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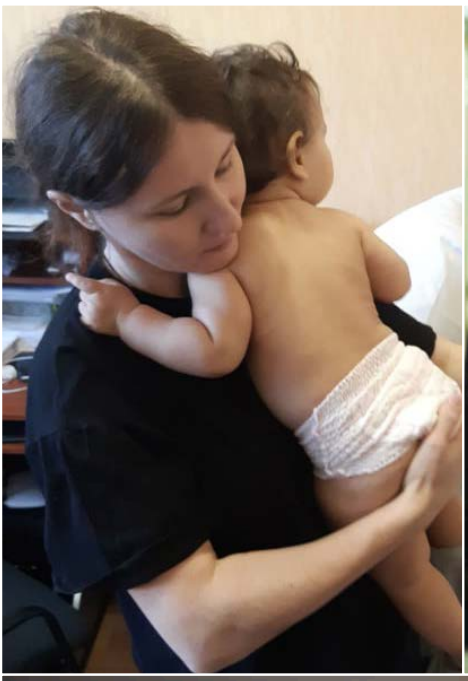

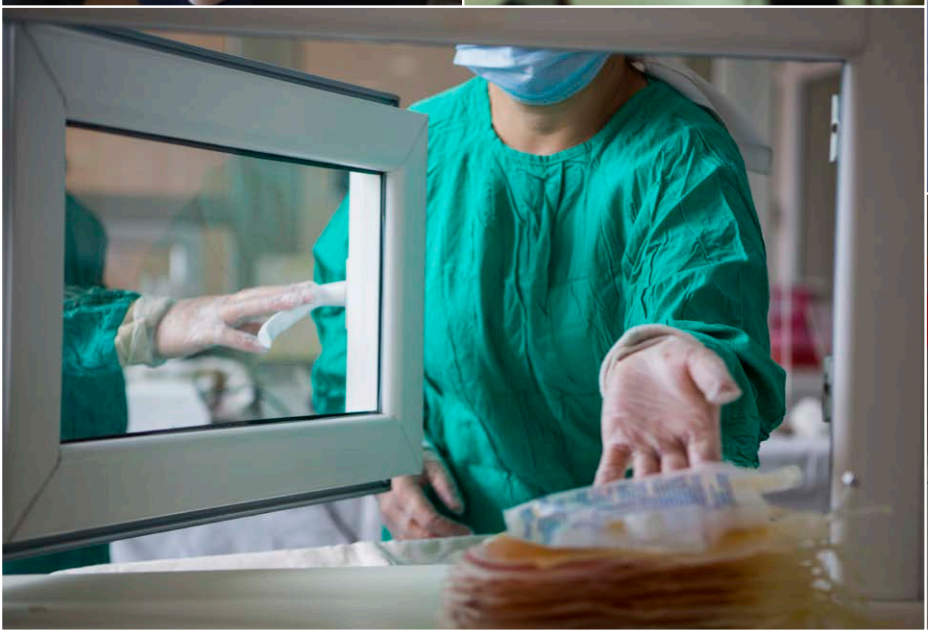

Compendium of good practices in the health sector response to viral hepatitis in the WHO European Region

World Health Organization
REGIONAL OFFICE FOR Europe

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ABSTRACT

In line with implementation of the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region, the WHO Regional Office for Europe launched an official call for good practices on viral hepatitis in May 2019. National health authorities, intraregional programmes, national technical focal points and programmes, civil society organizations (CSOs) and nongovernmental organizations (NGOs) responding to viral hepatitis were invited to submit exemplary practices. The narratives were collected over six months from May to November 2019, compiled and evaluated against pre-defined criteria, and technically reviewed by WHO experts in the Regional Office. This compendium includes 34 practice examples from 18 Member States in the WHO European Region authored by various actors in the collective response to viral hepatitis, including government and national viral hepatitis programmes, academia, public health/research institutes and NGOs and CSOs.

Keywords
VIRAL HEPATITIS
MODEL OF CARE
INTEGRATED TESTING
POINT OF CARE
LINKAGE TO CARE
HARM REDUCTION

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CONTENTS

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The WHO Regional Office for Europe would like to thank all Member States, civil society organizations, and national and international experts from the Region who contributed to the good practices described in this compendium.

Authors

Austria

ELIMINATE: laboratory-based patient tracing strategy for elimination of HCV in eastern Austria
Authors: Caroline Schmidbauer, David Bauer and Thomas Reiberger.

Hepatitis C elimination among people living with HIV in Austria
Authors: Benedikt Simbrunner, David Bauer, David Chromy, Mattias Mandorfer and Markus PeckRadosaljevic.

Testing and treatment of hepatitis C in MSM in Austria
Authors: Benedikt Simbrunner, David Bauer, David Chromy, Teresa Binter and Thomas Reiberger.

Belarus

Ensuring a high level of hepatitis B immuniation coverage in Belarus
Authors: Iryna Hlinskaya, Natalia Kolomiets, Tamara Svetahor, Veranika Vysotskaya and Viatcheslav Grankov.

State-funded hepatitis C treatment and local production of DAAs in Belarus
Authors: Igor Karpov, Oleg Skripko, Sviatlana Lykshyk, Dzmtry Danilau, Dmitry Litvinchuk and Viatcheslav Grankov.

Belgium

The Antwerp Model: an integrated multidisciplinary model of care with strong peer-support to ensure continuum of HCV care for PWID
Authors: Catharina Matheï, Griet Maertens, Stefan Bourgeois and Tessa Windelinckx.

Croatia

Móbile InfoHep Centre – mobile clinic
Authors: Boris Lukšić, Diana Nonković, Magda Pletikosa Pavić and Tatjana Reić.

National coordination, local implementation and scale-up of needle and syringe programmes in Croatia
Authors: Dunja Skoko-Poljak, Iva Jovović and Tatjana Nemeth Blažić.

Partnershps and synergy in the response to viral hepatitis in Croatia
Authors: Adriana Vince, Arian Dišković, Davor Dubravić, Ivana Portolan Pajić, Maja Erceg Tušek, Tatjana Nemeth Blažić and Tomislav Beganović.

Georgia

HCV core antigen testing and improved access to diagnosis in Georgia
Authors: Amiran Gamkrelidze, Gvantsa Chanturia, Maia Alkhazashvili, Nazibrola Chitadze, Paata Imnadze and Roena Sukhiashvil.

Hepatitis C treatment integrated into harm reduction services in Georgia
Authors: Amiran Gamkrelidze, Francisco Averhoff, George Kamkamidze, Irine Tskhomelidze, Lia Gvinjilia, Maia Butsashvili, Maia Kajaia, Maia Tsereteli, Marine Gogia, Muazzam Nasrullah, Shaun Shadaker and Tinatin Kuchuloria.

Integrated screening and diagnosis of HCV, HIV and TB in Georgia
Authors: Alexander Turdziladze, Amiran Gamkrelidze, Ekaterina Ruadze, Irma Khonelidze, Ketevan Stvilia, Maka Danelia, Nino Chikovani and Vladimer Getiai.

Integrating HCV screening and simplified treatment and care serrvices in primary health care in Georgia
Authors: Akaki Abutidze, Ekaterine Adamia, Lali Sharvadze, Nikoloz Chkhartishvili, Tengiz Tsertsvadze and Vakhtang Kerashvili.

Unidad Móvil de Cribado (Mobile Screening Unit) in Spain
Authors: Jorge Valencia and Pablo Ryan.

Ukraine

A national policy to improve access to hepatitis C treatment with lower prices and generic medicines in Ukraine
Authors: Iryna Ivanchuk, Serhiy Dmitriev and Volodymyr Kurpita.

Integrated hepatitis C management for high-risk and vulnerable populations in Mykolaiv, Ukraine
Authors: Karam Kamble, Larysa Kolomiiets, Svitlana Ivanchenko and Viktoriia Klychko.

Social support, adherence to hepatitis C treatment, and prevention of HCV reinfection in key populations in Ukraine
Authors: Dina Marumko, Zahedul Islam and Zhanna Tselinova.

United Kingdom

A home-based care pathway for the stratified treatment of HCV infection in England
Authors: Breanne Dilks, Elizabeth Blackwell, Jasmina Khaldi, Kathryn Jack, Samantha Bird, Sherelle Smith, Stephen Ryder and Brian Thomson.

A national patient re-engagement exercise to find and treat people who have previously been diagnosed with hepatitis C in England
Authors: David Geddes, Georgina Ireland, Graham Foster, Helen Bennett, Helen Harris, Mary Ramsay, Rachel Halford, Ruth Simmons and Sema Mandal.

Estimating the cascade of care for hepatitis C virus in England through data linkage: providing a benchmark for monitoring progress and early impacts of the new treatments
Authors: Brian Eastwood, Caroline Sabin, Georgina Ireland, Helen Harris, Koye Balogun, Mary Ramsay, Matthew Hickman, Ross Harris, Ruth Simmons, Samreen Ijaz, Sema Mandal and Will Irving.

Transitioning from the hepatitis C action plan to an elimination strategy in Scotland: successes and the way forward
Authors: David J Goldberg, Hamish Innes, John Dillon and Sharon J Hutchinson.

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ABBREVIATIONS

3TC	lamivudine
anti-HCV	hepatitis C antibodies
APRI	aspartate aminotransferase to platelet ratio index
CAHIV	Croatian Association for HIV and Viral Hepatitis
CI	confidence interval
CIPH	Croatian Institute of Public Health
CME	Continuing Medical Education
CNM	National Centre for Microbiology of the Institute of Health Carlos III (Spain)
CPTDA	Centres for the Prevention and Treatment of Drug Addiction (Slovenia)
CSO	civil society organization
DAA	direct-acting antiviral
DDD	defined daily dose
DOT	directly observed therapy
EOT	end of treatment
ESLD	end-stage liver disease
ETV	entecavir
FDC	fixed-dose combination
GECCO	German hepatitis C cohort
GEL	Georgian lari
GHSS	Global Health Sector Strategy on Viral Hepatitis 2016–2021
GP	general practitioner
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HCVcAg	hepatitis C virus core antigen
IEC	information, education and communication
LTFU	lost to follow-up
M&E	monitoring and evaluation
MIHC	Mobile InfoHep Centre (Croatia)
MOP	Mobile Outreach Programme (Portugal)

MoU	memorandum of understanding
MRCPCIS	Mykolaiv Regional Centre for Palliative Care and Integrated Services (Ukraine)
MSF	Médecins Sans Frontières
MSM	men who have sex with men
NAT	nucleic acid amplification test
NCDC	National Center for Disease Control and Public Health (Georgia)
NDTMS	National Drug Treatment Monitoring System (United Kingdom)
NGO	nongovernmental organization
NHS	National Health Service (United Kingdom)
NHSE	National Health Service England (United Kingdom)
NSP	needle and syringe programme
NUH	Nottingham University Hospitals (United Kingdom)
ODN	Operational Delivery Network (United Kingdom)
OST	opioid substitution therapy
PCR	polymerase chain reaction
PDS	Personal Demographics Service (United Kingdom)
PHC	primary health care
PHE	Public Health England (United Kingdom)
PLHIV	people living with HIV
PWID	people who inject drugs
PWUD	people who use drugs
RDT	rapid diagnostic test
RNA	ribonucleic acid
SVR	sustained virological response
SVR12/24	sustained virological response 12/24 weeks after the end of HCV treatment
TB	tuberculosis
TraP HepC	Treatment as Prevention for Hepatitis C (Iceland)
UHID	University Hospital for Infectious Diseases “Dr Fran Mihaljevic” (Croatia)
UMC	Unidad Móvil de Cribado [Mobile Screening Unit] (Spain)
US CDC	United States Centers for Disease Control and Prevention
VCT	voluntary counselling and testing
VUHSK	Vilnius University Hospital Santaros Klinikos (Lithuania)

EXECUTIVE SUMMARY

At the 66th session of the WHO Regional Committee for Europe in September 2016, all 53 Member States endorsed resolution EUR/RC66/R10, on the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region. The action plan guides Member States in accelerating their response to the viral hepatitis epidemic. Its goals and targets are in line with the United Nations 2030 Agenda for Sustainable Development and the WHO Global Health Sector Strategy on Viral Hepatitis, 2016–2021.

The goal of the action plan is the elimination of viral hepatitis as a public health threat in the European Region by 2030 through the reduction of transmission of hepatitis viruses and of the morbidity and mortality due to viral hepatitis and its complications, and by ensuring equitable access to comprehensive prevention and recommended testing, care and treatment services for all.

In line with implementation of the action plan, the WHO Regional Office for Europe launched an official call for good practices on viral hepatitis in May 2019. National health authorities, intraregional programmes, national technical focal points and programmes, civil society organizations (CSOs), and nongovernmental organizations (NGOs) responding to the epidemic were invited to submit exemplary practices. The narratives were collected over six months from May to November 2019, compiled and evaluated against pre-defined criteria, and technically reviewed by WHO experts in the Regional Office.

The compendium includes 34 practice examples from 18 Member States in the European Region authored by various actors in the collective response to viral hepatitis, including government and national viral hepatitis programmes (23), academia and public health institutes/research institutes (9) and NGOs and CSOs (9).

Chapters are organized by Member State, and best practices are presented in alphabetical order and categorized according to the strategic directions of the action plan: (1) information for focused action, (2) interventions for impact, (3) delivering for equity, (4) financing for sustainability, and (5) innovation for acceleration. This compendium is the first WHO Regional Office for Europe project to consolidate good viral hepatitis practices in the Region.

INTRODUCTION

Background

In the WHO European Region, an estimated 15 million people are living with chronic hepatitis B and around 14 million people are infected with hepatitis C. In addition to being a global and regional public health issue, chronic viral hepatitis also represents a clinical challenge, with high morbidity and mortality, as people may not show symptoms for a long time, sometimes for years, until the disease is advanced with liver cirrhosis and eventual hepatocellular carcinoma.

Considering its major burden on health systems and threat to the well-being of individuals, in September 2016, all Member States in the Region adopted the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region, reinforcing the global goal of elimination of viral hepatitis and identifying priority actions adapted for the regional context and response.

The priority actions span a range of topics and levels of care – including surveillance, harm reduction, immunization, people-centred care, community engagement, outreach activities, early diagnosis, and adequate treatment and care. These require effective public health policies, intersectoral collaboration and synergy among stakeholders for a collective response.

In line with the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region and in collaboration with WHO country offices, the WHO Regional Office for Europe has continuously provided technical assistance and guidance towards reaching the viral hepatitis elimination targets.

Areas of technical assistance have included: (i) viral hepatitis surveillance and development of national estimates, (ii) collaboration with partners and participation of civil society organizations (CSOs) in the response, (iii) implementation of national plans, (iv) communication guidance for World Hepatitis Day and awareness and prevention campaigns, (v) immunization and prevention of perinatal transmission, (vi) blood and tissue safety, (vii) safe injections and strengthening infection prevention and control, (viii) harm reduction, (ix) national guidelines for testing and treatment, (x) building political commitment and sustained financing, and (xi) operational research and innovation *(1).*

Viral hepatitis elimination faces many challenges across the European Region. In February 2019, the First Regional Consultation on Viral Hepatitis in the WHO European Region was held in Tbilisi, Georgia, bringing together stakeholders, international experts, academics, and representatives of Members States, international humanitarian organizations, patients' associations, CSOs, professional associations and WHO Collaborating Centres to discuss achievements, opportunities and barriers to the elimination of viral hepatitis *(2).*

The aims of this compendium are to expand this exchange of good practices and advise on the action points and next steps for scaling up the viral hepatitis response within the Region. The compendium of good practices also functions to support the monitoring and evaluation of Member States' commitment to implementing the action plan.

Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region

The action plan is an implementation plan for adapting the WHO Global Health Sector Strategy on Viral Hepatitis, 2016–2021, to the epidemiological, social and political contexts of the Region. It ensures that the Region is able to achieve the global goal of ending viral hepatitis as a public health threat by 2030, which the World Health Assembly adopted by consensus in May 2016. The action plan continues the momentum generated through both the 2030 Agenda for Sustainable Development and Health 2020, the Region's policy for health and well-being.

Since implementation of the action plan began, access to treatment for hepatitis C has increased overall in the Region; many Member States have removed treatment access restrictions based on the stage of liver disease, in line with the current WHO recommendation to treat all patients with chronic hepatitis C virus (HCV) infection; and two Member States have been added to pre-existing expanded access programmes. Thirty-two Member States have active national strategies, action plans, roadmaps for the elimination of viral hepatitis or national guidelines for treatment and care.

Both the action plan and this compendium of good practices are structured around the following five strategic directions.

Strategic Direction 1. Information for focused action

Develop strong strategic information systems to understand viral hepatitis epidemics and focus responses to them.
Strategic Direction 1 addresses the need to generate and use high-quality strategic information about viral hepatitis epidemics and responses to them, as a basis for focused national strategic planning, urgent and accelerated programme implementation, and advocacy to garner political commitment.

Strategic Direction 2. Interventions for impact

People should receive all the hepatitis services they need.
Each country should define a set of essential interventions, services, medicines and commodities relevant to the country context, to be included in the comprehensive health sector response to viral hepatitis. These essential interventions should be included in the national health benefit package, with no out-of-pocket expenses, to ensure affordability and overall sustainability of the health sector response to viral hepatitis. These interventions should cover the entire continuum of hepatitis services, including prevention, diagnosis, treatment and care, delivered through integrated services in which a public health approach is adopted and which are managed within the context of universal health coverage.

Strategic Direction 3. Delivering for equity

All people should receive the hepatitis services they need, and such services should be of adequate quality.
Strategic Direction 3 responds to the need for an enabling environment and optimization of service delivery using a public health approach under a model of universal health coverage. Interventions to address viral hepatitis, and the health and community-based systems that provide them, should respect the principles of equity and human rights. The continuum of hepatitis services should be people-centred, integrated, accessible, equitable, community-based and of high quality, to ensure that no one is left behind.

Strategic Direction 4. Financing for sustainability

Strategic Direction 4 identifies the need for sustainable financing models for the health system response to viral hepatitis and for cost-saving approaches that allow people to access the services they need without incurring financial hardship. This is possible when integrated and linked services are delivered under a model of universal health coverage.

Adequate investment in the full continuum of hepatitis services is necessary to achieve the targets for 2020 and to move towards the global goal of eliminating viral hepatitis as a public health threat by 2030. Member States in the European Region are diverse in terms of political and socioeconomic context, and the organization of their health systems varies. Some priority actions (e.g. joint procurement procedure) may be more relevant for the Region's European Union/European Economic Area Member States; other actions will apply specifically to lower-middle-income countries from the eastern part of the Region.

Strategic Direction 5. Innovation for acceleration

Research and innovation provide opportunities to change the trajectory of the regional and national health sector response to viral hepatitis, improve efficiency and quality of services, and maximize impact. Innovations are required across the entire continuum of prevention, diagnosis, treatment and care services. They need to be backed up with operational research and collaboration between researchers and policy-makers to ensure that research findings are translated into policy rapidly and on a sufficient scale to achieve the desired impact.

Member States should play a critical role in defining priorities for innovation, facilitating research by establishing multisectoral inclusive partnerships and collaborative opportunities focused on innovation and best practice. These should include collaborating with public and private sector organizations, documenting early implementation experiences, and taking the lead on operational research.

Selection criteria for good viral hepatitis practices in the European Region

The examples presented are the joint work of the authors listed for each practice.[1] This compendium is not intended to highlight every strong practice in each Member State: editors reviewed the submissions to ensure that the quality and conditions of the shared practices meet pre-defined criteria (Table 1). These criteria are adapted from Ng & de Colombani (2015) for selection based on efficacy, efficiency, sustainability and innovation in addressing inequities in health and fulfilling the call of the United Nations 2030 Agenda for Sustainable Development – to leave no one behind *(3)*.

Good practices in the response to viral hepatitis in the European Region may include one or more strategies for the prevention, diagnosis, treatment and care of viral hepatitis – including harm reduction, immunization, point-of-care testing, integrated models of care and increased access to medicines.

National health authorities, including national viral hepatitis programmes, ministries of health, ministries of justice or any other relevant responsible government organization; partner organizations; and nongovernmental organizations (NGOs) responding to viral hepatitis in the Region were invited to submit examples of good practices through an open call and submission form available in both English and Russian.

[1] Submissions were received from regional partners, research conglomerates, national governments (e.g. ministries of health, ministries of justice), national HIV programmes (public health institutes, HIV/AIDS centres), implementing partners, nongovernmental organizations (NGOs) and CSOs.

Analysis

The narratives were collected over six months from May to November 2019, compiled and evaluated against pre-defined criteria, and technically reviewed by WHO experts in the Regional Office. The compendium includes 34 practice examples from 18 Member States in the European Region authored by various actors in the collective response to viral hepatitis, including government and national viral hepatitis programmes (23), academia and public health institutes/research institutes (9) and NGOs and CSOs (9).

Member States and partners should sustain, replicate and scale up these and other similar good practices.

Table 1. Selection criteria for good practices for the prevention and control of viral hepatitis in the WHO European Region

Criteria	Definition
*Relevance	Must address one of the targets or areas of intervention of the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region as outlined above
*Sustainability	Implementable or able to be maintained over a long period of time (including policy decisions) without any massive injection of additional resources
*Efficiency	Must produce results with a reasonable level of resources and time
*Ethical appropriateness	Must respect the current rules of ethics for dealing with human populations
Equity/gender	Addresses the needs of key populations and/or gender in an equitable manner
Effectiveness	Must work and achieve results that have been measured
Possibility for scale-up	Can be scaled up to a larger population
Partnership	Involves satisfactory collaboration between several stakeholders
Community involvement	Involves participation from the affected communities
Political commitment	Has support from the relevant national or local authorities

* Required

AUSTRIA ELIMINATE: laboratory-based patient tracing strategy for elimination of HCV in eastern Austria

Strategic Direction 1 | Strategic Direction 2

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[2] Vienna HIV & Liver Study Groups, Medical University of Vienna, Vienna

Background

In Austria, laboratories and treating physicians have been obliged by law to report all people testing positive for HCV infection to the public health authorities since 2014. Yet, very few physicians voluntarily report and only laboratories are systematically reporting HCV cases, resulting in an incomplete national database for HCV infection. The information available in the database is also not shared with treating physicians or hepatology specialists at the treatment centres – where hepatitis C treatment with direct-acting antivirals (DAAs) is provided and is reimbursed by Austrian health insurance – negatively affecting patient tracing and linkage to care.

Description of the good practice

ELIMINATE is a laboratory-based patient tracing strategy created in 2019 to improve both the quality of the national database for HCV infection and the much-needed linkage to care. It was approved by the relevant Austrian authorities in 2018. The strategy consists of identifying all HCV test results conducted in hospitals where the treatment centres are located and eliminating duplicates, deaths and registries of cured patients. Out of 7 treatment centres, 5 agreed to participate in ELIMINATE. The resulting records made a fairly complete list of patients tested positive for HCV infection yet never treated for hepatitis C. This list of patients was shared with all treatment centres so that they could contact them and offer hepatitis C treatment with DAAs, increasing treatment uptake and improving linkage to care.

Evidence of impact

ELIMINATE has assisted in the identification of about 4000 people with hepatitis C and in need of treatment in Vienna and eastern Austria. Taking into account an approximation of the number of deaths, duplicate entries (e.g. through management or linkage at two or more centres), and the number of patients with spontaneous cure or cure by therapy at other centres, we expect the number of patients that remain HCV-RNA (ribonucleic acid) viraemic to be about 3000 out of these 4000. Due to the high mobility of these patients, the poor linkage to care, the lack of valid contact data and the lack of willingness to attend clinical visits/blood assessment, the number of patients will likely fall to about 2000. Overall at the participating treatment centres more than 1000 HCV patients have already been treated with DAA therapies.

Sustainability

We expect an increase in the number of people with hepatitis C and in need of treatment as the project progresses. Our specialists have already been invited to join other treatment centres to increase their capacity. The patient tracing facilitated by ELIMINATE has significantly improved treatment uptake and linkage to care, without additional investments.

AUSTRIA Hepatitis C elimination among people living with HIV in Austria

Strategic Direction 2 | Strategic Direction 3

Chromy, David[1,2,3] | Mandorfer, Mattias[1,2] | Bauer, David[1,2] | Simbrunner, Benedikt[1,2] | Peck-Radosavljevic, Markus[1,4] | Reiberger, Thomas[1,2]

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Background

Two population groups contribute to the majority of the approximately 45 000 people living with hepatitis C virus in Austria: people who inject drugs (PWID) *(4)* and men who have sex with men (MSM) *(5)*. HIV/HCV coinfection is common in both groups and HIV infection significantly affects the transmission of HCV and retention in health care.

In Austria, treatment and care for HIV and HCV are not fully integrated, even in the case of coinfection, and the responsibility for each infection is assigned to different specialists – hepatitis C to the hepatologists and HIV to the HIV specialists. In order to be reimbursed by Austrian health insurance, treatment for hepatitis C must not be prescribed by an HIV specialist.

The separate health-care structures for HIV and HCV pose a significant barrier to treatment access for those with coinfection, and can negatively affect the resulting outcomes. Therefore, health-care facilities should develop and implement proactive strategies to improve access to hepatitis C treatment and care for people living with HIV (PLHIV).

Description of the good practice

An outpatient clinic dedicated to people living with HIV/HCV coinfection was opened at the Vienna General Hospital (Division of Gastroenterology and Hepatology, Department of Medicine III) in 2002. Throughout the years, the outpatient clinic has proved itself important for various projects related to the treatment and care of hepatitis C in PLHIV, assisting in the funding and continuity of the services provided.

The outpatient clinic services are provided by a dedicated team of expert physicians with knowledge of both the management of HIV and hepatitis C. Importantly, these physicians operate a direct physician–patient phone hotline for any questions regarding viral hepatitis, which is available five days a week for 8 hours, with the option to leave a text or audio message outside operating hours. The direct communication allows these patients, who often have low socioeconomic status and poor linkage to care, easy access to integrated medical care (dermatology, infectious diseases, hepatology, internal medicine, etc.) and importantly also to DAA therapy against HCV.

We have been able to maintain a dedicated team of personnel for the outpatient clinic and the aforementioned activities for the majority of the time it has been operational, resulting in improvements in linkage to treatment and care of HIV and HCV, and progress towards the elimination of hepatitis C.

Evidence of impact

Since 2002, the number of treatments provided in the dedicated outpatient clinic has increased and the outcomes have changed significantly – categorized as: cure (sustained virological response, SVR), lost to follow-up (LTFU) or treatment failure. From 2002 to mid-2014, 152 interferon-based treatments were provided in the dedicated outpatient clinic, with only 48.6% of treatments achieving cure. Since then, more than 319 DAA-based treatments have been initiated, with more than 85.5% of patients cured (94.8% among those who have finished treatment) (Fig. 1).

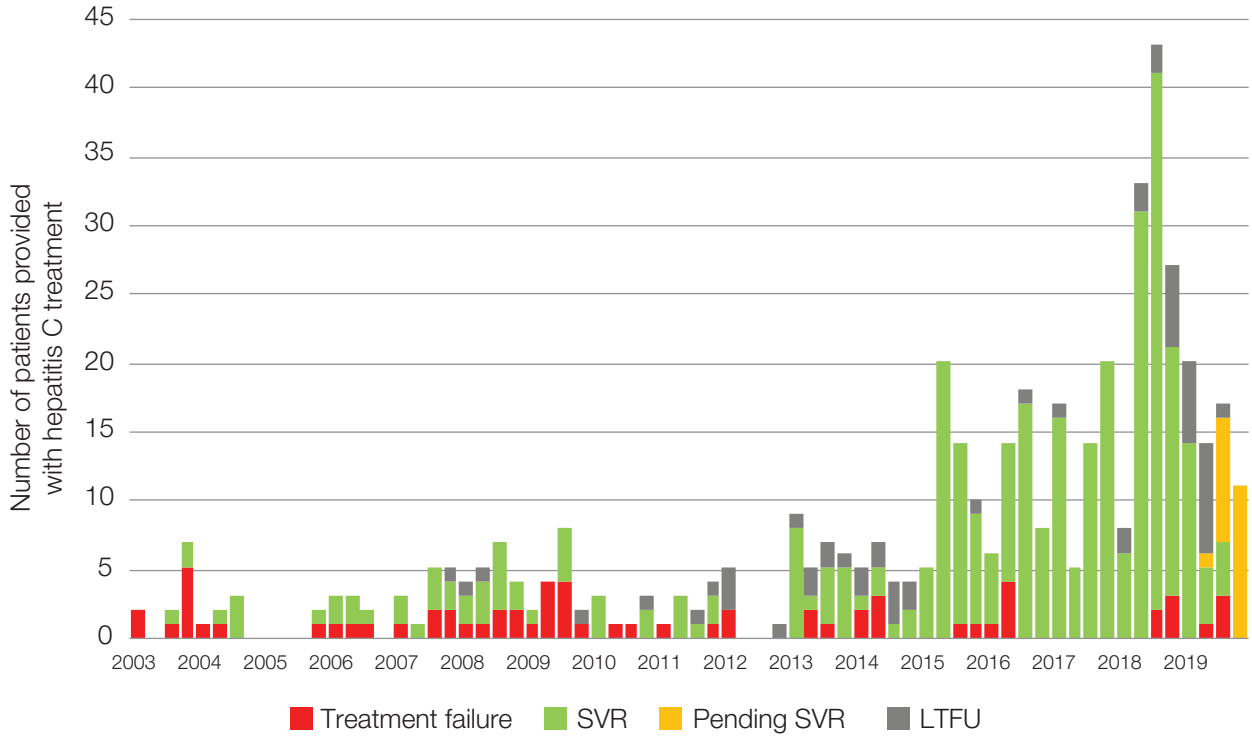
More than 470 people living with HIV/HCV coinfection received treatment for hepatitis C in the dedicated clinic, including 152 interferon-based and 319 DAA-based treatments. Throughout the years, multiple colleagues, including hepatologists and HIV specialists, have been engaged in our projects, allowing us to build and strengthen a tight network of dedicated health-care workers, improving the workflow and referral process. These improvements resulted in better access to treatment and overall care for our patients.

Sustainability

Our approach does not focus on scaling up diagnostics but rather improvement of linkage to care and has a well-defined list of required resources for constant

operation. These resources will be provided through projects for elimination of viral hepatitis in specific population groups. The demand for our activities depends on the effectiveness of our network of HIV specialists referring patients, and we have continuously worked to improve such collaboration. Our personnel at the clinic are highly experienced and able to provide the necessary knowledge to link diagnosed patients to treatment and appropriate follow-up. We can confidently recommend our model to others working under similar public health policies.

Fig. 1. Patients treated for hepatitis C at the dedicated HIV/HCV coinfection clinic, Vienna (2002–2019)



Source: Authors.

AUSTRIA Testing and treatment of hepatitis C in MSM in Austria

Strategic Direction 2 | Strategic Direction 3

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Background

In Vienna, cases of hepatitis C among MSM due to sexual transmission have considerably increased over the years. Between 2014 and 2016, MSM accounted for 61% of all incidents of HCV infection diagnosed at the Medical University of Vienna – a tertiary care centre hosting large HIV and HCV clinics – and 30–40% of patients with hepatitis C at the university's hepatitis clinic *(6,7)*. These findings are in line with reports from other European centres, describing a higher incidence of HCV infection not only in MSM living with HIV, but also in seronegative MSM, especially if they are receiving HIV pre-exposure prophylaxis. In addition to these initial findings, unprotected anal intercourse and nasal and/or intravenous drug use – relevant modes of transmission for HCV in the MSM population – have been commonly observed among MSM in Vienna. Hepatitis C tests are not reimbursed by the health insurance fund in Austria, significantly restricting access to free-of-charge testing and impairing the cascade of care and elimination of hepatitis C.

Description of the good practice

We established an efficient collaboration with primary health care physicians and gay health centres for free testing for viral hepatitis for MSM and timely referral to specialized services at the Medical University of Vienna. Our team implemented a hotline for medical appointments for hepatitis C (HCV Phone), decreasing the barriers for hepatitis C treatment and care for MSM in Vienna. Patients with confirmed HCV infection (defined by detectable HCV-RNA) that make use of the hotline have their appointments scheduled within seven days.

The project has kept reliable records of its operations, including the number of patients tested, positive test results, hepatitis C epidemiology and test acceptance in the MSM community.

Evidence of impact

The project is ongoing. It will be evaluated in December 2021.

Sustainability

Early diagnosis and treatment of hepatitis C in the MSM population has the potential to positively impact on epidemiology and contribute to the elimination of hepatitis C. Reducing barriers for diagnosis and treatment may be associated with increased costs for HCV testing, yet successful HCV treatment and thus prevention of repeated HCV transmission reduces long-term HCV-related health-care costs.

BELARUS Ensuring a high level of hepatitis B immunization coverage in Belarus

Strategic Direction 1 | Strategic Direction 2

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Background

Before the introduction of hepatitis B vaccination in the national immunization programme in 1996, Belarus had an incidence of hepatitis B of 80.57 cases (acute and chronic) per 100 000 people *(8)*. Among children aged 0–14 years, 110 cases of acute hepatitis B were registered every year – more than 60% of all paediatric cases occurred in those aged 7–14 years.

Description of the good practice

When hepatitis B vaccination was introduced into the national immunization programme in 1996, it was initially dedicated to blood donors, health workers and other population groups at risk of infection with hepatitis B virus (HBV). The recommendations for hepatitis B vaccination were extended in 2000 to include children aged 0–13 years, in accordance with recommendations issued by WHO and the Expanded Programme on Immunization (EPI) *(9)*.

In 2007, the national policy for hepatitis B vaccinations was once again updated and the national immunization schedule was extended to cover the following groups: family members of hepatitis B surface antigen (HBsAg) positive patients or patients with acute or chronic HBV infection, regular recipients of blood and blood products, patients on haemodialysis, haematology-oncology patients, people who had contact with HBV, medical students, unvaccinated patients before elective surgery and others.

During 2012–2014, the list was expanded to children born from HBsAg-positive mothers, people who have had sex with an HBsAg-positive person, MSM, PWID, PLHIV and people who travel to HBV endemic countries.

In 2018, the national immunization programme transitioned to a 4-dose schedule for hepatitis B immunization of children: with one dose within 24 hours of birth followed by a second, third and fourth dose of hepatitis B containing vaccines.

Evidence of impact

Hepatitis B vaccination had positive effects in Belarus, quickly reducing the incidence of acute HBV infection – incidence in children decreased tenfold and the incidence in the general population decreased by 19.5

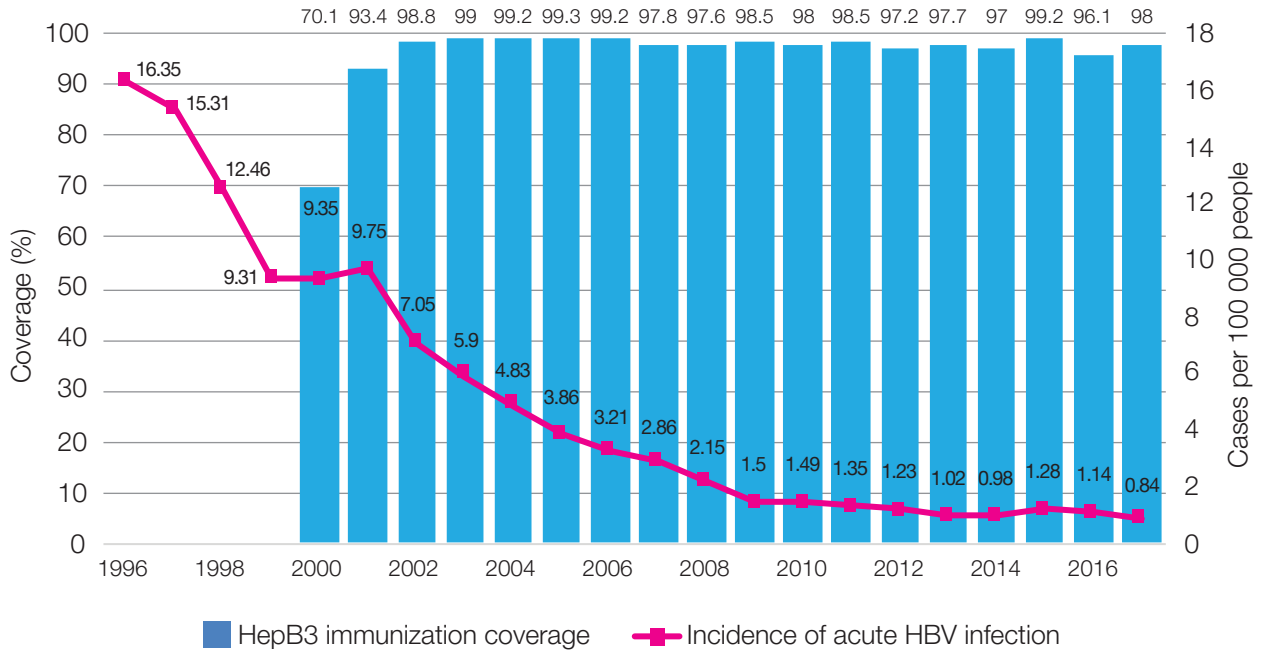
times (Fig. 2). The total number of people living with chronic hepatitis B infection decreased by a factor of 4.5.

Since 2007, very few cases of acute HBV infection have been registered in Belarus, approximately 1–2 cases among unvaccinated children aged 0–2 years. There are practically no cases of acute HBV infection among children older than 3 years.

A strong inverse correlation has been established between the incidence of acute HBV infection and the coverage of childhood HBV vaccination ($r = -0.85$; $p < 0.05$). This is consistent with data observed by other researchers in different settings. Universal childhood immunization also led to a significant decrease in the incidence of acute HBV infection in the adult population, dropping from 12.45 cases per 100 000 people in 1998 to 1.04 in 2017.

