programmes for transmissible diseases (syringe exchange programmes,

education strategies for health...) has had satisfactory results³². The rate of Infected has halved since 2000

Figure 9.

Evolution of the prevalence of HCV infection at Spanish prison institutions



Source: Spanish Home Office. Prevalence of HIV and HCV infections at prison institutions, 2013

40% of inmate patients with HCV are coinfecting by HIV³³ and 24-25% of inmates with HCV treated with biotherapy in Spanish prisons had fibrosis greater than or equal to 3³⁴.

Reinfections between inmates who have successfully completed the treatment are high, particularly amongst injecting drug users.

Table 3.

Reinfection incidences by subgroup

Risk factor	Incidence
Methadone	1,64
IDU who did not inject	2,57
Overall	5,27
IDU Background	6,25
Tatoos	7,19
Infection by HIV	13,41 (p=0.01)
Sex involving risk	18,5
IDU during or after treatment	33,01 (p<0.001)

Source: Marco, A. et al. Hepatitis C virus reinfection among prisoners with sustained virological response after treatment for chronic hepatitis C. J Hepatol. 2013 Jul;59(1):45-51

³² Hernández-Fernández, T. y Arroyo-Cobo, J.M. Results of the Spanish experience: an overall approach to HIV and HCV in prisons. Rev Esp Sanid Penit 2010; 12: 86-90

³³ Saiz de la Hoya, P. et al. Hepatitis C and B prevalence in Spanish prisons. Eur J Clin Microbiol Infect Dis. 2011 Jul;30(7):857-62

³⁴ Marco, A. et al. "Efficacy of treatment with pegylated interferon alfa-2a plus ribavirin in prison inmates with or without personality disorder. Subanalysis of the PERSEO study". London, UK: 49th Annual Meeting of the European Association for the Study of the Liver (EASL), April 9-13, 2014

At present, the Ministry of Justice or the Home Office is the body responsible for health in the prison environment in the vast majority of European countries that are members of the World Health Organisation (WHO). In Spain, the party responsible is the Home Office in the majority of AC. In recent years, some member countries have transferred responsibility to the Ministry of Health. This is the case of Norway, France, the UK and Italy³⁵.

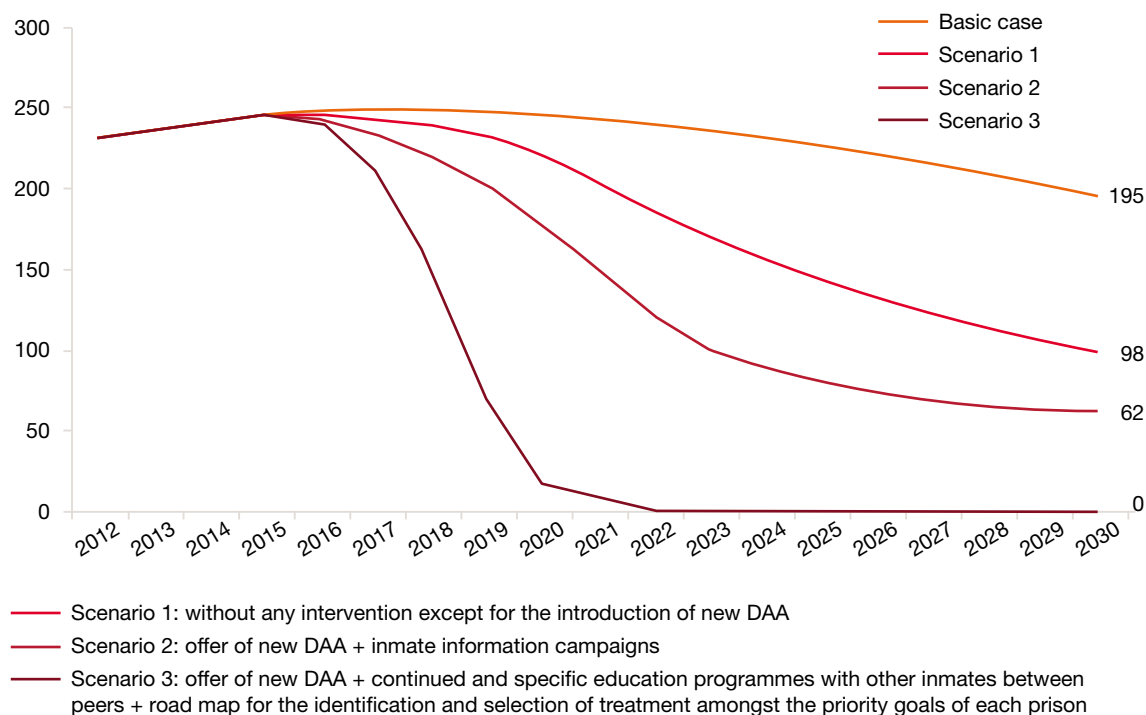
Some Swiss “cantons” and two Spanish AC (Basque Country and Catalonia) have implemented similar reforms.

In Spain, upon entering prison, a study if offered of the HCV infection which is carried out, unless it is a very short stay or

a refusal by the inmate. According to a study carried out on inmates in Catalonia, there is serology in around 85% of cases and it is positive in 18-20% of the inmates studied³⁶.

As regards treatment, in 2013 prison institutions treated 2.8% of inmates with positive HCV, representing 0.4% of the total population who entered³⁷. The treatment of hepatitis C in prisons had advantages (care is at hand, surveillance of compliance...) and drawbacks associated with imprisonment (releases, transfers between prisons...). The discontinuity of the treatment based on Interferon and Ribavirin in inmates was 22.5% and, in the main, it was due to prison release (36.1%) in the period 2007-2009³⁸.

Figure 10.
Mortality associated with liver disease in Italian prisons, 2012-2030



Source: Courtesy of Prof. F. S. Mennini Research Director, CEIS Economic Evaluation and HTA (CEIS-EEHTA) Università degli studi di Roma «Tor Vergata»

³⁵ WHO Europe

³⁶ Descriptors estadistics. Disponible en: http://www.gencat.cat/justicia/estadistiques_serveis_penitenciaris/1_pob.html

³⁷ Prevalence of HIV and HCV infections at prison institutions, 2013. Home Office

³⁸ Juan, J.D. et al. Multicenter study on the discontinuation and efficacy of chronic hepatitis C treatment in the Spanish penitentiary population (EPIBAND study). Eur J Gastroenterol Hepatol. 2014 Oct;26(10):1083-9

Treatment with combinations which include Sofosbuvir is cost-effective in inmates³⁹, but they are combinations which, up till now, have not been used much in the inmate population in Spain.

According to a study carried out by the *Centre for Economic and International Studies* (CEIS Tor Vergata)⁴⁰, mortality owing to hepatitis C may be eliminated in ten years with the combination of the new direct-acting antivirals, suitable inmate education strategies and internal policies in terms of treatment.

As a case of good practice in Spain, we can highlight the introduction of protocols at the prison centre of Fontcalent de Alicante and at the Infectious Diseases Ward of the General Hospital of this city who, in 1999,

drew up the first operating protocol to control treatment of infection by the AIDS virus and in 2001, for infection by the hepatitis C virus. The result was an increase in the number of patients treated as they suffered from an HIV infection of 45-48% to 50-54%; treatment at 60% of patients with hepatitis C whereas before they had not been treated; a reduction in the numbers of visits to hospitals by more than 50%; and the carrying out of more than 80 biopsies by 2005 when before virtually none had been carried out⁴¹.

