VHPB TECHNICAL MEETING

The role of international organisations in the elimination of viral hepatitis in Europe

Achievements, challenges and the way forward

ANTWERP, BELGIUM

5-6 April 2023

BACKGROUND DOCUMENT

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VHPB Secretariat

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MEETING INFORMATION

MEETING OBJECTIVES

- Provide an overview of the current viral hepatitis situation in Europe, in relation to the renewed WHO global health sector strategies 2022-2030
- Discuss initiatives, achievements, best practices and challenges from international organizations in the prevention and control of viral hepatitis
- Assess the needs to achieve elimination of viral hepatitis as a major public health threat by 2030 as set out in the new WHO Global Health Sector Strategies 2022-2030
- Investigate potential collaborations
- Discuss successes, good practices, issues and barriers to overcome and the way forward.

TARGET AUDIENCE

- Public health experts, policy makers, healthcare workers, academics/experts involved in prevention and control of viral hepatitis
- VHPB advisors
- Some selected observers

INTENDED IMPACT

Mapping all existing initiatives involved in the elimination of viral hepatitis in Europe, providing an update on the achievements, initiatives, needs and plans of international organisations to reach the 2030 elimination targets, investigate potential collaborations to move forward together.

MEETING VENUE

University of Antwerp - City Campus

Klooster van de Grauwzusters

Gebouw S

Lange Sint-Annastraat 7

2000 Antwerp

Belgium

NOTE: This pre-meeting document contains general background information on the topic(s) of the VHPB meeting. It contains a list of recent selected abstracts/references from a Pubmed MEDLINE and Google search of January 2023 on different search terms depending on the topics discussed in the session of the meeting (limited to abstract from 2020-now).

The references are sorted by publication year. This document should guide you in the preparation of the meeting, it should not be considered as complete literature review, but hopefully, it will give an overview of what has been published on the topics of the meeting.

BACKGROUND DOCUMENT

INTERNATIONAL ORGANISATIONS

VIRAL HEPATITIS PREVENTION BOARD

The Viral Hepatitis Prevention Board (VHPB) is an international board of experts in viral hepatitis, offering a platform for dissemination of scientific infromation related to viral hepatitis. <u>Board members</u> meet twice a year to discuss technical and country specific issues. The Board has a <u>permanent scientific secretariat</u>, located at the <u>Centre for the Evaluation of Vaccination</u> (CEV) of the University of Antwerp.

Focus audiences are, in first instance, opinion leaders, policymakers, and health care professionals.

Mission statement

The objective of VHPB is to contribute to the control and prevention of viral hepatitides:

- 1. by drawing the attention to this important public health problem
- 2. by issuing prevention guidance and catalyse the development of recommendations, and
- 3. by encouraging actions to improve control and prevention.

VHPB has, in support of its main objective, a wide range of functions, including the following:

- 1. To monitor and evaluate the currently implemented immunisation programmes.
- 2. To bring together, during VHPB meetings, an international forum of specialists to examine, discuss, and judge on specific topics, closely related with the control and prevention of viral hepatitis.
- 3. To produce and distribute a number of publications, including Viral Hepatitis newsletter, a short reports of VHPB meetings.
- 4. To provide guidance and catalyse the development of viral hepatitis control and prevention recommendations/ guidelines for the health care workers and policymakers.
- 5. To closely collaborate with international agencies dealing with control and prevention of viral hepatitis (World Health Organisation, Centres of Disease Control and Prevention, European Centre for Disease Prevention and Control, Bill and Melinda Gates Children's Vaccine Program, European Commission, and Non Governmental Organisations) in order to maximise the impact of the efforts.
- 6. To organise international meetings to facilitate the introduction of immunisation programmes.
- 7. To promote the implementation of WHO recommendations on viral hepatitis control and prevention.
- 8. To assist implementation of national plans of action for the introduction of vaccines.

Website: VHPB News | Viral Hepatitis Prevention Board

WORLD HEALTH ORGANISATION (WHO)

WHO leads global efforts to expand universal health coverage. We direct and coordinate the world's response to health emergencies. And we promote healthier lives – from pregnancy care through old age. Our Triple Billion targets outline an ambitious plan for the world to achieve good health for all using science-based policies and programmes.

Website WHO HQ: World Health Organization (WHO)

Website WHO EURO: WHO/Europe | Home

EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL (ECDC)

The European Centre for Disease Prevention and Control (ECDC) was established in 2005. It is an EU agency aimed at strengthening Europe's defences against infectious diseases.