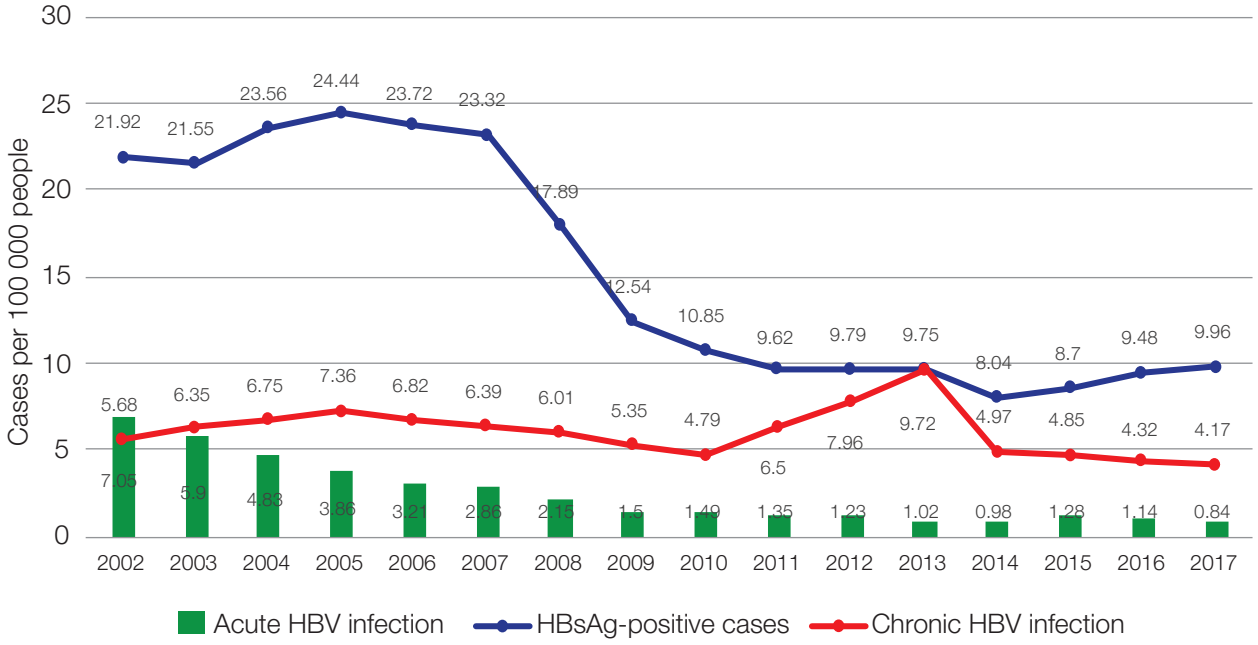
The average annual rate of decline in the incidence of acute HBV infection was –14.5% ($p < 0.05$) during 2002–2017. At the same time, there was a steep decrease in the numbers of HBsAg-positive cases, at an annual rate of –5% ($p < 0.05$) and a moderate upward trend in the incidence of chronic HBV infection (+1.5%, $p < 0.05$) (Fig. 3). This is to some extent a consequence of improved testing and diagnosis.

Fig. 2. Coverage of three-dose HBV vaccination among infants and incidence of acute HBV infection among the general population, Belarus (1996–2017)



HepB3 = Three-dose HBV vaccination.
Source: National Centre of Hygiene, Epidemiology and Public Health.

Fig. 3. Incidence of HBV infection, Belarus (2002–2017)



Source: National Centre of Hygiene, Epidemiology and Public Health.

In the past five years, adults over 30 years of age have had larger shares of acute, chronic and latent forms of HBV infection. This is most likely related to low vaccination coverage in these age groups and the year that mass immunization campaigns became available.

Sustainability

Strong and continuous political commitment in implementing and scaling up the immunization programme and promoting positive public perceptions and attitudes towards vaccines, while achieving low vaccine hesitancy and high coverage levels, indicate the sustainability of this good practice.

BELARUS State-funded hepatitis C treatment and local production of DAAs in Belarus

Strategic Direction 2 | Strategic Direction 4

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Background

The incidence of hepatitis C in Belarus is estimated at 3000 new cases every year, 90% of them occurring among the working-age population. The highest rates of new cases are found among those aged 30–39 years. During the past five years, screening coverage for hepatitis C has been significantly expanded and a steady upward trend was observed in numbers of newly diagnosed cases *(10)*.

It is estimated that 100 000 people live with chronic hepatitis C in Belarus – an estimation based on 1.3% prevalence of hepatitis C antibodies (anti-HCV) in the general population *(11)*. To date, approximately 33 000 cases of hepatitis C have been registered in the country, including 201 in children and adolescents. Liver cirrhosis due to chronic hepatitis C is the most common indication for liver transplantation in Belarus, representing 44% of all indications for liver transplantation in 2015 and 38% in 2016.

Description of the good practice

Since February 2018, patients with chronic hepatitis C have been treated with DAAs purchased from the state budget. In accordance with Ministry of Health Order No. 51 of 24 January 2018, the priority groups for treatment include: patients with liver cirrhosis and advanced fibrosis (METAVIR F3, F4), pre- and post-transplantation status, hepatocellular carcinoma, and haemophilia; PLHIV; women of childbearing age who plan to become pregnant, including through in vitro fertilization; health-care workers; and other population groups. The Ministry of Health purchased 2000 12-week treatments and distributed them among health facilities in all regions of the country.

Following the release of new WHO treatment guidelines in 2018, the national working group, supported by specialists from the WHO Regional Office for Europe and the WHO Country Office in Belarus, developed the national clinical protocol "Diagnosis and treatment of patients (adult population) with chronic viral hepatitis B and C" *(12)*. The protocol was approved by Ministry of Health Decree No. 19 of 19 March 2019 and regulates the process of diagnosis, treatment and care of patients with chronic hepatitis C.

Simultaneously, a time-bound hepatitis C treatment coverage plan for 2019–2028 was developed. In 2019, 6000 courses of the pangenotypic regimen of sofosbuvir and daclatasvir were procured from the state budget and distributed to health facilities.

Following its commitment to ensure the sustainability of state-funded hepatitis-related activities, the Government of Belarus has established local production of generic DAAs, including components of the recommended pangenotypic regimen comprising sofosbuvir and daclatasvir.

As of 1 September 2018, the cost of a 12-week treatment regimen was 1487 Belarusian roubles (approximately US$ 706). The Ministry of Health continues to work to further reduce the cost of the treatment in close cooperation with the pharmaceutical industry, representatives of patient organizations, infectious diseases specialists and international partners.

This collective work coordinated by the Ministry of Health will assist in improving the efficacy of public spending related to viral hepatitis and ensure the sustainability of the national strategy.

In November 2018, Belarus hosted the Eastern Europe and Central Asia (EECA) Second Regional Consultation on Expanding Access to Affordable and Quality Assured Medicines and Diagnostic Technologies. During the meeting, Belarus, among other countries, committed to make continued use of the best global and regional practices and tools to ensure the quality, safety and efficacy of essential HIV, tuberculosis (TB) and hepatitis C medicines and diagnostics and, at the same time, reduce their prices.

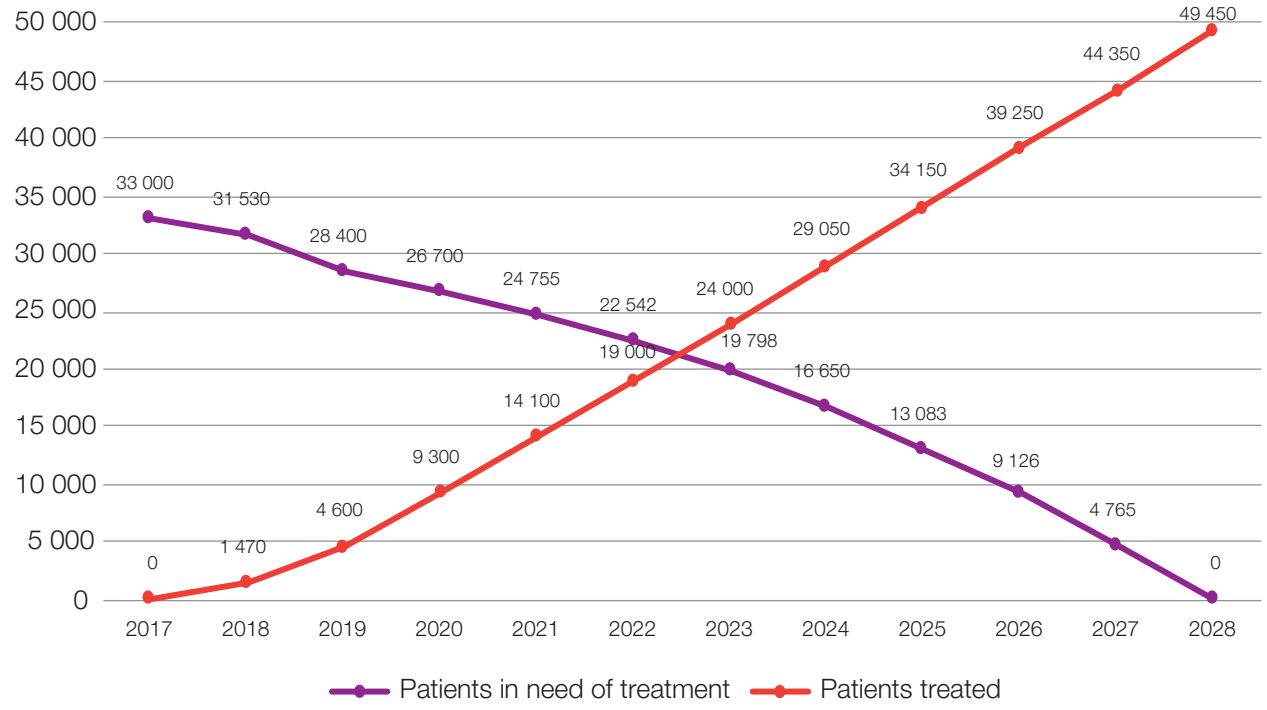
Evidence of impact

Among 6074 patients treated in 2018–2019 with known treatment outcomes, 6062 (99.8%) had successful treatment. Additional enrolment of patients for hepatitis C treatment will contribute to the effective implementation of the national strategy for elimination of hepatitis C as a public health threat by 2028 (Fig. 4) *(13)*.

Sustainability

The Ministry of Health has shown strong political commitment to ensuring access to highly effective hepatitis C treatment and to supporting local manufacturers. This has enabled the national production of DAAs and allowed more people with chronic hepatitis C infection to receive the required treatment and care, while safeguarding the interests of the national pharmaceutical industry and significantly reducing the financial burden of viral hepatitis on the health system.

Fig. 4. Planned patients treated and patients in need of treatment with DAAs, Belarus (2017–2028)



Source: Ministry of Health of the Republic of Belarus.

BELGIUM The Antwerp Model: an integrated multidisciplinary model of care with strong peer-support to ensure continuum of HCV care for PWID

Strategic Direction 3 | Strategic Direction 4 | Strategic Direction 5

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Background

Hepatitis C treatment has improved substantially over the last few years leading to highly successful, shorter regimens, better tolerated by patients, with minor side-effects. In addition to these significant changes, people with a history of injecting drug use can be treated as easily as any other person living with hepatitis C. Yet, there is a need to improve linkage to care for hepatitis C for this population group.

Free Clinic, a harm reduction service provider based in Antwerp, started an intensive collaboration with Ziekenhuis Netwerk Antwerpen (ZNA) to apply a comprehensive approach for hepatitis C case management for people who use drugs (PWUD), dubbed the Antwerp Model, assisted by the peer-support programme of the C-Buddies project.

Description of the good practice

The Antwerp Model aims to enhance hepatitis C testing, linkage to care and treatment uptake through: (i) screening with anti-HCV rapid diagnostic tests (RDTs) and off-site confirmatory tests for viraemic infection; (ii) integrated hepatitis C treatment and care delivered by professionals in a low-threshold harm reduction setting; (iii) community-based nurse-led evaluation, and information, education and counselling (IEC); (iv) timely referral to hepatitis specialists when needed; (v) non-invasive assessment of liver fibrosis with transient elastography; and (vi) continuous peer support for IEC, scheduling appointments, follow-up of special situations, tracing of patients referred to other services, home visits and patient navigation at the hospital.

The Antwerp Model is based on four main pillars: (i) the NGO, Free Clinic providing pre-test counselling, testing, IEC, referral, comprehensive follow-up and the opportunity to talk about safer drug use; (ii) established needle and syringe programmes (NSPs), distribution of injection equipment and referral to care; (iii) ZNA specialists assisting with additional testing, staging, referral, treatment and follow-up; (iv) the C-Buddies project providing peer support through the continuum of care. The model of care is highly flexible and can be quickly adapted to the needs of users and partners. The teams are trained to be streetwise in their actions.

C-Buddies project peers establish first contact with PWUD in hotspots, homeless shelters and other low-threshold facilities. They can deliver hepatitis C screening on site and on demand, assist PWUD to come to appointments and remind them by using text messages.

All PWUD who come to appointments with the hepatology specialist are welcomed at the entrance of the hospital and assisted in the navigation by a peer. In the case of absentees and exceptional situations, both the hepatology specialist and peer always work together to devise creative solutions, considering social determinants of health and the fact that people may not be ready for abstinence from alcohol and drugs.

Evidence of impact

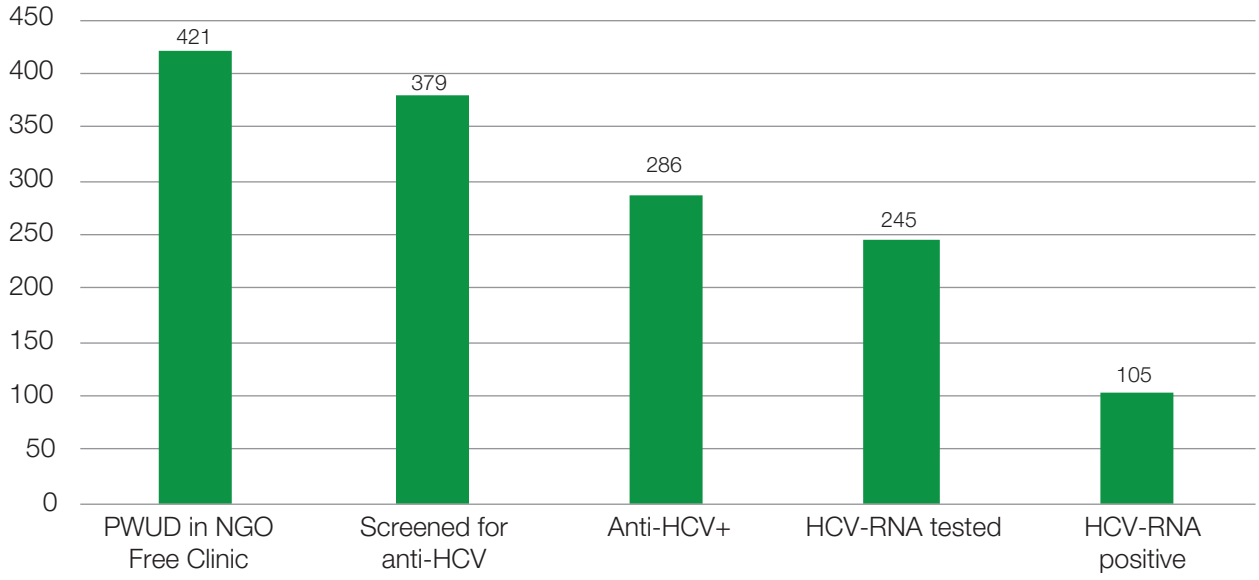
In 2017, approximately 90% of PWUD assisted by this model were successfully screened for hepatitis C, with diagnosis being confirmed in 105/245 of them (Fig. 5). In 2018, approximately 130 PWUD benefited from these testing activities. The reimbursement of hepatitis C treatment with DAAs to those with social security numbers was implemented in 2019 and improvements in treatment uptake are expected in the near future.

Thanks to the Antwerp Model and the C-Buddies system, the most vulnerable population group has improved access to hepatitis C diagnosis and the continuum of care.

Sustainability

Free Clinic and C-Buddies receive funds from the Flemish government through the Health Promotion in Injecting Drug Use programme (Gezondheidspromotie bij Injecteren Gebruik) with funding secured for activities until 2023. C-Buddies activities have been recognized by the Flemish Parliament *(14)*. An expansion of the services in the Flemish region is planned for the future, with a pilot project already conducted in Sint Niklaas in 2018. The team contacted treatment and care services, reached out to PWUD, provided RDTs and referral to a local hepatology specialist and even initiated some treatments. Other initiatives include the creation of ExpertC centres in every Flemish region and support for local initiatives, development of the cascades of care and improvement of the provision of strategic information and the overall continuum of care.

Fig. 5. Cascade of care for PWUD at Free Clinic, numbers tested for hepatitis C and supported by peers from the C-Buddies project, Antwerp (2017)



Source: Authors.

CROATIA Mobile InfoHep Centre – mobile clinic

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 5

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Background

The prevalence of HCV infection in Croatia has been estimated at 0.9% or approximately 40 000 people at risk of liver cirrhosis, hepatocellular carcinoma (HCC) and liver failure *(15,16,17)*. Approximately 200 newly diagnosed cases of hepatitis C are officially reported in the country every year. All newly diagnosed cases are reported to the National Public Health Information System (Nacionalni javnozdravstveni informacijski sustav, NAJS) of the Croatian Institute of Public Health (CIPH).

Testing for HCV infection in key populations and those subject to geographical barriers is still insufficient and the quality of medical records on diagnosis of hepatitis C and aetiology of liver cirrhosis and primary liver cancer prevents a more comprehensive understanding of the burden of the disease.

Regarding follow-up and treatment, liver elastography and DAAs have already been introduced and have since become the standard for treatment and care of chronic HCV infection in Croatia *(18)*. Yet, the underreporting of new cases, particularly in rural areas, results in significant delays in the lead time between request for antiviral treatment and treatment initiation, negatively affecting the lives of patients.

Historical events, a large proportion of the population living in rural settings and unique terrain, with islands and isolated villages, are some of the reasons for the low number of patients reported. Stigma and discrimination can also negatively affect access to health services, including specialized care, and the low awareness of viral hepatitis among patients and health-care workers impairs the detection of risk factors, signs and symptoms.

Description of the good practice

The Mobile InfoHep Centre (MIHC) stands as the most complete service for linkage to care for viral hepatitis in Croatia. Created in 2014 and implemented in 2015, the MIHC is a mobile clinic with medical staff and volunteers that is also fully equipped with state-of-the-art health services for diagnosis of viral hepatitis. The unit is a development of the InfoHep Centre, launched in 2007 thanks to the enthusiasm of a few highly motivated people from different sectors, dedicated to testing, consultations and legal support for beneficiaries in Split, Croatia.

The MIHC provides excellent medical care for patients throughout the country and has been praised by many, including the government, health providers, academia, civil society and key populations.

Mobility enables the delivery of treatment and care to key populations and people facing barriers in access to health, including transportation and geography – this includes people in prisons and closed settings, homeless people, war veterans, people living on islands, rural communities and those recovering from substance use disorder. The unit provides direct contact between the newly diagnosed patient and assigned physicians, and promotes delivery of equity in access to social and health services.

Equipped with liver elastography, the MIHC has been requested by small communities throughout Croatia, and neighbouring countries. The model is innovative and has brought together government, the private sector and civil society. Some of the collaborations include working with the Ministry of Justice to test people in prisons, coordinating public health activities with war veterans' associations, health promotion and prevention of viral hepatitis in schools, and promoting awareness and empathy in health-care settings to address stigma and discrimination experienced by patients.

The MIHC offers:

- free and anonymous HCV and HIV testing;
- IEC for patients, family and loved ones;

- free liver elastography tests;
- health education for health-care workers (e.g. general practitioners and nurses) with lectures, presentations and/or brochures.

All activities are performed in collaboration with local public health experts, civil society organizations and treating physicians from local or regional hospitals.

The following protocol is in place:

- Local civil society organizations are responsible for contact with the local target population and other logistics.
- Local public health doctors focus on testing and counselling and work together with the team of experts in the mobile unit and with local clinicians in the setup of lectures for local health care workers.
- Local clinicians interview and examine patients in the mobile clinic and perform liver elastography if needed.
- Based on the results of medical evaluations, patients are linked to care with appointments scheduled in few days or in the upcoming week to set up any additional steps.

Evidence of impact

According to the Croatian Bureau of Statistics, approximately 10% of the Croatian population resides in Split-Dalmatia County *(19)*. During 2010–2015, prior to the implementation of the MIHC, the county recorded 24–46 newly reported cases of HCV infection, 10–20% of the total number of cases reported in Croatia.

After the implementation of the MIHC, both the number of newly diagnosed HCV infections in Split-Dalmatia County and patients treated for hepatitis C in Croatia increased, with the proportion of patients newly diagnosed in Split-Dalmatia County leaping from 16.5% in 2014 to 48.8% in 2018 (Table 2).

This significant increase in case-finding for Split-Dalmatia County shows the success of the good practice and enables the MIHC and team of experts to promote and implement activities throughout Croatia and neighbouring countries.

As of 2019, of 1870 people tested, 1268 were male (67.8%), 415 were 38–48 years of age (22.19%), 303 identified themselves as PWUD/PWID (16.2%) and 188 were war veterans (10.05%). Active HCV infection was diagnosed in 615 people (32.88%) (authors, unpublished data).

Among those with active HCV infection, advanced liver fibrosis (METAVIR F3/F4) was detected in 182 patients submitted to medical examination (25.59%). These patients were immediately referred for antiviral treatment. Advanced liver fibrosis unrelated to HCV infection was detected in 11.89% of people tested, and medical treatment in accordance with WHO guidelines was recommended.

Table 2. Incidence of HCV infection and patients treated for hepatitis C in Croatia (2012–2018)

Year	Reported newly diagnosed HCV infection		Patients treated for hepatitis C in Croatia
	Split-Dalmatia County (%)	Croatia (total)	
2012	39 (22.80)	171	-
2013	39 (19.30)	202	-
2014	24 (16.50)	145	150
2015	42 (27.30)	154	150
2016	96 (52.17)	184	300
2017	96 (45.28)	212	350
2018	102 (48.80)	209	440

Source: Authors.

Based on the excellent results in increasing diagnosis and treatment in Split-Dalmatia County, and the overwhelmingly positive response from beneficiaries, the media, health-care workers and the general public, it is accurate to describe the mobile clinic as a successful initiative of great potential in the response to viral hepatitis, the delivery of equity in access to health, and the fight against stigma and discrimination.

Sustainability

The successful implementation of the MIHC in Split-Dalmatia County, the experience acquired and lessons learned have enabled the extension of the mobile clinic approach to the other parts of Croatia and neighbouring countries, reaching as many patients as possible, linking them to care and scaling-up the response to viral hepatitis.

The CIPH developed a project plan for the mobile clinic which focuses on areas where social-health services and support are inadequate and strategic information regarding key populations is insufficient (e.g. rural, remote or isolated areas, such as Dalmatian hills, and Slavonian villages and islands).

The network of partners, beneficiaries, stakeholders and donors, and the optimization of local resources, be they financial or human, are essential to the long-term sustainability of the project. The pharmaceutical industry provides part of the financial support necessary to maintain the good practice.

CROATIA National coordination, local implementation and scale-up of needle and syringe programmes in Croatia

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 4

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Background

The prevalence of hepatitis C in the general population in Croatia is relatively low. However, the prevalence among PWID is high – with proportion of individuals testing anti-HCV positive as high as 44.7% in a respondent-driven sampling survey conducted Rijeka, Split and Zagreb during 2014–2015 *(20)*. A capture-recapture study performed in 2010 indicated that Croatia had 10 726 opioid users *(21)*.

NSPs were introduced in Croatia in 1996 *(22)* and have since been implemented by NGOs at the local level, funded by national and local authorities *(23)*. NSPs have been integrated into national public health and strategic documents *(24,25)* and are coordinated by NGOs specialized in prevention and outreach.

It is important that NSPs have shared standards – including a system of codes and protocols for clients, and uniform reporting mechanisms to donors – and exchange information on gaps and geographical barriers to improve the coverage of services throughout Croatia.

Description of the good practice

Harm reduction services, including NSPs, were introduced in Croatia in 1996, with an increase in political support and recognition from the Croatian Parliament *(26)*. The NGO "Help" implemented the first NSP in Split with financial support from the Open Society Foundations.

During 1996–2003, civil society organizations expanded their activities to include harm reduction and NSPs, and implemented these initiatives in larger cities such as Pula, Zadar and Zagreb in 1998. Financial support was provided by the Global Fund to Fight AIDS, TB and Malaria during 2003–2006, and eventually harm reduction and NSPs fully transitioned to domestic funding – securing sustainability and even scaling up activities in some established services.

In 2015, technical guidelines on harm reduction were introduced to ensure high standards and the safety of clients. Today, NSPs are regularly implemented by seven NGOs in 102 geographic locations (6 fixed sites,

41 sites attended by outreach workers and 55 sites attended by mobile units).

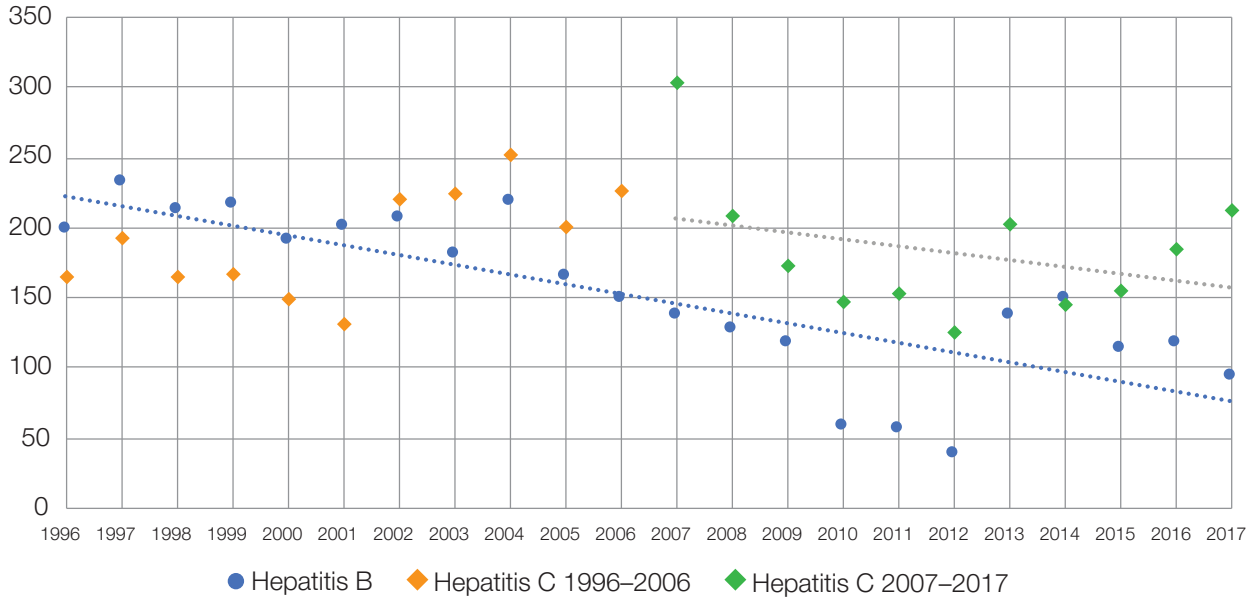
It is estimated that 5000 PWUD are reached by these services on a regular basis. Approximately 245 000 syringes were distributed in 2017 *(27)*.

Evidence of impact

The incidence of hepatitis B has been decreasing since 1996, and the incidence of hepatitis C has been decreasing since 2007, reaching an average of 165 new cases per year in the last decade *(28,29,30,31)* (Fig. 6). During the first half of 2019, 26 cases of hepatitis B and 74 of hepatitis C were registered.

The decline in the number of cases of hepatitis B and C in Croatia can be attributed to improvements in prevention, including successful implementation of NSPs, with a smooth transition to domestic funding, continuous provision of IEC and support to PWUD.

Fig. 6. Number of new cases of hepatitis B and C, Croatia (1996–2017)



Source: Croatian Institute of Public Health (CIPH).

The significant experience acquired in the response to HIV and the financial support provided by the Global Fund have contributed to this success; however, there is still room for improvement, such as better coordination of civil society organizations with local hospitals that treat hepatitis C.

In Croatia, harm reduction services give out needles and syringes and other injecting paraphernalia and equipment, and offer voluntary, anonymous and free-of-charge counselling and testing. About 5000 PWUD are reached by these services on a regular basis. The programmes also print and distribute information material about safer drug use. In recent years, they have contributed to the prevention of overdoses and have focused on the reduction of other health-related risks among their clients. In 2017, six NGO-run harm reduction programmes distributed around 245 000 syringes, with the majority given out by the NGO "Help" *(32)*.

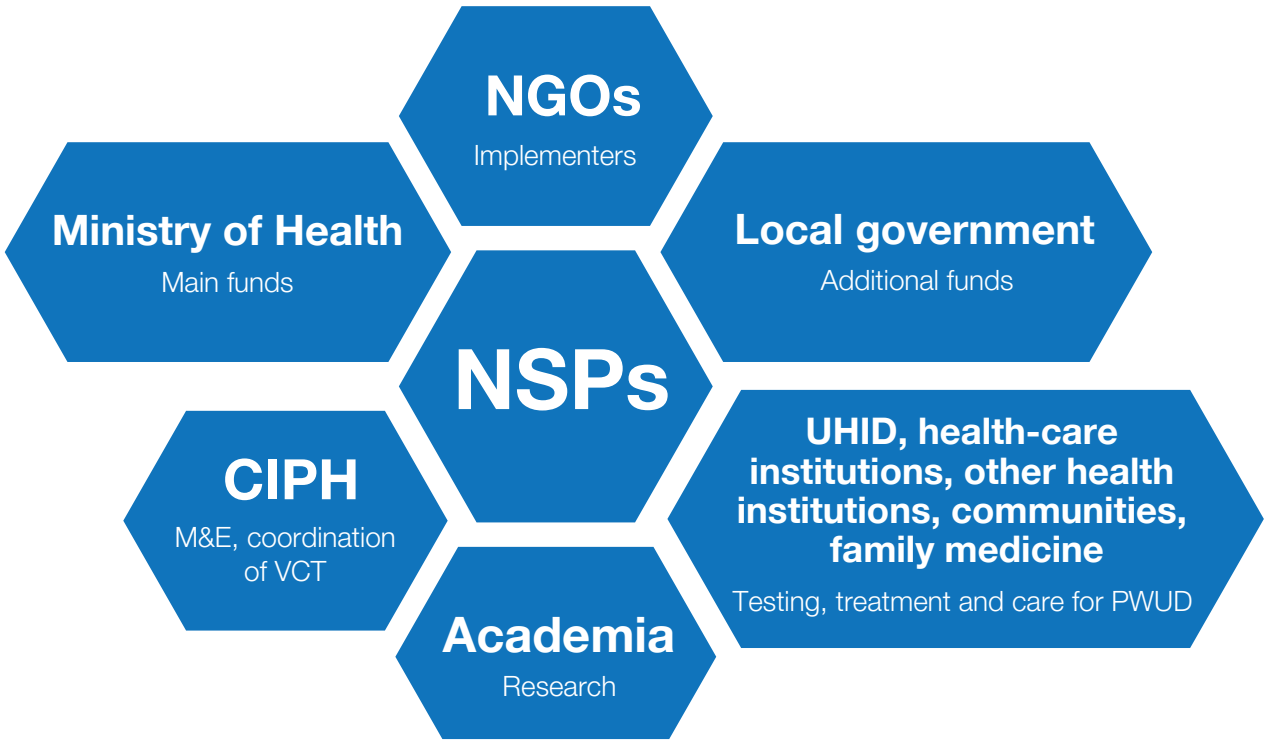
Good practice in the viral hepatitis response has also set standards for effective collaboration in prevention of other diseases and in other areas of work – including networking, monitoring and evaluation by public health authorities, and reporting to international treaties – inspiring stakeholders to come together, forging a greater team and bringing good results to the national level.

Sustainability

Collaboration

NSPs are conducted and supported technically and financially through synergistic collaboration between NGOs, the Ministry of Health, local government, academia, the CIPH, the University Hospital for Infectious Diseases "Dr Fran Mihaljević" (UHID), national health institutions, other health-care institutions, communities and family medicine clinics (Fig. 7).

Fig. 7. Synergistic collaboration in NSPs in Croatia



M&E = monitoring and evaluation.
Source: Authors.

Stakeholders meet every year for team building and to exchange information and enhance cooperation. A national mailing list is also in place.

Funding

The Croatian model has set calls for proposals for NSPs for three-year periods, guaranteeing NGOs that programmes will be financially secure and easing the burden of continuous applications for financial support, though agreements must be signed every year after submitting financial and descriptive reports to the Ministry of Health.

The financial resources are placed under the "Prevention, early detection, treatment, rehabilitation and harm reduction" portion of the state budget (Table 3).

Local authorities also provide funding for NGOs on an annual basis, and premises for drop-in centres and offices, free of charge or at low cost.

Table 3. "Prevention, early detection, treatment, rehabilitation and harm reduction" portion of the state budget, Croatia (2017–2021)

	2017	2018	2019	2020[a]	2021[a]
Croatian kuna	13 082 423	11 025 419	12 977 150	13 365 240	13 754 416
Euro	1 767.89	1 489.92	1 753.66	1 806.11	1 858.70

[a] Planned.
Source: Authors.


8
PULL DOWN FLAP
TO OPEN HOLE
TO FILL
AND VIEW WIN
FULL
BIOHAZARD
KOJAK

CROATIA Partnerships and synergy in the response to viral hepatitis in Croatia

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 5

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[3] University Hospital for Infectious Diseases "Dr Fran Mihaljević" (UHID), Zagreb
[4] City Office for Health, Zagreb

Background

Croatia has low prevalence rates for hepatitis B and C (below 1% in the general population). Epidemiological surveys in the general population have shown rates of 0.2–0.7% for HBV infection and 0.5–0.9% for anti-HCV *(33)*. These figures result in estimations of 25 000 people living with chronic hepatitis B, and up to 40 000 people living with chronic hepatitis C *(34)*, mostly unaware of their HCV status and not linked to care.

Regarding incidence, the CIPH estimated an average of 120 new cases of HBV infection and 180 new cases of HCV infection in 2015–2019. As of May 2019, 26 cases of HBV infection and 74 cases of HCV infection had been registered for that year (CIPH, unpublished data, 2020).

While the prevalence of hepatitis B in children and in the general population has been decreasing since the introduction of hepatitis B vaccination into the national immunization programme *(35)*, the prevalence rates of hepatitis B and C remain high in key populations *(36)*. Examples of such groups include PWID (29.1–65%), people in prisons (8.3–44%) and PLHIV (15%), with a range of values that far exceed those observed in the general population *(37,38,39,40,41,42,43).*

The prevention of new infections is one of the main public health challenges in Croatia. Voluntary counselling and testing (VCT) centres offer free and anonymous testing for HBV and HCV. Tests are also available through the CIPH and NGOs, covering 15 different locations throughout the country.

Despite such efforts, targeted testing for viral hepatitis remains a challenge and scale-up and outreach to key populations are needed. In order to achieve these goals, it is essential to connect with communities, strengthen prevention and awareness activities, improve linkages to care, and educate health-care workers, especially general practitioners – the first contact in the health system for many patients.

Treatments for hepatitis B and C are available in the country. Antiviral treatment with DAAs is provided through the Croatian Health Insurance Fund *(44)*. The first draft national action plan for combating viral hepatitis was developed in 2018 *(45)*.

Description of the good practice

The Croatian Association for HIV and Viral Hepatitis (CAHIV) has been successful in the development and implementation of community-based responses to viral hepatitis through collaborations with the Referral Centre for Diagnostics and Treatment of Viral Hepatitis of the Croatian Ministry of Health at the UHID, the CIPH, and the Zagreb City Office for Health.

The partnership with key stakeholders and health experts has enabled several activities in health promotion, prevention of viral hepatitis, and combating stigma and discrimination – leading to improved health and social outcomes, especially for key populations and those living with the infection.

1. CAHIV activities include the following: Community-based counselling and testing at CheckPoint Zagreb *(46)*

   Established by CAHIV in 2013, CheckPoint Zagreb offers IEC and VCT for HIV and HCV for both key populations and the general population, as well as psychosocial support, linkage to care and assistance throughout the continuum of care. Operational protocols were designed in collaboration with the UHID, with testing performed with on-site supervision by experts from both the UHID and CIPH.

2. Digital and online educational platform and mobile application *All about hepatitis (47)*

   As a means to further promote education on the risks of viral hepatitis, CAHIV introduced a new digital approach in 2017, with the development of

the portal "hepatitis.hr" and free mobile application *All about hepatitis* (*Sve o hepatitisu*). The app received professional support and was reviewed by both the CIPH and UHID.

All about hepatitis offers information on prevention, symptoms, testing and treatment of viral hepatitis. Additionally, users are given access to an interactive risk calculator for HBV and HCV infection, and recommendations on how to lower risk for viral hepatitis, which prevention services are available, where additional information and support may be sought and where to get tested. The app also features "ask the expert", a free counselling service which users may use to ask questions related to viral hepatitis.

3. Psychosocial support for people affected by viral hepatitis in community centres and health-care settings

CAHIV psychologists provide interdisciplinary care and psychosocial support to people living with hepatitis at the CAHIV centre for psychosocial support. They also help patients connect with the health system and assist them in their efforts to initiate and maintain their treatment and care. Psychological support allows true collaboration between health-care workers and the community.

4. Education for health-care workers, with events, courses and educational materials developed in collaboration with health-care institutions

Since 2014, CAHIV has organized the professional course "Chronic infectious diseases: HIV and viral hepatitis" for primary health care (PHC) and social welfare workers, in collaboration with UHID experts as lecturers. Courses are evaluated by professional bodies.

5. National health promotion campaigns

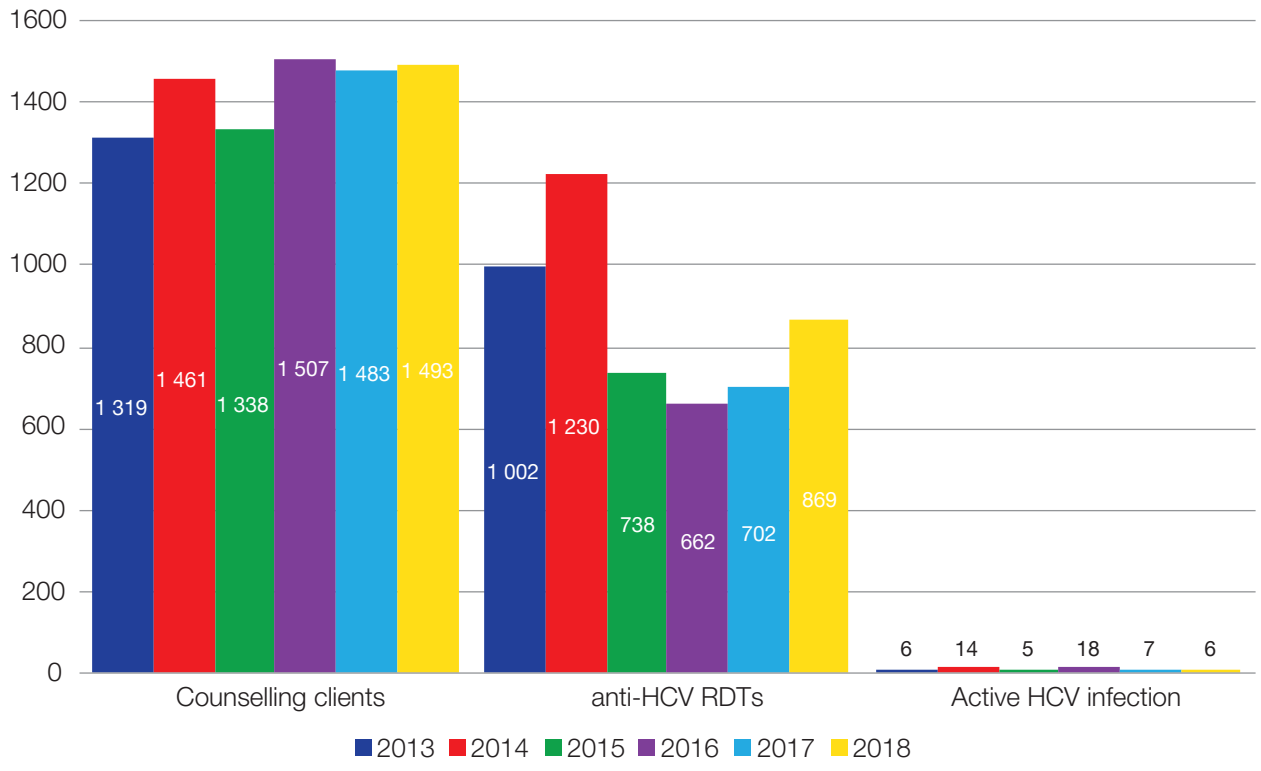
CAHIV has been conducting prevention and awareness campaigns and health promotion activities since 2013, supported by the UHID, CIPH and other stakeholders.