It should not be forgotten that prisons are a hotbed for diseases and they constitute a public health problem owing to the high concentration of Infectious Diseases. An intense interaction between prison health and public health is unanimously claimed



³⁹ Liu, S. et al. Sofosbuvir-based treatment regimens for chronic, genotype 1 hepatitis C virus infection in U.S. incarcerated populations: a cost-effectiveness analysis. *Ann Intern Med.* 2014 Oct 21;161(8):546-53

⁴⁰ Courtesy of Prof. F. S. Mennini Research Director, CEIS Economic Evaluation and HTA (CEIS-EEHTA) Università degli studi di Roma Tor Vergata

⁴¹ Sociedad Española de Sanidad Penitenciaria

as inmates have permission and receive visits and, what's more, the vast majority will leave prison and be reintegrated into society⁴².

Challenges

Although they have fallen in recent years, the **rates of prevalence and reinfection are still very high** at Spanish prison institutions (prevalence of 21.3% in Spain compared with 10.6% in the UK or 4.8% in France)⁴³ as well as between injecting drug users.

As regards treatment, access is not homogeneous at Spanish prisons. On the one hand, the inmates in Catalonia and the Basque Country, where prison health competences are transferred, have less restrictive access to treatments. On the other hand, in the rest of the AC where the prisons are answerable to the Home Office, the Secretariat-General of Prison institutions is answerable to the Home Office, access to new, latest generation drugs has been restricted. In the event that the inmate is selected to receive treatment, the condition is transferred to a Madrid prison for treatment at Hospital Gregorio Marañón where treatment has been centralised⁴⁴.

Opportunities

The great opportunity is to **treat high-incidence collectives according to the same principle of fairness as the general population**.

In the USA a project⁴⁵ was carried out in the state of New Mexico to provide care to a socially isolated population, as in the case of prisons, under the same conditions of equality, safety, efficacy and results in health as in university hospitals. The Project was based on the use of telemedicine to provide training

to professions in this area from university hospitals. Owing to the success of the Project, it was extended to other clinical pathologies.

At present in Spain the necessary technology is available for the diagnosis of the disease and the obtaining of the genotype and viral burden easily and speedily to which end there is a collection of patients who have been perfectly diagnosed and who are liable to receive treatment. Staying in prison or belonging to collectives who are vulnerable to who have a risk of social exclusion is to a contraindication for treating hepatitis C. In the event that it is decided to start treatment, the patient must be controlled by the prison doctors, NGOs or other health organisations with the support of specialists (hepatologists, infectologists etc.) from reference hospitals with a view to minimising the impact on the system.

The keys to success

- 1. Integrating prison institutions into the health services**, as occurs in some European countries. Prisons should have professional structuring which is integrated into the public health system in such a way as to allow a follow-up of inmates once they leave prison.
- 2. Undertaking specific elimination programmes** which include a tactical strategy of eliminating the virus at a certain number of prisons in the short-medium term before attaining the elimination of the disease at all prison institutions. The establishment of European leadership which shares ethical principles and shared protocols can help to implement international policies which result in an

⁴² World Health Organization. Good governance for prison health in the 21st century. A policy brief on the organization of prison health. 2013

⁴³ Health Without Barriers (HWB). Board of Directors Meeting. Barcelona, October 2014

⁴⁴ Pro Human Rights Association of Andalusia (APDHA). Restrictions on access to treatments of Hepatitis C. March 2014

⁴⁵ Arora, S. et al. Project ECHO: Linking University Specialists with Rural and Prison-Based Clinicians to Improve Care for People with Chronic Hepatitis C in New Mexico. Public Health Rep. 2007; 122(Suppl 2): 74–77

improvement in prison health. These programmes should include:

- **Consensual coordination protocols between prison health services and reference hospitals** for the control of infection by the hepatitis C virus. These protocols should be led by a coordinator responsible for implementation.
- **Training plans for medical professionals** from prison institutions with regard to the hepatitis virus. The vast majority of doctors at prisons are general practitioners and they require training in the most frequent diseases in the prison environment (mental health, Infectious Diseases and sexually transmitted diseases). Training courses should be fostered from an institutional perspective.
- **Courses in education for risk collectives** (población reclusa y sus cuidadores) que permitan disminuir los riesgos de transmisión. La reducción del consumo de drogas por vía parenteral y los programas de intercambio de jeringuillas, así como la eliminación de las hepatitis postransfusionales, han determinado que la incidencia de nuevas infecciones se haya reducido progresivamente⁴⁶. No obstante, hay que continuar informando y formando a estos colectivos para lograr eliminar la enfermedad.

3. Realizar campañas de screening a la entrada y salida de prisión. (inmate population and their carers) which allow a reduction in transmission risks. The reduction



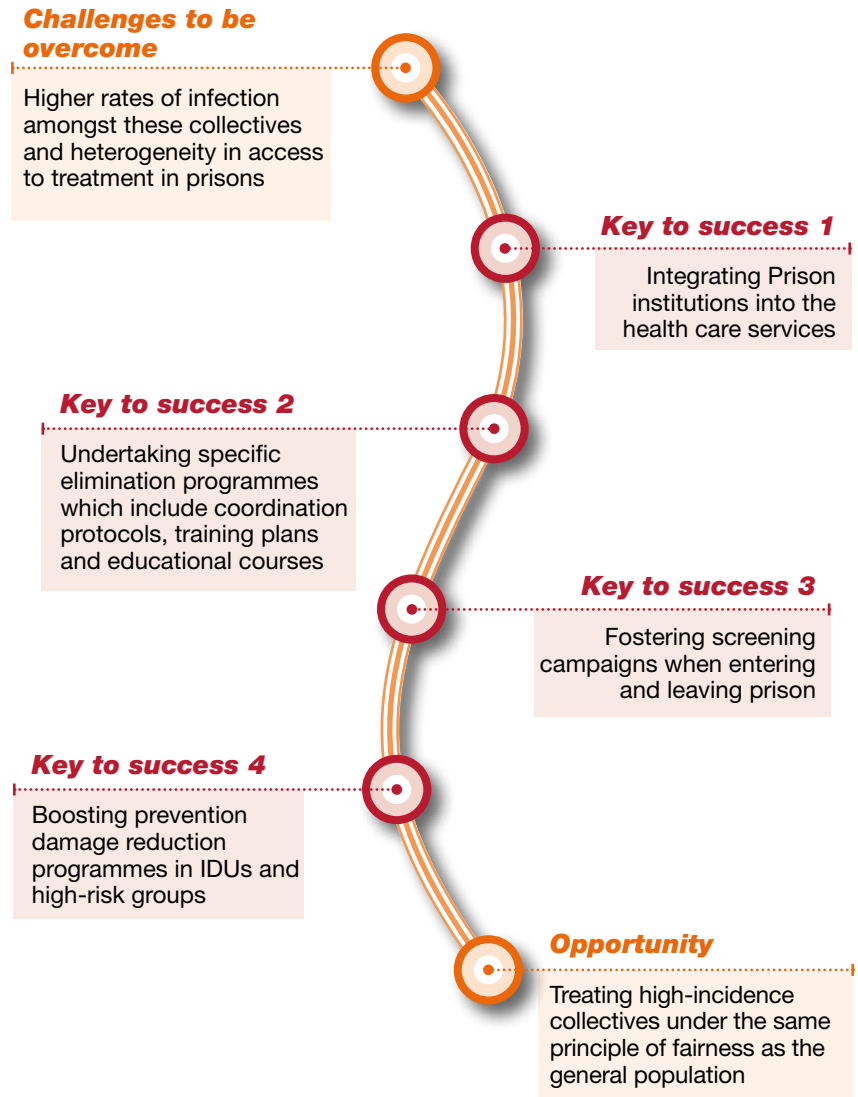
in injecting drugs consumption and the syringe exchange programmes as well as the elimination of postransfusional hepatitis, have led to the progressive reduction in the incidence of new infections⁴⁶. Notwithstanding, these collectives must continue to be informed and trained to manage to eliminate the disease.