Evidence of impact

CheckPoint Zagreb

During 2013–2018, CheckPoint Zagreb provided counselling to 8601 people, and conducted 5203 tests for anti-HCV, with 56 cases of confirmed active HCV infection (1.08%) (Fig. 8).

Fig. 8. Counselling, rapid diagnostic tests and active HCV infection numbers at CheckPoint Zagreb (2013–2018)



Source: Authors.

All about hepatitis

The mobile application *All about hepatitis* is at the centre of public health campaigns and effectively attracts public interest. The mobile application and the portal "hepatitis.hr" were implemented in June 2017. In 2017–2018 the app was downloaded 692 times and recorded 13 242 screen views; (by the end of 2019 it had been downloaded more than 1000 times). In the same period, the portal "hepatitis.hr" was visited 33 727 times, with 86 008 views. Another application, *Sexual health* (*Spolno zdravlje*), and the related portal "spolnozdravlje.hr", also cover viral hepatitis. *Sexual health* has the option of making inquiries, and has many more downloads and screen views as it is intended for the general public. *All about hepatitis* and "hepatitis.hr" are more specific, and so naturally receive more inquiries about viral hepatitis and related concerns. The risk calculator and "ask the-expert" features were the most popular tools used. In combination these apps are making a big impact, reaching many people.

Psychological support

In 2018, CAHIV psychologists and health-care experts received and replied to more than 1000 inquiries and attended to 814 people. The CAHIV psychologist team had 1441 individual counselling sessions, including by phone, online and face to face.

Education for health-care workers

CAHIV organized seven courses for health-care workers, reaching hundreds of professionals in the country. In collaboration with the UHID, CAHIV launched the *Guide for early detection of HCV* for health-care workers *(48)*. The material includes recommendations for risk assessment, clinical features of hepatitis C, and testing guidelines. In 2018, the guide was distributed at most relevant events, with 2000 copies handed out to physicians.

National health promotion campaigns

CAHIV has organized national campaigns since 2012, progressively reaching out to key populations and the general population, and improving visibility and awareness for viral hepatitis. Printed materials are available for download at the CAHIV portal *(49)*.

Sustainability

The sustainability of CAHIV activities is guaranteed by mutual trust, effective communication and transparency with its partners, including CAHIV sponsors.

Sponsors recognize the importance and success of CAHIV work and have continuously supported the association, so it can continue to connect community and health-care services, fight stigma and discrimination, and assist in the response to viral hepatitis in Croatia.

GEORGIA HCV core antigen testing and improved access to diagnosis in Georgia

Strategic Direction 2 | Strategic Direction 5

Alkhazashvili, Maia[1] | Chitadze, Nazibrola[1] | Chanturia, Gvantsa[1] | Sukhiashvili, Roena[1] | Imnadze, Paata[1] | Gamkrelidze, Amiran[1]
[1] National Center for Disease Control and Public Health (NCDC), Tbilisi

Background

According to the seroprevalence study on viral hepatitis in Georgia undertaken in 2015, national anti-HCV prevalence is estimated at 7.7% *(50)*, resulting in approximately 200 000 people in need of confirmatory tests for hepatitis C in the country.

However, a significant number of patients did not have access to nucleic acid amplification tests (NATs) as the test was not fully covered by the national hepatitis C elimination programme at the time of the seroprevalence survey, with out-of-pocket payments of 30% for key populations (33 Georgian lari (GEL)) and 70% for the general population (77 GEL).

In December 2017, the government of Georgia approved HCV core antigen (HCVcAg) testing as an alternative to the NAT, and made all diagnostic services from autonomous laboratory service providers free

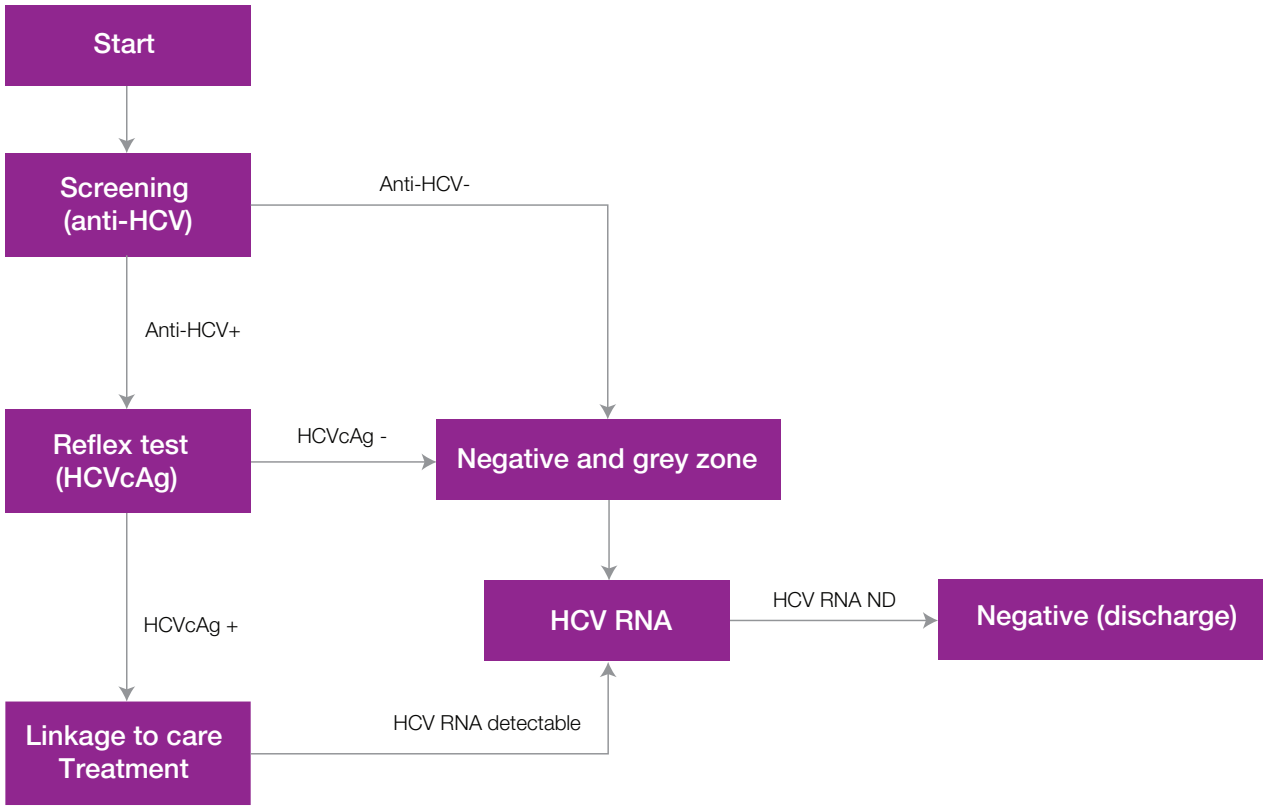
of charge to patients, reimbursing them through the Social Services Agency.

Description of the good practice

This project was designed to assess the feasibility of HCVcAg as a cost-effective and productive alternative to the NAT in diagnosis and medical follow-up during hepatitis C treatment with DAAs. The project had two parts: (i) development of a new testing algorithm for hepatitis C, with reflex testing with HCVcAg for confirmation of active HCV infection (Fig. 9); and (ii) a feasibility study of the HCVcAg test as a tool for monitoring patients on treatment with DAAs.

The first part of the project involved testing 4235 serum samples obtained from sites participating in the national hepatitis C elimination programme. These included blood banks, clinics, screening centres and the premises of the Georgian Harm Reduction Network (GHRN). Samples from the national seroprevalence survey were also used.

Fig. 9. New testing algorithm for hepatitis C with reflex testing with HCVcAg for confirmation of active HCV infection



ND = not detected.
Source: Authors.

The second part of the project comprised the analysis of 976 serum samples, collected at baseline, week 4, end of treatment (EOT), and 12 weeks after treatment completion. Samples were provided by three clinics in Georgia, and the HCV RNA and genotyping tests were conducted with NATs at the clinics. Samples were also tested with HCVcAg assay at the Richard Lugar Center for Public Health Research in Tbilisi – the National Center for Disease Control and Public Health (NCDC) reference laboratory for viral hepatitis. The percentage of agreement between HCVcAg and HCV RNA was calculated based on qualitative results.

Since January 2018, the Richard Lugar Center for Public Health Research and the NCDC have been providing free-of-charge reflex testing with HCVcAg for all blood donors and pregnant women screened positive in state funded programmes. In March 2018, services were expanded to include people screened positive at NCDC laboratory sites and inpatients. Hospitals were

responsible for reporting screening within 24 hours of service provision and sample collection.

Evidence of impact

The new algorithm for reflex testing with HCVcAg, for confirmation of active infection in patients tested positive for anti-HCV, has been successfully developed and implemented in Georgia.

Regarding the accuracy and feasibility study, the overall agreement between HCVcAg and HCV RNA test results was 97.7% (1258/1284), except for 10 samples that fell into the grey zone. In the case of smaller samples in the grey zone, the test was not performed and was reported as indeterminate. The agreement between HCVcAg and HCV RNA test results was 98.3% (414/421) at pre-treatment, 96.5% (334/346) at week 4, 98.9% (186/188) at EOT and 100% (21/21) at 12 weeks after treatment completion.

The findings suggest that the HCVcAg test could be used as an alternative to the NAT as a confirmatory test for active HCV infection among people who previously tested positive for anti-HCV and for the follow-up of treatment with DAAs.

From December 2017 to August 2019, more than 24 000 people received HCVcAg testing – an average of 1153 tests per month (Fig. 10). The median age was 52 (interquartile range 41–64) and the majority were male (n=16 240; 67.1%). Overall, 72.9% of HCVcAg tests were positive, resulting in the identification of 17 638 people in need of hepatitis C treatment.

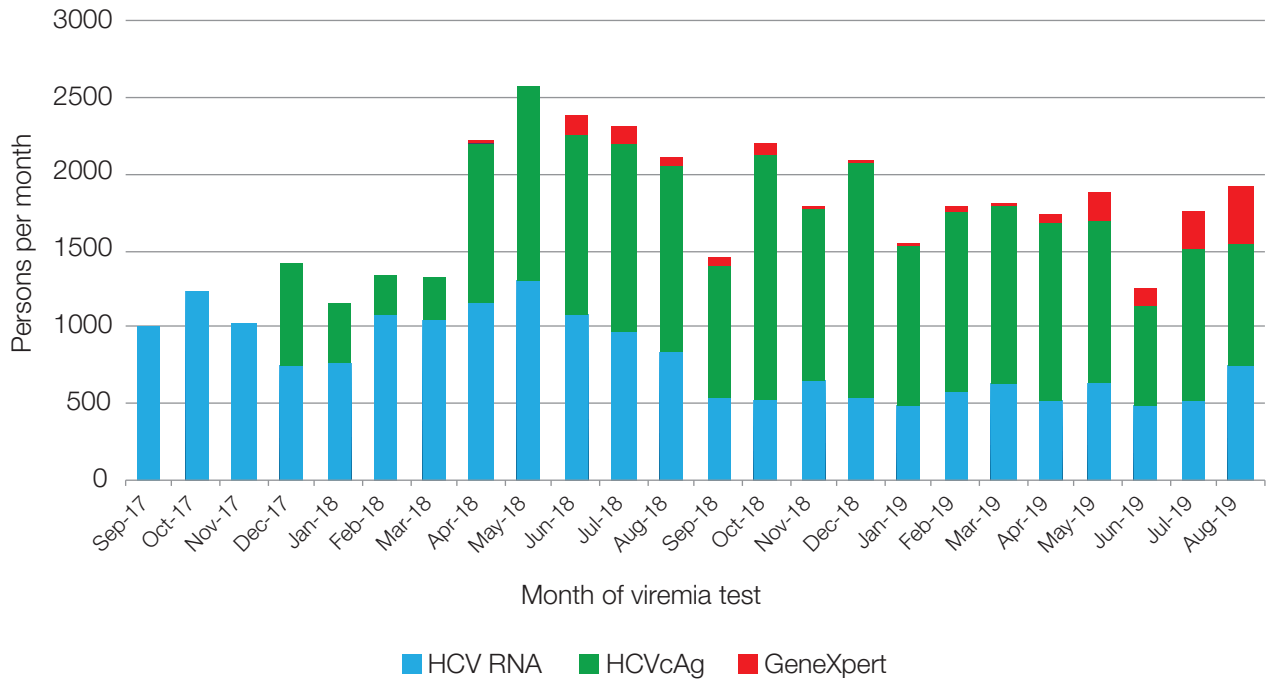
After the introduction of HCVcAg testing among the hospitalized patients, the average number of tests per month increased, eventually reaching 1897 tests per month during March 2018–August 2019.

HCVcAg testing helped to identify greater numbers of people with active infection; however, one unintended effect was that treatment initiation rates among those identified with active infection decreased *(51)*.

Sustainability

The introduction of free-of-charge tests with the innovative algorithm for HCVcAg reflex testing in hospitals, antenatal clinics and blood banks has improved the numbers of people diagnosed in Georgia, although funds are still required to ensure the sustainability of the good practice. Nevertheless, Georgia remains steadfastly committed to the elimination of hepatitis C.

Fig. 10. Confirmatory testing for HCV infection, Georgia (September 2017–August 2019)



Source: NCDC.

GEORGIA Hepatitis C treatment integrated into harm reduction services in Georgia

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 5

Butsashvili, Maia[1] | Kajaia, Maia[2] | Averhoff, Francisco[2] | Nasrullah, Muazzam[2] | Shadaker, Shaun[2] | Gamkrelidze, Amiran[3] | Tsereteli, Maia[3] | Gvinjilia, Lia[4] | Kuchuloria, Tinatin[4] | Tskhomelidze, Irine[4] | Gogia, Marine[5] | Kamkamidze, George[6]

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[4] Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET), Tbilisi
[5] Georgian Harm Reduction Network, Tbilisi
[6] Clinic Neolab, Tbilisi

Background

Georgia has a high burden of hepatitis C, with a prevalence of anti-HCV of 7.7% and active HCV infection of 5.4% among adults. PWID account for the largest proportion of people living with HCV infection, with an estimated HCV prevalence of 63.2%, according to integrated biological and behavioural surveys performed in 2017 *(52)*.

In 2015, the Ministry of Internally Displaced Persons from the Occupied Territories, Labour, Health and Social Affairs (Ministry of Health) of Georgia, supported by technical assistance from the United States Centers for Disease Control and Prevention (US CDC), implemented a national HCV elimination programme, focusing on case detection, treatment with DAAs and reducing prevalence of HCV infection *(53)*.

Initially, policy-makers and health-care workers had concerns about potentially lower rates of treatment compliance among PWID, possibly resulting in SVR rates inferior to those reported in the general population. These incorrect assumptions were rapidly dismissed once no significant difference was observed between the SVR rates of the two groups *(54)*.

The integration of hepatitis C treatment services into harm reduction facilities could potentially improve the enrolment of PWID with active HCV infection in the elimination programme – accelerating the response. Therefore, in 2018, the Ministry of Health established a working group for decentralization of hepatitis C treatment services among PHC facilities and harm reduction centres.

Description of the good practice

Four harm reduction centres were selected to implement integrated hepatitis C treatment and care: an opioid substitution therapy (OST) centre in Tbilisi and three NSP centres, in Tbilisi, Zugdidi, and Batumi. These three NSP sites continuously perform HCV serology testing with RDTs and confirmation of active HCV infection using NAT for HCV RNA on site (GeneXpert®).

The simplified laboratory testing algorithm implemented at the selected sites required fewer baseline and monitoring investigations, and follow-up visits to the treatment sites.

This pilot project received funds from the Task Force for Global Health, the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) and US CDC.

Health-care workers and patients were surveyed at the four selected sites to assess the effectiveness of integrated hepatitis C treatment at harm reduction centres. The survey included analysis of acceptability (providers) and satisfaction (patients) regarding the integrated care services.

Evidence of impact

The most significant challenges during the implementation of the project were the regulatory procedures required by the Ministry of Health to register harm reduction centres as hepatitis C treatment providers. A simplified procedure could be useful in the expansion of integrated treatment.

Overall, 62 staff members of harm reduction services were surveyed. Most respondents were supportive of hepatitis C treatment integrated into harm reduction centres (n=60; 96.7%) and the most common argument in favour of treatment integration was “patient/client convenience” (57/60; 95%).

The patient survey (n=146) showed that patients did not face major barriers regarding enrolment in the

national HCV elimination programme. The location of the medical facility was considered convenient by 142 patients enrolled at OST/NSP sites (97.2%) and its conditions were considered satisfactory by 144 patients (98.6%). Most patients reported a good attitude from health-care workers (>95%) and having received completely adequate information about hepatitis C treatment procedures and medications (98%). All of the surveyed beneficiaries treated at the centres reported that they would recommend others to enrol in the national HCV elimination programme.

During the first 10 months of integrated services, the four sites screened a total of 1977 beneficiaries, and performed 255 NATs for HCV RNA, with 209 positive results (82.0%). Nearly two thirds of the 385 patients evaluated for liver fibrosis had a fibrosis 4 (FIB4) score of <1.45 (n=240; 62.3%). Out of 215 patients who initiated treatment, 149 (69.3%) completed the course, 58 were referred for HCV RNA testing and 55 (94.8%) achieved a sustained virological response 12 weeks after the end of HCV treatment (SVR12).

Sustainability

Integration of hepatitis C treatment into harm reduction centres is feasible, and is highly acceptable for health-care workers and patients receiving care. The Ministry of Health is planning to further decentralize hepatitis C treatment throughout the country, ensuring the sustainability of the good practice conducted in this pilot project.

GEORGIA Integrated screening and diagnosis of HCV, HIV and TB in Georgia

Strategic Direction 2 | Strategic Direction 4 | Strategic Direction 5

Gamkrelidze, Amiran[1] | Danelia, Maka[1] | Khonelidze, Irma[1] | Stvilia, Ketevan[1] | Ruadze, Ekaterina[1] | Chikovani, Nino[1] | Turdziladze, Alexander[1] | Getia, Vladimer[1]

[1] National Center for Disease Control and Public Health (NCDC), Tbilisi

Background

Georgia has one of the highest prevalence rates for hepatitis C in the world – more than 5% of the adult population are chronically infected with HCV and two thirds of people infected with HCV are unaware of their status *(55)*.

The country also has a high incidence of TB, albeit considerably lower than in recent years: the total number of TB notifications has decreased by 41% and the number of new and relapse cases by 34% since 2012 (personal communication between the authors and National Center for Tuberculosis and Lung Diseases, 2019).

The prevalence of HIV in the country is low (0.4%) and concentrated in key populations. Yet, it has been steadily increasing in recent years. It is estimated that 40% of PLHIV in the country are unaware of their status and late presentation is the prevailing obstacle in the public health response to HIV *(56)*.

Coinfections are of special concern for Georgia. It has been identified that among PLHIV, up to 22% had active TB and 22.4–32.6% had latent TB; and among people with TB, 21% had HCV infection, significantly increasing risks for hepatotoxicity during treatments *(57)*.

Georgia is transitioning between international donors and domestic funding of the national response to HCV, TB and HIV. Therefore, the development and implementation of sustainable and people-centred models of care is a priority for the country.

The integration of the health system responses to HCV, TB and HIV and integrated testing in PHC centres represent opportunities for collaboration, coordinated efforts and synergistic results, improving system efficiencies, saving operational costs, and increasing access to health services – particularly for key populations.

Description of the good practice

Integrated testing for HCV, HIV and TB was introduced to the region of Samegrelo-Zemo Svaneti in April 2018. With a population of 330 000 people and a significant share of internally displaced people, the region has experienced significant public health challenges due to the conflict in the bordering Abkhazia region and has

the highest burden in the country of all three diseases (Table 4).

The project set an ambitious goal in 2018: to provide integrated testing to 40% of the adult population of the region, approximately 97 000 people, by the end of that year.

Table 4. Burden of HCV, HIV and TB, Samegrelo-Zemo Svaneti, Georgia (2017)

Indicators	Samegrelo-Zemo Svaneti	Georgia
Prevalence of anti-HCV (%)	11.0	7.0
Active HCV infection (%)	7.2	5.4
Prevalence of HIV (per 100 000)	251.0	132.0
Incidence of TB (per 100 000)	120.0	78.5

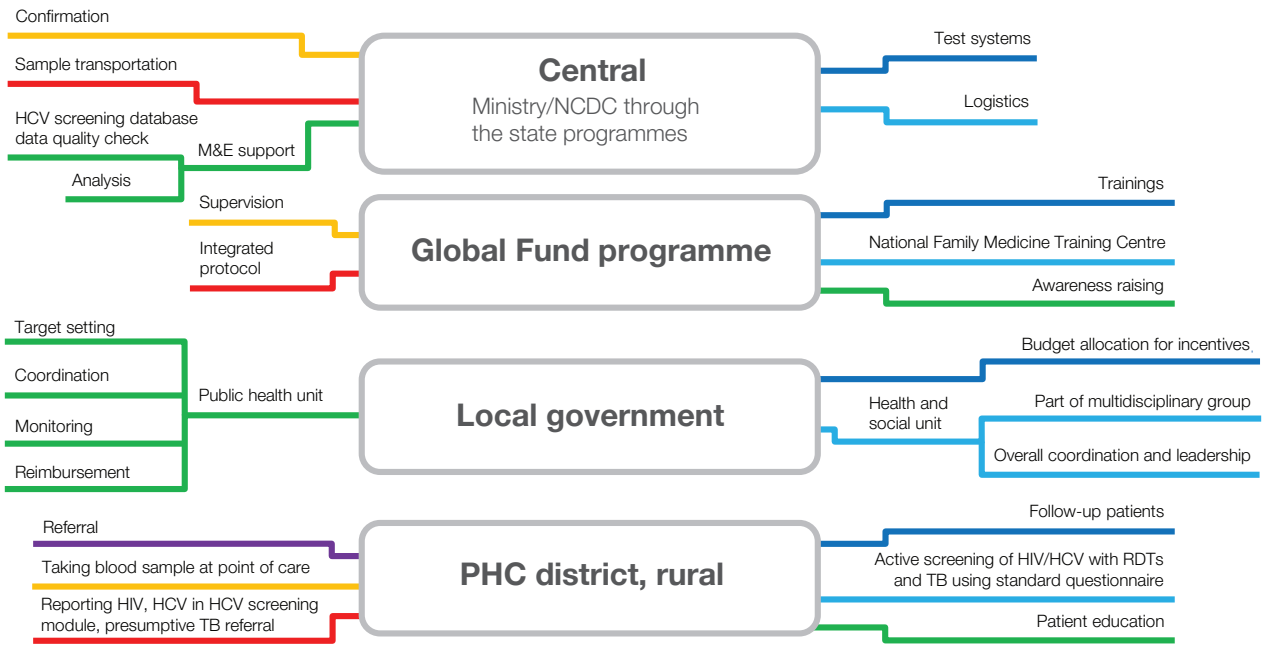
Source: NCDC.

Before the start of the programme, a regional campaign comprising advocacy, communication and social mobilization was conducted to raise awareness about HCV, HIV and TB among all relevant stakeholders. Involved parties include the Ministry of Health, the NCDC, local government, PHC providers (public and private) and civil society organizations. Memoranda of understanding (MoU) with defined roles and responsibilities were signed between the partners during September and October 2017 (Fig. 11).

The integrated screening protocol and training module were developed by the National Family Medicine Training Centre. Over 400 PHC providers in the region were trained to ensure ethical conduct and quality of diagnostic procedures, and case recording and reporting through a web-based platform. Trained PHC physicians currently provide triple screening for patients seeking care at medical facilities, and active case-finding with a door-to-door approach and reaching out to people at congregate settings and public establishments.

Supervision and additional support was provided by the National Family Medicine Training Centre. A questionnaire on TB signs and symptoms and risks has been used for identification of presumptive TB cases.

Fig. 11. Partner roles and responsibilities



Source: Authors.

Presumptive TB or diagnosed TB cases are referred to specialized clinics for further diagnosis and care.

A regional steering committee was established to improve advocacy and to lead the implementation of the programme. The committee was supported by the Ministry Health, the NCDC and the national TB, hepatitis C and AIDS centres.

Multidisciplinary district teams with representatives of local public health centres, government and private services were established for programme monitoring and support. The team members were trained to build monitoring capacity and raise understanding of their role and functions.

Evidence of impact

The programme enhanced public interest in testing for the three diseases, contributing to the number of people screened. Within seven months of operations, 88 178 people had been screened (exceeding the last three years combined – 58 500 people), and integrated testing was able to identify 1 277 cases of active HCV infection, 11 new cases of HIV and 22 of active TB (Table 5).

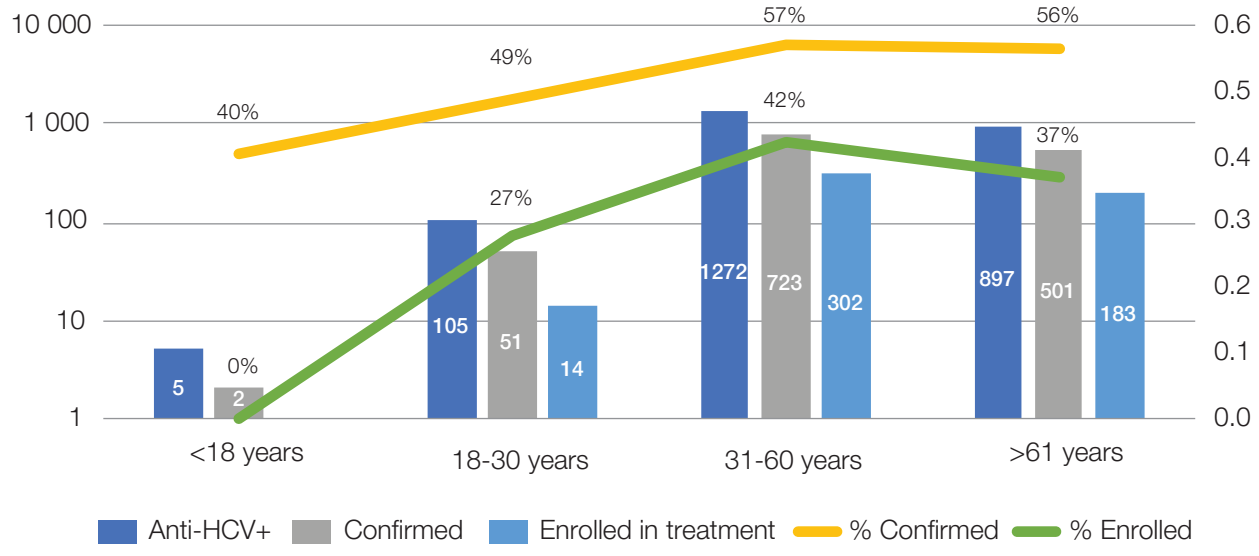
The region is on track to achieve hepatitis C elimination, likely to be the first to achieve the strategic objective of the national plan – to identify 90% of HCV-infected people by 2020 *(58)* (Fig. 12)

Table 5. Results of integrated screening and diagnosis, Samegrelo-Zemo Svaneti, Georgia (2018)

	Total (n = 88 178)	%
Anti-HCV	2 279	2.58
Active HCV infection	1 277	1.45
HIV	37	0.04
New cases of HIV	11	0.01
Presumptive TB	192	0.22
Active TB	22	0.02

Source: Authors.

Fig. 12. Hepatitis C cascade of care distributed by age groups, Samegrelo-Zemo Svaneti (April–October 2018)



Source: Authors.

The project enabled first-time partnerships between the NCDC, local government and private health service providers, promoting early diagnosis, a patient-centred approach and decentralized diagnosis to non-specialized facilities at district level.

Additionally, integrated service delivery in PHC is also useful in overcoming barriers in access to health, such as stigma and discrimination, as well as helping meet common operational requirements such as waste management, transparency and accountability.

Rejection of integrated screening and diagnosis by patients was rare.

Sustainability

The Global Fund provided the initial technical assistance for the development of the model for integrated screening and diagnosis of HCV, HIV and TB. They also supported awareness-raising and capacity-building for health providers.

Tests and supplies were provided through state programmes within the limit of the approved budget. Incentives for PHC providers were covered by the local government.

Local municipalities allocated a total of 181 000 GEL for the programme and the local government of Samegrelo-Zemo Svaneti allocated a similar amount to enable operations throughout 2019. Integrated screening and diagnosis of HCV, HIV and TB have been initiated in other regions of Georgia.

GEORGIA Integrating HCV screening and simplified treatment and care services in primary health care in Georgia

Strategic Direction 2 | Strategic Direction 4 | Strategic Direction 5

Tsertsvadze, Tengiz[1,2] | Sharvadze, Lali[1,2] | Chkhartishvili, Nikoloz[1] | Abutidze, Akaki[1,2] | Kerashvili, Vakhtang[1] | Adamia, Ekaterine[3]

[1] Infectious Diseases, AIDS and Clinical Immunology Research Centre, Tbilisi
[2] Faculty of Medicine, Ivane Javakhishvili Tbilisi State University, Tbilisi
[3] Ministry of Internally Displaced Persons from the Occupied Territories, Labour, Health and Social Affairs of Georgia, Tbilisi

Background

It is estimated that 5.4% of the adult population of Georgia are living with hepatitis C – approximately 150 300 people – the fifth largest prevalence in the world *(59)*. In the face of this public health challenge, the country substantially stepped up its efforts against hepatitis C and implemented one of the first national HCV elimination programmes in the world – launched in April 2015. The Georgian HCV elimination programme received technical assistance from the US CDC and donated DAAs from the manufacturing company *(60,61)*.

Georgia's hepatitis C elimination programme has made substantial progress since its initiation. Over the first four years, more than 77 000 people were diagnosed and more than 60 000 of them initiated antiviral treatment. Treatment was successful in 98.7% of patients assessed for SVR and in 98% of patients with advanced liver fibrosis assessed for SVR.

Despite the success of the programme, the analysis of programmatic data indicated that patients' enrolment in treatment had been slowing down since 2018, probably due to deficiencies in testing and linkage to care.

In response to this new challenge, the country implemented free-of-charge diagnosis, including all tests required during pre-treatment and follow-up, and integrated screening, treatment and care in PHC throughout the country. The decentralization of hepatitis C services to PHC is an important instrument for overcoming barriers in access to diagnosis and treatment of hepatitis C *(62,63,64,65)*.

Description of the good practice

The Ministry of Internally Displaced Persons from the Occupied Territories, Labour, Health and Social Affairs of Georgia developed a special Continuing Medical Education (CME) programme, and hepatitis C integrated model of care and guidelines for PHC physicians. The

model of care was built upon the "one-stop shop" approach – with patients receiving tests, treatment and care at PHC centres.

In June 2018, 10 PHC centres located in districts and regions with a high prevalence of HCV infection were selected to provide decentralized hepatitis C treatment and care. The centres were also chosen based on the considerable distance patients would otherwise have to travel to receive specialized services for hepatitis C.

Patients receiving care at the selected centres were offered HCV RDTs and informed that they could choose to decline or defer testing. Reflex testing and confirmatory tests were also available to assist in the diagnosis of hepatitis C.

Following confirmation of infection, patients were given information about hepatitis C and the treatment options. Patients were also offered to enrol in the Georgian HCV elimination programme, and once registered, were provided with treatment and attended by their regular PHC providers at the one of the 10 selected centres. The PHC providers had already been trained in hepatitis C treatment and care by the CME programme and were further supported through the ECHO platform, which connects local PHC physicians with specialists via video conferencing.

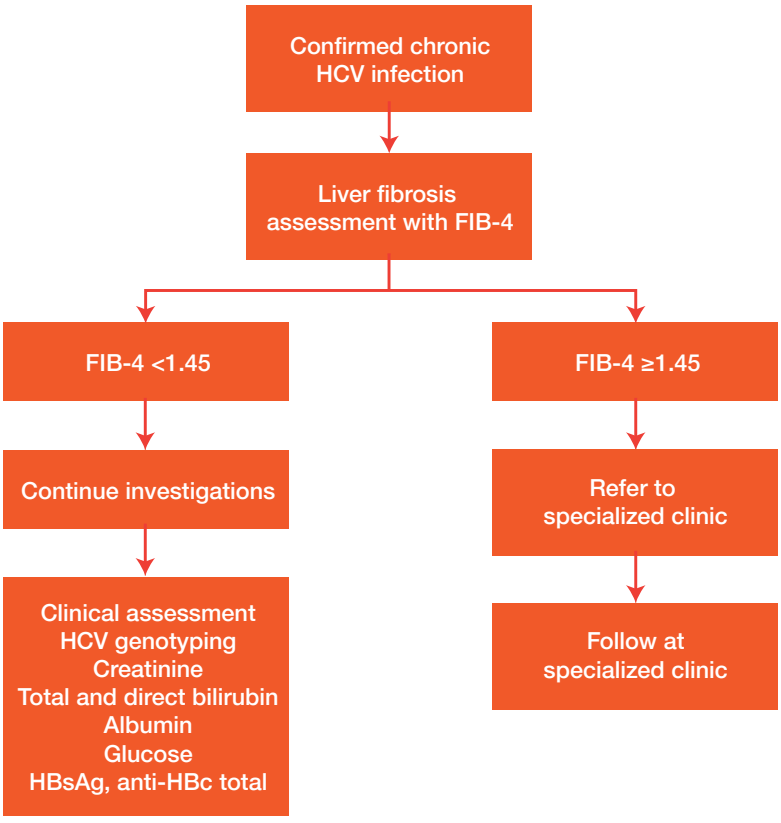
During the first phase of implementation, the PHC centres only attended to treatment-naïve patients with no or mild liver fibrosis, using simplified diagnosis and treatment monitoring algorithms. Patients with more advanced fibrosis (FIB4 >1.45) were referred to specialized clinics instead (Fig. 13).

Patients with HCV genotype 1 received ledipasvir and sofosbuvir without ribavirin, and patients with HCV genotype 2 and 3 received ledipasvir and sofosbuvir with ribavirin, until the introduction of velpatasvir and sofosbuvir in December 2018.

Once on treatment, a simplified monitoring procedure is followed:

1. Patients receive a clinical assessment by a physician and an alanine aminotransferase (ALT) test and make an appointment with a nurse every four weeks.

Fig. 13. Pre-treatment evaluation algorithm



anti-HBc = hepatitis B antibodies.
Source: Authors.

2. Patients taking ribavirin get a complete blood count every four weeks.

3. Nurses make routine phone calls to patients until the end of treatment to enable early detection of adverse events and potential drug interactions, and ensure adherence to treatment.

4. Patients receive a quantitative HCV viral load test 12 or 24 weeks after the end of treatment.

The Infectious Diseases, AIDS and Clinical Immunology Research Center together with other partners provided guidance and supervision for the implementation of the integrated model of care.

Evidence of impact

As of August 2019, a total of 941 people had received HCV-RNA or core antigen tests, with active HCV infection confirmed in 784 (83.3%). Of these, 639 (81.5%) were linked to care and tested for FIB-4, with more than two thirds (68.2%) with FIB-4 less than 1.45.

A total of 355 patients initiated antiviral treatment with DAAs (81.4%), 241 completed the treatment regimen, and 146 were eligible for SVR assessment – 108 were tested and cure was achieved in 107 of them (99.1%). These remarkable results show the feasibility and effectiveness of integrating simplified HCV diagnosis and treatment in PHC (Fig. 14).

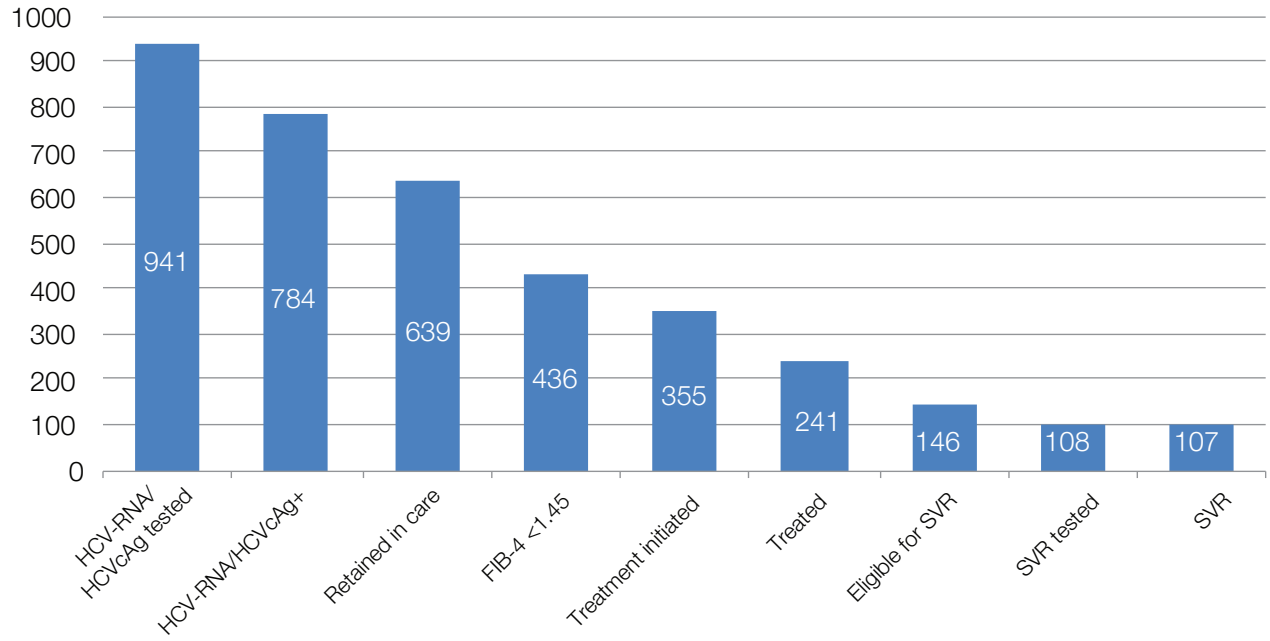
The expansion of this good practice is essential to overcome gaps in the cascade of care for hepatitis C. A full-scale decentralization and integration of hepatitis C services in PHC will significantly increase the diagnosis and linkage to care and improve treatment uptake – facilitating the goals of the Georgian HCV elimination programme.

Sustainability

The programme has received substantial government support since it was launched, and hepatitis C remains a priority for the health sector in Georgia. Strong political commitment has played a key role in the smooth implementation of the programme and its success so far.

Integrated testing, treatment and care in PHC is a cornerstone of the Georgian HCV elimination programme today, with a strong base that includes CME for PHC physicians, simplified diagnosis and treatment monitoring algorithms, and a unified web-based information system. Along with the continuing governmental commitment and productive partnerships, integrated testing, treatment and care in PHC ensures the long-term sustainability of the good practice without requiring substantial additional resources.