4. Boosting prevention and damage reduction programmes amongst injecting drug users (IDUs) in order to increase the availability of Access and use of sterile material. The Health Ministry drew up the “Action plan for Drugs 2013-2016” which is part of the “EU Strategy on the fight against drugs 2013-2020”. This Plan is respectful towards the various strategies, plans and actions of the various AC and includes amongst its aims a reduction in the damage associated with consumption.

⁴⁶ Bruguera, M. and Forn, X. Hepatitis C in Spain. Med Clin (Barc). 2006 Jun 17;127(3):113-7

Figura 11.

Esquema de las claves de éxito en la estrategia nacional hacia la eliminación en población de alta incidencia



Source: In-house

5

National Strategy for elimination: Recommendations to optimise diagnosis Importance of primary care, prevention services and private health organisations



Present situation

Acute infection by HCV owing to its silent form of progression is rarely diagnosed and hence the real rate of incidence is unknown⁴⁷. People who become chronic, in turn, may remain undiagnosed until they get liver failure⁴⁸.

The **National Strategic Plan** already stipulates, in one of its strategic lines, the need to establish appropriate prevention measures. The specific goals include primary prevention (reducing the incidence of hepatitis C), secondary prevention (promoting early diagnosis in priority populations) and tertiary prevention (preventing morbidity and mortality and the complications deriving from chronic HCV infection).

As regards primary prevention, in recent years the incidence of the virus has fallen in Spain as transmission by haemoderivatives has fallen and universal precautions have been applied in medical actions⁴⁹.

As regards secondary prevention, early diagnosis by means of a serological test is presented as the first step towards preventing transmission of the virus. Some countries recommend the examination of people with a high risk of infection. In the case of the USA, since 2012 the Centers for Disease Control and Prevention (CDC) recommend the carrying out of the HCV antibodies test on adults born between 1945 and 1965

who represent 27% of the population but account for 73% of the deaths associated with HCV⁵⁰. However, in Spain a study⁵¹ carried out in the area of the University Hospital of A Coruña has already suggested that the US recommendations to test on those born between 1945 and 1965 may not be applicable to other countries. In Galicia it was observed that the highest prevalence occurred in those born between 1956 and 1975 with higher peaks in those born between 1961 and 1970. Another study revealed that in Spain 75% of those Infected are those born between 1950 and 1980⁵². The high consumption of injecting drugs in the 1980's could explain these differences.

On the other hand, the "Toronto Declaration" of 2014⁵³ recommends that all countries should develop a national and/or regional Action plan against HCV infection with a view to, amongst other aspects, diagnosing 75% of infected patients before 2018 through screenings in high-risk populations (injectable drug consumers, immigrants from endemic countries, receivers of blood products) and populations with a high prevalence (populations cohorts).

As regards tertiary prevention, the new direct-acting antiviral drugs prove to be highly effective and their advantage over previous treatments is noted particularly in those populations with worse response to conventional treatments such as people waiting for a transplant or post-transplanted people⁵⁴.

⁴⁷ Martínez-Rebollar, M. et al. Current state of acute hepatitis C. *Enferm Infecc Microbiol Clin*. 2011; 29(3):210-215

⁴⁸ Ghany, M.G. et al. American Association for the Study of Liver. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology* 2009;49:1335-74

⁴⁹ Aguilera Guirao, A. et al. Microbiological diagnosis of viral hepatitis. Spanish Society for Infectious Diseases and Clinical Microbiology (SEIMC). 2014

⁵⁰ Testing recommendations for Hepatitis C virus infection. Centers for Disease Control and Prevention (CDC). Reviewed September 24, 2013

⁵¹ Mena, A. et al. (2014) Seroprevalence of HCV and HIV Infections by Year of Birth in Spain: Impact of US CDC and USPSTF Recommendations for HCV and HIV Testing. *PLoS ONE* 9(12): e113062

⁵² Wedemeyer, H. et al. Strategies to manage hepatitis C virus (HCV) disease burden. *J Viral Hepat*. 2014 May;21 Suppl 1:60-89

⁵³ 1st International Meeting on Hepatitis Cure & Eradication. 5-6 November 2014, Toronto, Canada

⁵⁴ Manns, M. et al. Ledipasvir/sofosbuvir with ribavirin is safe and efficacious in decompensated and post liver transplantation patients with hcv infection: preliminary results of the prospective SOLAR 2 trial. *EASL - The International Liver Congress 2015, 50th annual Meeting of the European association for the Study of the Liver*. Vienna, Austria. April 22-26 2015



Some experts advocate greater participation and involvement by primary care professionals in the handling and follow-up of hepatitis C, particularly with the appearance of new drugs which shorten and simplify treatment at the same time as reducing side effects compared with Interferon-based treatments. However, although the present treatment has been simplified with direct-acting antivirals, very sound knowledge is required to establish better treatment. Furthermore, it should not be forgotten that although effectiveness is very high with rates of 90%⁵⁵, 5-10% of treatments will fail and will require very strict control.

Some general practitioners trained to this end and interested in this pathology may cover the limitations of the system in some geographic areas or in various situations in which the needs for diagnosis and treatment cannot be covered. In actual fact, there are studies which demonstrate that suitably and specifically trained general practitioners

can provide treatment against HCV effectively and safely. According to a study carried out in the USA, sustained virological response rates (viral load of HCV undetectable 24 weeks after completing the treatment) were similar both in patients who received treatment from their primary care doctor as in those who were prescribed it by a specialist⁵⁶. To carry out the project, suitable training was provided to primary care doctors and they were subsequently supported by video and teleconferences.

In Spain it is recommended to carry out serological tests if infection is suspected, not only on patients with clinical manifestations, but also on those who have been exposed to the risk of infection (risk population groups are, inter alia, people who have injected drugs, people infected by HIV and people who have received transfusions). In terms of primary care, suspicions of infection may occur owing to, amongst other symptoms, high transaminases⁵⁷.

⁵⁵ Spanish Association for the Study of the Liver

⁵⁶ Arora, S. et al. Outcomes of Treatment for Hepatitis C Virus Infection by Primary Care Providers. *N Engl J Med.* 2011; 364:2.199-2.207

⁵⁷ Aguilera Guirao, A. et al. Microbiological Diagnosis of viral hepatitis. Spanish Society for Infectious Diseases and Clinical Microbiology (SEIMC). 2014

Table 4.

Priority population for screening programmes

Priority Population
Injecting and sniffing drug users
Patients treated with blood products before 1990
Patients exposed to nosocomial infection by hepatitis C
People who cohabit with patients suffering from chronic hepatitis C
People with tattoos or piercings and exposed to procedures who use a sharp instrument without appropriate hygiene-sanitary controls (acupuncture and mesotherapy)
Children of mothers with HCV infection
Health professionals exposed to procedures which involve biological risks.
Patients in haemodialysis
Men who have risky sexual relations with men
Patients coinfectd by HIV
Patients coinfectd by HBV or TBC
Inmates at Prison institutions

Source: Marco, A. et al. Hepatitis C virus reinfection among prisoners with sustained virological response after treatment for chronic hepatitis C. J Hepatol. 2013 Jul;59(1):45-51

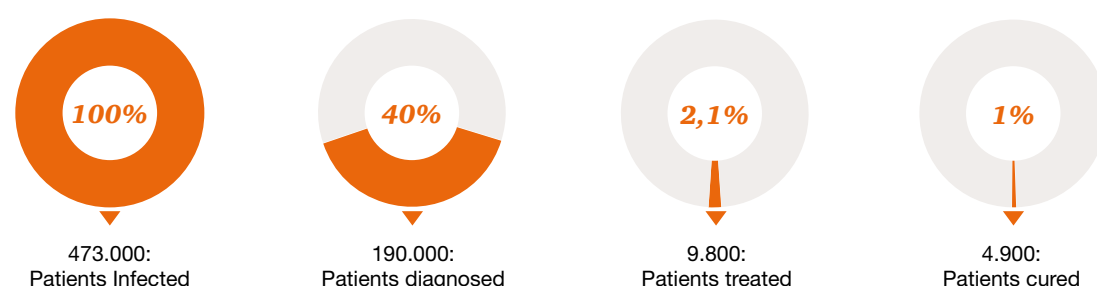
The National Strategic Plan makes it clear that screening programmes are required to avoid the silent progression of the disease, bearing in mind that owing to their greater risk of infection the priority populations are those shown in table 4.