Fig. 14. Cascade of care for decentralized hepatitis C treatment and care in 10 PHC centres in the Georgian HCV elimination programme (2019)



Source: Authors.

GERMANY From pills to patients: how many people have been treated in Germany since the introduction of DAAs?

Strategic Direction 1 | Strategic Direction 5

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Background

The total number of people diagnosed with HCV in Germany was estimated at 160 000 in 2014 *(66)* and approximately 4500 cases are notified every year *(67)*. Prevalence is estimated to be low in the general population (0.3% anti-HCV *(68)*) and high in population groups most vulnerable, such as PWID, MSM living with HIV and migrants *(69,70,71,72,73)*. Treatments for hepatitis C with DAAs have been available in the country since 2014.

At the moment, Germany has no nationwide registry for the medical follow-up of patients with hepatitis C or nationwide registry of antiviral treatments prescribed by various private medical doctors, mainly specialists in hepatology or infectious diseases. This is a barrier to the development of the cascade of care and appropriate monitoring and evaluation of the national response.

Yet, antiviral drug prescriptions are reported by billing centres for pharmacies that cover about 99% of the nationwide pharmacy sales for all people covered by the statutory health insurance, approximately 85% of the population of Germany – representing an interesting alternative for strategic information.

Description of the good practice

Our good practice estimated the number of people treated for hepatitis C in Germany during 2014–2018 and the costs of medications for the health system, based on the data from pharmacy sales. By doing so, we were able to improve strategic information and overall progress towards elimination.

After collecting all available information, we combined prescriptions for 28 days' worth of treatment into full treatment regimens according to German clinical guidelines *(74)*. Treatment duration was determined from the German hepatitis C cohort (GECCO) data *(75,76)* and treatment recommendations *(9)*. Additional details and results of our research are available in other publications *(77)*.

We have developed a step-by-step approach for those who wish to estimate the number of people treated for hepatitis C per year based on prescriptions for DAAs identified in data from pharmacy sales:

1. Identify a source (e.g. nationwide, regional or local prescription data; cohort data; or other) that contains the prescribed or delivered medications against the infection. Determine the representativeness of the source for the country or setting to determine the proportion of those not covered by the source (used for the extrapolation in step 6).

   Important: The source must be representative for future extrapolation.

Example: Nationwide anti-HCV prescription data of individuals with statutory insurance (~85% of the German population).

2. Categorize medications in fixed-dose combination (FDC) or part of a treatment regimen with a marker substance. Determine the number of units (e.g. pills, injection-pens, packages).

   Treatment for hepatitis C with DAAs is available as a FDC or combination of antivirals taken mostly simultaneously with sofosbuvir – the marker substance in this case.

3. Determine the defined daily dose (DDD) for the drugs and apply a drug/unit-factor if necessary.

   The calculation is based on packages, with one 28-day package of DAAs combined into treatment regimens equivalent to one month's worth.

4. Choose the smallest or most useful unit of time to observe a period.

   Important: Note that the observation over time does not mean tracking the same population over time, since new people will initiate treatment and others will leave/die, significantly altering the denominator.

   DAAs have been observed quarterly or yearly since their market release in Germany in 2014.

5. Sum up and calculate the DDD for the marker substances or packages or units chosen representing people treated per day, month or other time frame.

   Sum up the 28-day packages for the regimen combinations, which results in the number of people treated in the month.

6. The proportion of people who might not be covered by the source should be added to the quantity and extrapolated.

   Important: Prescribing patterns of the source should be representative for the rest of the population.

   We only focused on the statutory health insurance system. No extrapolation was required.

7. Real world treatment data or guideline recommendations for the duration of regimens per year multiplied by the number of 28-day packages results in the number of treated individuals per year. Assuming a cure rate of ~95% results in the number of cured patients.

   Treatment duration of the different regimens was derived from real world treatment data from a German cohort of hepatitis C patients for the years 2014–2015 (9). For the year 2016–2017 treatment duration was based on recommendations for treatment of hepatitis C (9) (Table 6).

Evidence of impact

Monthly prescriptions of DAAs progressively increased during 2014–2015, reaching a peak of approximately 6600 prescriptions in March 2015. There was a significant decrease in pegylated interferon and ribavirin, and the majority of treatment regimens were sofosbuvir-based in the beginning.

After March 2015, the number of prescriptions decreased, with slight increases due to the market release of pangenotypic drugs in 2016 and 2017. In 2018, 73% of DAA prescriptions were for pangenotypic treatments, with approximately 2000 prescriptions issued every month (Fig. 15).

We estimated the approximate number of people treated with DAAs per year to be: 7000 (2014), 20 100 (2015), 13 200 (2016), 11 600 (2017) and 9900 (2018), adding up to a total of 61 800 (Table 6).

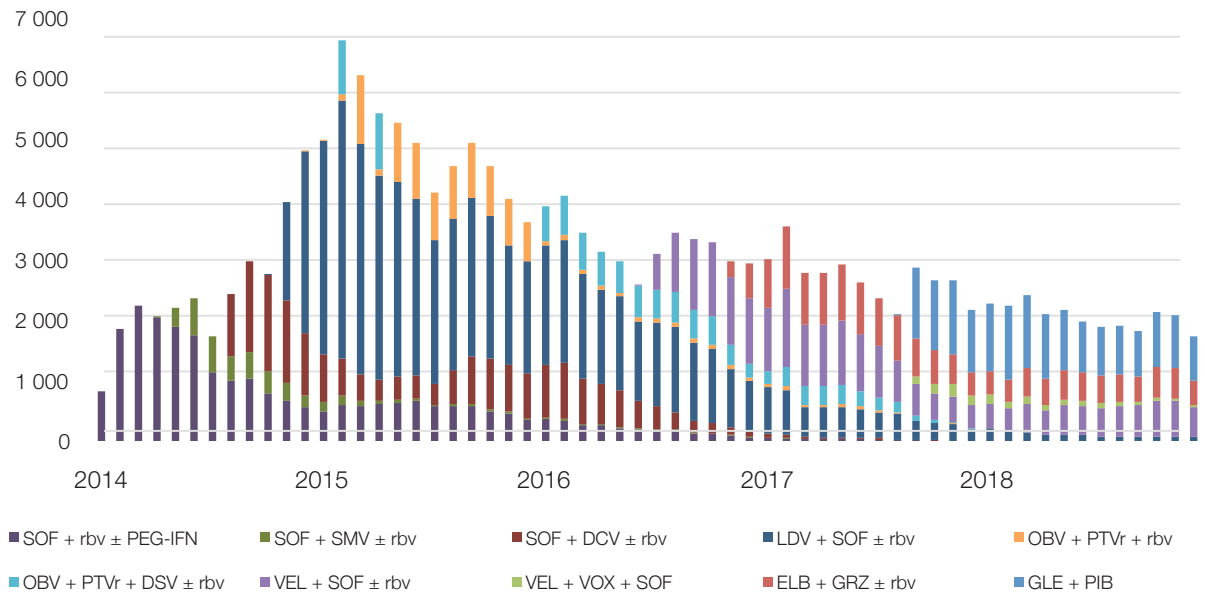
Since treatment duration has been standardized since 2017, the calculations can be based simply on treatment recommendations, without the need for real-world data on the duration of different treatment regimens. With the release of pangenotypic substances, the definition of a marker substance is also no longer needed.

Sustainability

The Robert Koch Institute is the principal German public health institute and has, among other tasks, the responsibility to monitor the viral hepatitis epidemic in Germany and to publish and report data on the WHO indicators set out in the elimination strategy. The HCV antiviral treatment numbers are estimated and published annually. The data are used to determine and initiate targeted measures for HCV prevention, testing, treatment and care in Germany.

Using the same approach, expanded to TB, HCV and HIV treatment and OST, we also published the results of a study analysing the treatment of people in prison in Germany *(78)*.

Fig. 15. Monthly prescriptions of HCV antiviral regimens (regimen months), in people with social health insurance, Germany (2014–2018)



DCV = daclatasvir; DSV = dasabuvir; ELB = elbasvir; GLE = glecaprevir; GRZ = grazoprevir; LDV = ledipasvir; OBV = ombitasvir; PEG-IFN = pegylated interferon α; PIB = pibrentasvir; PTV = paritaprevir; PTVr = paritaprevir/ritonavir; rbv = ribavirin; SMV = simeprevir; SOF = sofosbuvir; VEL = velpatasvir; VOX = voxilaprevir.
Source: Authors.

Table 6. Number of 28-day packages, mean treatment duration and number of people treated with DAAs per year, Germany (2014–2018)

Year	Number of 28 day packages	Mean treatment duration (weeks)	Estimated number of patients treated
2014	25 462	14.6[a]	7 000
2015	60 912	12.1[a]	20 100
2016	39 890	12.1	13 200
2017	32 730	11.3	11 600
2018	24 909	10.1	9 900
2014–2018	–	–	61 800

[a] Based on data of GECCO *(9,10)*.
Source: Authors

GERMANY The epidemiology of hepatitis B, C and D in Germany: a scoping review

Strategic Direction 1

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Background

Germany is considered a low prevalence country for viral hepatitis B, C and D. However, the burden of viral hepatitis may be higher among certain subpopulations.

The aim of our project was to understand the baseline epidemiological situation regarding burden of disease, sequelae and care for viral hepatitis in the context of the elimination goals set in the Global Health Sector Strategy on Viral Hepatitis *(79)*, and to identify evidence gaps and research needs for further progress in the elimination of viral hepatitis in Germany.

Description of the good practice

We performed a comprehensive scoping review of the epidemiology of hepatitis B, C and D in the general population and those at risk for viral hepatitis in Germany to understand the current evidence, describe the baseline epidemiological situation, identify evidence gaps, formulate research needs and measure progress in the elimination of viral hepatitis.

The review was prepared following the PRISMA for Scoping Reviews checklist *(80)*. A broad search string with relevant search terms was used to identify eligible studies describing the burden of disease in different outcome categories (prevalence, incidence, transmission routes, distribution of genotypes, coinfections with hepatitis viruses or HIV, quality of life, and outcome of infection) and the management of viral hepatitis (vaccination, diagnosis, therapy and liver transplantation).

We searched six online databases (Embase, PubMed, Europe PMC, Scopus, Base Bielefeld and CC Med) for original work published between January 2005 and March 2017 in English or German languages. We assessed the eligible literature and developed a matrix illustrating the available evidence by population group and outcome category, enabling us to map existing evidence and research gaps.

The broad search string allowed us to identify a large set of publications on all population groups and epidemiological topics. The collected evidence can now be used to describe the baseline epidemiological situation of viral hepatitis in Germany and guide further research. Evidence gaps have been identified and provide an opportunity for future research initiatives.

We assessed the existing body of evidence regarding several epidemiological topics relevant for the response to viral hepatitis in Germany. The broad search string was an important strength in this review, as it covered multiple research questions in one search to obtain a complete overview of available published evidence on viral hepatitis epidemiology.

The search was done in English and German languages, which was important as some key evidence for Germany is published in German language only. Population groups were not defined in the search to capture groups not previously considered. The large dataset and topics retrieved resulted in a comprehensive overview of available key data to monitor the response to viral hepatitis in Germany.

Screening and analyses of the large dataset required many resources and were time consuming. This needs to be considered by others who wish to perform such a review. If the required resources are not available, others may consider performing a narrower search with specific research questions covering some topics and/or population groups to ensure good review progress and to make it possible to complete the review well and efficiently.

It was difficult to identify all existing unpublished studies and ongoing research. Additional resources

are required for the identification and review of grey literature and this should be considered for similar reviews in the future.

Evidence of impact

The inclusion criteria were met by 104 scientific publications, covering 299 outcomes for viral hepatitis in Germany. The research revealed a good amount of evidence for prevalence of hepatitis B and C, and hepatitis B vaccination coverage, and large evidence gaps in incidence, mortality and hepatitis D (Table 7).

The evidence also varied between the different population groups. In the case of prevalence of hepatitis B and C and hepatitis B vaccination coverage, good evidence was found only for the general population and proxy populations. The evidence for the outcomes in populations at risk for viral hepatitis, such as PWID, MSM, people in prisons and closed settings, and migrants was weaker.

Outcomes on sequelae due to viral hepatitis and care were mainly covered by studies in clinical populations of people living with viral hepatitis. The proportions of people with viral hepatitis related to acute liver failure, hepatocellular carcinoma and liver transplantations were not covered by any studies in the general population or populations at risk.

For some population groups, we found significant evidence gaps in all outcome categories with few to no publications identified by our review. These groups included sex workers (not covered in any hepatitis B or C studies), people in prisons and closed settings (covered by a single study on prevalence and treatment of hepatitis C) and household contacts of people living with viral hepatitis.

Based on the results of this review, future research can be planned to fill the identified gaps in evidence. Data on the general population identified in this survey provide good baseline evidence about the epidemic but should be updated regularly to comply with monitoring and evaluation needs. The inclusion of testing for viral hepatitis in the large population-based health surveys conducted in the general population is of critical importance to monitor the progress of elimination.

Table 7. Number of identified publications/outcomes by outcome category and pathogen

	HBV	HCV	HDV
Burden of disease			
Prevalence	46/55	44/46	4/4
Incidence	4/6	7/12	0
Mortality	2/2	2/2	1/1
Genotype distribution	1/1	13/13	0
Transmission routes	7/7	14/14	1/1
Sequelae			
Acute liver failure	2/2	3/3	1/1
Liver cirrhosis	10/10	11/11	1/1
Hepatocellular carcinoma	10/11	8/9	4/6
Quality of life	2/2	1/1	0
Care			
Diagnosis	4/4	6/6	0
Therapy	9/9	16/16	1/1
Liver transplantation	3/3	2/2	1/1
Vaccination coverage	43/46	–	–

HDV = hepatitis D virus.
Source: Authors.

Despite PWID being at high risk for viral hepatitis, large evidence gaps were identified among this population. Emphasizing these research needs can impact policy change and the availability of resources for future research. A proposal has already been submitted to the Federal Ministry of Health (Bundesministerium für Gesundheit) to establish an ongoing monitoring system in low threshold services across the country to improve data collection for PWID.

Estimates for the number of people living with hepatitis B and C in the general population and populations at high risk should be performed using the workbook approach. This will allow better targeting of resources for prevention, testing and treatment for HBV and HCV infection in Germany.

Sustainability

With the developed methodology and search string, the search can be updated regularly to maintain an overview of new evidence on viral hepatitis epidemiology. The search string is reproducible and can also be adapted to a different setting and country. The data extraction form can be made available for similar reviews.

Sharing our experience and the lessons learned in mapping evidence is important. Our ideas to improve the methods may ease the process for others performing such reviews.

This best practice provided a good baseline of epidemiological data for monitoring the progress of viral hepatitis elimination in Germany, planning new research, identifying policy focus areas and targeting available financial resources.

GREECE HCV elimination in Greek prisons

Strategic Direction 2 | Strategic Direction 3

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Background

HCV prevalence in the adult population of Greece is estimated at 74 000–134 000 adults. In Greece there are approximately 3700 new infections per year, and 7 out of 10 new infections are associated with injecting drug use *(81)*.

In Greece, PWID are over-represented in prisons, due to the criminalization of minor drug offenses. While in prison, PWID continue to inject drugs and remain at risk of communicable diseases such as hepatitis C. Following their release from prison they risk transmitting the disease beyond the prison population.

According to data from the Ministry of Justice, Transparency and Human Rights, out of a total prison population of 9560 people in 2017, 2829 (29.6%) were detained for drug offenses *(82)*. This ratio is possibly an underestimation given that many PWID may have been held for other offenses which are closely related to drug use.

The Hellenic National Plan for Hepatitis C, issued in 2017, aims to improve access to prevention, counselling and support for people in prisons to reduce the incidence of hepatitis *(83)*.

Description of the good practice

In response to this scenario and the impaired access to health care and treatment experienced by people in prisons and other closed settings, the Hellenic Liver Patients Association "Prometheus" implemented a comprehensive testing and treatment programme for hepatitis C, with the aim of eliminating the infection in Greek prisons. The programme is conducted in collaboration with hepatology clinics and the prisons.

The activities of the programme include mapping, outreach and communication, logistics, rapid diagnostic testing and confirmatory testing (HCV RNA), and linkage to care for patients eligible for treatment, while implementing integrated patient health records, including treatment received, and a therapeutic registry.

The first cycle of the programme was successfully completed in Diavata Prison in Thessaloniki during 2018–2019 in collaboration with the 4th Pathology Department of Ippokrateio General Hospital. The programme was quickly implemented and covered

almost the entire prison. Despite a minor procedural issue with transfer and release of participating patients, the appropriate follow-up was conducted and linkage to care was not obstructed.

The programme coordinators are required to ensure that the participants have a social security number, the only prerequisite to accessing the National Health System in Greece.

Evidence of impact

During 5 months of operation (December 2018–April 2019), 516 RDTs for hepatitis C virus were performed, out of the total population of 553 inmates in Diavata Prison (93.3% coverage). Consent for a hepatitis C test was not given by 37 people. Among those tested, 87 individuals tested positive for anti-HCV and 61 had detectable HCV RNA.

All 61 participants with confirmed hepatitis C were linked with the hepatology clinic for medical follow-up. The referring physician registered 60 entries for antiviral treatment (1 person had already started treatment and had an existing file). The mean time from diagnosis to registry completion was approximately one month (Fig. 16). The next steps are to assess cure, defined as SVR12.

The success of this first cycle led to the expansion of the programme to three other Greek prisons.

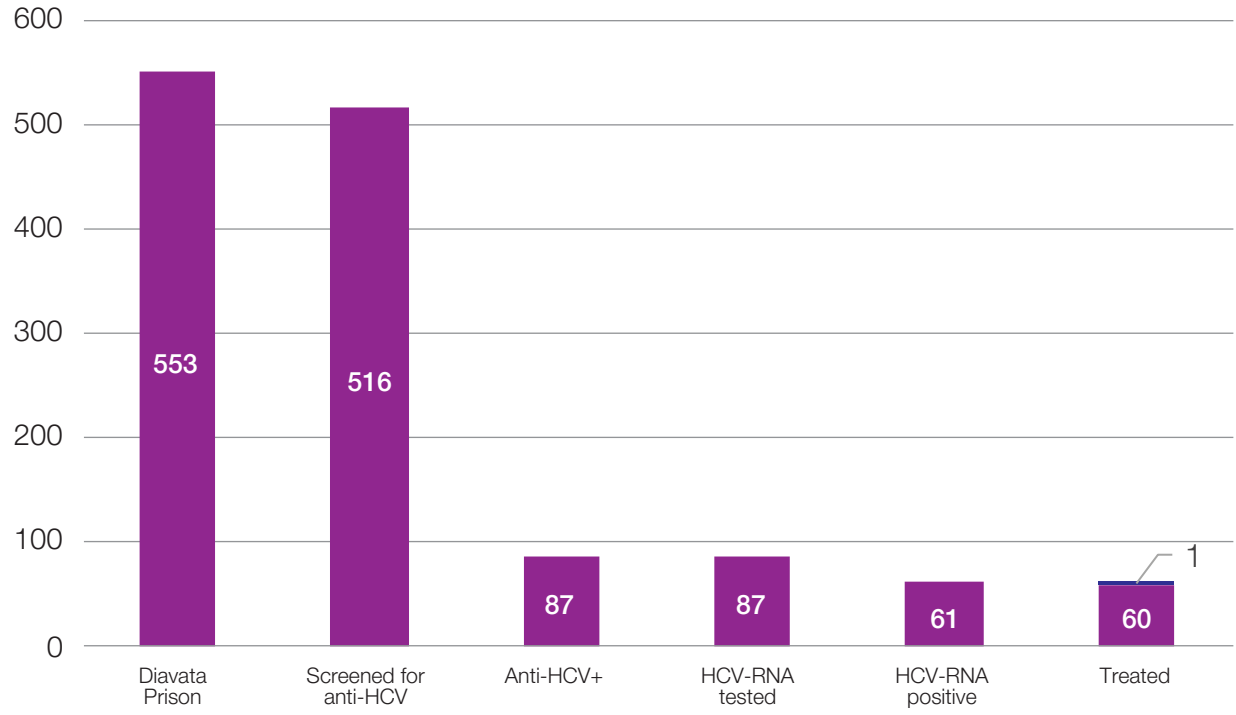
Sustainability

PWID remain one of the population groups most affected by hepatitis C, sustaining high incidence and prevalence rates in many countries. Rates of screening and linkage to care in prisons are very low and face significant barriers such as discrimination. Our model represents a short-term public health intervention with significant outcomes. It can be replicated in other prisons and closed settings.

The programme was cost-effective, time-bound and successful in addressing hepatitis C in prison settings. It can be used to avoid obstacles in the elimination of hepatitis C. Sustainability can be achieved once the programme is handed over to policy-makers and public authorities.

Our best practice also resulted in greater awareness of viral hepatitis and the importance of prioritizing the health needs of vulnerable population groups. It also highlighted a need to review Greek law on drugs that results in further discrimination of PWID and transmission of hepatitis C.

Fig. 16. Cascade of care for people in Diavata Prison, tested for hepatitis C and supported by the Prometheus project (2018–2019)



Source: Authors.

ICELAND Cascade of care in the Treatment as Prevention for Hepatitis C programme in Iceland

Strategic Direction 1 | Strategic Direction 2

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Background

Over the past two decades, 40–70 new cases of HCV infection have been diagnosed in Iceland annually. In 2015, the prevalence of hepatitis C was estimated at 800–1000 people, approximately 0.3% of the population of Iceland *(84)*.

Injection drug use accounts for nearly all cases of hepatitis C and new HCV infections in Iceland. Although most PWID are routinely tested for HCV, the uptake of hepatitis C treatment in this population group had been insufficient and did not have an effect on lowering the incidence of HCV infection.

Iceland intends to overcome these challenges, improve the cascade of care for hepatitis C and meet the goals of the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region *(85)* and the Global Health Sector Strategy on Viral Hepatitis 2016–2021 (GHSS) *(86)* by 2030.

Description of the good practice

In January 2016, the Treatment as Prevention for Hepatitis C (TraP HepC) programme was launched in Iceland with the following characteristics:

- The programme grants the opportunity to receive hepatitis C treatment with DAAs to all patients with HCV infection and aims to eliminate the transmission of HCV and decrease the incidence of HCV infection in the country.
- The programme is based on collaboration between three medical specialties (infectious diseases, hepatology and addiction medicine) and a multidisciplinary team approach, with physicians, nurses and social support services, including shelters for homelessness.
- A central project manager oversees the coordinated efforts, and the penitentiary system of Iceland is also involved in the programme.
- The antiviral treatment with DAAs is offered to all patients aged 18 years and older with detectable HCV RNA who are covered by Icelandic health insurance. People in prisons are systematically offered testing for hepatitis C and antiviral treatment if the diagnosis is confirmed.
- The programme has led to increased public awareness, with communication products dedicated to physicians.
- Harm reduction efforts have been scaled up simultaneously to the implementation of the programme, leading to improved access to testing, NSP and OST services
- DAAs have been donated by the pharmaceutical industry.
- Early case-finding and treatment for PWUD have been emphasized in the programme and prioritized for those at highest risk for progression to cirrhosis or severe complications of chronic hepatitis and liver disease, and people in prisons and closed settings.
- Patients who were not treated are identified and linked to care by cross-referencing multiple data sources, including the National HCV Registry maintained by the Directorate of Health in Iceland

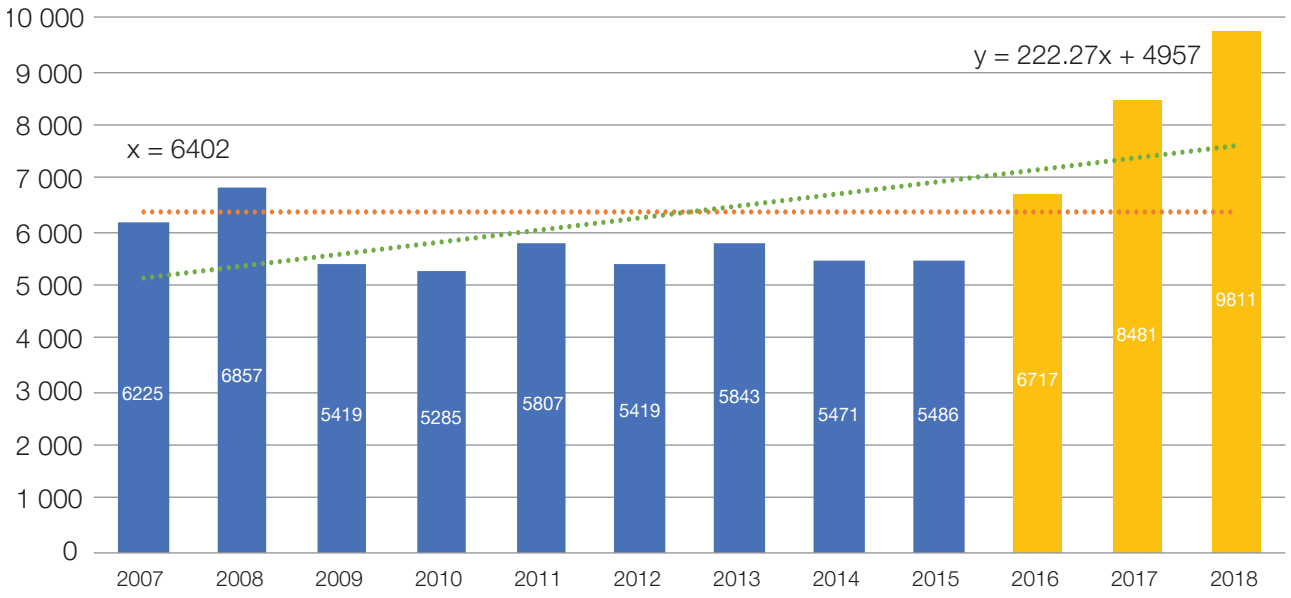
and the Vogur Addiction Hospital database (the most important health facility for treatment of substance use disorder in the country).

Evidence of impact

The TraP HepC programme had a significant impact in tracking potential patients and improving linkage to care. A total of 1287 people who had tested positive for anti-HCV were identified in the National HCV Registry in 2016 and another 161 cases were identified in 2018, adding up to 1448 people screened positive for hepatitis C. As of November 2018, 741 cases of hepatitis C had been confirmed with detectable HCV RNA test results *(84)*.

The programme also had a positive impact on the number of hepatitis C tests in Iceland, significantly increasing the annual figures since its implementation – by 81% since 2015 (Fig. 17).

Fig. 17. Annual number of anti-HCV tests performed in Iceland (2007–2018)



Source: Authors.

It is likely that more than 90% of the HCV infections acquired in Iceland have been diagnosed with extensive screening among key populations such as PWID, people in prisons and other closed settings, PLHIV, recipients of blood and blood products prior to 1992, MSM and people with abnormal liver test results (e.g. alanine aminotransferase) without other explanation. It is estimated that the total number of people with active HCV infection at the beginning of the TraP HepC programme (2016) and new infections through 2018 adds up to 800 people.

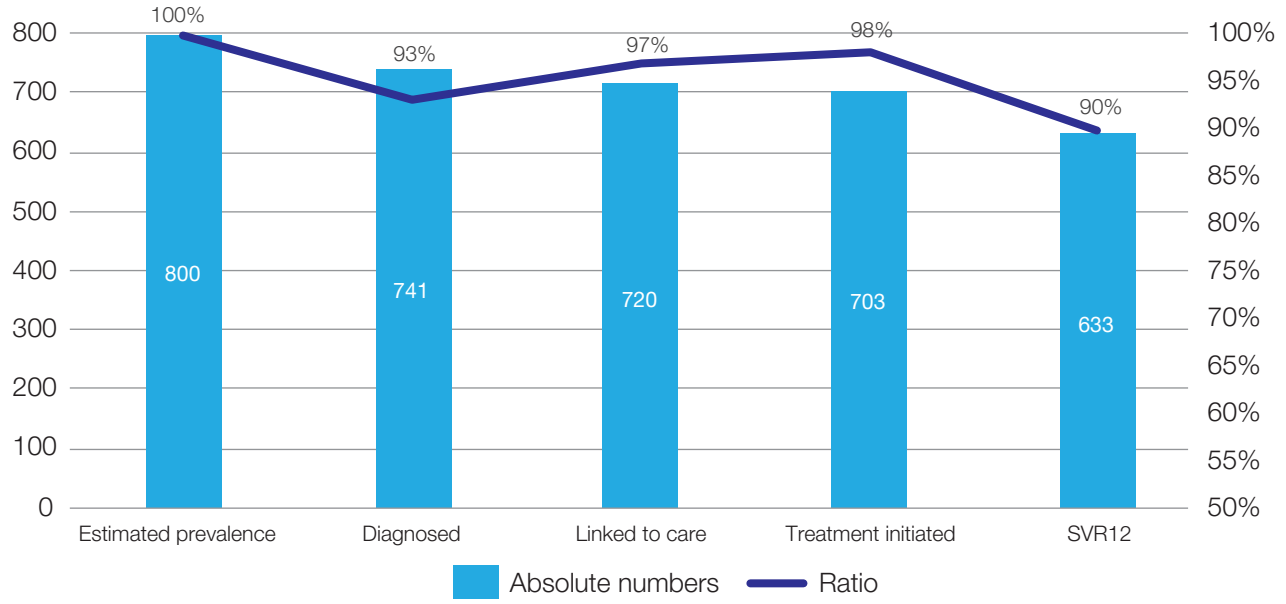
Additional findings during the TraP HepC programme indicate that there are very few undiagnosed HCV infections acquired in Iceland:

- No new HCV infections were identified with outreach point-of-care testing among key populations and other population groups at high risk for the infection.
- The prevalence of hepatitis C was found to be 30% among people in prisons. All patients had been previously diagnosed and were subsequently treated by the programme.
- Out of 3998 people who attended a fertility clinic during 2014–2018, four individuals (0.1%) had detectable HCV RNA, and all but one had been previously diagnosed.

As of November 2018, 720 patients (97% of those diagnosed) had been linked to care and given the baseline interview for antiviral treatment. A total of 703 patients initiated antiviral treatment with DAAs (Fig. 18).

The scale-up in testing and treatment for hepatitis C in Iceland resulted in high rates of engagement in treatment and cure. It seems that Iceland may already have reached the 2030 WHO service coverage targets

Fig. 18. Cascade of care of TraP HepC, Iceland (2016–2018)



Source: Authors.

of 90% diagnosis, and treatment of 80% of eligible patients, in 2018. It is hoped these results will translate into the elimination of HCV as a major health threat in Iceland.

Sustainability

Long-term maintenance of these achievements after the treatment phase could be a challenge. A large part of the programme has been built upon existing health-care services provided through universal health insurance and a welfare system based on high taxes (personal income tax in Iceland is expected to be 45% by the end of 2020).

While testing and treatment for hepatitis C is already established at the main health facility for treatment of substance use disorder and in prisons, it is essential to further integrate the health services, outreach and other activities provided by the TraP HepC team into other systems, including the penitentiary system.

Threats posed to the programme include a recent large increase in drug use, including injection drug use, a small group of actively injecting patients who have been difficult to engage in care, and an increasing rate of homelessness.

ITALY Use of point-of-care testing to enhance diagnosis and treatment of hepatitis C among PWID

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 5

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Background

The prevalence of HCV in Italy is estimated to be 1–2%, or about one million people *(87)*. A large study conducted in public services for treatment of substance use disorders revealed prevalence rates among PWID of 63.9% for anti-HCV and 43.0% for active HCV infection *(88)*.

Italy has 561 clinics for treatment of substance use disorder, with approximately 120 000 patients on

follow-up for opioid use and 25 000 for cocaine use. The national coverage of HCV screening in these services stands at 43.9% *(89)*.

A total of 180 000 hepatitis C treatments have been initiated in Italy since 2014. Yet, more than 200 000 people, many of then PWID, remain untreated and out of reach of conventional services *(90)*.

In order to improve diagnosis, linkage to care and access to treatment, we have developed a model of care and a multidisciplinary approach, with point-of-care tests and hepatitis C treatment integrated into services for treatment of substance use disorders.

Description of the good practice

In 2017, a task force of various professionals was established at San Paolo University Hospital, Milan, to improve HCV diagnosis and treatment for PWID already enrolled in treatment for substance use disorder. Forze Armate clinic was selected to pilot point-of-care diagnosis with oral swab tests and nucleic acid tests. Patients are only referred to the hospital for abdominal ultrasound and transient liver elastography. The staff involved in the treatment of substance use disorders were trained on hepatitis C diagnosis, treatment and care by infectious disease specialists.

Oral swab tests are routinely offered to OST clients as they attend the clinic for therapy, effectively doubling the screening coverage of the population group. Diagnostic point-of-care testing (GeneXpert® HCV VL Fingerstick) is offered to all OST clients who screen positive from oral swab tests, including people previously tested with other methods.

Patients with active HCV infection have blood samples collected for genotyping, haematology and biochemistry tests. Those who test negative are offered IEC materials on prevention of HCV infection and health promotion.

Patients are evaluated at the OST clinic by an infectious disease specialist on two separate occasions and, thanks to an agreement with the hospital pharmacy, are provided with antiviral treatment together with OST.

Abdominal ultrasound and transient liver elastography before initiating treatment are only considered for patients with high aspartate aminotransferase to platelet ratio index (APRI) scores.

Evidence of impact

The screening coverage of OST clients (n=350) has increased from 34% to 62% during project implementation, enabling the diagnosis of 140 patients with active HCV infection. Among PWID on OST (n=233), the screening coverage has increased from 43% to 77%, adding up to 117 people.

The new model of care and multidisciplinary approach with diagnostic point-of-care tests have significantly improved the cascade of care for OST clients. Data collection and analysis are in progress.

Only one patient has required abdominal ultrasound and transient liver elastography before initiating antiviral treatment with DAAs, due to signs of advanced liver disease (high level of aspartate transaminase and low platelet count). Only two patients with active HCV infection have been LTFU. Some patients have already finished treatment, although most of them are currently on treatment or ready to start.

Additional major benefits of the new model of care include improved doctor–patient relationships, reduced lead time between outreach and treatment, and the successful implementation of non-invasive tests to accelerate treatment and recovery of patients.

Sustainability

The project has benefited from improved communication and collaboration between the different departments involved (Addiction Rehabilitation Programme, Central Pharmacy, Central Laboratory, Infectious Diseases Unit and Azienda Socio-Sanitaria Territoriale (ASST) Santi Paolo e Carlo) and has not required additional financial resources.

The equipment and consumables for diagnostic point-of-care tests were provided by an external sponsor. The authors are grateful to the sponsor for this collaboration that will enable the programme to further address gaps in the cascade of care for hepatitis C.

The creation of a dedicated mobile task force comprising specialists in infectious diseases and substance use disorder could improve cost-effectiveness and accelerate the response to hepatitis C, thus achieving its elimination as intended.

This good practice could be cyclical – alternating between different substance use disorder clinics every

few months – with teams continuously developing experience, increasing the screening coverage of people with hepatitis C infection and quickly identifying patients for antiviral treatment.

LITHUANIA Monitoring HBV resistance to antivirals in Lithuania

Strategic Direction 1 | Strategic Direction 2

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Background

In Lithuania, incidence of acute cases of hepatitis B are reported to have declined since 1990 *(91)* and the prevalence in the general population is reported to be at 2.03% (1.37–2.69) *(92)*. With regards to vulnerable populations, prevalence is reported to be 10.5–82.0% among PWID *(93,94)*, and 3.6% among MSM *(95)*. Different studies have registered vaccination for hepatitis B at 7.5% for PWID *(96)* and 20.7% for MSM *(97)*.

Hepatitis B vaccination was introduced to immunization calendar in Lithuania in 1998 with the first dose given within 24 hours of birth followed by 2 or 3 doses to complete the vaccination series. The first hepatitis B treatment guidelines were issued in 2005. Lithuania does not have a national programme for viral hepatitis.

As for treatment of chronic hepatitis B, lamivudine (3TC) is still widely used in Lithuania, mainly due to its price, availability and full reimbursement policy. Until 2016, the antiviral accounted for more than 95% of the treatments provided in the country, even though it presents a low barrier to resistance and is no longer recommended in the WHO guidelines for treatment of hepatitis B *(98)*. The reimbursement for entecavir (ETV) was introduced in February 2016, but was available only for patients who had HBV resistant to 3TC. Since 2017, the reimbursement for ETV has also been available for naive patients.

The recommended medications, tenofovir alafenamide fumarate (TAF) and tenofovir disoproxil fumarate (TDF) are not fully available in the country: TAF remains unregistered; TDF is provided through personal name-based application to the Lithuanian Sick Fund and is given to very few patients *(91).*

EVT is subject to resistance that occurs frequently in people with 3TC resistance *(97)*, raising significant concerns over the widespread use of 3TC and the potential selection of drug-resistant mutations, leading to cross-resistance for preferred regimens for the treatment of hepatitis B in Lithuania, thus threatening the country's progress in the elimination of the disease.

Description of the good practice

Our good practice comprises a retrospective study on patients treated for chronic hepatitis B at the Vilnius University Hospital Santaros Klinikos (VUHSK) Centre of Infectious Diseases, to assess the efficacy of ETV and compare resistance between 3TC-naive and 3TC-experienced patients. Efficacy was measured by quantitative molecular viral level testing during treatment; an increase of viral DNA during treatment was a marker of resistance to ETV.

We expect that this study will contribute to improvements in hepatitis B treatment in Lithuania, using the evidence previously established in international guidelines and that observed in our cohort.

Evidence of impact

This research comprised the retrospective collection of data on all 122 patients currently on treatment for chronic hepatitis B at the VUHSK Centre of Infectious Diseases. Of the 122 patients, 43 were female (35.2%) and the mean age of patients was 45.4±14.4 years.

For the analysis, 59 patients who were treated with ETV for at least 12 months were selected and divided into groups according to previous experience with 3TC – 3TC-naive (21) and 3TC-experienced (38) (Table 8). The 63 patients on treatment with pegylated interferon or 3TC were excluded from the evaluation.

Table 8. Distribution of patients on treatment for chronic hepatitis B according to previous experience with 3TC at the VUHSK Centre of Infectious Diseases

3TC status	ETV for ≥12 months
3TC-naive	21
3TC-experienced	38
Total	59

Source: Authors.

Resistance to 3TC was identified in 33 out of 38 patients previously experienced with 3TC (87%).

We compared the occurrence of resistance to ETV according to patients' previous experience with 3TC, with 9 (24%) patients displaying resistance to ETV after 38.4±25.2 months of treatment (Table 9).

With this brief assessment of our cohort, we were able to observe that patients previously experienced with 3TC were at great risk of developing cross-resistance to ETV, potentially forcing patients to seek other available options at their own expense or continuing treatment with ineffective medication in the future.

These findings support the need for a change in treatment options in Lithuania that follow international guidelines and WHO recommendations.

This good practice represents the first monitoring of HBV resistance to antivirals in Lithuania in the cohort of patients treated for hepatitis B at the VUHSK Centre of Infectious Diseases. It has also resulted in scientific publications that will assist with the development of research in viral hepatitis and in building capacity at the university and in the country.