To be precise, the Plan stipulates, amongst its actions to reduce incidence, the implementation of newborn screening programmes in women with a greater risk of exposure to the infection.

Some ACs also have individual initiatives for detecting a greater diagnosis volume. In Catalonia, for example, the Societat Catalana de Digestologia has drawn up a strategic plan for evaluating the prevalence of hepatitis C and B in Catalonia by using rapid diagnosis serological tests. In Galicia, a study⁵⁸ was carried out during the period 2008- 2012 to establish the impact of applying the recommendations of the CDC in the US in the health area of A Coruña, thereby detecting pockets of patients with a

Figure 12.

Estimate of patients diagnosed, treated and cured in Spain, 2013



Source: Razavi, H. et al. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. Journal of Viral Hepatitis, 2014, 21, (Suppl. 1), 34-59

⁵⁸ Mena, A. et al. (2014) Seroprevalence of HCV and HIV Infections by Year of Birth in Spain: Impact of US CDC and USPSTF Recommendations for HCV and HIV Testing. PLoS ONE 9(12): e113062

greater prevalence by age groups. Andalusia, in turn, has announced that it will draw up a Comprehensive Care Plan for patients suffering from hepatitis C⁵⁹ which will essentially be focused on raising awareness, training professionals and early detection and prevention of the disease.

There is an evident need to improve the screening, diagnosis and treatment methods if we look at the treatment cascade which shows that only 2% of everyone suffering from chronic hepatitis C receives treatment.

Challenges

The primary care area is part of a health system characterised by a high organisational complexity in which there is a coexisting multitude of levels, organisations and agents with duties which are very often in silos. This situation may it difficult for general practitioners to participate in the strategies drawn up with specialists. Coordination will be a key aspect to be looked at to achieve a cohesive system.

Furthermore, political decisions are based on short-term planning criteria to obtain short-term results. The error made is that there is no longer-term vision for devising prevention, diagnosis and treatment strategies which manage to achieve the elimination of the disease in certain population groups or even eradication nationwide.

Finally, it is worth highlighting that some segments of the population have certain system access barriers. On the one hand, the population residing in rural areas and the elderly population with mobility problems, may face access barriers to diagnosis and treatment as

they find it hard to travel to the hospital and cannot receive treatment at their local health centres. On the other hand, illegal immigrants, the homeless or drug users may have barriers to access to diagnosis as they do not have the appropriate information about the rendering of services in Spain or do not have a health card.

Opportunities

The great opportunity in the context of primary care is to achieve the systematic participation of primary care structures and coordination to ensure elimination. With this in mind, there are two fundamental aspects: diagnosis and treatment⁶⁰.

Thus, participation and cooperation with microbiology services is important to diagnose the disease.

As far as diagnosis is concerned, the inclusion of hepatitis C on the list of notifiable diseases⁶¹ will allow the monitoring of new diagnosis cases. In addition, the National Strategic Plan puts forward several actions to promote early diagnosis in priority populations, including the drawing up of a handbook of recommendations for the early diagnosis of HCV in priority populations in the field of primary care.

As far as treatment is concerned, the recent commercialisation in Spain of second generation antiviral drugs allows efficacy rates of 90% to be attained⁶².

Podrá erradicarse el VHC en los próximos años y reducir el número de complicaciones asociadas, únicamente, si se establecen estrategias, de cribado y tratamiento, activas, eficientes y adaptadas a nuestra población.

⁵⁹ Diario de Sevilla. Díaz announces a comprehensive care plan for patients suffering from hepatitis C. April 9th 2015. Available at <http://www.diariodesevilla.es/article/andalucia/2002674/diaz/anuncia/plan/integral/atencion/para/los/patients/hepatitis/c.html> (consulted on 07/05/2015)

⁶⁰ Mena, A. and Pedreira, J.D. Towards the eradication of hepatitis C virus. *Galicia Clin* 2014; 75 (4): 164-166

⁶¹ Order SSI/ 445/ 2015 of March 9th

⁶² Spanish Association for the Study of the Liver



The keys to success

- 1. Specifying the screening criteria and adjusting the risk groups to carry out screening** programmes on population groups with a greater risk of being infected by HCV, bearing in mind cost-effective criteria. It is necessary to define how (how many times per year, methodology...) and to whom (by age groups, risk factor ...) these programmes must be aimed at.

Despite the fact that the World Health Organisation already identifies the higher risk groups⁶³, there needs to be consensual drawing up of the risk groups specific to the case studies of Spain and include both criteria by risk factor (drug users, transfused patients etc.) and criteria by age groups for the general population as the prevalence is low in this segment

- 2. Configuring warning systems in the electronic health records to contribute to early diagnosis.** These systems are useful for raising the awareness and surveillance to levels that allow early detection, contribute to the definition of risk groups or prevent

the cases diagnosed from giving rise to significant outbreaks.

- 3. Incorporating patient screening and patient access to care into the primary care goals.** With a view to boosting the commitment of the primary care doctor, new goals may be incorporated associated with the diagnosis of patients in the AC programme contracts.
- 4. Drawing up practical, consensual operating protocols/guidelines** between the two care levels, primary care and specialised care, actively involving primary care and occupational medicine companies. To develop them the coordination between specialists and general practitioners is key, both in the public and private area. The progressive implementation of the clinical record by processes would make coordination between both levels easier.
- 5. Involving private insurance companies in the strategy to tackle Hepatitis C in Spain as it is a notifiable infectious disease.** There is a broad collective

⁶³ WHO. Guidelines for the screening, care and treatment of persons with hepatitis C infection. April 2014



of patients whose passage through the care circuit is limited to access to the insurance companies. The coordination of the public sector with the private sector is vital in order for clinical staff in the private sector to have the same tools and knowledge that can be offered to the public sector.

6. Developing continuous training programmes aimed at primary care and occupational medicine professionals

to raise awareness amongst these collectives about disease control if appropriate detection programmes are carried out. It must be remembered that many workers do not enter the primary care circuit as they are treated directly by occupational doctors.

7. Fostering raising awareness campaigns aimed at the population through educational prevention plans

to facilitate early diagnosis, prevent contagions and avoid reinfection. As regards the risk of reinfection, although it is low in the general population, it is 8.5% within 5 years in injecting drug users and inmates

prison institutions and is as much as 23.4% in these same collectives if they are coinfecting by HIV⁶⁴.

In this regard, there is a lot to learn about raising awareness campaigns for AIDS prevention. There is a wide range of campaigns from different organisations which have been successful and on an important scale amongst the population.

Hence, it becomes necessary to raise the awareness of the population, without alarming it, about the disease's symptoms and its consequences as well as the transmission mechanisms and universal precaution measures. In this regard, in October 2013, the Spanish Association for the Study of the Liver (AEEL) had already implemented a campaign to raise awareness of HCV infection at 13,000 pharmacies in Spain⁶⁵.