It is expected that once provided with local evidence, public health policy-makers will consider improvements not only in the recommendations for first-line treatment, but also in the reimbursement policy for tenofovir, contributing to better access to health for those living with hepatitis B.

Sustainability

The retrospective review of clinical data and treatment outcomes from our patients is not a costly practice and it could facilitate potential changes in public health policy on viral hepatitis. It could also support sustainability by strengthening strategic information, particularly for planning the substitution of 3TC for entecavir, reviewing reimbursement policy for tenofovir and estimating overall costs of medications.

Table 9. Patients on treatment for chronic hepatitis B according to previous experience with 3TC, and resistance to 3TC and ETV, VUHSK Centre of Infectious Diseases

	Resistance to 3TC[a]	Resistance to ETV[a]
3TC-naive (21)	0	0
3TC-experienced (38)	33 (87%)	9 (24%)
Total	33	9

[a] After 38.4±25.2 months of treatment.
Source: Authors.

LUXEMBOURG Combination disease prevention in prisons: a comprehensive programme in Luxembourg

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 4 | Strategic Direction 5

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Background

In Luxembourg, 4346 people, approximately 1% of the population, tested positive for anti-HCV during 1990–2013 *(99)*. It is estimated that 77% of them present active infection and most cases of hepatitis C are males with a median age of 37 years.

Injecting drugs is the predominant route for HCV transmission among the general population in Luxembourg. It is also the most important risk factor for the infection in people in prisons *(100)*. In 2015, it was estimated that approximately 1500 PWID resided in Luxembourg *(101)* and that 75% of them would test positive for anti-HCV *(102)*. Therefore, incarceration is an important opportunity to offer prevention, diagnosis and treatment of hepatitis C, among other health services, to underserved population groups such as PWID.

There are 689 people in prison in Luxembourg – most of them are not citizens of the country. The prison population is divided into two state prisons: a closed setting with 615 people (including 320 pre-trial detainees) and a semi-open prison with 74 people. The turnover of the prison population in Luxembourg is high – at an approximate rate of 1000 people per year. About one third of the prison population (228/689) has been incarcerated for drug-related offences and/or has suffered from substance use disorders.

In 2003, the HCV-UD programme (l'hépatite C au sein des usagers de drogues au Luxembourg) was implemented in the two state prisons – providing systematic case-finding of infectious diseases, linkage to care, treatment, immunization and a combination of prevention measures, including NSPs, OST and educational training. This comprehensive approach aimed to prevent communicable diseases in prisons and improve the overall health of PWID with viral hepatitis.

Description of the good practice

Test and treat

Due to the high prevalence of viral hepatitis, HIV and other complications of an infectious nature related to drug use in prisons, a standardized approach was implemented in 2009 to offer diagnosis, linkage to care, treatment, immunization and prevention of infectious diseases in prisons under a specialized medical department (COMATEP) *(103)*.

Two nurses oversee the COMATEP programme in the prison. The work is done in collaboration with the National Service of Infectious Diseases and ensures that all inmates can receive early treatment and care for infectious diseases.

All inmates are systematically offered screening for HIV, hepatitis A virus (HAV), HBV, HCV, TB and syphilis during a consultation with a doctor within 24 hours of arrival in prison. The acceptance rate of the screening protocol is very high (>95%). In the case of a positive test result, a consultation with an infectious diseases specialist is immediately organized in the prison clinic for the initiation of appropriate antiviral therapy, follow-up on viral load, immunization for HAV and HBV, and/or ultrasound tests.

Liver elastography tests (Fibroscan) are performed by one of the nurses. Antiviral treatment for hepatitis C is provided within the prison clinic when the duration of the treatment with DAAs fits with the period of incarceration.

Nurses also organize counselling and make appointments with infectious disease specialists outside the prison and with NGOs upon the discharge of

inmates. They are also responsible for the transcription of medical and blood analysis reports. Educational sessions on infectious diseases are also organized by the nurses for prison staff.

Clinical history and treatment information have been systematically collected since 2003, and in 2017 an epidemiological survey on risk behaviours and patterns of drug use (HCV-UD study) was implemented in prisons *(104)*. All participants provided written informed consent.

Harm reduction

Different harm reduction services have been implemented in prisons since 2005, including OST, NSPs, condom distribution and, more recently, a "safe tattoo" project. The OST is delivered by the psychiatric service and requires full compliance from the patient and a formal contract. Methadone, buprenorphine and naloxone are available only to registered patients.

OST is given as a directly observed therapy (DOT). Since 2014, 15–18% of inmates have received OST – roughly 63 to 80 patients per day, at an average duration of 140–151 days.

The NSP programme was established in 2005. Information is provided at entry by the medical doctor. A contract is signed between the patient and the medical service, with a one to one exchange rule, and counselling is provided by a nurse. By 2018, 427 NSP kits had been distributed and 12 428 syringes had been exchanged by the medical service. Regarding unprotected sex, condoms are readily available in different locations in the prisons. Their provision is generally well accepted but no figures are available on their actual use.

Safe tattoo

Launched in March 2017, this project was initiated by a trainee nurse and Erasmus+. Half the prison population in Luxembourg has tattoos and a third of these tattoos were performed during incarceration – increasing the risk of infectious diseases and complications. Therefore, a safe tattooing room was installed in the prison. Inmates are trained in tattooing, hygiene and infectious diseases. Under the supervision of a nurse, 528 hours of tattooing were performed during 196 appointments up to June 2018. Training was received by 14 tattooists and 120 people got at least one tattoo.

Evidence of impact

Since 2013, 4218 communicable disease tests have been performed, with 737 positive results for anti-HCV (17.47%). HIV infection was found in 103 cases (2.44%) and syphilis in 101 (2.39%). Approximately one third of inmates became aware of their seropositive status for all infections during the screening performed upon arrival at the prison. Due to reincarceration, it is possible that patients were tested more than once and that duplicates could exist.

During 2013–2018, out of 2186 patients, there were 160 consultations with the infectious disease specialist; 1100 liver elastography tests and 769 ultrasounds were performed. Since 2012, 3828 vaccinations against hepatitis A/B have been provided.

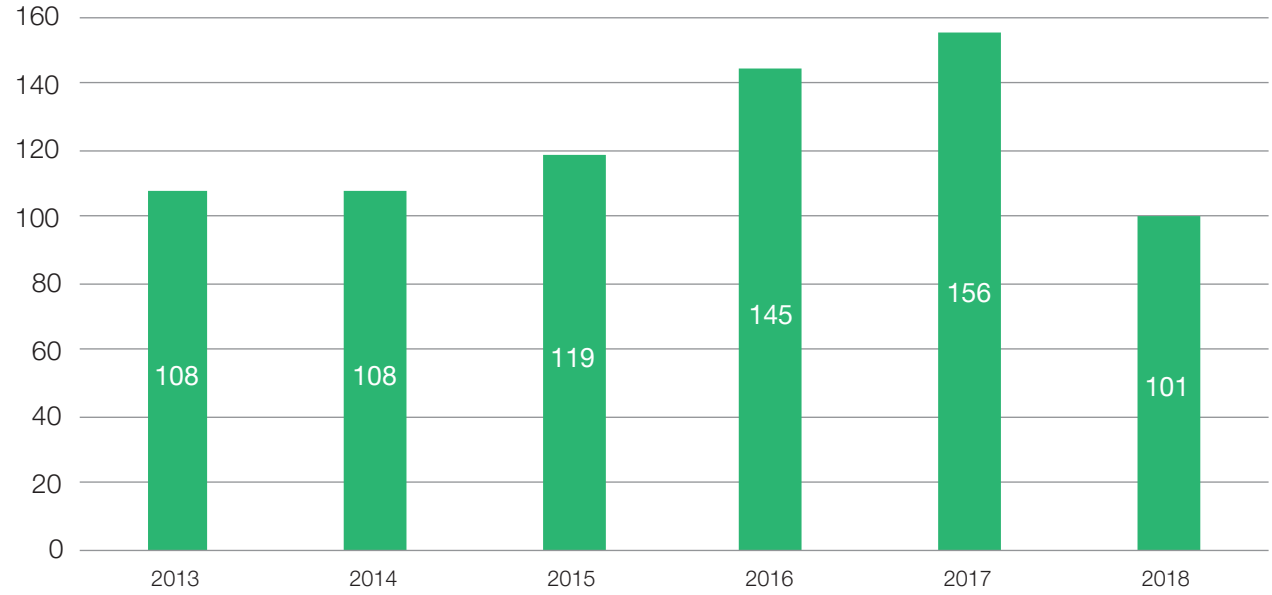
The number of inmates testing anti-HCV positive upon arrival has been stable during the last few years, between 101 and 156 people each year (ranging from 13.3% in 2014 to 14.5% in 2018) while the high turnover of the prison population was sustained (Fig. 19).

We conducted a retrospective study of hepatitis C treatment in prison from 2003 to 2015, when the combination of pegylated interferon and ribavirin was still in use *(105)*. Among 665 inmates tested positive for anti-HCV, 209 received hepatitis C treatment, and 204 received follow-up without antiviral treatment (due to contraindications to pegylated interferon or prioritization of treatment). Although 31.9% of patients (95% confidence interval (CI): 25.85–38.54) were LTFU, the SVR was registered in 136 patients who were followed for a median of 4.4 years (interquartile range = 1.54–6.54) or a total of 429 years at risk. During this period, 32 patients were assumed to be reinfected outside of prison, so the incidence of reinfection was 7.4/100 person-years at risk (95% CI: 5.3–10.3).

Reinfection was confirmed by genotype change in 13 cases (40.6%). The overall reinfection rate was 23.5% (95% CI: 19.50–28.22). The linkage to OST after discharge from prison has been intensified and monitoring of reinfection inside and outside prison after DAA therapy was implemented in 2017.

Since 2012, DAA treatment has been provided in the prison clinic as DOT. Treatment has been offered to 90 patients and 83 finished treatment (92%) during incarceration. Among these patients, 80 achieved an undetectable viral load at EOT (96%),

Fig. 19. Number of positive anti-HCV test results in the prison population (2013–2018)

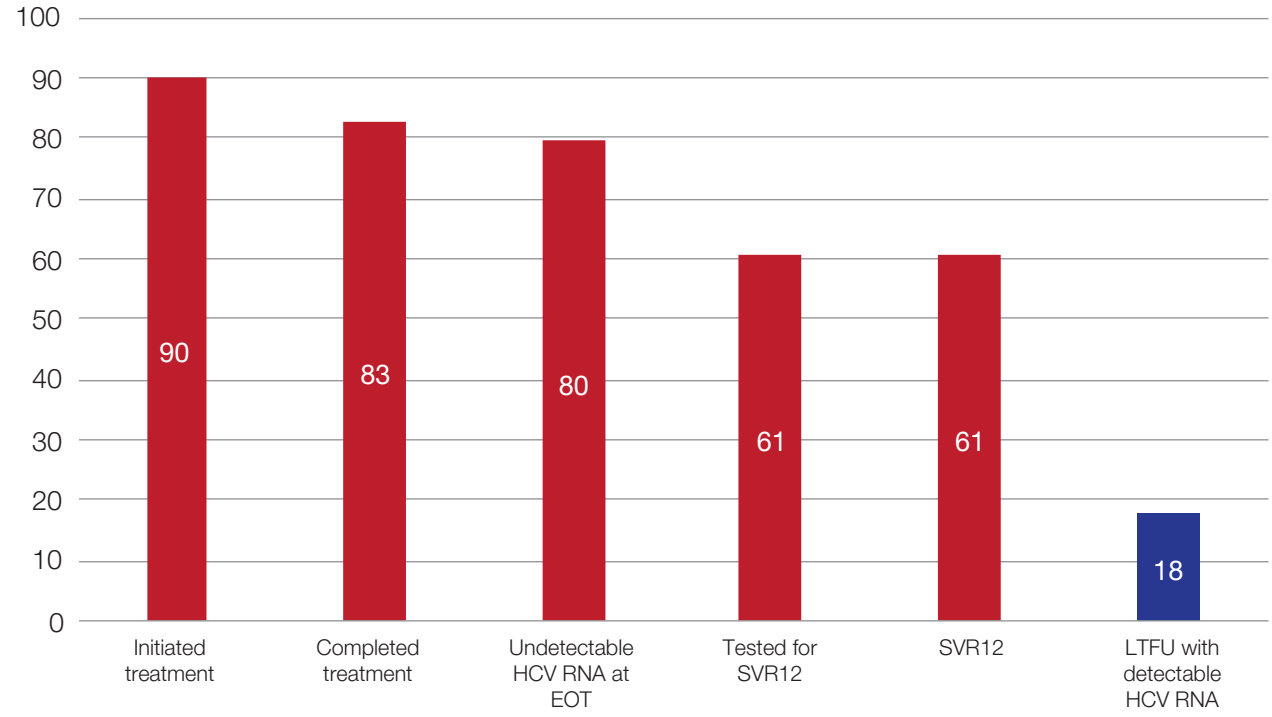


Source: Authors.

61 were submitted to HCV RNA test 12 weeks after EOT, and 61 achieved SVR12 (Fig. 20). In the LTFU group, 18 patients presented detectable HCV RNA, a potential consequence of treatment discontinuation or reinfection. In 2019, only two reinfections were registered, which took place outside the prison. The majority of cured patients were LTFU in 2019.

In conclusion, there is an effective opportunity to test and treat underserved population groups, including PWID, in prisons. Inmates have very limited access to treatment, care and education for prevention and control of infectious diseases and drug use. Combination prevention programmes should include harm reduction services with OST, NSPs, condom distribution, immunization and education.

Fig. 20. Cascade of care for hepatitis C with treatment with DAAs in two state prisons, Luxembourg (January 2012 to June 2019)



Source: Authors.

Following the introduction of DAA treatment in Luxembourg, the screening and treatment of hepatitis C inside and outside of prisons have contributed to a decrease in the overall prevalence of HCV infection among PWID in the country. Since 2015, we have established an interventional programme, HCV-UD, to conduct the screening and the linkage to care of PWID in five harm reduction centres (OST/NSP programmes and one supervised drug consumption facility) in Luxembourg – with excellent results in the enrolment of participants and decrease in prevalence of HCV infection.

Sustainability

The programme, including the safe tattoo project, is funded by the Ministry of Justice as part of the general health care for people in prisons. Various ideas on how to improve the existing system include simplification of the NSP programme in prison, attention to women and their access to harm reduction services, and safe piercing and naloxone projects.

There is a diamorphine project running outside prisons that, once evaluated, could also be introduced in prisons. Any projects inside prisons in Luxembourg should be "living" projects – continuously evaluated and improved when necessary. Prevention of infectious diseases for inmates should be strengthened through peer-support programmes and NGOs, as suitable for the interventions. Social reintegration and housing upon discharge from incarceration are also essential, to sustain the good practice initiated inside prisons.

MALTA A clinical strategy for the elimination of hepatitis C in Malta

Strategic Direction 1 | Strategic Direction 2 | Strategic Direction 5

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Background

A retrospective analysis of the demographics of patients who had tested positive for anti-HCV at the Mater Dei Hospital, the main hospital in Malta, was carried out in 2013 *(106)*. This study estimated that 1000 people are living with hepatitis C in Malta.

Intravenous drug use is the most common mode of transmission of hepatitis C infection in the country.

A national strategy to eliminate HCV infections in Malta was launched in 2018 *(107)*. The aim of the strategy is to treat 200 patients per year over a five-year period. By mid-2019, seven consultants in infectious diseases and gastroenterology had treated the first 200 patients with hepatitis C.

Description of the good practice

A single-tablet combination of sofosbuvir/ledipasvir is used to treat patients with a genotype 1 or 4 HCV infection; while sofosbuvir/velpatasvir is used in patients with a genotype 2 or 3 HCV infection. The duration of DAA treatment is 12 weeks. The endpoint of treatment is defined as undetectable HCV RNA in serum at 24 weeks after the end of treatment (SVR24) – deemed to be consistent with a cure of the hepatitis C infection.

It was decided to prioritize patients with hepatitis C at high risk of complications and/or accelerated disease progression. Patients with hepatitis C and any of the following selection criteria were prioritized for DAA treatment:

- decompensating liver cirrhosis secondary to HCV infection;
- liver cirrhosis secondary to HCV infection;
- rapidly progressive hepatic fibrosis secondary to HCV infection;
- liver transplantation;
- type 2 or 3 essential mixed cryoglobulinaemia with end organ damage secondary to HCV infection;
- significant renal disease secondary to HCV infection;
- HCV infection in the context of immunosuppression.

Evidence of impact

In the first couple of months, DAA treatment was initiated in a total of 45 patients, who were prioritized for HCV treatment according to the selection criteria. The majority of treatments were assigned to patients with liver cirrhosis or HIV/HCV coinfection.

Twenty treatment courses were reserved for patients with any of the prioritization criteria who presented during the year. The remaining 135 DAA treatment courses were utilized to treat other patients with HCV under the care of the seven consultants.

Before initiating DAA treatment, all patients are screened for possible hepatitis B and/or HIV coinfections. A full drug history is taken from each patient, and any drug interactions noted and acted on accordingly. All patients initiating DAA treatment are strongly advised to avoid alcohol intake, especially during the duration of the treatment.

Once treatment is started, patients are contacted for assessment of adherence to treatment and questioned regarding any adverse events related to treatment. The cure rate cannot be accurately assessed at this point because most patients are still undergoing DAA treatment or still awaiting their SVR24 result.

Sustainability

According to the national strategy, 200 patients with hepatitis C should be treated every year for the next four years. Some treatment courses will always be reserved for patients who might present the prioritization criteria during the year. The remaining DAA treatment courses will be used to treat all patients with hepatitis under the care of the consultants.

It is estimated that towards the third year of the local/national strategy, most patients with known HCV infection who are already linked to care will have been treated. Therefore, other patients could be identified through an active screening programme and eventually treated.

The screening programme will target groups at high risk of HCV infection, such as people attending the Substance Misuse Out-Patients Unit (Detox Centre) and people in prisons and other closed settings. In addition, it is planned that any patients who have tested positive for HCV infection and are still not linked to care will be contacted and offered treatment.

Our goal is to achieve more than 75% coverage for hepatitis C treatment for eligible patients and at least a 90% cure rate – aligning with goals set in the GHSS for 2020.

The local/national strategy is entirely funded by the public health system.

PORTUGAL The Mobile Outreach Programme (Ares do Pinhal) in Portugal

Strategic Direction 2 | **Strategic Direction 3** | **Strategic Direction 4**

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Background

In Portugal, the prevalence of anti-HCV in the general population has been estimated at 0.54%, with peak prevalence among people aged 35–64 years *(108)*. Among PWID, the prevalence of anti-HCV has been reported to be higher than 88.45%, according to official sources *(109)*, and injecting drug use is a major risk factor for HCV transmission in the country *(110)* – with higher rates of anti-HCV seroconversion among PWID than in PWUD *(111)*.

In 2016, a study on a cohort of 825 clients of the Mobile Outreach Programme (MOP) (Ares do Pinhal) found prevalence rates of HCV infection of 67.6% (558/825) and detectable HCV RNA of 68.4% (307/449) *(112).*

Description of the good practice

Ares do Pinhal is a non-profit organization created in 1986 that takes a multidisciplinary approach to support capacity-building, personal autonomy and social inclusion *(113)*.

The organization is highly experienced in the assistance of PWUD, having provided services to approximately 500 people in a derelict district of Lisbon during the 1990s. Since the implementation of the MOP in 2001, the organization has been of assistance to approximately 1600 people a year, attending to around 1200 individual appointments a day. From January 2018 to June 2019, the MOP assisted 1884 people, screened 1416 of them for HCV infection and detected infection in 860 (60.7%) of those. Ares Do Pinhal estimates that there are about 400 people with active infection in need of treatment for hepatitis C who are served by the MOP.

The MOP comprises three vans (two OST mobile units, one medical care and psychosocial support unit), one support car for patient transportation and back-up for the vans, and a back office. The three vans operate seven days a week, 365 days a year, with daily stops at five strategic spots in Lisbon. Services are provided throughout the morning and the afternoon.

The MOP offers the following main features:

- improved access, with units operating close to underserved areas and population groups;
- prompt response to requests for admittance, simplified admittance procedures and referral to health and social services;
- promotion of better living conditions;
- a low-threshold methadone programme;
- an NSP and distribution of condoms and tinfoil.

Additionally, the programme offers clients the screening of infectious diseases with blood tests and chest radiography, administration of medications and follow-up, including for HCV infection, with a competent team of medical doctors, nurses and psychosocial workers.

The MOP integrated model of care addresses prevention and screening of hepatitis C, linkage to care, treatment, and the prevention of reinfection and relapse. The goal is to provide screening for major infectious diseases to all PWUD of the MOP and eliminate any existing barriers in the access to hepatitis C treatment.

Two general hospitals in Lisbon and their respective gastroenterology and hepatology departments partner with the programme – either improving access to specialized consultations or assigning a medical doctor of their own to assist in the mobile units. The hospitals contribute significantly with clinical procedures required before the treatment for hepatitis C is initiated.

Some of the strategies to promote awareness and prevention of hepatitis C include True or False games and IEC sessions in the field – with strong participation by peer workers. These methods have been quite effective in engaging patients in their treatment and remain an important part of the MOP.

The MOP offers two pathways to care:

- Pathway 1:
  1. First appointment at the hospital – North Lisbon Hospital Centre (partner).
  2. Appointments at the hospitals are scheduled by the MOP.
  3. Transportation to the hepatologist appointment and HCV RNA testing at a partner hospital. Navigation performed by an MOP technician.
  4. Medications are transferred from the partner hospital to the mobile units.
  5. DOT is performed in the mobile units.
  6. Follow-up by the MOP (for patients with advanced liver disease or cirrhosis).

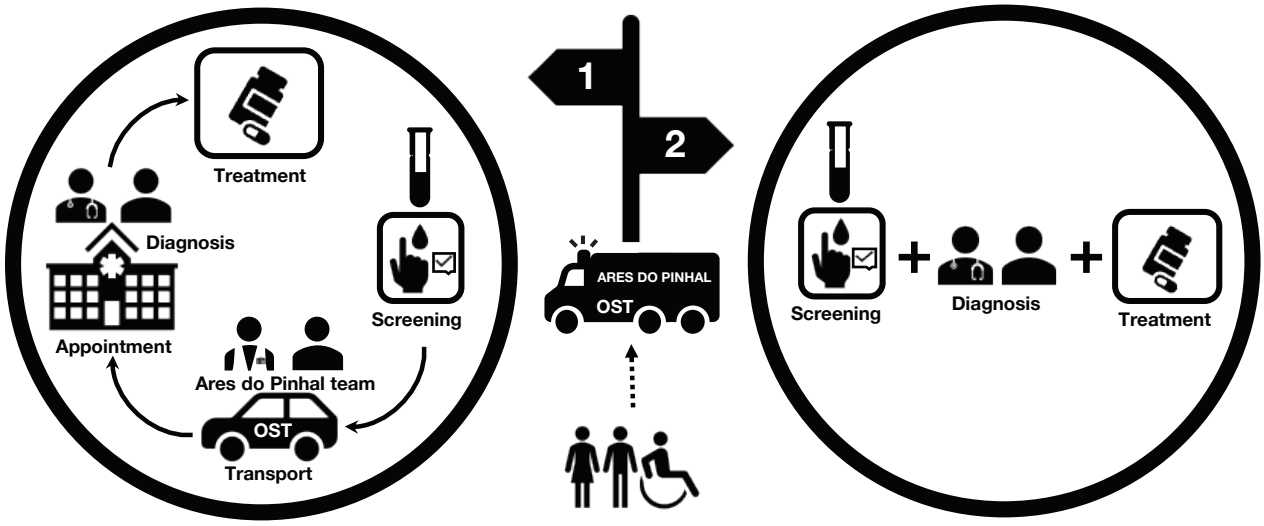
- Pathway 2:
  1. First appointment at the MOP – Western Lisbon Hospital Centre (partner).
  2. Appointments with hepatologist at the mobile units.
  3. Blood samples collected in the mobile units and transported to the partner hospital for HCV RNA testing.
  4. Medications are transferred from the partner hospital to the mobile units.
  5. DOT is performed in the mobile units.
  6. Follow-up by the MOP (for patients with advanced liver disease or cirrhosis).

Fig. 21 illustrates these two pathways to care.

Evidence of impact

The MOP integrated model of care improved access to health and hepatitis C treatment for many clients

Fig. 21. Hepatitis C patient-centred model of care in Lisbon Mobile Outreach Programme



Source: Authors.

who could not have complied with all the stages and processes demanded by conventional health facilities.

Regarding linkage to care and adherence to treatment, both pathways had better results than referral to a family doctor, the conventional procedure before MOP implementation. In Pathway 1, 273 clients were scheduled appointments, 123 (45%) received consultations, 75 completed treatment, 4 treatments are in progress, and 10 cases are pending laboratory results. In Pathway 2, 85 clients were scheduled appointments, 68 (80%) received consultations, 11 completed treatment, 10 treatments are in progress, and 57 cases are pending laboratory results. A total of 100 people had their treatments initiated through the MOP with no LTFU patients (Table 10).

The good practices in the MOP also increased patients' adherence to appointments with hepatologists in the partner hospitals (45%) and in the mobile units (80%).

Some patients reported their general health conditions before treatment and after being cured: "I thought this state of mind was normal, but now I've made it [through treatment] I realized it was the hepatitis C virus", "I gained a new life", "I've been tired for 30 years", "In a job interview, I'm no longer afraid to be tested for hepatitis C, because despite being positive [for anti-HCV] I'm already cured" (translation from Portuguese). Clients also expressed their gratitude for the resources invested in treatment by the state and their wish to contribute to society.

Sustainability

The MOP is supported by public funds through the General Directorate for Intervention on Addictive Behaviours and Dependencies (SICAD) an entity of the Ministry of Health and the Municipality of Lisbon. The programme is monitored by the Department for Intervention on Addictive Behaviours and Dependencies (DICAD) of the Ministry of Health of Portugal.

The sustainability of the project is driven by innovative solutions and partnerships with a wide range of stakeholders, including: public and private organizations; civil society; those working on harm reduction, health, substance use disorder and security; local parishes, charitable funds and philanthropic organizations; PWID/PWUD associations; peers; public hospitals; academia; and government.

"Social Return on Investment – SROI" is a multimethod study coordinated by Ares do Pinhal and Universidade Atlântica. Implemented in late 2018, the study aims to assess the impact of treatment on the quality of life of people with HCV infection – such as the assistance provided by the MOP – and the ways it can lead to additional social and economic benefits to society *(114)*.

Table 10. Preliminary cascade of care for hepatitis C before and during the MOP, Lisbon (2015–2019) (number of patients)

Model	Duration	Scheduled	Consulted	Adherencea	Treatment ongoing	Treatment complete	Pending lab results
Before MOP (family doctor)	2015–2017	307	30	10%	–	–	–
Pathway 1	Oct 2017–ongoing	273	123	45%	4	75	10
Pathway 2	Feb 2019–ongoing	85	68	80%	11	10	57

[a] Percentage of all patients who attended scheduled appointments.

Source: Authors.

RUSSIAN FEDERATION Establishing the National Viral Hepatitis Patient Registry

Strategic Direction 1 | Strategic Direction 5

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Background

Both acute and chronic hepatitis B and C are notifiable diseases in the Russian Federation and have been the subject of extensive epidemiological surveillance and public health interventions, such as the hepatitis B vaccination programmes initiated in 1990 and made universal in 2007 *(115,116,117)*.

After increasing in the 1990s, the incidence of acute hepatitis B dropped from 43.8 per 100 000 people in 1999 to 4.0 in 2008, and eventually to 0.67 in 2018. The incidence of chronic hepatitis B also decreased significantly during the period, dropping from 14.2 cases per 100 000 in 2008 to 9.27 in 2018 *(118)*. The incidence of hepatitis C remained high, though steadily decreasing, dropping from 40.85 cases per 100 000 in 2009 to 32.7 in 2018 *(119,120)*.

The prevalence of hepatitis B and C has been estimated at 2% and 4%, respectively. Since 1999, more than 2.9 million cases of HCV infection have been registered, yet only 600 000 people have sought medical attention *(121,122)*. The attributable fraction of deaths due to hepatitis B and C is not available.

Treatment programmes for hepatitis B and C are limited in the Russian Federation and data on treatment rates are unreliable.

Description of the good practice

A National Viral Hepatitis Patient Registry was developed and implemented in the Russian Federation in 2012 to improve the existing disease surveillance system and the health care of patients with hepatitis B, C and D. The Registry is a medical information system based on cloud technology, provided to the user through the internet. Physicians can use computers, tablets or smartphones connected to the internet to access the system.

The Registry provides the following functions:

- registration of patients with newly diagnosed viral hepatitis and new cases/reinfection cases in previously registered patients;
- search for duplicate patient records;
- data collection on risk factors and route of transmission;

- data collection on comorbidities;
- registration of chronic viral hepatitis outcomes;
- input of relevant laboratory test results and instrumental examinations (e.g. ultrasound, liver fibrosis assessment) performed during follow-up and antiviral treatment;
- selection of patient groups based on different criteria for planning and implementation of a treatment programme;
- monitoring and evaluation of antiviral treatment efficacy;
- monitoring of treatment programme implementation and effectiveness;
- relevant statistical information for all involved parties (physicians, programme managers, regional and federal Ministry of Health employees) according to their role and level of access;
- infographics for monitoring key progress indicators;
- access to the library of information materials on viral hepatitis (e.g. diagnosis and treatment guidelines, acts of the Ministry of Health).

The National Viral Hepatitis Patient Registry has a distributed hierarchical structure, and patient data entry is performed by physicians in clinics for treatment and care of viral hepatitis – the primary source of information. At higher hierarchical levels (district, regional and national), specialists have access to the aggregated data according to their administrative level and access rights. All personal information in the system is kept strictly confidential in accordance with the Russian Federal Law on Personal Data *(123)*.

As of the beginning of 2019, the Registry had been implemented in 73 of 85 regions of the Russian Federation. More than 3600 physicians in 2100 clinics have been using the system in their daily practice.

Evidence of impact

The Registry is a useful tool for monitoring the key indicators of the GHSS *(124)* and the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region *(125)*, and supports the development of programmes for the prevention, diagnosis and treatment of viral hepatitis B, C and D. It is also a useful resource for the advocacy, development and implementation of treatment and care programmes in several regions of the Russian Federation.

The Registry indicates that the number of patients treated for hepatitis C annually increased from 820 people in 2012 to 7143 in 2018, and that treatment efficacy increased from 60% in 2012 to 90% in 2018.

Sustainability

The sustainable development of the Registry is related to its further integration with the digital health service infrastructure, which is currently being developed and implemented as part of the Strategy for the Development of the Information Society in the Russian Federation for 2017–2030 *(126)*.

SLOVENIA Elimination of hepatitis C in population groups at high risk of HCV infection in Slovenia

Strategic Direction 1 | Strategic Direction 2 | Strategic Direction 3

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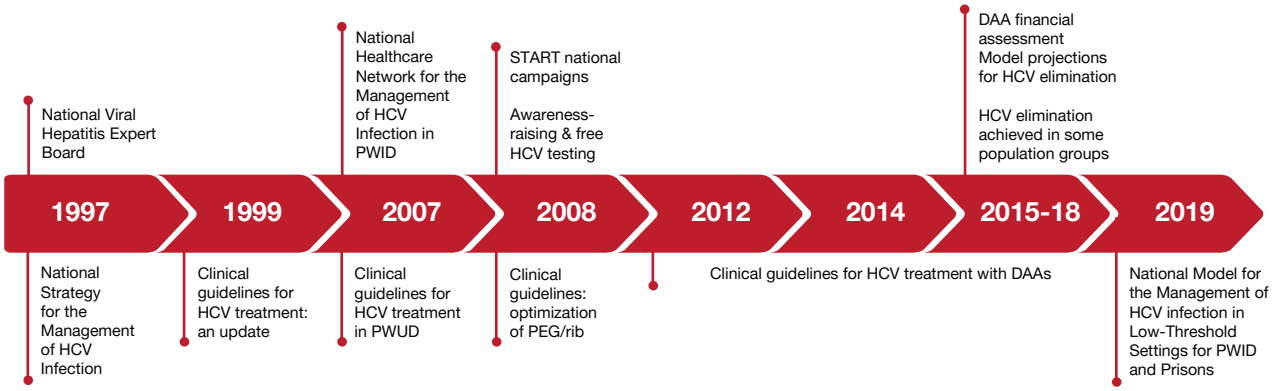
Background

The National Viral Hepatitis Expert Board initiated the Slovenian response to hepatitis C in 1997, with the launch National Strategy for the Management of HCV Infection and the development and implementation of hepatitis C treatment guidelines *(127)*.

This self-founded multidisciplinary body of experts from various public medical institutions has been collaborating with the Ministry of Health of Slovenia and the National Health Insurance System, as well as with civil society organizations, to improve the national response and cascade of care for hepatitis C (Fig. 22).

Among the achievements led by the National Viral Hepatitis Expert Board are the creation of a national register of people treated for hepatitis C in Slovenia since 1997, regular follow-up of treatment efficacy at the national level and, in collaboration with partners, estimation of the burden of HCV infection and assessment of the national response *(128)*.

Fig. 22. Timeline of the national strategy for HCV management in Slovenia



PEG/rib = pegylated interferon plus ribavirin.
Source: Authors.

The prevalence of hepatitis C in Slovenia is currently estimated at 0.2%, and two thirds of those infected report drug use as the mode of infection *(129,130,131,132,133)*. Up until 2014, before the introduction of DAAs, it was estimated that 6500 people were infected; 20% of them were successfully treated with interferon-based regimens, particularly after 2008 when the optimization of interferon-based treatment was introduced (82% overall SVR) *(6,7,134,135)*. With the advent of DAAs, the proportion of patients linked to care that have ever received HCV treatment has increased to 52%; of them, 97% have been successfully cured *(136)*.

Historically, all options for hepatitis C treatment have been available and accessible to everyone in Slovenia. Entirely funded by the National Health Insurance System, treatment only required prescription by a nominated specialist (infectious diseases or hepatology) according to the national guidelines. Treatment was partly restricted to prioritized groups of patients only during 2015–2017 because of the high prices of DAAs.

A statistical projection for HCV elimination in Slovenia proposed that with the use of highly effective DAAs and by steadily increasing the proportion of newly diagnosed and treated patients, the elimination goal can be achieved by 2030.

Therefore, in 2017, besides greatly increasing the continuum of services available within the framework

of routine national health-care activities (awareness-raising, testing, linkage to care and treatment), the National Viral Hepatitis Expert Board decided to take additional, parallel action to achieve multiple elimination goals for targeted population groups. These groups include those at highest risk of HCV infection, groups with known high prevalence rates and those for whom treatment and prevention could be delivered more quickly and efficiently with targeted methods, accelerating treatment.

Description of the good practice

The population groups chosen for targeted HCV elimination in 2017 included: (i) patients with hereditary bleeding disorders, (ii) patients on haemodialysis, (iii) organ transplant recipients, (iv) patients with end-stage liver disease (decompensated cirrhosis etc.), (v) people living with HIV/HCV coinfection, and (vi) PWID (Fig. 23).

Below we describe the good practice in two of these groups (i) patients with hereditary bleeding disorders and (ii) PWID.

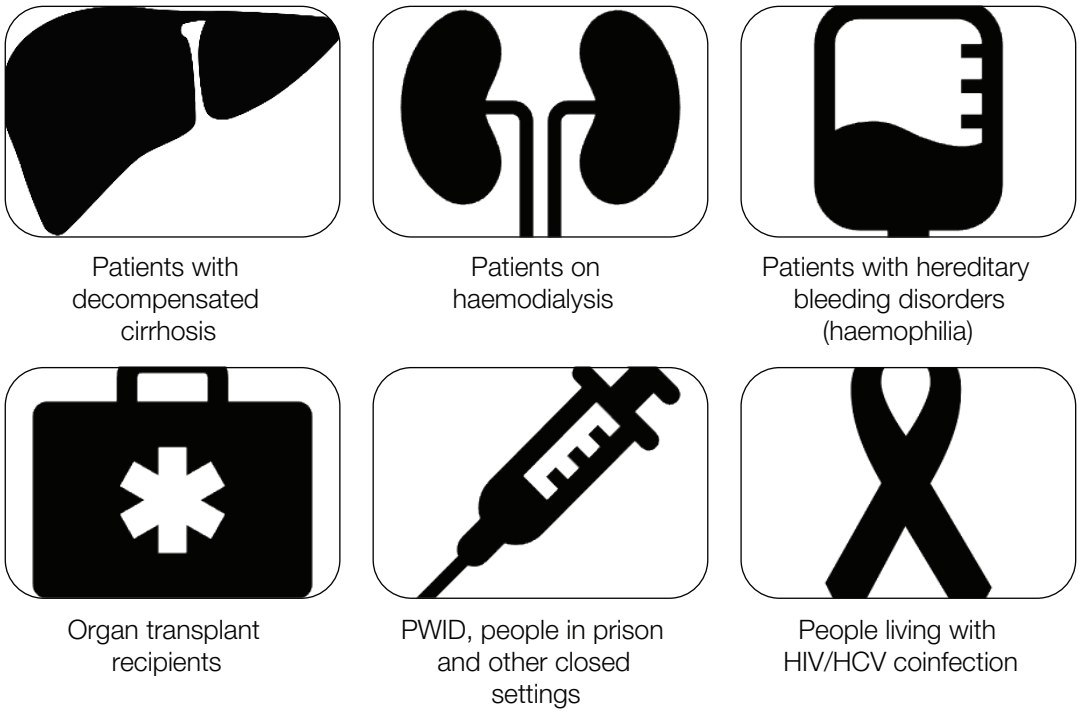
Patients with hereditary bleeding disorders

HCV infection represents a significant comorbidity for people with hereditary bleeding disorders (e.g. haemophilia) who were treated with transfusion of blood and blood products prior to the introduction of general HCV screening for blood donors and viral inactivation procedures. In Slovenia, haematologists organized a comprehensive system for management of patients with hereditary bleeding disorders in 1967 – leading to a national screening programme for bloodborne viruses in the early 1990s and the implementation of continuum of care for those with hepatitis C *(137)*.

Many haemophiliacs refused interferon-based treatments for hepatitis C because of the adverse events they caused. Therefore, after the introduction of DAAs, a national strategy for the elimination of hepatitis C in this group was prepared by a multidisciplinary expert team (infectious diseases and haematology specialists). The strategy comprised finding all untreated and previously unsuccessfully treated HCV-infected haemophiliacs and treating them with DAAs immediately.

All patients with hereditary bleeding disorders with detectable HCV RNA during the screening programme were identified from the national register of haemophiliacs and the database of people infected with HCV at the Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana. Registries were matched to records of people treated for hepatitis C held by infectious diseases specialists.

Fig. 23. Population groups chosen for elimination of hepatitis C in Slovenia (2017)



Source: Authors.

Patients who had not yet been successfully treated for hepatitis C were actively reached by telephone and invited for an appointment with an infectious diseases specialist who immediately introduced treatment with DAAs *(138)*.