Scotland, in turn, has celebrated the World Hepatitis Day for two years running (2013 and 2014). It organised various events all around its country, including a bus with the campaign "Have you ever shot up? Get the test done now! Hepatitis C is curable"⁶⁶.

⁶⁴ Andrew Hill. Effects of Sustained Virological Response on the risk of liver transplant, hepatocellular carcinoma, death and re-infection: meta-analysis of 129 studies in 34,563 patients with Hepatitis C infection. AASLD, Boston, USA, 10th November 2014. [Abstract 44]

⁶⁵ Calleja, J.L. y Crespo, J. Spanish Association for the Study of the Liver. Libro Blanco de la Hepatología en España, 1ª ed. Madrid; 2015

⁶⁶ World Hepatitis Day Scotland 2014. Evaluation Report

Figura 13.

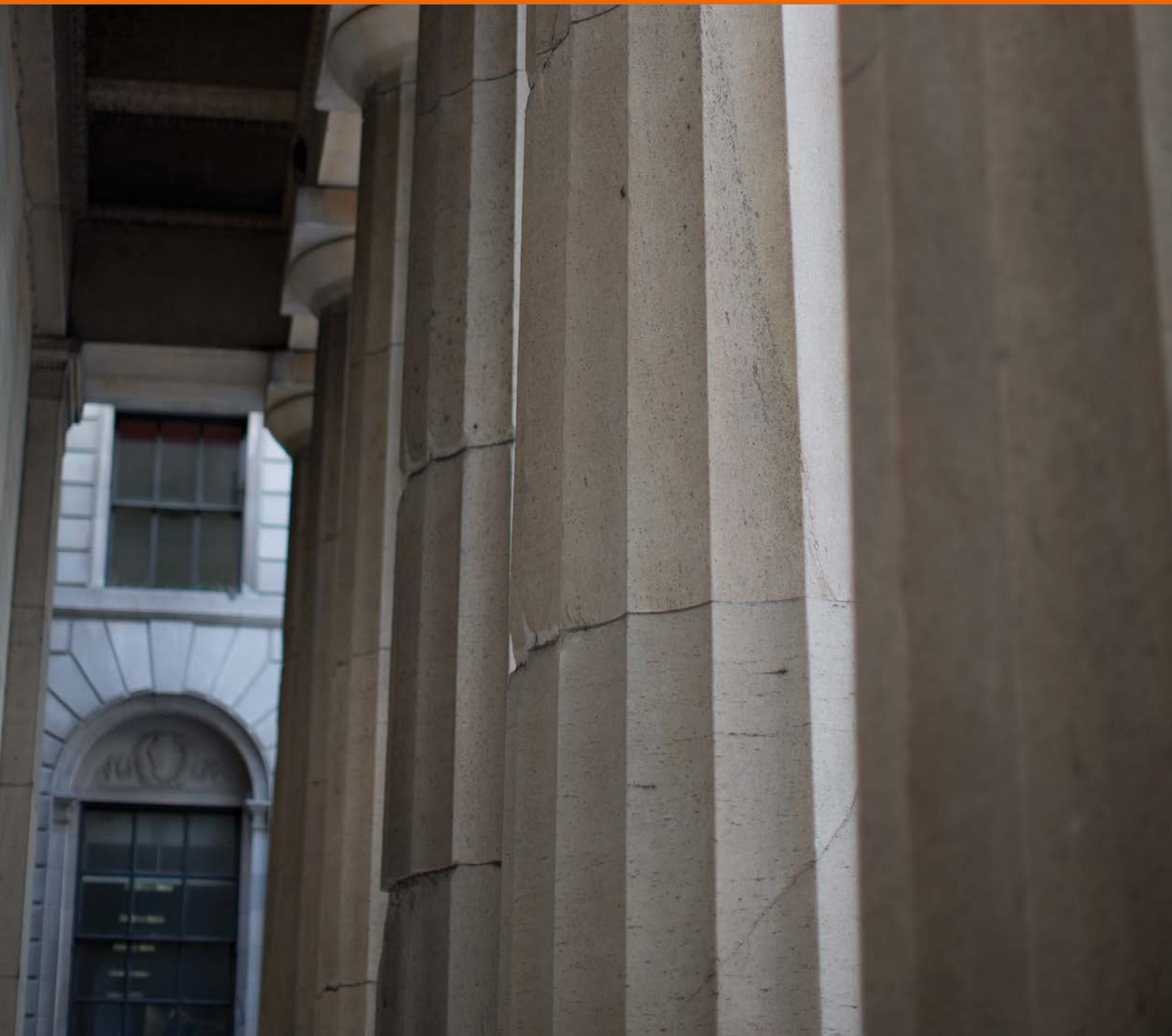
**Diagram of the keys to success in the National Strategy for elimination:
Recommendations to optimise diagnosis**



Source: In-house

6

*Investment in health strategy is key
in a Comprehensive Plan to tackle
Hepatitis C in Spain*





Present situation

The situation for HCV treatment may be compared with the HIV treatment situation in late 1990 when therapy with antiretroviral drugs drastically reduced mortality amongst patients⁶⁷. In Spain various planning instruments of the National Aids Plan were set in motion and the expenses were assigned to specific chapters.

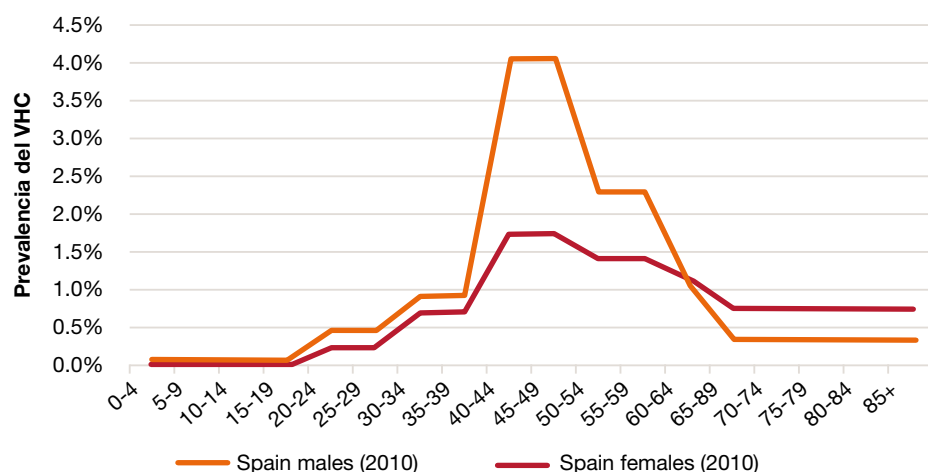
The commercialisation of the new direct-acting antiviral drugs against

hepatitis C, which are more effective, safer and have less side effects, drive forward the need to analyse the cost of the pathology versus the health outcomes. Morbidity and mortality owing to HCV entails a major public health problem in Spain. Furthermore, the disease affects to a larger extent people at a prime age and attains its maximum peak in men aged between 45 and 55 years old, entailing an impact on the employment market.

A study carried out in the USA demonstrates that despite the fall in the

Figure 14.

Prevalence of Hepatitis Viral C in Spain by age and gender, 2010



Source: Bruggmann, P. et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. Journal of Viral Hepatitis, 2014, 21, (Suppl. 1), 5-33

⁶⁷ Ford, N. et al. Simplification of antiviral hepatitis C virus therapy to support expanded Access in resource-limited settings. J Hepatol. 2014 Nov; 61 (1 Suppl) S132-8

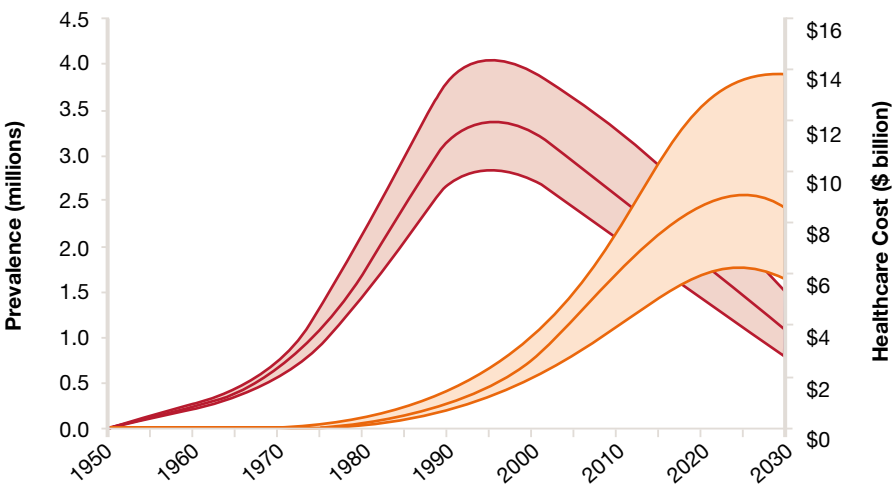
prevalence of HCV in the forthcoming years thanks to a lower incidence of infections, the health costs associated with the disease (excluding the antiviral treatment costs) will continue to rise.

This increase in costs can be put down to the fact that the population with HCV infection is getting older and the

prevalence of sufferers with an advanced degree of the disease will keep growing unless measures are adopted to halt the progression of the disease.

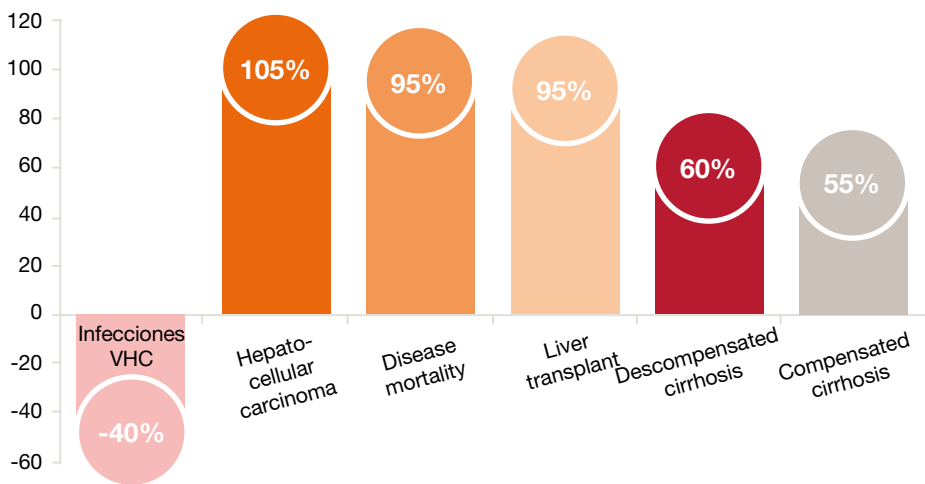
The complications associated with the advance of the disease have a high budgetary impact. Liver cirrhosis

Figure 15.
Projection of prevalence and associated health costs in the USA



Source: Razavi, H. et al. Chronic Hepatitis C Virus (HCV) disease burden and cost in the United States. Hepatology 2013; 57:2164-2170

Figure 16.
Variation in the disease burden in the period 2013-2030 in Spain



Source: Razavi, H. et al. The present and future disease burden of hepatitis C virus (HCV) infection with today's treatment paradigm. Journal of Viral Hepatitis, 2014, 21, (Suppl. 1), 34-59

produced by HCV, with or without associated hepatocellular carcinoma, is the cause of around 40% of liver transplants in adults⁶⁸. In Spain a liver transplant costs around 130,000 euros and in 2013 1,093 liver transplants were carried out⁶⁹. According to a study

carried out in the US, looking after a patient infected by hepatitis C with decompensated cirrhosis costs 550% more than looking after a patient without cirrhosis⁷⁰. Hence, the seriousness of the complications increases the cost of caring for patients with advanced fibrosis.

Table 5.

Evolution in public health spending. Millions Euros, percentage of GDP and Euros per inhabitant. Spain, 2008-2013

	2009	2010	2011	2012	2013 (P)
Millions euros*	72.939	71.080	69.240	64.479	63.006
% PIB**	6,7%	6,6%	6,5%	6,2%	6,0%
€/ inhabitant**	1.510	1.475	1.442	1.357	1.337

Source: *General Intervention of State Administration (IGAE), Finance Ministry and Public Administrations. **Public health expense statistics 2012: main results. April 2014 edition. 2013 Data: % GDP calculated in line with IGAE data. Expense per capita calculated in line with the municipal register of inhabitants as at January 1st 2013

According to a study carried out in the US, looking after a patient infected by hepatitis C with decompensated cirrhosis costs 550% more than looking after a patient without cirrhosis⁷⁰. Hence, the seriousness of the complications increases the cost of caring for patients with advanced fibrosis.

According to a study presented in 2013, the impact on the disease burden caused by hepatitis C in Spain falls at different speeds in line with the implementation of public health strategies. Hence, as shown in the figures below, adopting public health strategies and bearing in mind the effectiveness and safety of the direct-acting antivirals which allow an increase in the number of eligible patients, the prevalence of hepatitis C can be reduced significantly as well as its complications and mortality.

The *Comprehensive Plan to tackle Hepatitis C* has arisen in an environment of budgetary restrictions. In recent years, public health expenditure in Spain was cut by almost 10.1

million Euros (period 2009- 2013), meaning 13.6% less.

The solution to the financing announced by the Health Ministry is that the Finance Ministry will lend the Autonomous Communities 727 million euros to treat almost 52,000 patients with advanced liver fibrosis over the next three years. The credits will have a repayment period of 10 years, being financed in the first year at 0% and they will not be posted as a deficit.

Challenges

Our system is facing the challenge of achieving **sufficient financing for the health system in the light of disruptive innovations**. The fragmentation of the financing system involves distancing between the central and autonomous level. Whilst the setting of prices for newly marketed drugs is paid for by the Interministerial Drug Pricing Commission (CIPM), the payment of drugs is the competence of the ACs. If