PWID

Approximately 4500 out of an estimated population of 6000–8000 PWID receive high-threshold services at the 18 regional Centres for the Prevention and Treatment of Drug Addiction (CPTDA) in Slovenia *(139)*. The prevalence of HCV RNA among 1450 PWID served by the CPTDA was 15.6% in 2006 and only 4% received treatment for hepatitis C *(140)*. In order to increase the proportion of PWID treated, and achieve the best outcomes, a multidisciplinary national network for treatment and care of PWID with hepatitis C was established in 2007, regionally linking the 18 CPTDAs and five hospital-based clinics specialized in viral hepatitis treatment *(141,142).*

The network includes different health-care providers (addiction therapists, infectious disease specialists and hepatologists), counsellors (nurses and social workers), trained psychiatrists, peers and other members of patient support systems such as family, friends and co-workers. All health professionals and members of the support teams collaborate and participate in annual national conferences. The Clinic for Infectious Diseases and Febrile Illnesses at the University Medical Centre in Ljubljana serves as the reference institution.

The Slovenian guidelines for treatment of hepatitis C in PWID were also established in 2007 *(13)*. The guidelines set forth best practices for the comprehensive management and care of patients, including screening and identifying patients, providing them with high-quality education on HCV, counselling and motivation. In clinical settings, these best practices are performed before, throughout and after the treatment period, with close cooperation between infectious disease specialists and addiction therapists.

With the advent of DAAs, a national strategy for elimination of viral hepatitis in PWID was developed and statistical methods indicated that elimination would be feasible by 2026 with the existing model of care and twice the treatment rate. This led to the implementation of testing, linkage to care, fibrosis assessment with liver elastography and treatment at the CPTDA *(143)*.

PWID in Slovenia also have low-threshold programmes at their disposal, though only harm reduction is currently offered in these services. A pilot project was implemented to assess the targeted interventions for elimination of hepatitis C in PWID. The project integrated infectious disease specialists, a hepatitis patients' association (Slovenia HEP) and an NGO with a low-threshold programme (Stigma). PWID at six regional centres with low-threshold programmes (NSPs and homeless shelters) were offered anti-HCV tests onsite and liver fibrosis assessment with transient elastography.

Evidence of impact

Patients with hereditary bleeding disorders

Since 2018, Slovenia has had no people with hereditary bleeding disorders and HCV infection. The country is the first to completely eliminate hepatitis C in this group. During 1997–2018, of the 105 people with haemophilia, 66 were treated for hepatitis and 65 were cured – 82% with interferon-based treatments and 18% with DAAs *(12)* (Fig. 24).

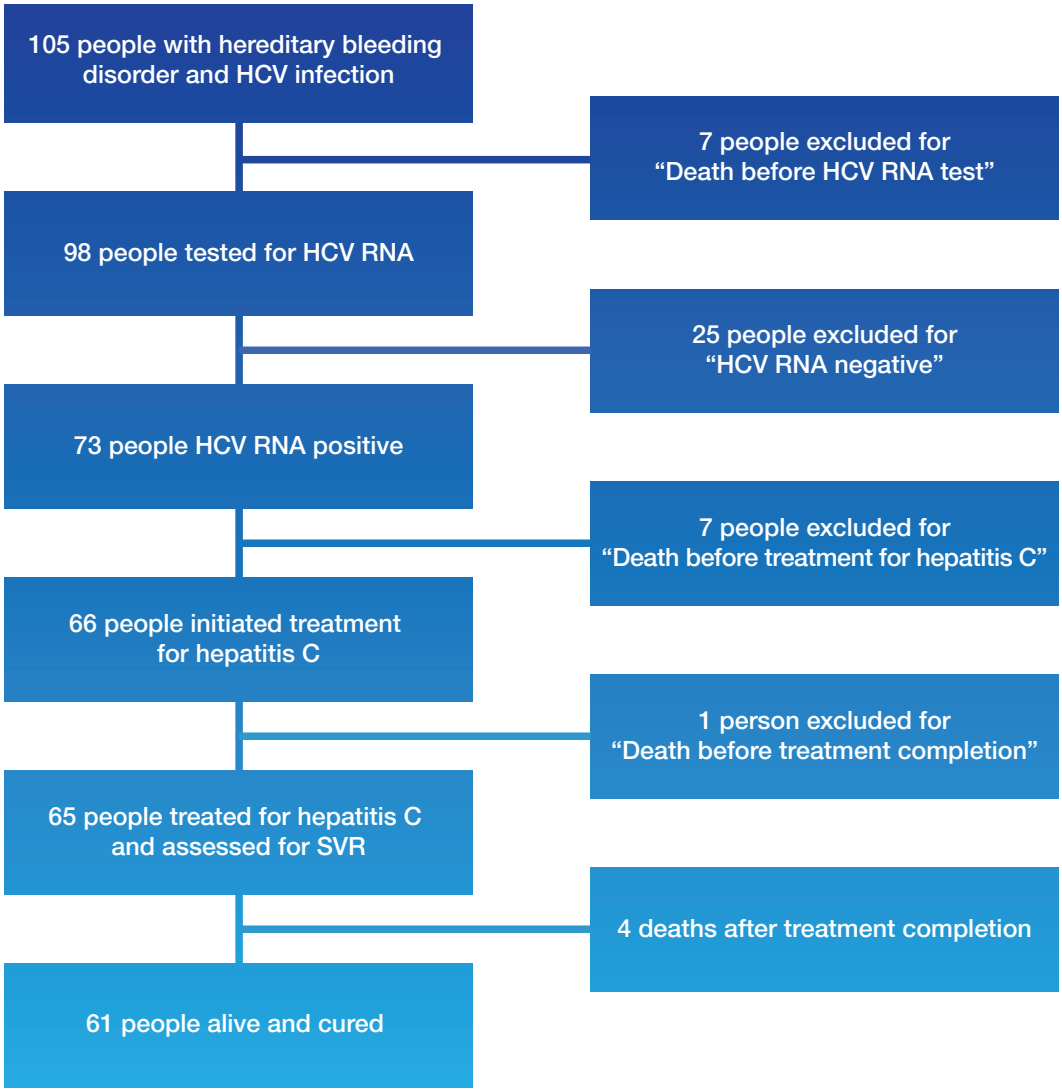
PWID

Before the introduction of the multidisciplinary model in 2007, PWID represented the following proportions of all patients treated for hepatitis C in Slovenia: 5% in 1997–1999, 16% in 1999–2001 and 36% in 2002–2004; whereas, after the introduction of the model, in 2008–2010, this proportion increased to 78% *(3,4,15,16)*. It is remarkable that by the end of 2010, approximately 13% of all HCV-infected PWID at CPTDA had already received hepatitis C treatment (Fig. 25).

During 2015–2017, 45% of all the patients treated with DAAs reported injecting drug use as a mode of infection *(18).* The percentage of SVR in PWID and non-PWID was the same (97%) *(10).* In the CPTDA, 31% of the PWID not treated for hepatitis C had advanced liver disease, and 21% of them had not been linked to care *(145)*. Receiving the results of liver elastography turned out to be an excellent motivator for PWID, since 45% of those with advanced liver disease demanded immediate linkage to care and treatment with DAAs.

Hepatitis C screening and liver elastography in low-threshold settings indicate a prevalence of HCV infection of 38–42% in PWID, with 12% of them with advanced liver fibrosis *(146)*. Thus, counselling, testing, onsite liver fibrosis assessment and immediate linkage to care need to be ensured.

Fig. 24. Diagnosis, treatment and outcomes for people with hereditary bleeding disorders and HCV infection in Slovenia (1997–2018)



Source: Authors.

The pilot project resulted in a partnership with the Ministry of Health to provide a mobile unit with anti-HCV screening and NAT, transient liver elastography and linkage to care for treatment with DAAs. The continuous provision of those services will be offered to all PWID outside the CPTDA throughout the country.

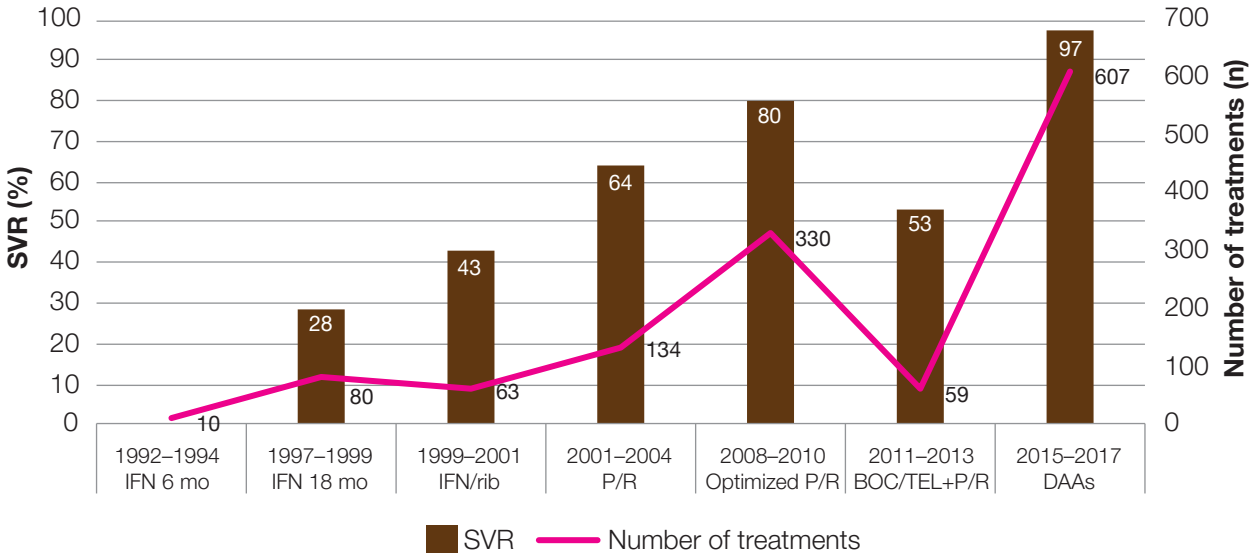
According to the most optimistic scenario and recent studies, approximately 75% of HCV-infected people in Slovenia have been diagnosed and 54% cured for hepatitis C (Maticic M, unpublished data, 2019). The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) recognized the Slovenian approach to hepatitis C in PWID as a model of good practice *(147)*.

Sustainability

The elimination of hepatitis C in populations with concentrated infection is a result of the implementation of the National Strategy for the Management of HCV Infection, created over 20 years ago. The strategy included the integration of hepatitis C elimination into the already existing health-care system and the introduction of new highly effective and safer treatments.

The strategy to eliminate hepatitis C in PWID has involved systematic introduction of various harm reduction initiatives since the early 1990s, and the implementation of a multidisciplinary model for the management of HCV infection, integrating facilities and the use of DAAs.

Fig. 25. PWID treated for hepatitis C and treatment efficacy (SVR), Slovenia (1994–2017)



BOC/TEL = boceprevir or telaprevir; IFN = interferon; IFN/rib = interferon plus ribavirin; P/R = pegylated interferon plus ribavirin.
Source: Authors *(129,130,141,142,144)*.

The future of hepatitis C elimination for Slovenia includes the implementation of mobile units for management of HCV infection in PWID, and improving the management of HCV infection in people in prisons. While HCV testing and treatment for people in prisons have already begun, activities aiming towards the elimination of hepatitis C in this population started at the beginning of 2019 and a multidisciplinary project was to be prepared by the end of that year.

Regardless of the positive results in some population groups, it is still necessary to provide care for those remaining patients with the infection, and regular hepatitis C screening to find new HCV infections and monitor those at risk of reinfection.

SPAIN Control of HCV infection in prisons in Catalonia, Spain

Strategic Direction 1 | Strategic Direction 2 | Strategic Direction 3

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Background

Catalonia is an autonomous region in Spain with a population of 7.5 million people. The region has nine prisons and as of 2016, a prison population of 14 137– an estimated incarceration rate of 110.7 per 100 000 people *(148)*.

In 2002, approximately 40% of people in prisons were found to be anti-HCV positive – a scenario that would eventually lead to the development and implementation of the Prison Hepatitis Programme. The programme was originally aimed at preventing transmission of viral hepatitis and providing diagnosis and treatment, and in recent years has incorporated the goal of elimination of hepatitis C, aligning itself with the GHSS *(149)* and Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region *(150)*.

Description of the good practice

In order to meet the goals of the elimination strategy, it is essential to diagnose HCV infection and implement the following: (i) harm reduction and OST; (ii) universal access to antiviral treatment (including for HCV-infected and reinfected patients) and timely delivery; (iii) epidemiological surveillance focusing on new cases and reinfections after treatment in population groups at high-risk for transmission; and (iv) improved coordination of services inside and outside prisons

for continuous follow-up and treatment, especially for patients with advanced liver disease after their release from prison.

Worldwide, the prevalence of HCV infection in people in prisons and other closed settings is very high *(151)*. Although such prevalence has notably decreased in Catalonia in recent years, it is estimated that 2.7% of people in prisons remain HCV infected *(148).* This is 5.5–3.5 times higher than the prevalence rates found in the non-prison population (0.2–0.5%) *(152,153).*

There is a good quantity of quality data on HCV infection among people in prisons in Catalonia – practically all people undergo HCV screening upon admission. Procedures for diagnosis include ELISA tests and arrangements to prevent double blood collection for confirmatory tests. Though screening upon admission is voluntary and people in prisons are free to refuse it, the coverage rate for the screening is high (83.7%) *(148)*. Screening is not performed for those staying for less than 7 days.

In general, people in prisons who admit engaging in practices with risk of infection agree to undergo the screening. Those who reject the tests, usually claim that they do not engage in these practices, even though it is still possible that they may have acquired the infection at an earlier time when the current mechanisms to ensure blood safety were not available.

The emergence and use of DAAs has revolutionized the treatment of hepatitis C. The effectiveness of treatment with DAAs is as high as 90–100% in most scenarios. Between January 2015 and September 2018, 117 452 patients were treated with DAAs in Spain *(154)* and 130 000 patients were expected to have received the antiviral treatment by the end of June 2019.

Spain is among the eight countries in the world that have treated the highest proportion of patients per population, and is one of the nine countries estimated in a recent study to be on track for eliminating hepatitis C by 2030 *(155)*. Since the beginning of treatment with DAAs, people in prisons in Catalonia have been treated without any type of discrimination – that is, under conditions similar to those provided to the non-prison population, while obtaining the same results in terms of efficacy *(156)*.

Providing treatment to this population is essential to achieve the elimination of hepatitis C *(157,158)*.

Evidence of impact

The programme implemented in Catalonian prisons has achieved excellent results; however, the target population requires complementary actions to prevent reinfection and guarantee continuity for follow-up, treatment and care after release.

Prevention of reinfection

Our research identified that for people in prisons in Catalonia, both PWID and PLHIV with a history of injection drug use have a higher risk of reinfection after successful treatment for hepatitis C *(159,160)*. Therefore, prisons can play a key role in the detection and treatment of HCV reinfection. In order to detect reinfection, our programme provides HCV RNA tests twice a year for each patient who is successfully treated for hepatitis C and yet continues practices associated with risk of reinfection. The follow-up is combined with counselling and optimized harm reduction, including OST and NSPs.

The incidence rate of reinfection among people in prisons in Catalonia is 2.9 per 100 person-years (p-y); 3.9 per 100 p-y in PWID, and 5.6 per p-y in PLHIV with a history of injection drug use (Fig. 26).

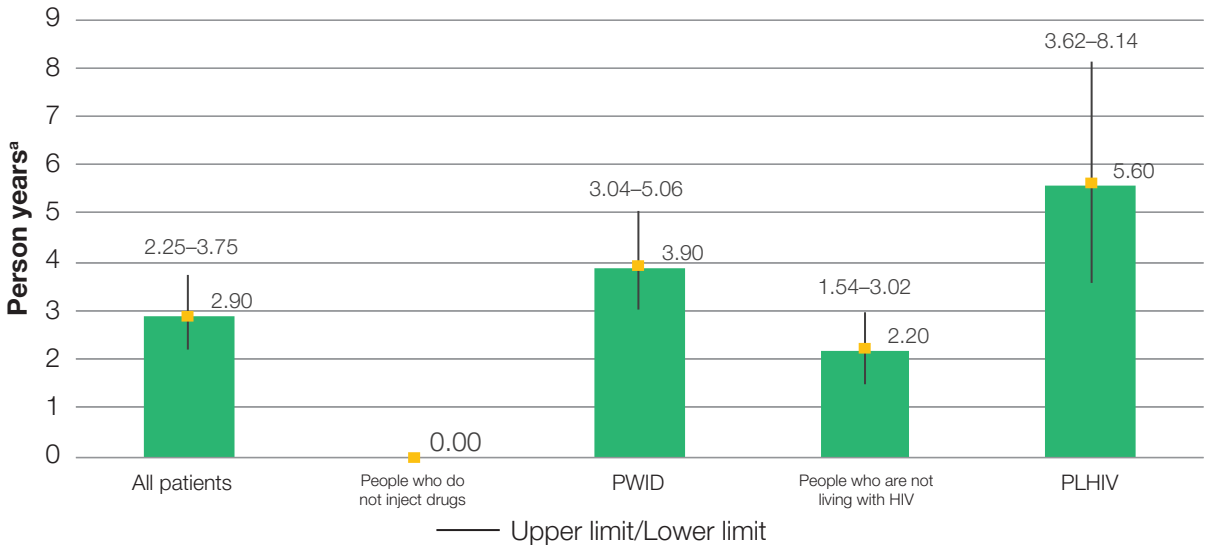
Continuity after release

Release from prison may take place earlier than is expected by prisons health services, putting the continuity of prevention, treatment and care at risk. In Catalonian prisons, treatment discontinuation rates due to patient decisions or adverse effects is very low but increases after release from prison *(156)*. In order to support treatment after release, the Prison Health Programme of the Catalan Institute of Health created the position of “liaison nurse” in late 2017. The liaison nurses are responsible for improving coordination with out-of-hospital services, following-up HCV infected people and monitoring their compliance with hepatitis C treatment.

The recently published preliminary results of this practice are very positive *(161)*, and are likely to improve as more experience is gained, thus optimizing the coordination of health services inside and outside prisons.

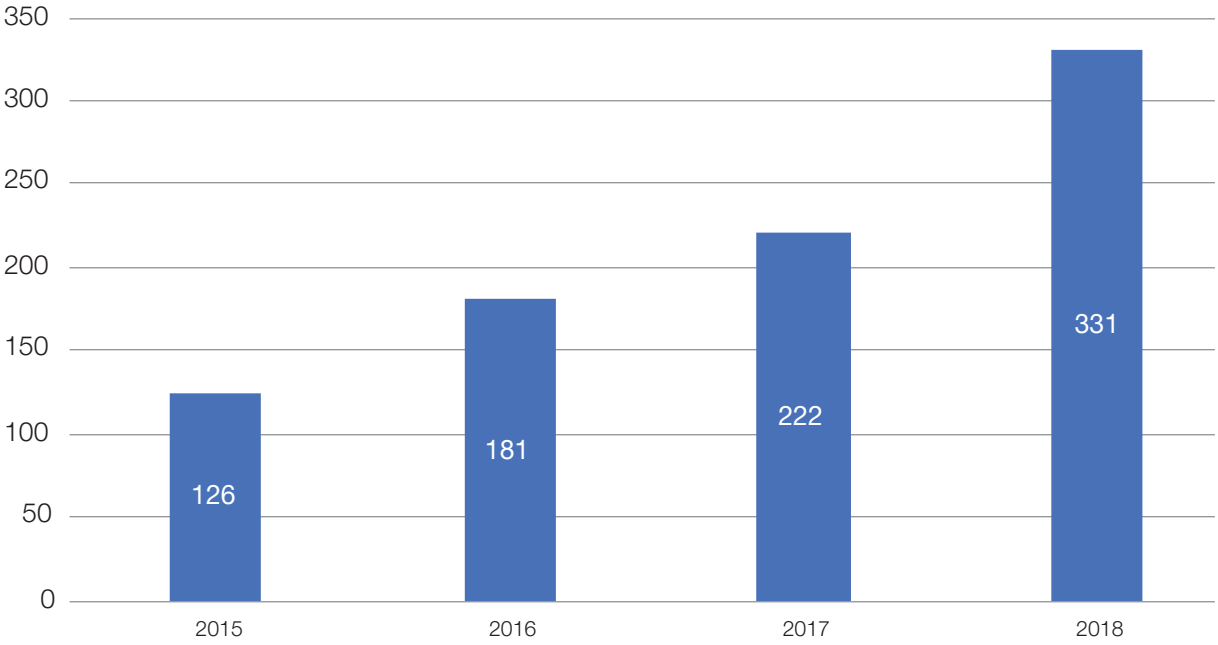
In Catalonia, 860 people in prisons were treated with DAAs between 2015 and 2018 (Fig. 27).

Fig. 26. Incidence of reinfection in people in prisons after successful treatment for hepatitis C (SVR), Catalonia, Spain (2018–2019)



[a] The product of the total time between successful treatment and reinfection (in years) times the number of people in prisons who were successfully treated and monitored.
Source: Authors.

Fig. 27. Number of people in prisons treated with DAAs, Catalonia, Spain (2015–2018)



Source: Authors.

This impressive uptake in hepatitis C treatment brought a steady and progressive reduction of HCV viraemia in Catalonian prisons. The prevalence of HCV viraemia has been reduced by 2.2% annually. In September 2019, the prevalence in Catalonian prisons was 1.6% (Fig. 28).

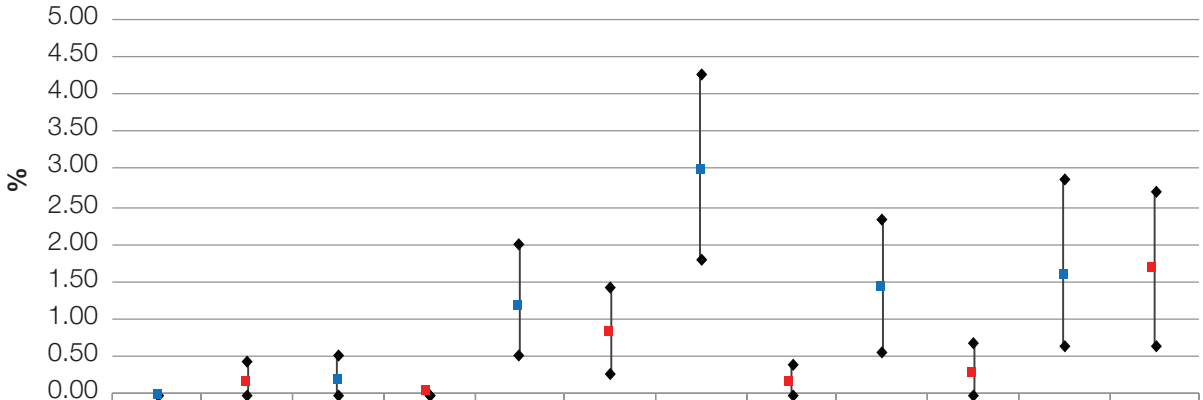
A recent study with linear exponential smoothing (LES) based on diagnosis and therapeutic time series in Catalonian prisons over a 15-year period, stated that hepatitis C could be eliminated from Catalonian prisons by the end of 2021 *(162)*. The quality and quantity of the data used for this estimation has substantially improved in recent months, raising the possibility that elimination might be achieved earlier than calculated.

Sustainability

To make our best practice sustainable, scientific associations and the regional public health and prison services must continue to work together. The purpose of

the Prison Hepatitis Programme is to continue with the goal of eliminating hepatitis C in a short period of time.

Fig. 28. Prevalence of HCV viraemia in people in prisons, Catalonia, Spain (2019)



	20 to 29 (1997-1988)		30 to 39 (1987-1978)		40 to 49 (1977-1968)		50 to 59 (1967-1958)		60 to 69 (1957-1948)		70 to 80 (1947-1937)	
	M	F	M	F	M	F	M	F	M	F	M	F
CI 95% UL	0.00%	0.45%	0.54%	0.00%	2.00%	1.43%	4.29%	0.42%	2.35%	0.67%	2.89%	2.72%
CI 95% LL	0.00%	0.00%	0.00%	0.00%	0.51%	0.26%	1.79%	0.00%	0.58%	0.00%	0.63%	0.64%
Prevalence	0.00%	0.15%	0.18%	0.00%	1.20%	0.79%	3.00%	0.14%	1.43%	0.27%	1.61%	1.65%

Source: Authors.

SPAIN Prevalence of hepatitis C in Spain: results from a national population-based survey in 2017–2018

Strategic Direction 1

Working Group of the HCV Prevalence Study in Spain in 2017–2018 *(163)*

Background

In 2015, the Spanish Interterritorial Council of the National Health System approved the Strategic Plan to Address Hepatitis C in the National Health System (PEAHC) *(164)*. This plan aims to reduce morbidity and mortality rates in the Spanish population, addressing the prevention, diagnosis, treatment and monitoring of HCV infection. Between January 2015 and June 2019, 131 582 patients in Spain were treated with DAAs, with a therapeutic efficacy of 95.7%. The plan is structured along four strategic lines; the first aimed at measuring the extent of the problem, describing the epidemiological characteristics of people with HCV infection and establishing prevention measures.

Until 2018, most of the studies on prevalence of HCV infection carried out in Spain were limited to certain regions and lacked information about viraemic confirmation. An extrapolation of studies published in 2014 showed an estimated national prevalence of anti-HCV of 1.7% and of viraemia of 1.2% *(165)*. A higher prevalence of anti-HCV has been found in populations at risk: 47–85% in PWID *(166,167,168)*, 3.2% in MSM with HIV coinfection *(169)*, 1.6% for adult migrants (7.1% in those from certain European areas and 3.1% from sub-Saharan Africa) *(170)*, and 10.6% in prison settings (3% for viraemia) in 2018 *(171)*.

Description of the good practice

Decision-making in public health needs to be supported by the best available epidemiological evidence. To this end, and in the context of the first strategic line of the PEAHC, a population-based study was conducted to estimate the prevalence of HCV infection in Spain.

This study was part of the second seroprevalence study in Spain: a descriptive cross-sectional study on the immune status against vaccine-preventable diseases and other important diseases for public health of the general population aged 2–80 years living in Spain. Fieldwork was carried out between May 2017 and May 2018 *(163)*.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A detailed description of the study methodology has been published *(172)*. A two-stage sampling strategy was conducted considering the size of the population ascribed to the primary health centres. First-stage sampling units were primary health care centres with blood collection facilities. Second-stage sampling units were individuals attending a blood test, randomly selected from the blood extraction queue. Where necessary, the sampling process was completed with simple random selection among the eligible population registered with a given health centre. The number of people born outside Spain was monitored so that it would not exceed the proportion of the general population. People who were identified as having any condition and/or treatment leading to immunodeficiency (which included AIDS but not HIV) were excluded.

In the case of HCV, laboratory testing was conducted at the National Centre for Microbiology (CNM) of the Institute of Health Carlos III through:

- a study of the presence of anti-HCV with chemiluminescence assay (accredited by Entidad Nacional de Acreditación);
- HCV RNA detection through nested polymerase chain reaction polymerase chain reaction (PCR) of the 5'NC region (method developed by CNM, estimated sensitivity 1000 UI/ml);
- HCV genotype determination in RNA positive samples, by amplification of NS5B regions and population sequencing (method developed by CNM, estimated sensitivity 10 000 UI/ml);
- two anti-HCV substantive tests through Western blot, considering negative, positive or undetermined values, as prescribed by the manufacturer.

Cases were classified in the following categories:

- Positive cases:
  - presence of anti-HCV
    - cases with reactive total antibodies in the chemiluminescence assay and HCV RNA detection;
    - cases with reactive total antibodies in the chemiluminescence assay and one or both positive confirmatory tests;
  - active HCV infection: cases with detectable HCV RNA.
- Negative cases: people without reactive total antibodies in the chemiluminescence assay or people with reactive antibodies but negative HCV RNA and negative results in both antibody confirmatory tests. People with reactive total antibodies in the chemiluminescence assay, negative HCV RNA and undetermined results in both antibody confirmatory tests were not considered confirmed HCV cases. Those results could correspond to residual antibodies against HCV or false positives, but only rarely to active HCV infection cases.

For confirmed and undetermined cases of HCV infection, a letter was sent to the corresponding health professional providing the results, requesting further information be provided to the public health services of the autonomous communities regarding whether the HCV infection case was previously known or not, as well as requesting additional information on HCV risk factors, linkage to care and treatment with DAAs.

The adjusted prevalence of anti-HCV and active HCV infection was obtained using weighting inverse to the selection probability. Confidence intervals at 95% were calculated to estimate prevalence using bootstrapping techniques.

Evidence of impact

The HCV prevalence study within the second seroprevalence study in Spain approached 17 496 people, of whom 9103 agreed to participate and met inclusion criteria. Out of the 9103 samples analysed, 9002 were negative and 101 were reactive to anti-HCV in the chemiluminescence assay. After verifying with RNA or Western blot in those with negative RNA, 66 cases were confirmed, which corresponded to a weighted prevalence of anti-HCV of 0.69% (95% CI: 0.50%–0.87%). In 17 of those cases, HCV RNA was detected, yielding a weighted prevalence of active HCV infection of 0.17% (95% CI: 0.08%–0.28%). No confirmed case of hepatitis C was found in people under 20 years of age, so the analyses focused on the population aged 20–80 years (sample of 7675 people).

In the population aged 20–80 years, the weighted prevalence of anti-HCV was 0.85% (95% CI: 0.64%–1.08%) and the weighted prevalence of active infection was 0.22% (95% CI: 0.12%–0.32%). The prevalence of positive antibodies and of active infection was higher in men, in the population aged 50–59 years and in underprivileged social classes (Table 11).

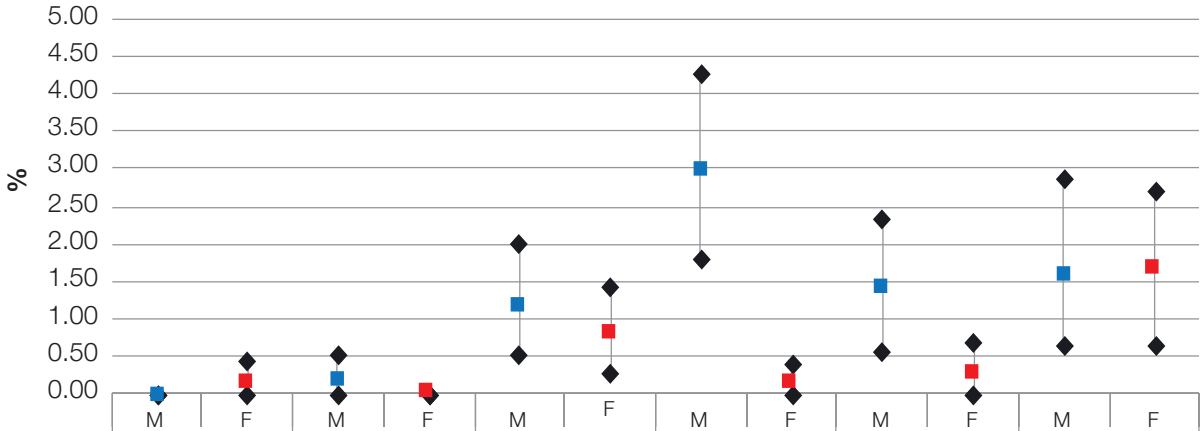
Table 11. Weighted prevalence of anti-HCV and active HCV infection according to sociodemographic variables in people aged 20–80 years, Spain (2017–2018)

Characteristics		Anti-HCV			Active HCV infection		
	N	n	%	95% CI	n	%	95% CI
Sex							
Male	3 670	48	1.24	(0.92–1.58)	14	0.35	(0.17–0.53)
Female	4 005	18	0.46	(0.28–0.66)	3	0.08	(0.01–0.18)
Age group (birth year)							
20–29 (1997–1988)	1 207	1	0.07	(0.00–0.15)	0	0.00	(0.00–0.00)
30–39 (1987–1978)	1 202	1	0.09	(0.01–0.17)	1	0.09	(0.01–0.17)
40–49 (1977–1968)	1 432	14	0.99	(0.57–1.48)	2	0.14	(0.00–0.28)
50–59 (1967–1958)	1 417	22	1.56	(0.99–2.27)	7	0.50	(0.22–0.85)
60–69 (1957–1948)	1 426	12	0.83	(0.48–1.25)	5	0.34	(0.06–0.69)
70–80 (1947–1937)	991	16	1.63	(0.87–2.49)	2	0.19	(0.00–0.39)
Country of birth							
Spain	7 186	59	0.81	(0.61–1.03)	15	0.20	(0.10–0.30)
Other	489	7	1.30	(0.44–2.44)	2	0.34	(0.00–0.96)
Community size							
<10 000	1 535	17	1.04	(0.59–1.53)	3	0.18	(0.00–0.38)
(10 000–50 000)	1 986	13	0.71	(0.41–1.07)	5	0.26	(0.06–0.49)
(50 000–100 000)	984	8	0.82	(0.32–1.35)	1	0.08	(0.00–0.29)
(100 000–500 000)[a]	1 860	18	0.94	(0.57–1.33)	4	0.24	(0.08–0.45)
>500 000	1 310	10	0.70	(0.27–1.19)	4	0.24	(0.01–0.52)
Formal schooling							
1st grade or lower	2 340	38	1.71	(1.22–2.24)	12	0.54	(0.28–0.84)
2nd grade, 1st cycle	1 478	9	0.62	(0.28–1.05)	1	0.07	(0.00–0.21)
2nd grade, 2nd cycle	1 756	13	0.66	(0.27–1.10)	3	0.14	(0.00–0.36)
3rd grade	1 888	5	0.27	(0.06–0.49)	1	0.05	(0.00–0.15)
Social class[b]							
I (privileged)	1 717	7	0.40	(0.16–0.71)	2	0.12	(0.00–0.29)
II (middle)	1 459	8	0.50	(0.16–0.85)	2	0.10	(0.00–0.30)
III (underprivileged)	4 246	51	1.20	(0.91–1.53)	13	0.31	(0.17–0.48)
Total	7 675	66	0.85	(0.64–1.08)	17	0.22	(0.13–0.31)

[a] Including provinces and capitals.
[b] According to the Spanish National Classification of Occupations (Clasificación Nacional de Ocupaciones/CNO-94) and Spanish Society of Epidemiology (Sociedad Española de Epidemiologia/CSO-SEE12).
Source: Authors.

A clear pattern by age and sex can be identified, with the highest anti-HCV prevalence among men older than 50 years and women older than 70. The highest prevalence of active infection is shown in men aged 50–59 and 60–69 years, with figures of 0.86% and 0.72%, respectively, and with the remaining groups under 0.20% (Fig. 29 and 30).

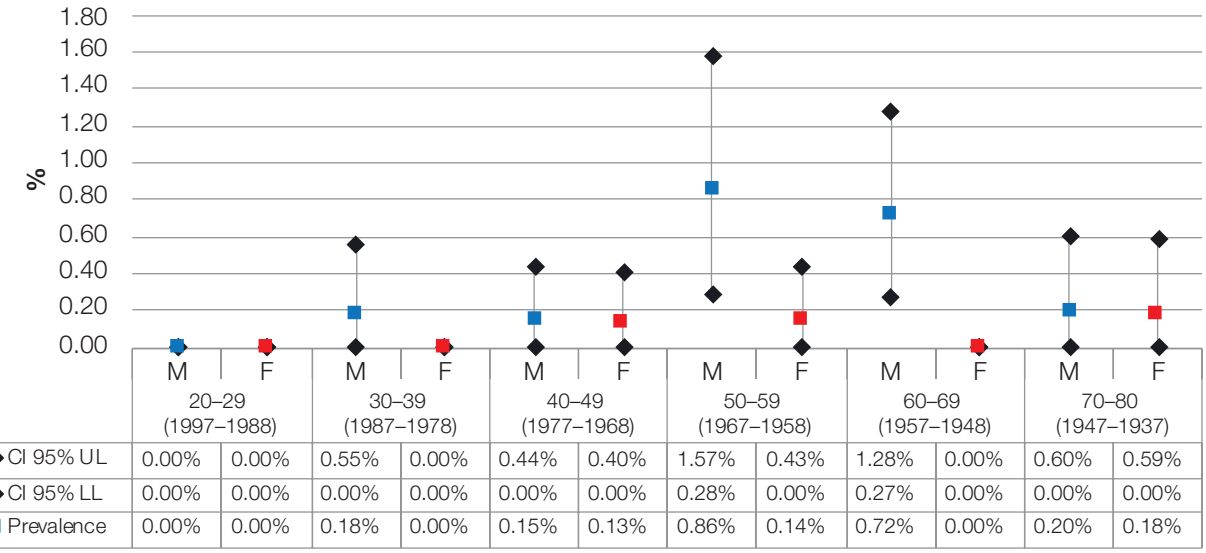
Fig. 29. Prevalence of anti-HCV by sex and age groups, Spain (2017–2018)



	20 to 29 (1997-1988)		30 to 39 (1987-1978)		40 to 49 (1977-1968)		50 to 59 (1967-1958)		60 to 69 (1957-1948)		70 to 80 (1947-1937)	
	M	F	M	F	M	F	M	F	M	F	M	F
CI 95% UL	0.00%	0.45%	0.54%	0.00%	2.00%	1.43%	4.29%	0.42%	2.35%	0.67%	2.89%	2.72%
CI 95% LL	0.00%	0.00%	0.00%	0.00%	0.51%	0.26%	1.79%	0.00%	0.58%	0.00%	0.63%	0.64%
Prevalence	0.00%	0.15%	0.18%	0.00%	1.20%	0.79%	3.00%	0.14%	1.43%	0.27%	1.61%	1.65%

LL = lower limit; UL = upper limit.
Source: Authors.

Fig. 30. Active HCV infection by sex and age groups, Spain (2017–2018)



	20–29 (1997–1988)		30–39 (1987–1978)		40–49 (1977–1968)		50–59 (1967–1958)		60–69 (1957–1948)		70–80 (1947–1937)	
	M	F	M	F	M	F	M	F	M	F	M	F
◆ CI 95% UL	0.00%	0.00%	0.55%	0.00%	0.44%	0.40%	1.57%	0.43%	1.28%	0.00%	0.60%	0.59%
◆ CI 95% LL	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.28%	0.00%	0.27%	0.00%	0.00%	0.00%
■ Prevalence	0.00%	0.00%	0.18%	0.00%	0.15%	0.13%	0.86%	0.14%	0.72%	0.00%	0.20%	0.18%

Source: Authors.

The undiagnosed fraction for anti-HCV was 18.6% and for active HCV infection was 29.4%. Of those cases where the active HCV infection was previously known by the health system, 50% were verified as having started treatment with DAAs, in 17% there was an absence of DAA treatment (both were PWID) and in the remaining 33% this information was not available.

Regarding genotype characterization of HCV cases with active infection, the most frequent was genotype 1b (41.2%), followed by 1a (23.5%), 3a (11.8%), 2c (5.9%), 4a (5.9%) and inconclusive (11.8%).

This study has provided an accurate description of the epidemiology of HCV infection, which places Spain at a low level of prevalence of active infection and provides key information for decision-making to fulfil the commitments towards the elimination of HCV as a public health problem in Spain by 2030. In this sense, and in the context of the objectives of the Strategic Plan to Address Hepatitis C, these results will inform

the recommendations on the HCV screening strategy in the National Health System.