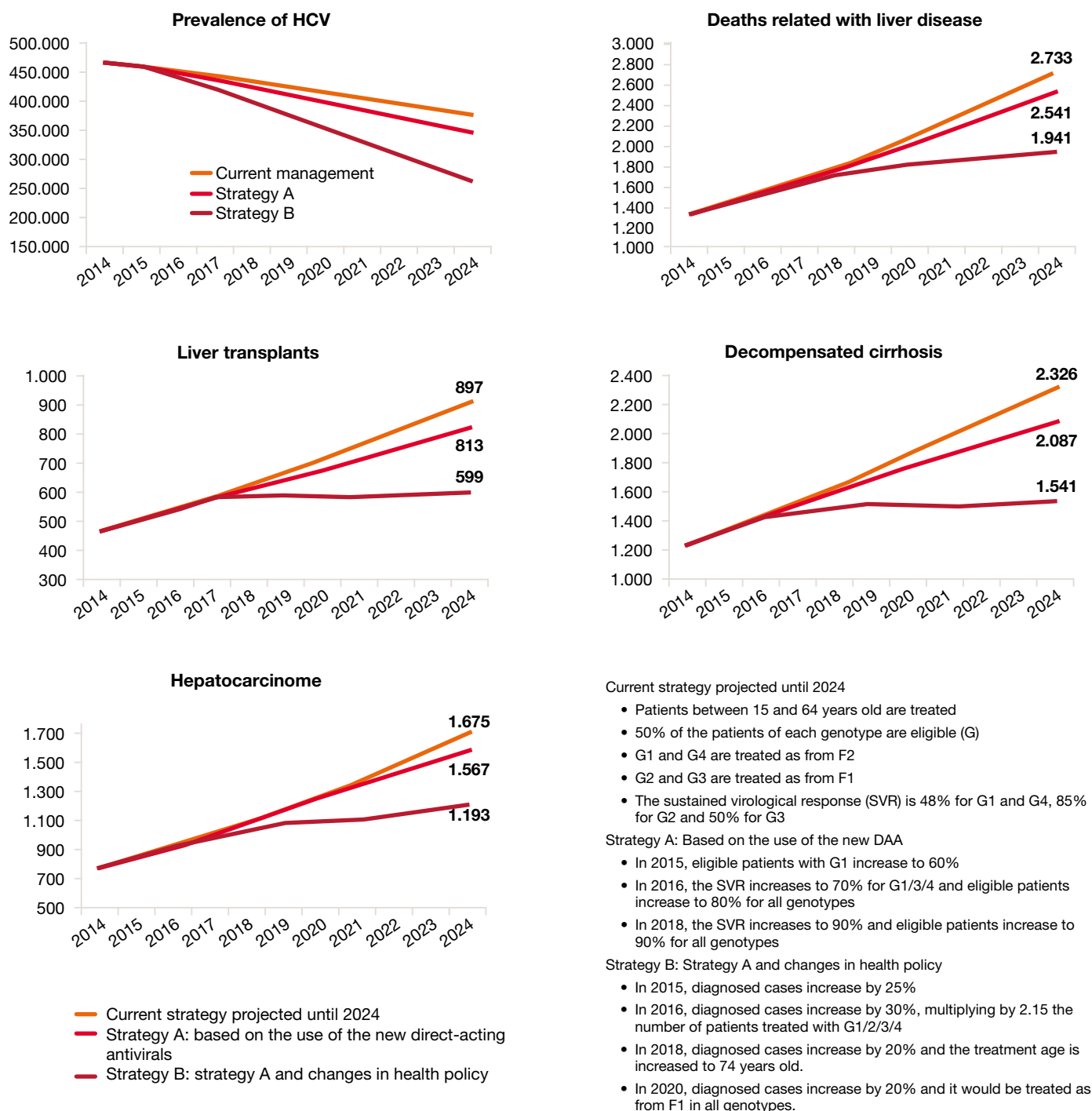
⁶⁸ Associació Catalana de malats d'hepatitis

⁶⁹ National Transplant Organisation

⁷⁰ Stuart C. Gordon et al. Impact of disease severity on healthcare costs in patients with chronic hepatitis C (CHC) virus infection - Hepatology - Volume 56, Issue 5, pages 1651-1660, November 2012

Figure 17.

Dynamic model of systems for evaluating the progression of hepatitis C, 2014-2024



Source: Buti, M. et al. Reduction in the disease burden caused by hepatitis C in Spain based on a comprehensive public health model. XXXIX Spanish Foundation for the Study of the Liver, Spanish Association for the Study of the Liver. P-123. Madrid, 18-21 February 2013



we add the fact that the procedure for inclusion in the financing of the system is not transparent nor predictable⁷¹ and that price negotiations with industry are carried out centrally, we can find certain obstacles between levels.

The Ministry of Health is aware that if it wishes to ensure fairness and avoid any region having to wait to obtain cheaper drugs owing to the population segment criterion established, it has to share the treatments of each segment and price in line with the population of each autonomy. The health minister has announced that this will be procedure when negotiating credits⁷².

Opportunities

The critical juncture of the case of hepatitis C must be taken advantage of well beyond the present moment in time. This is an opportunity to make the financing mechanisms adapted to multiannual health programmes flexible. The vast majority of new drugs that have been marketed in Spain were regarded as incremental innovations. However, the antivirals for HCV is regarded as disruptive innovation as it radically changes the paradigm of the disease. It is to be expected that in the future new disruptive drugs will arise in

other pathologies. It is thus necessary to come up with new financing formulas which can be adapted to the new innovations gradually being incorporated onto the market.

The keys to success

1. Incorporating the return on investment into decision-making process to avoid endpoints whose costs are very high. Treatment with the new oral direct-acting antivirals entails a short-term benefit in patients though the benefits to the system are medium and long-term.

On the one hand, the patient is released from the disease (effectiveness rates of 90%) and on the other, the health system is slightly released from a very heavy, expensive care burden when the disease reaches its final stage (liver transplant, hepatocellular cancer or cirrhosis). In addition, the incorporation of those who are no longer ill onto the employment market, results in greater productivity and a reduction in indirect costs. It is thus the time to incorporate the results of the analysis of benefits that a new drug

⁷¹ National Commission for Markets and Competition. Report on the draft Royal Legislative Decree approving the reworded text of the Law on guarantees and the rational use of drugs and health products, March 12th 2015

⁷² Statements made by the Health Minister, Alfonso Alonso, on March 26th 2015



brings to society as a whole and to the Spanish socioeconomic fabric in particular when deciding about its financing by the National Health System.

2. Rigorously incorporating the economic evaluation into the technical analyses.

It is necessary for financing decisions to be presided over by the criteria of scientific evidence of cost-effectiveness and an economic evaluation, bearing in mind the budgetary impact which takes into account a diagram showing the price associated with the real value that the drug or health product brings to the system⁷³.

3. Assuming multiannual and flexible budgets to avoid short-term decisions and allow the AC to adapt its own policies to the scale of the problem. Hence, the AC could finance not just the treatments but also their own screening campaigns, epidemiological studies or any other project they might wish to carry out in due time and in a way to suit the decision-making process.

4. Making the financing mechanisms more flexible. The

National Plan has opted for an alternative financing formula as it will be the Finance Ministry that will pay the invoices pertaining to the payment of the drugs that the communities keep sending them and which they will then have to reimburse on very beneficial terms depending on whether they have signed up to the Autonomous Liquidity Fund (FLA) or to the Financial Facility fund. In addition, the law considers that the inclusion of drugs in system financing is made possible by selective and not indiscriminate financing, bearing in mind the general, objectives and published criteria⁷⁴. Setting up alternative financing mechanisms such as that proposed by the Ministry is an effective measure in light of the problems on a scale such as those which concern us here.

5. Establishing health investment and disinvestment recommendations. A strategic review should be carried out to boost the incomings and outgoings of new drugs based on the scientific evidence in addition to the displacement effect which may occur owing to the speed of new additions onto the market. In the UK, for

⁷³ Royal Decree-Law 16/2012 of April 20th on urgent measures to guarantee the sustainability of the National Health System and improve the quality and safety of its services

⁷⁴ Royal Decree-Law 16/2012 of April 20th on urgent measures to guarantee the sustainability of the National Health System and improve the quality and safety of its services

example, the National Institute for Health and Care Excellence (NICE) sets the priorities of the population, identifying the clinical practices they recommend not to use because they do not bring benefits or owing to the lack of evidence to support their use. These recommendations are on the “Do not do” data base which contains all the

recommendations since 2007. They are obtained from the guided and are updated or replaced if a new guide is published. Each record contains not only the specific recommendation but also additional information about the intervention, the theme and the guide where it comes from.

Figura 18.

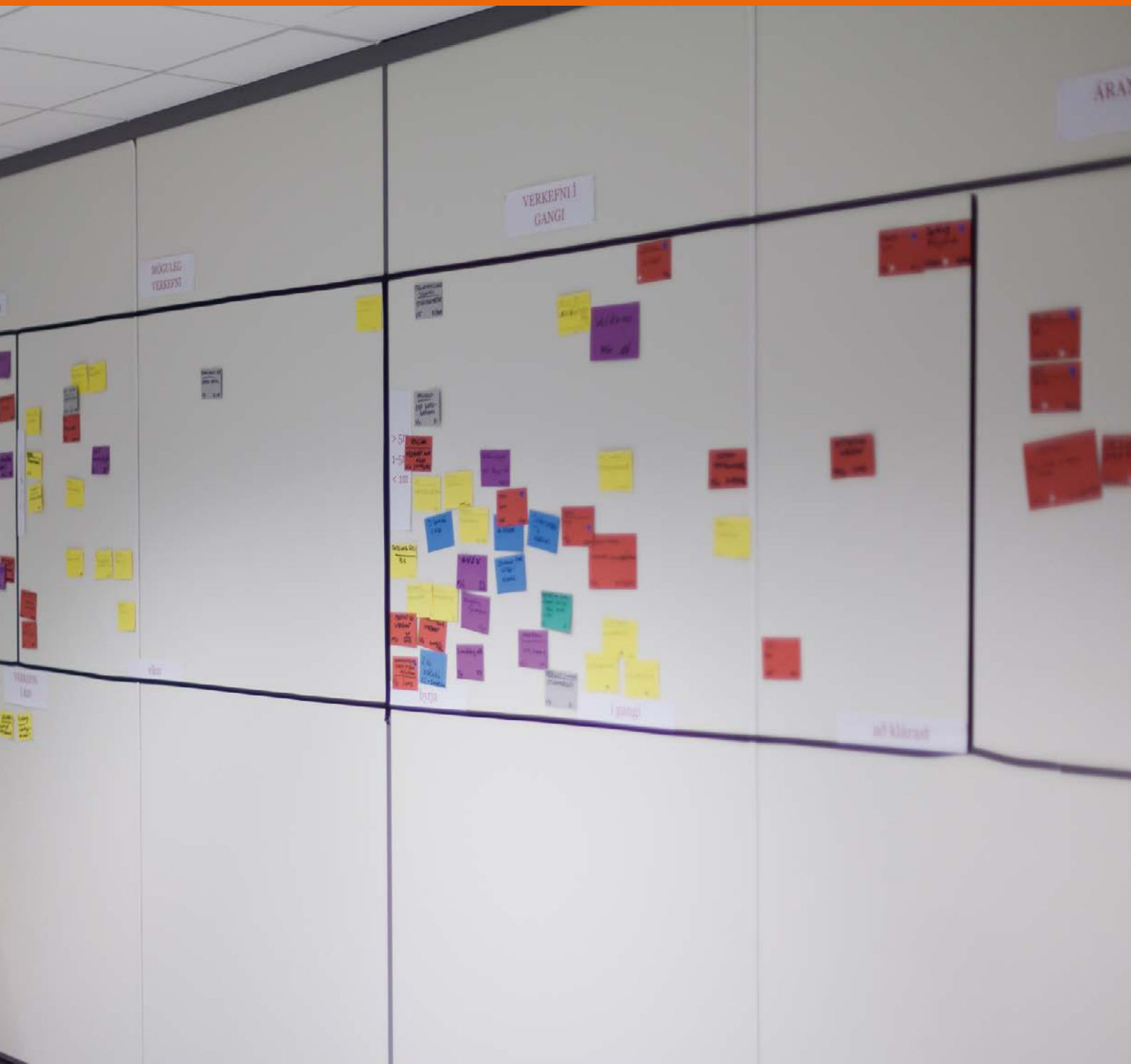
Diagram of the keys to success in the Health investment Strategy key in a Comprehensive Plan to tackle Hepatitis C in Spain



Source: In-house

7

Importance of the effective implementation of a health plan



Policies for shared governance

Against a backdrop of autonomous health competences, as is the case of Spain, it is the regional governments which finance, plan and offer health services. Decentralisation has great potential in the sense of the emergence of different innovation poles in the system and greater flexibility when adjusting the health offer to the demands of the population. However, these advantages must not be eclipsed by a lack of transparency or coordination of certain aspects both of a strategic and technical nature which ensure fairness in Access by citizens to treatments.

In view of the autonomous decentralisation characteristics in Spain, our system is facing the challenge of establishing governance which strikes a balance between ensuring national leadership, guaranteeing that actions and resources are optimised and sharing knowledge, whilst concurrently maintaining autonomy that ensures an appropriate response is given to the heterogeneity of each region. At present, Spain has the Interterritorial Council of the National Health System (CISNS) as a mechanism for institutional cooperation between the central and autonomous level. It is a coordination body mainly aimed at ensuring fairness in the health services provided to all citizens from the different AC. However, the need to strengthen shared governance requires consideration of the dimensions of the problem from an overall perspective and with this in mind, shared visions must be provided of different agents so as not to end up with partial approaches, including primary care, specialised care, the pharmaceutical industry, the patients' associations and society as a whole.

The successful implementation of the strategy will depend on a shared

governance between the different stakeholders which is based on an operating model that drives forward and monitors the follow-up of the Plan.

In addition to the keys to success identified in the previous chapters above for the implementation of the *National Strategic Plan*, we have pinpointed three levers for success, necessary though not sufficient, on which all the actions to be undertaken to successfully ensure the goals of the Plan should be based.

Levers for success

1. Ministry leadership, ensuring the appropriate participation of the Autonomous Communities.

The first step to achieve this leadership is to obtain, an overall, innovative perspective which allows endorsement to be obtained from health decision-makers in any action geared towards providing a greater number of clinical, diagnostic, material and human resources. With this in mind, it is necessary to have both scientific and political leadership and genuine coordination between both to ensure the successful implementation of the strategies.

To facilitate the deployment of the strategy, it is proposed to configure a multidisciplinary Central committee which is responsible for coordinating all nationwide actions and creating technical participation structures at all levels in such a way that clear roles and functions of all the AC with well-defined responsibility can intervene in coordinated fashion.

2. Involving all stakeholders in the governance model, including the central and autonomous public administrations, clinical professionals, patients, the pharmaceutical industry and society in general.

They all play an important role as regards the development of capacities to attain the goals set. The clinical criteria should stand out for the definition and deployment of the strategy whereby an alignment should be carried out between the goals of health planning by the Administrations with the management goals of the clinical staff and hospitals.

The AC should follow the guidelines laid down by the Ministry at all levels (epidemiology, health information systems, primary care, health investment strategy ...) but with sufficient flexibility and capacity to adapt the policies established at a central level to its own political, economic and social context.

3. Ensuring the continuous follow-up and rendering of accounts with regard to the Plan's results. It will be necessary to carry out a follow-up which monitors the plan's results. The ultimate objective is to generate clinical evidence with the maximum transparency and communication of what is happening and thereby facilitate decision-making process in line with care and scientific knowledge. This model should include a group responsible for its implementation and some shared tools to measure and evaluate the impact in terms of health outcomes.

The keys to success identified should be endowed with a series of common characteristics in order to successfully attain the opportunities detected:



It thus seems crucial to reach a consensual agreement about how to guide in the future healthcare for HCV infection, making the most of the strengths of the different healthcare areas to improve the organisation of the

system and ensuring the quality and fairness throughout the State as well as a rational use of resources aimed at improving the health of patients and reducing transmission⁷⁵.

⁷⁵ Polo, R. Shared governance from the SPNS care area. II Round Table: Shared governance and the challenges of HIV/AIDS information systems in Spain. December 15th 2011

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