Sustainability

Population-based surveys are highly valued due to their representativeness of the general population. However, they have a significant cost and it is therefore essential to maximize their utility for decision-making in public policy. For this reason, in terms of the sustainability of this study, it is key to include the study of HCV infection in future seroprevalence surveys of vaccine-preventable and other diseases important for public health. The continuity of this type of survey, both at a national and at a regional level, will allow us to evaluate the policies implemented to reduce the prevalence of hepatitis C.

SPAIN Unidad Móvil de Cribado (Mobile Screening Unit) in Spain

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 5

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Background

Since the approval of DAAs for HCV treatment, more than 120 000 patients have been treated in Spain. Part of the reason this has been possible is because Spain has had free, universal health care and governmental policies facilitating therapy without any restrictions since 2015. However, according to a recent seroprevalence survey conducted by the Spanish Ministry of Health, it is estimated that around 80 000 people in Spain are anti-HCV positive and require HCV treatment. Many of the HCV infected patients who are awaiting DAA therapy have poor access to health care and treatment, mainly because they belong to vulnerable population groups.

In Spain, therapies with DAAs can only be prescribed by HCV clinics in hospital settings. This is the main barrier for many patients, as access to hospital is challenging and very limited among vulnerable populations.

To address this issue and facilitate testing for HCV and HBV and provide access to therapy in all districts of Madrid, we have implemented an alternative service, Unidad Móvil de Cribado (Mobile Screening Unit) (UMC), comprising a mobile unit to reach these vulnerable populations, test them for HCV, HBV and HIV, and ensure their prompt treatment at a hospital.

The mobile unit and accompanying service is used to reach the most vulnerable population groups, who might not be attending a hospital or clinic due to stigma and discrimination, injection drug use, homelessness and other social determinants that impair access to health services.

Description of the good practice

The mobile unit can promote equity in health by bringing anonymous prevention, screening and diagnosis with point-of-care testing and referral, and accompanying services provided by trained staff and volunteers, directly to the sites where the most vulnerable population groups gather in Madrid. These hot spots include Cañada Real shanty town, home of 40 000 residents, among them immigrants, refugees and Roma people; other housing and sheltering facilities; and places where sex work takes place.

The project promotes prevention and awareness and linkage to care by offering to take patients by car to University Hospital Infanta Leonor for additional blood tests, liver elastography, ultrasound (if cirrhosis is present), and medical evaluation. Patients can take any necessary medication from the hospital pharmacy on the same day.

Meanwhile, the project collects data on sociodemographic factors, consumption habits and acceptability of the approach using an open-source software platform – REDCap. The data collected make a valuable contribution to improving the understanding of social determinants of health, potential social transformation and the impact of diagnosis, retention and treatment of hepatitis C in the public health system. All patients sign an informed consent form.

Approval of the Gregorio Marañón Hospital ethics committee has been obtained.

Evidence of impact

The data collected in March–June 2019 are displayed in Table 12.

Table 12. Clinical, sociodemographic and epidemiological characteristics of people using the UMC, Madrid (2019)

	Total (786)		Homeless (547)		Foreigner (348)		Active drug user (263)	
	N	%	N	%	N	%	N	%
Age (mean years)		43		43		41		44
Male	585	74.6	416	76.2	283	81.3	204	77.9
No economic income	444	57.1	387	71.1	284	82.3	151	58.5
Irregular situation in the country	100	13.0	96	17.8	99	29.3	12	4.6
Alcohol consumption (>50g/day)	240	30.7	158	28.9	78	22.5	93	35.4
Smoker	607	77.8	423	77.6	228	66.3	252	95.8
Has ever had problematic drug use	394	50.8	233	43.2	91	26.4	263	100.0
Stable partner	169	21.6	89	16.3	60	17.3	60	22.9
Contact with family	431	55.2	229	42.1	205	59.2	123	47.3
Risky sexual behaviour in last year	457	58.8	290	53.6	202	58.7	193	74.8
Sex worker	9	2.0	7	2.5	4	2.0	8	4.3
Positive HIV rapid test	66	9.4	43	9.0	9	3.0	34	14.4
Positive HCV rapid test	210	27.5	133	25.0	47	13.9	121	47.3
Positive HCV PCR	74	40.7	52	43.3	16	39.0	40	37.7
Positive HBV rapid test	1	0.9	1	2.1	1	2.8	1	2.3
Needs linkage to care	71	36.4	49	45.4	16	29.1	39	42.9
Referral offered	61	9.0	44	8.8	16	5.0	29	12.6
Accompaniment to hospital by educator	53	7.9	38	7.7	14	4.4	26	11.5
Started therapy for viral hepatitis	21	91.3	18	44.6	4	25	10	25

Source: Authors.

The active search for cases with the mobile unit achieved a detection rate of 27.5% for anti-HCV and a prevalence of 9.4% for active hepatitis C among all clients tested. In the four-month period of implementation (March–June 2019), 53 patients were taken to a reference hospital by an educator or a navigator. Navigators provide patients with a direct path to the HCV clinic.

The UMC facilitated additional partnerships with the private sector for the continuous provision of services, particularly for RDT and resulted in an agreement with the Madrid City Council to open different community centres for screening hepatitis C.

Sustainability

The project is financed through several funds and organizations. It is not directly sponsored by the Government of Spain, yet its effective and simple strategy will enable the project to operate independently through the next 12 months.

UKRAINE A national policy to improve access to hepatitis C treatment with lower prices and generic medicines in Ukraine

Strategic Direction 1 | Strategic Direction 2 | Strategic Direction 4

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Background

Hepatitis C is a major threat to public health in Ukraine. It is estimated that 3.6% of the population – approximately 1 517 515 people – are infected with HCV. Yet, only 82 654 people have been registered in health-care facilities – approximately 5.4% of the total number of people believed to be infected.

Improving access to treatment is essential to the success of the global strategy to eliminate hepatitis C, the GHSS *(173)*. In order to meet the regional and global targets, Ukraine needs to make best use of its resources and maximize the number of patients treated with effective medicines purchased with public funds. Only by doing so, will the country be able to achieve the goal of treating 80% of eligible people with chronic HCV infection by 2030.

Description of the good practice

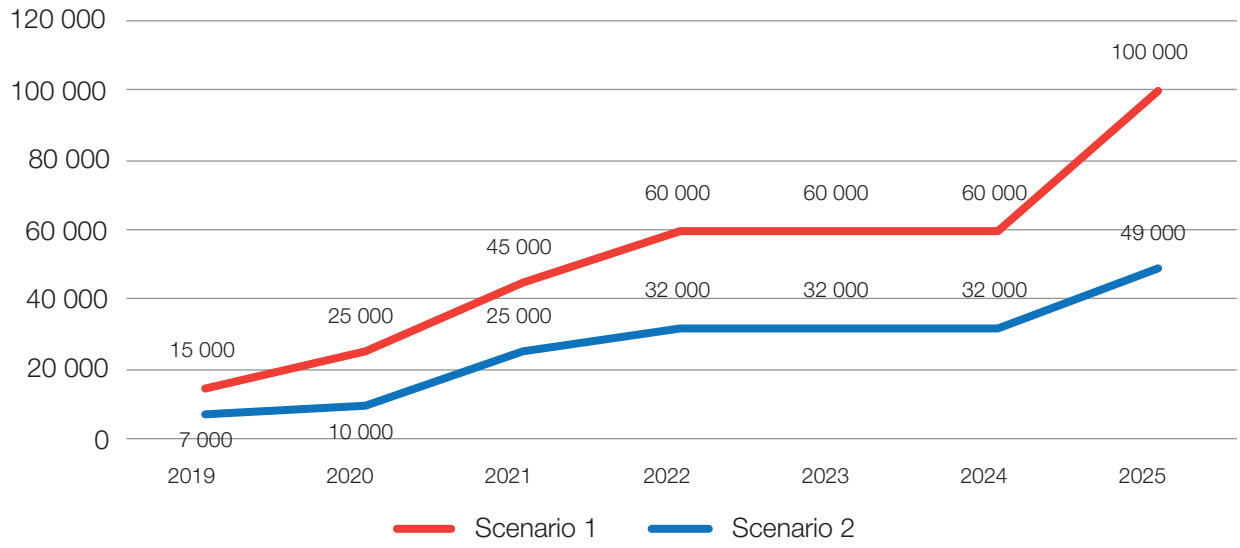
The Public Health Centre of the Ministry of Health is committed to supporting Ukraine in developing the appropriate response to hepatitis C and assisting the country in reaching the elimination goals. As a part of this, the Public Health Centre developed mathematical models for the elimination of hepatitis C. This work was concluded in 2018 and had support from WHO; the Centre for Disease Analysis; national experts in the fields of epidemiology, blood safety, infectious diseases and viral hepatitis; NGOs; and other stakeholders.

The mathematical models estimate the number of people that must be treated for hepatitis C in Ukraine each year – accounting for the scale-up of services and intent to meet the global objectives by 2030 (Fig. 31). Scenario 1 states that 15 000 people should be treated in 2019, 25 000 in 2020, 45 000 in 2021 and 60 000 every year from 2022 to 2025. After 2025, it would be necessary to treat 100 000 or more people every year. Scenario 2 states that to achieve 50% of the target for elimination of hepatitis C, it is necessary to treat 7 000 patients in 2019, 10 000 in 2020, 25 000 in 2021 and 32 000 every year from 2022 to 2025. After 2025, it would be necessary to treat 49 000 people every year.

Evidence of impact

The Ministry of Health provides the financial resources for the purchase of medicines for treatment of viral hepatitis B and C. Approximately US$ 14 million were

Fig. 31. Hepatitis C treatments estimated per year to reach 50% and 100% of the treatment goals in the GHSS



Source: Authors.

allocated for this purpose during 2013–2016, and US$ 15 million during 2017–2019. In these seven years (2013–2019), only 8000 people were treated for hepatitis C with medicines purchased with public funds.

Considering the number of treatments provided and the likelihood that the dedicated budget will not be increased soon, Ukraine would not be able to achieve the estimated number of treatments per year required to achieve the global goals for elimination if branded antivirals were purchased at their original prices – branded sofosbuvir/ledipasvir could be purchased at approximately US$ 900 per 12-week treatment course.

Therefore, making best use of the financial resources available in the state programme became the top priority for Ukraine. This resulted in a joint effort, coordinated by the Ministry of Health, to improve access to hepatitis C treatment – negotiating price, patents and the introduction of generic medicines through procurement with international organizations.

The negotiations received support from health-care workers, specialists, academia, civil society and pharmaceutical companies and resulted in a substantial reduction in prices for treatment with DAAs: sofosbuvir/ledipasvir and sofosbuvir/daclatasvir at US$ 89 per 12-week treatment course and sofosbuvir/velpatasvir at US$ 250 per 12-week treatment course.

The next step for Ukraine is to optimize programmatic information and future purchases of antivirals in line with WHO recommendations, and continuously improve access to treatment.

Sustainability

In 2018–2019, nine generic highly effective antivirals were registered in Ukraine, including daclatasvir, sofosbuvir and sofosbuvir/ledipasvir from different manufacturers, supporting competition and further price reduction. The availability of sofosbuvir and daclatasvir as a pangenotypic treatment regimen also contributed to a decrease in costs in the continuum of care by eliminating HCV genotyping tests.

The reduction of costs with these new prices will allow a tenfold increase in the current numbers of hepatitis C treatments in Ukraine.

UKRAINE Integrated hepatitis C management for high-risk and vulnerable populations in Mykolaiv, Ukraine

Strategic Direction 2 | Strategic Direction 3

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Background

It is estimated that 5% of the total population of Ukraine is infected with HCV (2 107 660), of which 3.6% (1 517 515) have chronic hepatitis C, of which only 82 654 are under medical supervision (authors, unpublished data, 2020). Mykolaiv Province has a high prevalence of HIV infection and the second highest number of patients under OST in the country. These population groups are at highest risk for hepatitis C. As of September 2017, Mykolaiv Regional Centre for Palliative Care and Integrated Services (MRCPCIS), the reference health service in the province, has identified 2769 anti-HCV positive patients.

The main challenge in Ukraine is the lack of availability of affordable diagnostic services and treatments. Generic DAAs had not been registered in Ukraine in 2017 when the project began, which meant higher costs and thus inaccessible treatment to many.

Description of the good practice

The objective of the project is to integrate hepatitis C services into existing harm reduction programmes such as OST services and at the MRCPCIS as a way to better address the needs of vulnerable groups. The project aims to ensure access to free hepatitis C diagnosis, liver fibrosis staging and treatment with DAAs, and to develop an adapted comprehensive case management

approach for hepatitis C which includes up-to-date technologies for diagnosis, liver fibrosis staging and treatment. It also aims to provide integrated counselling for adherence and health promotion, and training on hepatitis C for health-care workers.

In collaboration with the Ministry of Health of Mykolaiv Province, Médecins Sans Frontières (MSF) supports the testing and treatment of 1000 patients with generic sofosbuvir and daclatasvir, 750 PLHIV undergoing antiretroviral therapy, 150 OST clients and 100 health-care workers.

All patients with chronic hepatitis C are being treated using generic sofosbuvir and daclatasvir for 12 or 24 weeks depending on the genotype and presence of cirrhosis. Patients undergo elastography, and APRI is calculated before commencing treatment to assess the stage of cirrhosis. The current genotypic distribution of HCV is as follows: 1A, 11%; 1B, 41%; 2, 2%; 3A, 35%; 4, 0%. Patients undergo HCV viral load tests 12 weeks after completion of treatment, which decides the outcome of the treatment.

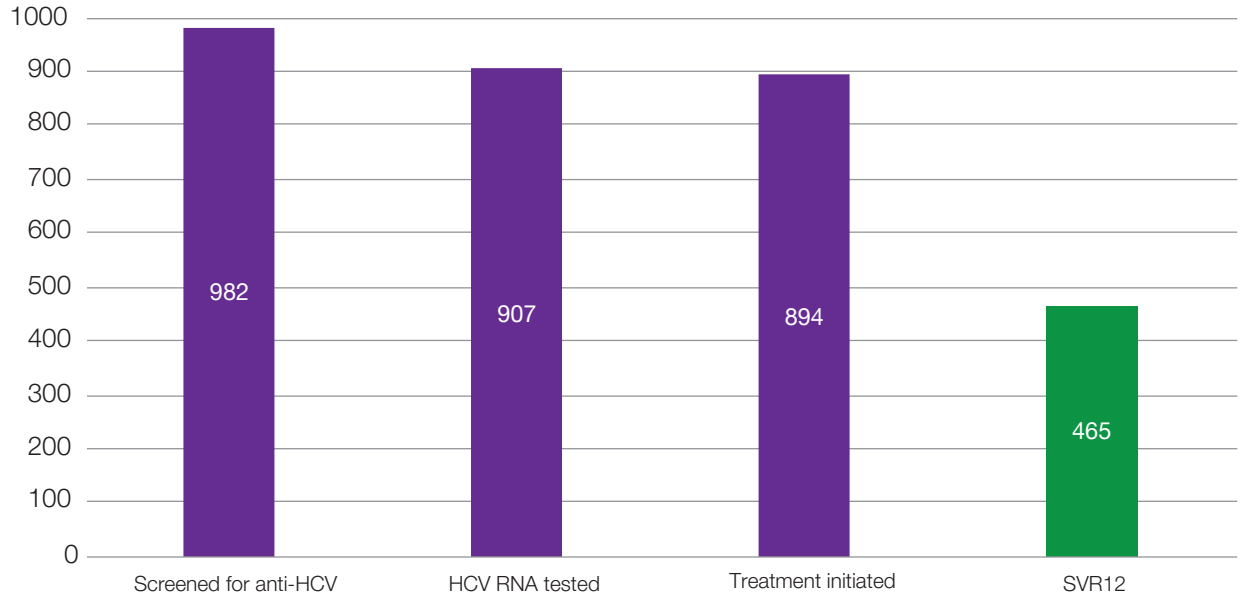
Treatment for HCV infection in patients with special needs is similar to the treatment of chronic diseases with respect to psychosocial support and the need for lifestyle modification. For this purpose a psychosocial team comprising social workers and peer educators is made available to the patients. The objective is to support each patient regarding different adherence barriers they may face during treatment and that affect treatment outcome. The patients undergo screening for depression with a Patient Health Questionnaire (PHQ-9) and Alcohol Use Disorders Identification Test (AUDIT). Patients on treatment are monitored for adherence, and encouraged to modify their lifestyles with respect to diet, alcohol use, safe sex practices, using clean needles and avoiding sharing needles. Patients needing professional support are referred to psychologists for further management. Patients who miss visits or are LTFU are contacted promptly by the psychosocial team and linked back to care.

Evidence of impact

A total of 894 patients have received or are currently on treatment for chronic hepatitis C. The cure rate is 97.4% with generic sofosbuvir and daclatasvir; the failure rate is 2% (Fig. 32). The rate of LTFU is 0.42%.

During November 2017 to June 2019, 993 patients were provided with patient support, education and counselling (PSEC) services. The main outcomes of such PSEC services are the stabilization of patients' conditions and the avoidance of risky behaviour. Patients demonstrate a high level of knowledge about hepatitis C (92%), and good adherence to treatment (94%).

Fig. 32. Cascade of care for hepatitis C in PLHIV, OST clients and health-care workers, Mykolaiv, Ukraine (2017–2019)



Source: Authors.

During the treatment, patients improve their psychological well-being: the percentage of patients with depression symptoms drops from 5.2% at the first session to 1% at the third session. Their awareness of the risks of HCV re-exposure increases: after the treatment, 73% of patients avoid contact with blood, 72% practice safe sex, 30% change their lifestyle (e.g. healthy nutrition, abstinence from alcohol) and 28% use sterile equipment (e.g. needles, razors).

In 2019 generic sofosbuvir and daclatasvir were successfully registered in Ukraine.

The project enabled training of four health-care workers in hepatitis C management and became a pilot for the management of hepatitis C in Mykolaiv Province and Ukraine.

Sustainability

The project shows the feasibility and effectiveness of a simplified model of care for HCV integrated into the public health system of Ukraine. With the registration of generic DAAs, hepatitis treatment can be more accessible in the country without being a financial burden on the country and its people.

UKRAINE Social support, adherence to hepatitis C treatment, and prevention of HCV reinfection in key populations in Ukraine

Strategic Direction 2 | Strategic Direction 3 | Strategic Direction 5

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Background

Ukraine has a high burden of viral hepatitis. Hepatitis C is estimated to affect approximately 1.5 million people alone, and between 6000 to 7000 new cases are detected in the country every year. According to official records, only 82 654 infected individuals are registered in the public health system *(174)*.

Ukraine also has a high number of PWID, estimated at 290 000–346 000 in 2017 *(175,176)*. This key population is at high risk for HCV infection. PWID also experience stigma and discrimination, especially in health facilities, and require a comprehensive approach for outreach, testing, referral, treatment and care for hepatitis C *(177)*.

At the time this project was initiated, Ukraine was not featured in expanded access programmes for DAAs and the costs of treatment exceeded the financial capacities of the population living with hepatitis C, particularly those experiencing treatment impaired by stigma and discrimination and reinfection caused by injecting drugs. The Alliance for Public Health, an international charitable foundation, pioneered hepatitis C treatment with DAAs in Ukraine and was essential to designing a project that could offer improvements to retention in care and adherence to treatment with affordable medication.

Description of the good practice

The Alliance for Public Health developed and implemented a hepatitis C model of care for key populations in partnership with the Ministry of Health, the Public Health Centre, 25 health-care facilities, and 19 local NGOs that provide social support to patients on treatment for hepatitis C – to maximize access to treatment. The implementation mechanism was organized through memoranda of understanding/ cooperation with partners and key stakeholders and sought to improve diagnosis, linkage to care, treatment outcomes and prevention of reinfection. The project provided successful antiviral treatment to 1907 people in the country.

Some of the activities developed with the Ministry of Health and Public Health Centre include selection of health-care facilities, distribution of medicines, organization of trainings, reporting and monitoring in the field, and discussion on deliverables.

Community representatives provided recommendations that were essential for the design and success of the project.

Pre-treatment phase

Social workers from local NGOs and community representatives assisted the project in defining criteria

for eligibility, identifying opportunities to promote health and referring potential patients to health facilities for consultations with doctors.

Each of the 25 participating health facilities was equipped with a multidisciplinary team comprising a doctor, a nurse and a social worker from one of the 19 local NGOs. Multidisciplinary teams coordinated the decisions on enrolment in the project and treatment initiation during regular meetings.

The Alliance for Public Health organized capacity-building for doctors and social workers, with workshops about hepatitis C treatment with DAAs performed by national experts.

People previously tested positive for anti-HCV were invited to take HCV RNA tests in private laboratories at the expense of the project.

Treatment phase

During the treatment phase, all patients were placed under the supervision of the multidisciplinary teams. Social workers were the first to establish contact with potential patients, providing explanations about consultations, the enrolment process and psychosocial support; doctors examined patients and requested tests according to the patients' clinical status, maintained medical records and assessed adverse events and complications during follow-up and treatment; nurses ensured timely delivery of medications, registered their consumption and assessed adverse events.

Social workers also kept track of patients using phone calls and a registry of medication intake, and provided patients with three sessions focused on prevention of reinfection, HCV transmission and safer practices. Patients were offered to invite family members and close companions for appointments with the social worker to inform them about hepatitis C, prevention of transmission and treatment, and to improve the patients' support network.

Post-treatment phase

Social workers kept in regular contact with patients and/or their families to remind them of the last appointment for assessment of treatment outcome, with cure defined as SVR12.

The project followed up with operational research regarding individual characteristics; organizational barriers and other factors that posed a threat to treatment adherence or were related to the risk of HCV reinfection; and the regression of liver fibrosis *(178)*.

Evidence of impact

The cohort of 1907 patients comprised 1531 PWID (80.3%) and 1400 PLHIV (73.4%). While PLHIV on antiretrovirals accounted for 1360 (97.1%), PWID on OST only accounted for 165 (10.4%) – a small coverage rate for OST. Sixty-seven patients were receiving only OST – 50 on methadone and 17 on buprenorphine.

The project also succeeded in reaching out to and enrolling partners of PWID (8.0%), MSM (3.6%), sex workers (4.3%) and other population groups (3.8%) – expanding the coverage of key populations. Approximately 44% of all patients enrolled in the project had an APRI score over 3.25, thus indicating advanced liver fibrosis (F3,F4). APRI and FIB4 scores calculated 48 weeks after SVR12 significantly improved in 302 and 326 patients respectively, out of 348 assessed.

Adherence to hepatitis C treatment was high (98.2%) and SVR12 was achieved in 95% of treatments (Fig. 33). Less than 2% of patients interrupted treatment (34), with 6 resuming follow-up and successfully restarting treatment.

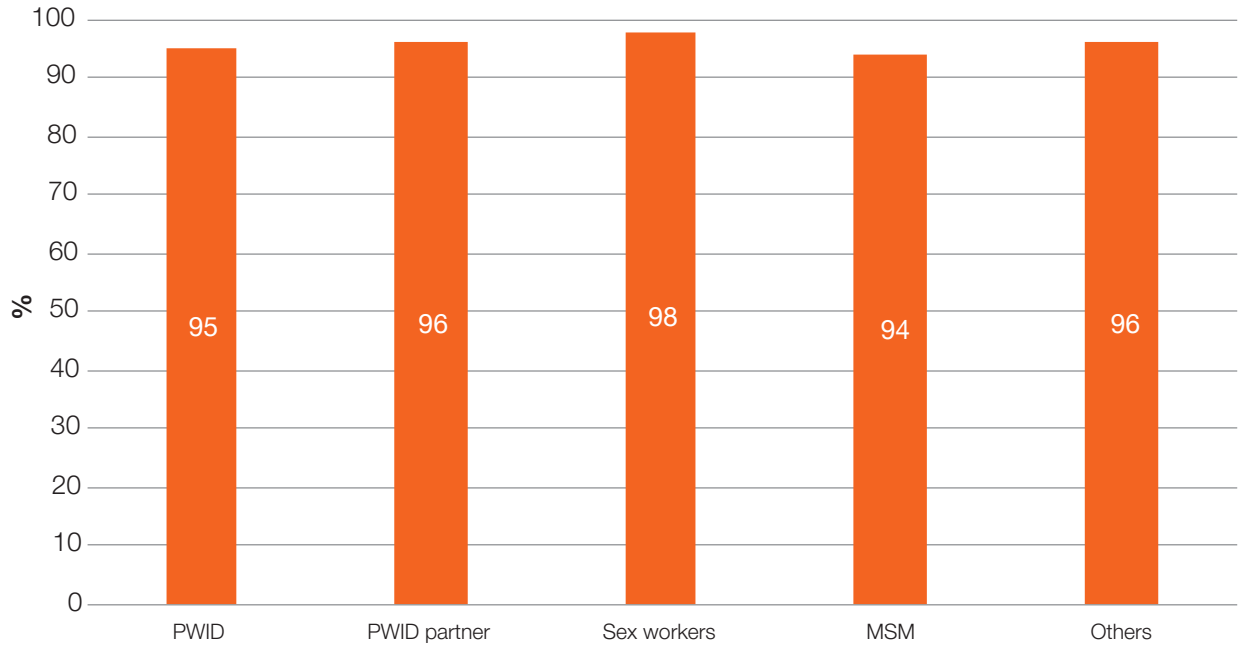
SVR12 had been assessed in 1837 patients by 2019 – and only 3% of those successfully treated presented detectable HCV RNA 48 weeks after achieving SVR12, indicating good adherence to prevention and low risk of reinfection.

It is understood that the project managed to raise general awareness about HCV among patients from key populations, while providing a friendly, comfortable environment, free of stigma and discrimination, and attending to the patients' needs for quality health-care services.

Interviews at beginning of follow-up, EOT and 12 weeks after EOT revealed that most patients lacked information about hepatitis C and HCV transmission at the beginning of their participation in the project, but improved their knowledge over time with the progression of appointments (Fig. 34).

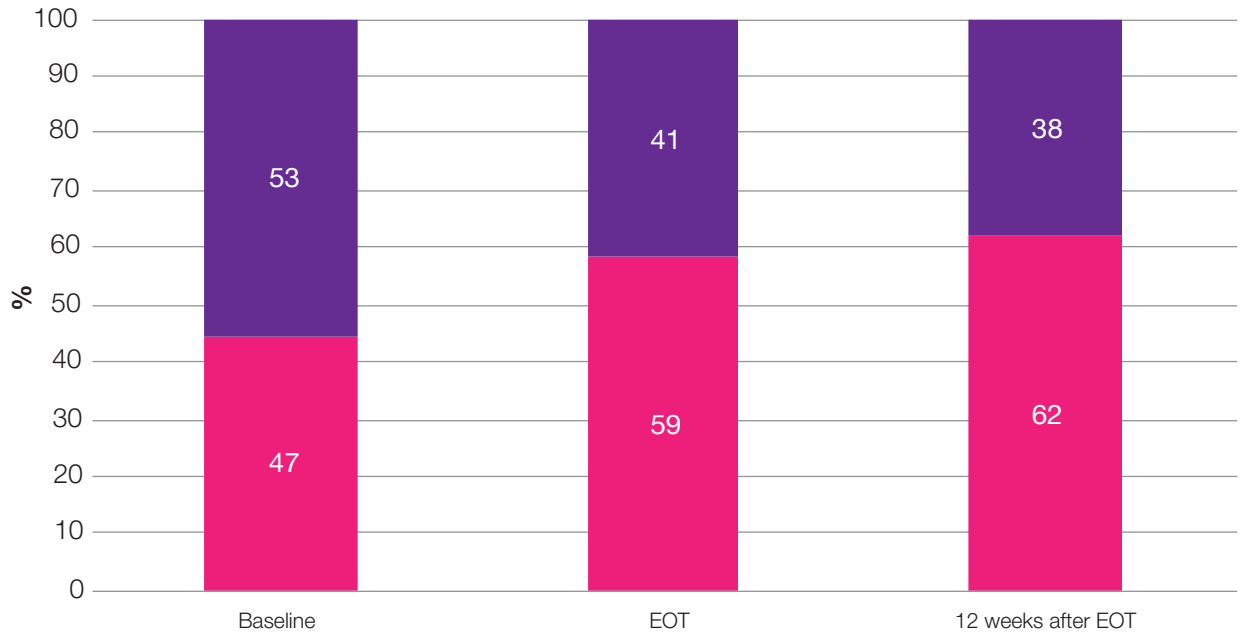
Patients mostly noted that they previously understood the possible risks of HCV transmission via non-sterile syringes or sex without a condom, but before the

Fig. 33. SVR12 in hepatitis C patients undergoing treatment from key populations, Ukraine (2015–2018)



Source: Authors.

Fig. 34. Hepatitis C awareness among patients, Ukraine (2015–2018)



Source: Authors.

start of treatment they were not aware of the risk of transmission through personal hygiene products (e.g. razors or manicure instruments).

Sustainability

This practice is in line with the decentralization and task-sharing of services, enabling optimization of health services and consolidating an effective and comprehensive service delivery model for a population at risk for reinfection, despite the very high rate of advanced liver disease (94%).

It also improved the awareness of patients and promoted integration of partners already acting on HIV, viral hepatitis and harm reduction without a massive input of financial resources, proving to be a sustainable activity for improving linkage to care and partnerships.

UNITED KINGDOM A home-based care pathway for the stratified treatment of HCV infection in England

Strategic Direction 2 | Strategic Direction 4 | Strategic Direction 5

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Background

The most recent estimates suggest that around 113 000 people in England are living with chronic HCV infection *(179)*. National Health Service England (NHSE), working through the HCV Operational Delivery Networks (ODNs), has reached milestones predictive of meeting the WHO GHSS 2030 targets of diagnosing 90% of infected individuals, treating 80% and reducing HCV-related mortality by 65% *(179)*.

Continued success will depend increasingly on implementing new strategies for engaging hard to reach groups. Nottingham has been at the forefront of developing patient-centred models of community care in settings which maximize engagement with vulnerable groups, such as drug and alcohol treatment centres and prisons *(180,181)*. As part of this stratified approach, we further hypothesized that the majority of HCV infected patients who are currently treated in secondary care do not need specialist supervision to safely complete DAA therapy.

To test this hypothesis, we have developed a home-based care pathway (Homecare) which minimizes the need to attend the hospital clinic following the decision to treat. This strategy offers patients the option of choosing treatment in a setting which minimizes disruption of professional and personal life and removes geographic inequality for those distant from our specialist centre.

Homecare is now the preferred option for most of our patients and has had a dramatic effect on activity in our hospital clinics. This innovation has been of major benefit to our patients and has allowed specialist staff to focus on patients with advanced comorbidities and the most challenging groups in the community.

Description of the good practice

All patients eligible for treatment with DAAs for HCV in Nottingham are screened for entry into a home-based care pathway. Individuals who for any reason are assessed as requiring supervision of therapy in secondary care, such those with significant liver comorbidity, are not routinely offered care at home. Patients with established cirrhosis without decompensation or who are coinfected with HIV/HBV are eligible. Patients considered for inclusion in the study should in addition: (i) be assessed as competent to adhere to therapy and attend scheduled blood tests without direct supervision; (ii) have no current evidence, or documented history, of liver decompensation; and (iii) be contactable by telephone. Patients who meet these screening criteria are then offered the choice of home or hospital-based care.

Following stratification to Homecare, the Nottingham ODN selects and prescribes the DAA regimen according to usual practice and NHSE guidelines. Patients sign consent forms permitting drugs to be delivered to their home and are provided with contact details of the Homecare coordinator and clinical team. The primary care physician (general practitioner (GP)) is informed of the decision to treat at home. Patients do not need to return to the hospital clinic before beginning Homecare. Once treatment begins:

- A schedule of testing and forms for monitoring DAA therapy is sent to the patient's home. Blood tests are performed either in the hospital or, more usually, the local GP surgery.
- DAAs are delivered to the patient's home on a monthly basis, using services contracted by Trust Pharmacy at Nottingham University Hospitals (NUH).
- The Homecare coordinator/clinical team access and review blood results.
- The coordinator/clinical team will inform the patient and GP in writing of results. Depending on

the patient, the clinical team may elect to make telephone contact to discuss progress and reinforce the importance of compliance.

- A 12-week post treatment SVR assessment is the endpoint of the study.

- Patients who have an SVR are discharged from medical care unless follow-up is required for underlying liver disease (i.e. cirrhosis). Patients who do not have an SVR are considered for retreatment.

The service is implemented and governed by a partnership between the ODN and Trust Pharmacy. The ODN is responsible for selecting and prescribing the DAA regimen in exactly the same way as for hospital-based patients. The process of dispensing and delivering DAAs to the patient's home is governed by Trust Pharmacy, who also employ the Homecare coordinator.

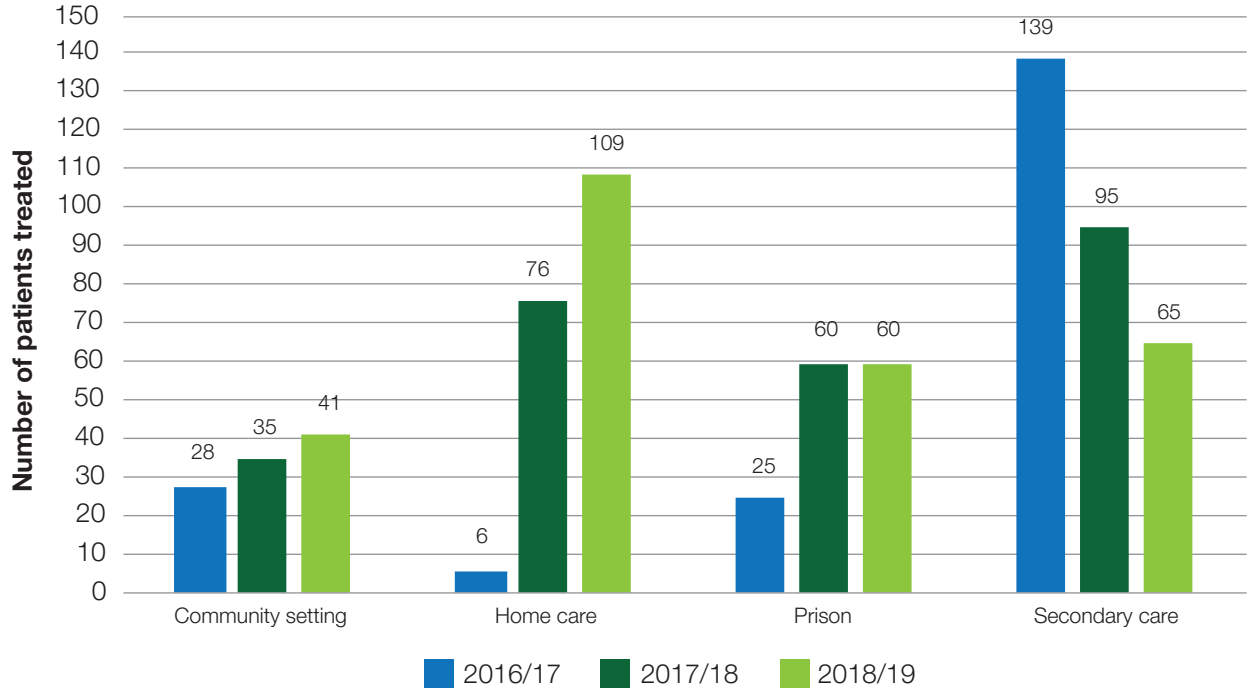
Evidence of impact

As of June 2019, 232 patients have been treated through our Homecare pathway. The distribution of gender, age and HCV genotype of the Homecare cohort is not significantly different from hospital-based patients. Of the 232 patients who have begun treatment, 188 have reached 12 weeks post-treatment and SVR data are currently available for 158. Of this group: 153 have achieved SVR (96.8%); 4 did not complete treatment (2.5%); and 1 relapsed (0.7%). Two patients opted to return to hospital-based care. This high SVR rate does not differ significantly from outcomes for hospital-based patients.

The care settings in which HCV infected patients were treated in Nottingham between April 2016 and March 2019 are shown in Fig. 35a and 35b. Community settings include drug and alcohol treatment centres and primary care. The numbers of patients treated in the community and prisons have both increased over the assessment period. The striking change, however, is the progressive and rapid shift from secondary care to the Homecare service (Fig. 35a, 35b and 36). Homecare has enabled a reduction in the proportion of patients treated in secondary care from 70% to 24% over the three-year period, and this trend is likely to continue. This transition has had a major impact on service delivery and planning in Nottingham, as set out below.

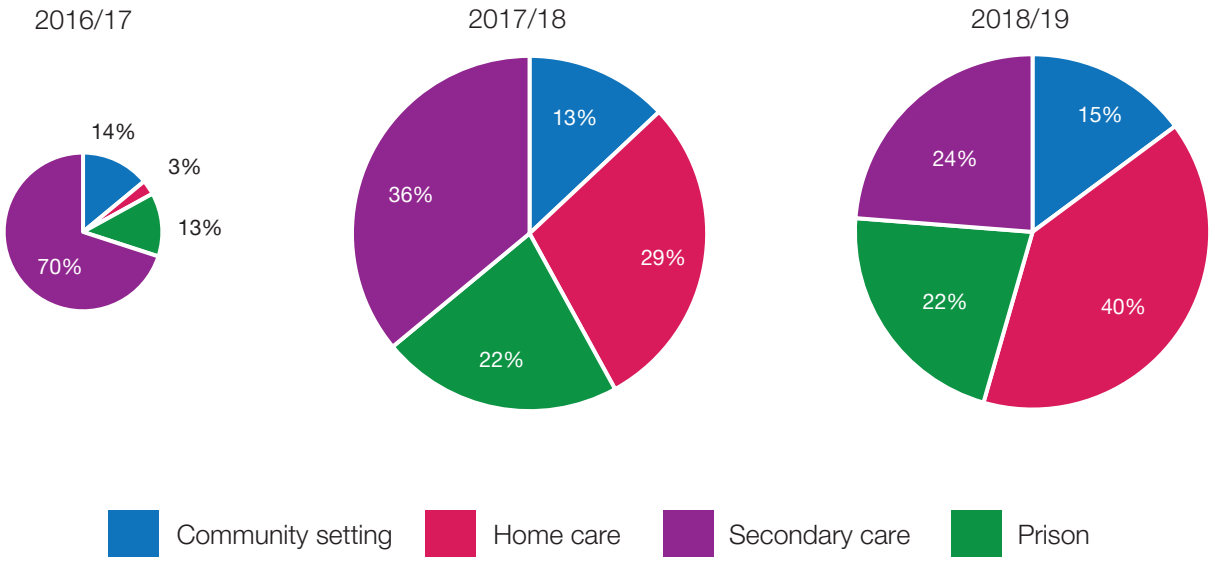
A further and key advantage of the Homecare model is its reach. In common with most regions in the United Kingdom, the NUH serves as a single HCV specialist centre to a large geographical area.

Fig. 35a. Numbers of patients treated in different health-care settings in Nottingham annually (April 2016 to March 2019)



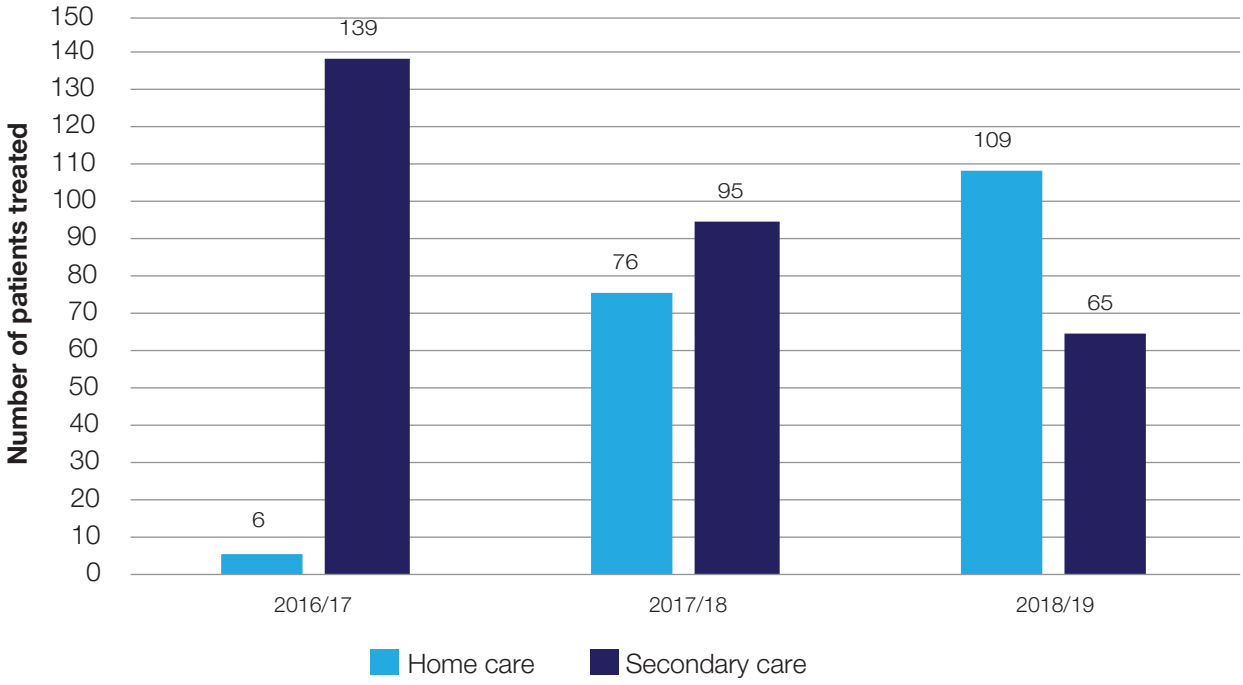
Source: Authors.

Fig. 35b. Percentages of patients treated in different health-care settings in Nottingham annually (April 2016 to March 2019)



Source: Authors.

Fig. 36. A direct comparison of numbers of patients treated in home care and secondary settings (April 2016 to March 2019)



Source: Authors.

Patients who live far from our centre must undertake long and often expensive journeys. Such patients do not therefore have equality of access, particularly as many of our patients are on income support benefits.

Overall the introduction of Homecare has had a major impact on HCV services provided by the NUH.

- Homecare was the preferred care pathway for more than 90% of patients offered the choice between hospital or home settings for treatment.
- Patient feedback is excellent.

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- Homecare has reduced the proportion of HCV patients treated in secondary care from 70% to 24% over the three years from inception.

- Waiting lists for treatment at home are much reduced as the availability of specialist staff and clinic facilities is no longer rate limiting.

- The Homecare model enables us to treat more patients – Nottingham increased the number of patients treated in 2018/2019 despite significant staff shortages.

- The Homecare model is ideal for those small but important group of patients with complex needs, notably mental health problems, which prevent them from accessing clinics. In these circumstances medication is delivered to the health-care setting and patients take their own therapy supervised by carers/clinical staff.

- The service reduces "geographical inequality" and makes it much easier for patients who live far from our centre to access and complete treatment.

- The reduction in the need for specialist staff in secondary care has enabled Nottingham to plan expansion of our services and treatment for hard to reach populations in the community. Within the next 12 months our main HCV hospital clinics will be closed and staff relocated to the community.

Taken together therefore, Homecare continues the Nottingham principle of a patient-centred service delivered in an environment designed to meet patient needs and promote the cost-effective use of scarce resources. Homecare is a new service conceived to preserve autonomy, minimize disruption to patients and their families, take full account of personal or professional needs, and reduce geographical and financial inequality. We therefore consider Homecare to be an ethical and highly effective intervention of major benefit to both patients and service. The service is now being adopted by other large hospitals in our region.

The Homecare model is a relatively straightforward care pathway and has not proved challenging to implement. The pharmacy is, however, key to its successful delivery and governance. Trust Pharmacy very much welcomed the opportunity to become directly engaged with the project and to assume a new form of leadership role in patient care. In order to achieve this, Trust Pharmacy had to review and revise internal governance structures, and will be very happy to share their experience with any organization who may wish to adopt the Homecare model. As in any new pathway, communication between the different staff groups and users – in this case Trust Pharmacy, specialist hepatology staff and patients – is key and it is critical that lines of communication are clear and adhered to by all parties.

The Homecare pathway has very much resulted in the impacts we had expected. We had, however, not fully anticipated the scale of the shift from secondary care to home-based care pathways (in the last three months, almost all our patients have entered Homecare) and its positive impact on our hospital services. The current drive to eradicate HCV as a major health-care threat by 2030 mandates a shift of focus from secondary to community care, and this process is likely to be enormously facilitated by adoption of the Homecare model.

Sustainability

The Nottingham Homecare Service does not use hospital outpatient infrastructure to provide patient care and greatly reduces the specialist clinical staff time allocated to supervising treatment. It is therefore intrinsically cost-effective.

The service has reduced waiting lists, increased treatment capacity and enabled redistribution of staff to more challenging settings. Homecare has been of clear and sustainable benefit to our patients and clinical teams. After a 12-month period of evaluation as a research project from April 2017, Homecare now forms the core of our clinical service and is funded by NHSE income. It is therefore demonstrably sustainable and ensures that our clinical services are deployed as efficiently and cost-effectively as possible.

UNITED KINGDOM A national patient re-engagement exercise to find and treat people who have previously been diagnosed with hepatitis C in England

Strategic Direction 2 | Strategic Direction 5

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Background

The United Kingdom is a low prevalence country for hepatitis C. Around 113 000 people are thought to be living with chronic infection in England.

Public Health England (PHE) and NHSE estimate that there are tens of thousands of people currently living with diagnosed hepatitis C infection in England who are not in contact with treatment services. Many of these people may have been diagnosed when the natural history of HCV-related disease was less certain and/or when treatment options were limited, with suboptimal outcomes. Now that new DAAs are available that can clear the virus in the great majority of patients, it is important that every effort is made to re-engage people with treatment services, so they can consider the treatment options now available to them.

As many of those infected with HCV come from vulnerable populations (migrants, PWID) who experience poorer access to treatment and outcomes, an active approach was considered likely to be of benefit.

This exercise is relevant good practice in that it addresses the strategic directions of the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region *(182)*: intervention for impact (Strategic Direction 2) and delivering for equity (Strategic Direction 3).

Description of the good practice

NHSE, with its ambition to deliver treatment and care to infected eligible patients, PHE, with its duty to monitor and control communicable diseases, and the Hepatitis C Trust, with its advocacy role as the national charity for people with hepatitis C, are all committed to re-engage previously diagnosed people with treatment services. This is part of wider concerted efforts to eliminate hepatitis C as a major public health threat in England before 2030.

With this in mind, in 2018, PHE obtained approval from the Caldicott Guardian (United Kingdom information governance leads on patient data) to share with the lead hospital clinician of the ODN (a network with a central coordinating hepatology clinical service), a list of people resident in their ODN area who were previously diagnosed with HCV in National Health Service (NHS) laboratories during 1996–2017 and reported to PHE (for surveillance purposes).

As laboratory reports contain patient identifiable information, PHE were able to match these patients to the NHS Spine Personal Demographics Service (PDS), and to other national surveillance datasets (deaths, transplants, HCV treatment) to generate a list of patients who were known to be alive, registered with a GP and not known to be already under specialist care or to have completed treatment with the new DAAs.

Laboratory reports are provided to PHE under the current PHE permissions for public health surveillance under Section 251 of the NHS Act 2006 and the Health Service (Control of Patient Information) Regulations 2002 (Regulation 3/'Section 251 support'). This allows PHE to process personal confidential data without consent. By giving the data to ODN leads PHE were changing permitted data flows and data sharing agreements, and hence needed specific Caldicott approval to do so.

The main information-governance risks were related to the fact that PHE-held laboratory data were submitted to PHE for public health surveillance purposes not for direct patient care, and hence completeness of identifier fields was variable. The main risks that were identified by the Caldicott panel for mitigation were:

- accidental disclosure as a patient letter is sent out to an old address (if the NHS Spine PDS is not up to date or the name is incorrect on the PDS or laboratory systems);

- incidental or inappropriate notification – whereby: (i) the letter is the first a person is informed of their diagnosis; (ii) the patient has been treated or has cleared infection spontaneously and is no longer HCV positive; (iii) the patient had actively chosen to not have contact with health services; or (iv) the patient did not want their diagnosis shared with their GP or other health services;

- false positives – whereby a person without hepatitis C is told they have it through the letter (because of erroneous coding at the testing laboratory or they were not removed following negative confirmatory test or the poorer performance of older assays);

- missed patients – whereby because of incomplete or incorrect information entered on NHS laboratory or PDS systems, a diagnosed patient could not be linked to a GP and identified for contacting as part of this exercise.

In view of the information governance risks, the data were provided to ODNs under conditions set out in in a memorandum of understanding (MoU). While the ODNs should decide locally how best to implement the exercise, there were expectations that the ODN should:

- mitigate information governance risks as required for Caldicott approval to release data, such as:
  - ensuring that only those professionals who need access to personal confidential data for direct care should have access;
  - ensuring data were not used, shared or published for any other purposes;
  - checking patient information against local systems prior to contact with the patient and their GP;
  - giving GPs sufficient time to respond with any concerns or reasons not to contact the patient;
  - reporting back any incorrect details so that PHE can correct their systems;
  - implementing and maintaining security standards, controls and procedures appropriate for patient confidential data;

- minimize workload on GPs by leading on contacting patients, doing confirmatory testing and managing contacts;

- ensure diagnosed patients had access to appropriate care pathways, including for other comorbidities, supportive care, substance misuse services, hepatitis vaccination and harm minimization advice.

Implementation of the exercise is supported by development of ODN, GP and patient FAQs and leaflets on hepatitis C and the exercise, in collaboration and with the endorsement of several stakeholders: NHSE, the Hepatitis C Trust, the Royal College of General Practitioners and the British Liver Trust. In addition, template letters were produced for ODNs to use to contact GPs and patients. All were available at a dedicated gov.uk webpage *(183)*.

PHE and NHSE jointly led a communications strategy with blogs, a press release and briefings at the launch in September, which was picked up in a news article in the BMJ. The Hepatitis C Trust also promoted the PHE news items on its webpage and offered a telephone helpline to be included in patient letters.

The implementation (i.e. contacting patients on the list and offering testing and treatment) is in progress, but lessons have already been identified and addressed.

Local implementation is variably resourced and so Gilead Sciences developed a toolkit in response to ODN's request for help with implementation (e.g. prioritization of patients on the list, undertaking data validation checks).

The provision of supporting documents (e.g. letter templates, background information (FAQs) for GPs and patients, MoU and posting on gov.uk) has helped local implementation, clear messaging and transparency.

It is vitally important to ensure that not only patients are engaged but other health providers outside of treatment services, such as general practices whose patients are being targeted and are the first point of call for patient queries.

One of the challenges identified was checking the data against local laboratory systems, due to cases that have been incorrectly reported as HCV and/or cases that have been tested outside of the ODN area – so their records are not available in local laboratories. These challenges were not unexpected, and innovative actions, such as including a flag to indicate that the patient has also been found with a positive HCV code (as per International Classification of Diseases, 10th Revision, ICD-10) in the hospital episode statistics

dataset and/or in the sentinel surveillance of bloodborne virus testing (positive and negative results extracted directly from 21 NHS reporting laboratories), gave us more confidence in the HCV diagnoses. A second column identified the first and most recent laboratory of diagnosis for patients, to support local searches and facilitate contact with the diagnosing laboratory if outside the ODN of patient residence.

Monitoring and evaluation

As this type of re-engagement has not been conducted previously for HCV at a national scale, using surveillance data, a formal evaluation is in progress to evaluate the process and outcomes, through qualitative, quantitative and economic methods. The main outcome is a patient initiating treatment. "Reengagement exercise" was added as a referral source within the national treatment database to estimate the yield from the exercise. To date, approximately 30 patients have been recorded with this referral source.

In order to assess the quality and utility of the laboratory data, feedback on PCR status, the source of data validation checks, whether the patient was contacted (and how) and the outcome of contact, have been requested though M&E fields on the dataset given to ODNs. Baseline interviews were conducted with the ODN leads on the utility of the data, resources required and patient contact approaches taken. Follow-up interviews will also be conducted along with a study of patient and GP perspectives on the acceptability of this approach.

Evidence of impact

The local implementation of this exercise is ongoing.

Advisory/strategy groups were set up in ODNs to oversee the process and engage local partners, contributing to the increase in profile and importance of case-finding activities in the ODNs.

Professional awareness of hepatitis C in the health sector has increased, which is much needed, especially among GPs, with pick up by the mainstream medical press (BMJ article) with a wide readership.

The evaluation of the exercise is expected to yield information on the utility and acceptability of this type of case-finding and is a springboard for other case-finding initiatives.

This exercise has set an information governance precedence in the United Kingdom for novel use of routinely collected surveillance data to support case-finding and direct patient care. Wales is also launching a similar exercise using the resources and similar approaches developed by England, and other projects to interrogate local clinical and laboratory databases containing hepatitis C patients are being scoped out (e.g. prisons, sexual health services, drug services).

This exercise also demonstrated the utility of data linkage methodologies, previously used to estimate the cascade of care, for improving patient care through lookback exercises.

Data on PCR positivity and whether PCR negative patients identified in the exercise reported spontaneous clearance or treatment will inform our understanding of the epidemiology and natural history of hepatitis C, and allow us to parameterize models estimating prevalence and burden.

Sustainability

Although this was a one-off exercise to re-engage people currently living with diagnosed hepatitis C infection who are not in contact with treatment services, initial feedback from interviews highlighted that resourcing to work through the lists was a major issue and varied by ODN.

ODNs were able to bid for funds from NHSE to support implementation of this exercise as part of wider case-finding activities. The process could be improved if some data validation with local laboratories was done by regional PHE teams prior to the release of data. However, the data were provided by PHE and engagement of NHSE and GPs was achieved without additional resources, which was recognized as a good example of a low/no-cost case-finding initiative by policy-makers.

Depending on the findings of the evaluation, a phase 2 re-engagement exercise may be considered, looking at the feasibility of contacting patients who were not matched to a GP and so not provided to the ODNs.

In addition, there is potential for building periodic laboratory-to-treatment database-matching into routine surveillance as a failsafe approach to ensure that all new diagnosed patients are offered treatment.

UNITED KINGDOM Estimating the cascade of care for hepatitis C virus in England through data linkage: providing a benchmark for monitoring progress and early impacts of the new treatments

Strategic Direction 1

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Background

When this work was started in 2014, little was known about engagement and retention in care for people with HCV in England. Establishing the cascade of care for HCV-infected patients is critical for identifying where and which groups drop out of the care pathway, to inform targeted interventions to promote case-finding, referral, treatment uptake and retention in care.

Historically, HCV treatment rates in England have been low, however, the treatment landscape for people with chronic HCV has dramatically changed in recent years, with the availability of DAAs. Furthermore, the United Kingdom has signed up to the WHO global strategy for elimination of viral hepatitis as a significant public health threat by 2030. It is therefore important to benchmark the burden of HCV-associated disease in the pre-DAA era. Through data linkage we produced baseline estimates against which PHE can monitor the impact of new curative treatments, monitor progress towards the WHO elimination goals and identify persistent barriers along the care pathway which can be addressed by partner organizations such as NHSE that deliver treatment and care services.

It is important to note the legal and ethical framework for disease notifications and surveillance in England as these provide the context in which PHE can undertake surveillance and data linkage work. Hepatitis is a notifiable organism and laboratories are mandated to report new diagnoses to PHE. For specific communicable and noncommunicable disease surveillance purposes, PHE has permission (under specific legislation) to collect and process patient identifiable information without patient consent.

This project enhances the surveillance and monitoring systems in PHE and NHSE, and is relevant in that it addresses the strategic directions of the Action Plan for the Health Sector Response to Viral Hepatitis in the WHO European Region *(184)*: information for focused action (Strategic Direction 1); and delivering for equity (Strategic Direction 3).

Description of the good practice

In 2018, we estimated the cascade of care for HCV in the era of ribavirin and pegylated interferon therapies through HCV testing data reported from sentinel NHS laboratories (21 across England), and presented data on testing, positivity, treatment uptake and SVR by patient demographics and setting/service of test. Appropriate treatment uptake was estimated by four or more sequential HCV RNA test results within a 390-day period following an initial positive RNA result. People with a final negative HCV RNA test result within the 390-day period were considered to have responded to therapy and achieved SVR.

To build on this work we used data linkage to establish baseline estimates of disease burden in an HCV tested and/or diagnosed population, by linking national laboratory-based new diagnoses and sentinel NHS laboratory HCV testing to disease registry and health-care utilization datasets – including the transplant registry, death registry, the hospital episode statistics, the cancer registry, the National Drug Treatment Monitoring System (NDTMS), the national HIV database, and the national TB database. We estimated crude incidence of end-stage liver disease (ESLD) and primary liver cancer admissions, crude incidence of liver transplants, age- and sex-adjusted mortality rates, coinfection rates, and HCV incidence for people engaging with drug services, and their cascade of care.

Through this work, we were able to provide baseline and monitoring data that identified gaps in health

service provision and care pathways, and inform monitoring of progress towards elimination by United Kingdom government agencies. Key findings include:

- Early evidence suggests a decrease in mortality, liver transplants, and hospital admissions of both ESLD and primary liver cancer in the post-DAA (compared to pre-DAA) era in an HCV diagnosed population.

- HCV testing among drug users testing in community addiction services was happening, but there were inefficiencies, with repeat testing prior to referral and poor linkage to HCV treatment and care.

- Although liver transplant rates associated with hepatitis C have fallen in HCV diagnosed patients, the short period from diagnosis to liver transplant suggests that late diagnosis with advanced liver disease is a problem.

- Mortality rates, particularly in younger individuals, were significantly higher in those with a diagnosis of HCV compared to the general population in England, highlighting significant health inequalities. The high mortality rates associated with common comorbidities, such as problematic drug and alcohol use, highlights the importance of integrated health and social care strategies, and commissioning to address the needs of this vulnerable population and reduce inequalities.

Lessons learned:

- Issues with the quality of hospital admissions data impacted our ability to link datasets, and unless addressed, will limit our ability to use hospital admissions for HCC and ESLD in people with HCV as a monitoring metric. The issue has been flagged with the data provider and corrective actions are being taken.

- There is substantial underreporting of HCV-associated deaths in the death register, and of HCV-associated hospital admissions for ESLD and HCC, which, without adjustments or linking to surveillance of HCV diagnoses, would lead to an underestimate of these monitoring metrics.

- The ability to link data is associated with data completeness, and the method used for data linkage is based primarily on the variables available within the dataset.

Evidence of impact

We have established baseline estimates of the cascade of care and outcomes with which we can monitor the impact of DAA treatments in England. We have shown early evidence of a decrease in mortality, liver transplants and hospital admissions for both ESLD and HCC in patients with a diagnosis of hepatitis C.

Monitoring the HCV cascade of care enables PHE and researchers to identify persistent barriers to access and retention in care that may hinder elimination efforts, which is of patient, health service and societal benefit.

Our findings indicate to NHSE and the local health economy where to focus efforts and resources, and guide intervention and prevention strategies to reduce gaps in the care cascade and increase care retention.

Our estimates and quantification of underreporting of hepatitis C in certain health-care datasets are contributing to the refinements being made to HCV prevalence and burden modelling being undertaken by PHE and partners, which are used to inform local and national prevention and intervention strategies.

Through the data linkage work with the NDTMS, we have been able to report back our findings, which has led to the NDTMS reconsidering the eligibility criteria for testing, following the identification of anti-HCV positive patients among those under treatment due to alcohol and not injecting drug use.

We have shown the importance of surveillance and of data linkage in monitoring uptake and impact of wider access to HCV treatment and also in efforts to meet the WHO elimination goals. As such, this work has increased the profile and usability of the data collected on hepatitis by PHE and has led to new collaborations to support hepatitis C case-finding and evaluation of interventions.

Findings have been presented at the European Centre for Disease Prevention and Control (ECDC) and published in peer-reviewed journals, so other countries may adapt and apply similar data linkage approaches in their surveillance systems and/or advocate for improved surveillance standards, such that meaningful

data can be collected to allow cascade of care and outcome monitoring to be established.

Sustainability

This work has shown the success and importance of data linkage, with a small capital investment to establish methods and collaborations with academic and clinical partners.

As the data linkage methods have been set up in PHE using existing population-based national surveillance systems, scalability is not an issue. PHE will continue to produce these estimates with existing funds and ensure they are incorporated into national surveillance and data outputs (e.g. surveillance reports and annual reports on hepatitis C in England and the United Kingdom), and made available to the cross-agency national expert group – the National Strategic Group on Viral Hepatitis – for monitoring our progress towards elimination.

UNITED KINGDOM Transitioning from the Hepatitis C Action Plan to an elimination strategy in Scotland: successes and the way forward

Strategic Direction 1 | Strategic Direction 2

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Background

Over 10 years have elapsed since the Scottish Government launched the Hepatitis C Action Plan for Scotland. In 2008, 38 000 people in Scotland (0.7% of the population) were estimated to be chronically infected with HCV, and over 90% of those had injected drugs *(185,186)*. The Action Plan was underpinned by significant funding – initially around £100 million, additional to the general NHS funding pot, was invested in services in 2008–2015 – and comprised numerous initiatives ranging from the education of children to the rapid scale-up of antiviral therapy *(185,186,187)*. We here review the good practice and associated impact of the Action Plan during the first decade (2008–2018) and further evidence informing the transition to Scotland's elimination strategy in 2019 *(188)*.

Description of the good practice

Coordination and monitoring

An infrastructure has been created by establishing:

- a nationally and locally coordinated, multidisciplinary and multiagency approach, involving the health service, local authority and third sector, covering all geographical areas, settings and spheres of service need (prevention, diagnosis, treatment and care);
- accountable and interlinked local and national networks vital for optimal service planning and development;
- a national monitoring, evaluation and research initiative, with the hub at Health Protection Scotland and Glasgow Caledonian University and spokes linking into NHS Boards and other universities.

Prevention services

During 2008–2018, it is estimated that 500–1500 people in Scotland were infected with HCV annually, almost all through drug injecting behaviours *(187,189)*. Prior to the Action Plan, uptake of harm reduction services (NSP and OST provision) among PWID in Scotland was among the highest anywhere *(189)*.

The Action Plan involved a further bolus of investment, directed mainly at providing PWID with other sterile injecting-related paraphernalia (mainly spoons, filters and water). The Action Plan initiated a national biennial survey of bloodborne viruses and behaviours among 2000–3000 PWID *(190)*.

Incidence is gauged by monitoring HCV (PCR RNA) among PWID who test negative for anti-HCV. By 2018, no sustained reduction in the incidence of infection among this population was observed; the rate remained

around 10–15 per 100 person-years of injecting *(190)*. It is possible that the benefits of scaling up harm reduction coverage have been offset by the detrimental effects of changes in drug taking behaviours *(191,192)*.

Mathematical modelling has shown that if HCV therapy is scaled up among PWID infected with HCV, there is likely to be a beneficial impact on the incidence of HCV in this population *(193,194,195)*. Studies are being undertaken in the United Kingdom (particularly Dundee) to shed light on the potential impact of this intervention in real world situations *(196)*.

Diagnostics, treatment and care

In 2006, 38% of Scotland's estimated 38 000 people living with HCV, had been diagnosed with their infection *(187,197,198)*. By 2018, the proportion had grown to 50% of an estimated 21 000 *(188,199)*. This increase appears modest but it does not take into account the estimated 13 000 people who have been diagnosed and successfully treated, and thus are no longer living with HCV *(188)*. More striking is the 55% reduction in the estimated number of infected people unaware of their infection (i.e. 23 500 in 2006 compared to 10 500 in 2018). Several factors account for this progress, including:

- "user friendly" dried blood spot sampling of PWID in harm reduction/drug treatment settings *(200)*;
- awareness-raising events/campaigns involving third sector (Hepatitis Scotland and the United Kingdom Hepatitis C Trust) and statutory organizations *(201)*;
- political and intersectoral support to address HCV in a relatively small country *(187)*.

Early experience of the Action Plan demonstrated the enormous challenge of transporting highly vulnerable people along the cascade of care; the proportion of those newly diagnosed with HCV attending specialist care year on year during the Action Plan period barely exceeded the 50% mark *(199,202)*. To address the challenges observed with referral to and attendance at specialist care located within hospital settings, and recognizing the different needs of people with HCV, one health board area (Tayside, incorporating the city of Dundee) developed a bespoke approach *(196,203)*. Depending on the circumstances and the needs of the person, treatment is provided in a single or a combination of secondary, primary or other community settings (including pharmacies, harm reduction services, drug treatment centres and prisons). This approach, involving tailoring of services to the individual, is advocated as part of Scotland's ongoing plan and is now evident in other parts of the country beyond NHS Tayside *(204)*.

Government treatment targets, informed by modelling *(195)*, were set annually from the beginning of the Action Plan *(187)*. These have risen over time from 500 in 2008/2009 to 2000 in 2018/2019, to ensure progress was made on scaling up efforts, while balancing demonstrated need with available resources *(204)*. The targets have been taken seriously, have generally been met and have usually been exceeded (Fig. 37a) *(187,188)*. The proportion of those treated with a successful outcome has increased – from just over 70% during 2010/2011 to 95% from 2015/2016 onwards (Fig. 37b) – as a consequence of the movement away from injectable interferon-based regimens to the oral DAA therapies in mid-2014 *(205)*. This progress over the Action Plan lifespan (2006–2018) is best demonstrated by the estimated cumulative numbers of infected people treated (16 000) and treated successfully (12 800) *(188)*.

Evidence of impact

Infection

The estimated number of people living with chronic HCV in 2018 was 21 000 (range 16 000–26 000) – representing a 17 000 (45%) reduction from 2006, when it was 38 000 *(188)*. The rate of decline in infection prevalence has accelerated recently due to the increasing Scottish Government treatment targets combined with the introduction of DAAs.

Disease

Between 2006 and 2013, the number of individuals with HCV at the time of presentation with decompensated cirrhosis increased from 71 to 141 (Fig. 39); it was predicted that the annual number would have continued to rise to at least the year 2020 in the absence of the DAA therapies *(188,205)*. With the introduction of such treatment in mid-2014, however, the number of decompensated cirrhosis presentations declined by 67% to 47 in 2018. It is estimated that approximately 330 cases of HCV-related liver failure were averted during 2015–2018 *(205)*. This translates to a potential saving of £30 million to the NHS in caring for patients with liver failure *(188)*.

Fig. 37a. Annual number of patients initiated on HCV antiviral therapy in Scotland and associated Scottish Government national target

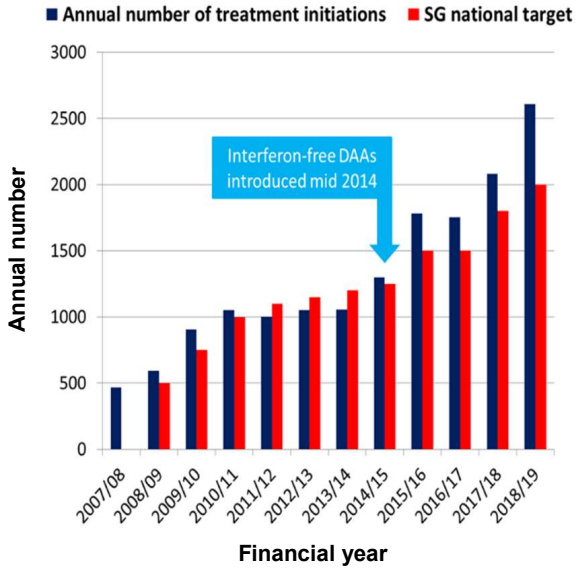
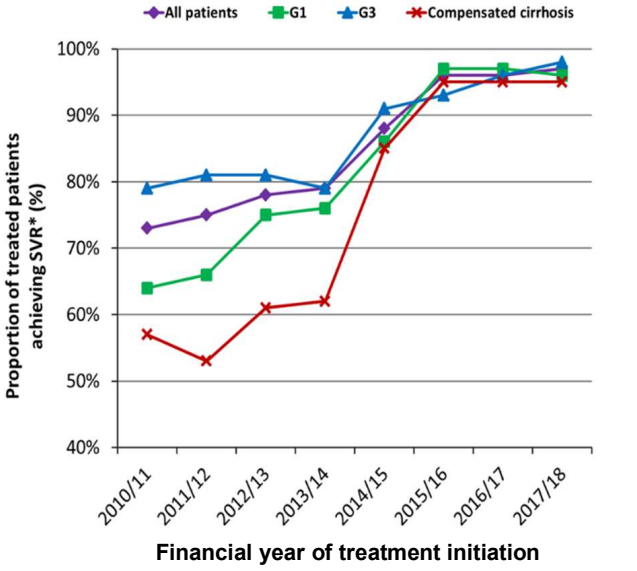


Fig. 37b. Rates of SVR among patients treated for HCV in Scotland



G1 = HCV genotype 1; G3 = HCV genotype 3; SG = Scottish Government.
Source: Health Protection Scotland *(188)*.

The number of people with chronic HCV at the time of presentation with HCC rose from 19 in 2006 to 58 in 2016; by 2018, however, the number of new presentations of HCV-related HCC had fallen dramatically by 69% to 18 *(188)*. This observation suggests that treatment is having a serious preventative impact on HCC.

The number of people with chronic HCV at the time of death for which there was a mention of decompensated cirrhosis and/or HCC on the death certificate increased from 33 to 67 between 2006 and 2015; since then, a 49% decrease has been observed to 34 in 2018 (Fig. 38) *(188)*.

Sustainability

New Scottish HCV elimination strategy: 2019 and onwards

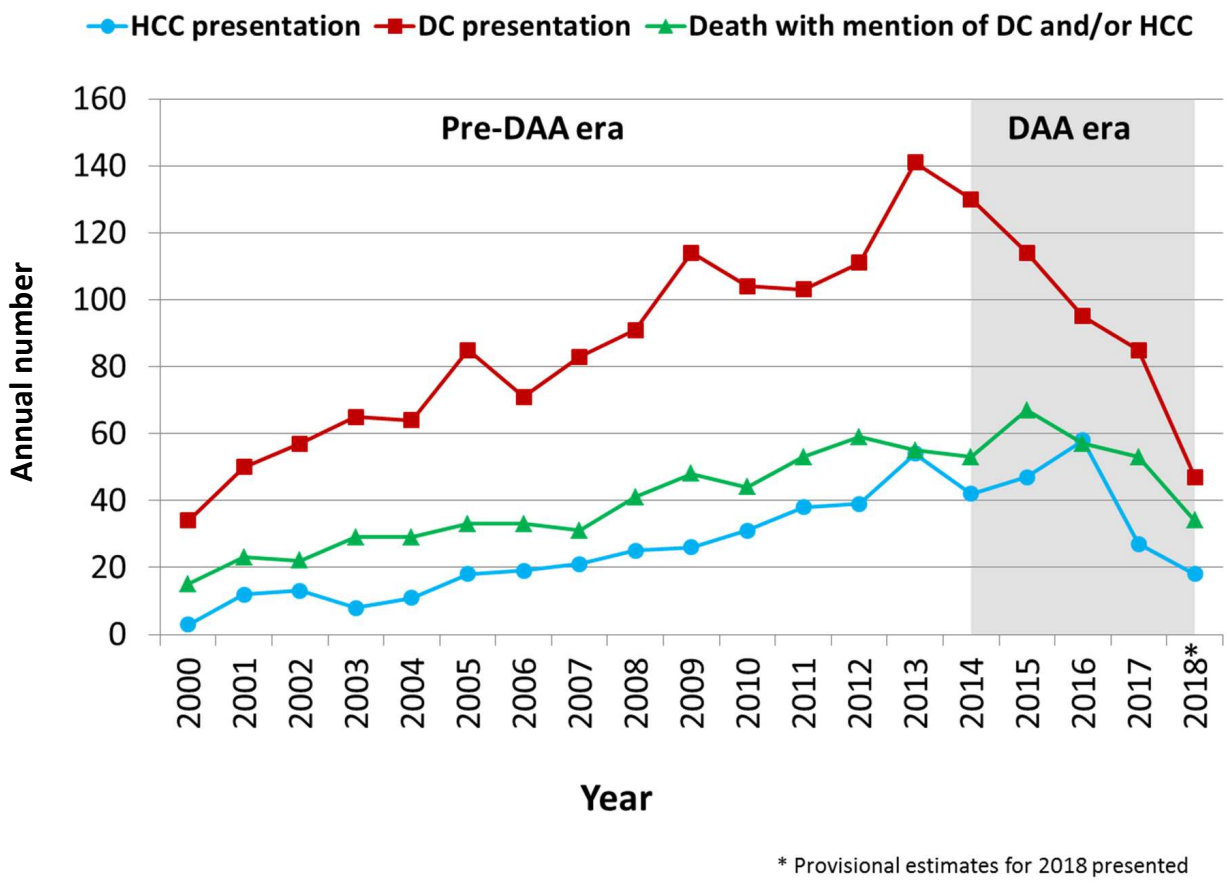
To inform the next phase of the Scottish Hepatitis C Action Plan, dynamic modelling, based on previous work for Scotland *(195),* was undertaken to assess the potential impact of different treatment target scenarios on the time when the elimination threshold – defined as 5000 people living with infection (i.e. a population rate of 1 per 1000) – would be reached, and to estimate the overall cost to the NHS (Fig. 39) *(188)*.

It is estimated that the overall costs associated with HCV to the NHS will be less if the elimination threshold is reached earlier rather than later. An elimination date of no later than 2024 has been endorsed by Scottish Government (Box 1). To achieve elimination, NHS Boards in Scotland, together with local authorities and third sector organizations, and supported by Health Protection Scotland, have been advised to:

- Treat a minimum of 2500 during 2019–2020, and 3000 people each year thereafter; it is predicted that this strategy will achieve elimination by 2024.

- Adhere to recommendations made by the National Short Life Working Group on Hepatitis C Case Finding and Access to Care *(206)*, with regard to intensifying efforts to identify those undiagnosed and to re-engage those diagnosed but not in contact with HCV services. An eclectic model of HCV care (i.e. the provision of services in both hospital and community settings, tailored to the needs of the patient) should be adopted.

Fig. 38. New presentations of decompensated cirrhosis and HCC, and deaths from these among people with chronic HCV infection (at time of presentation) in Scotland (2000–2018)



DC = decompensated cirrhosis.
Source: Health Protection Scotland *(188)*.

Box 1. Elimination of hepatitis C in Scotland

Vision

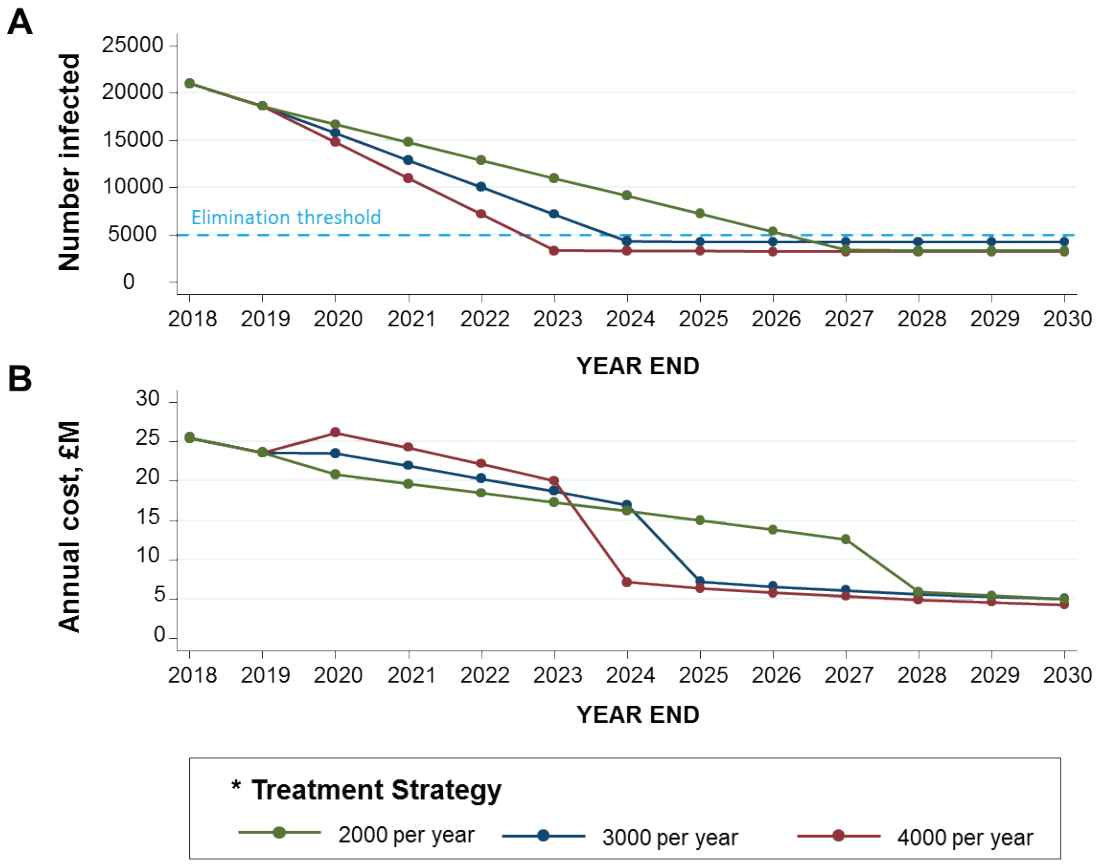
The elimination of hepatitis C infection and hepatitis C related severe disease and death as a major public health concern by 2024 at the latest.

Definition of elimination

- Infection: 5000 or less chronically infected people (i.e. 1 in 1000 people or less).
- Liver failure/liver cancer/death: for each outcome, less than 10 people with chronic HCV presenting per year.
- Compliance with WHO targets: targets, set by WHO in 2016, for the elimination of hepatitis C to be achieved by 2030.

Source: Authors.

Fig. 39. Predicted time when the elimination threshold will be reached, and estimated overall annual cost to the NHS: depending on numbers treated/year from 2020



A = Estimated number living with chronic HCV infection; B = Estimated total annual cost (£M), assuming a cost per treatment course of £3000, according to treatment strategy*.
Source: Health Protection Scotland *(188)*.

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