According to Article 3 of the <u>Founding Regulation</u>, ECDC's mission is to identify, assess and communicate current and emerging threats to human health posed by infectious diseases.

In order to achieve this mission, ECDC works in partnership with national health protection bodies across Europe to strengthen and develop continent-wide disease surveillance and early warning systems. By working with experts throughout Europe, ECDC pools Europe's health knowledge to develop authoritative scientific opinions about the risks posed by current and emerging infectious diseases.

Within the field of its mission, the Centre shall:

- search for, collect, collate, evaluate and disseminate relevant scientific and technical data;
- provide scientific opinions and scientific and technical assistance including training;
- provide timely information to the Commission, the Member States, Community agencies and international organisations active within the field of public health;
- coordinate the European networking of bodies operating in the fields within the Centre's mission, including networks that emerge from public health activities supported by the Commission and operating the dedicated surveillance networks;
- exchange information, expertise and best practices, and facilitate the development and implementation of joint actions.

Website: Homepage | European Centre for Disease Prevention and Control (europa.eu), Viral hepatitis (europa.eu)

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

CDC works 24/7 to protect America from health, safety and security threats, both foreign and in the U.S. Whether diseases start at home or abroad, are chronic or acute, curable or preventable, human error or deliberate attack, CDC fights disease and supports communities and citizens to do the same.

CDC increases the health security of our nation. As the nation's health protection agency, CDC saves lives and protects people from health threats. To accomplish our mission, CDC conducts critical science and provides health information that protects our nation against expensive and dangerous health threats, and responds when these arise.

Webiste: Centers for Disease Control and Prevention (cdc.gov)

INTERNATIONAL VIRAL HEPATITIS ELIMINATION MEETING (IVEM)

Convened by Academic Medical Education, Virology Education, and the Coalition for Global Hepatitis Elimination (CGHE), IVHEM is a global forum for the exchange of practical experiences for translating diagnostic and therapy advances of viral hepatitis into broad applications that accelerate progress towards the elimination of viral hepatitis as a public health threat by 2030.

Hepatitis B and C affect more than 320 million people globally and can lead to liver disease and mortality from liver failure and hepatocellular carcinoma. More than 248 million people (3.8% of the world's population) live with HBV, and over 700,000 deaths are attributable annually. An estimated 80 million people (globally, 1.1%) live with the hepatitis C virus (HCV), resulting in nearly 500,000 deaths annually.

Key issues to be addressed are how to translate research outcomes into public health policy and practice to meet the 2030 elimination targets. During this two-day meeting, experts in viral hepatitis from around the globe will examine current evidence on how to implement programs that improve the prevention of viral hepatitis and increase the number of people accessing testing and treatment.

The program includes practical examples of innovative intervention studies, country elimination programs, and novel funding mechanisms for testing and treatment.

Website: International Viral Hepatitis Elimination Meeting (IVHEM) 2022 - Hybrid Event - ICE-HBV

THE TASK FORCE FOR GLOBAL HEALTH - COALITION FOR GLOBAL HEPATITIS ELIMINATION

In the spring of 2018, John Ward, MD, a senior scientist at the U.S. Centers for Disease Control and Prevention (CDC), came to The Task Force for Global Health to develop a viral hepatitis elimination initiative called the Coalition for Global Hepatitis Elimination. Under Ward's direction, and in collaboration with the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and other partners, the Coalition was born.

The Coalition for Global Hepatitis Elimination (CGHE) works to eliminate viral hepatitis by strengthening the capacity of elimination programs around the world through technical assistance, knowledge generation, and advocacy among partners.

The Goals

The aim of the Coalition for Global Hepatitis Elimination is to build a "community of practice around viral elimination." Experts from around the globe will share the evidence-based information they've gathered while working on successful virus elimination programs to help at-risk countries create their own solutions. The program is centered around five main axes:

- 1. Building a community practice
- 2. Providing useful information
- 3. Offering technical assistance
- 4. Developing operational research
- 5. Raising public awareness.

To create a truly global movement, all of the information gathered will be made available in one central repository—www.globalhep.org. Its audience will include Coalition members working on viral hepatitis prevention, care, treatment, and elimination.

The Partners

To achieve its goals, the Coalition will rely on a number of financial and technical partners. Nonprofit sector partnerships include organizations such as the Clinton Health Access Initiative, which provides low-cost medications to the developing world, as well as Partners in Health, WHO, and the CDC. A number of private sector partners including industry and foundations are providing financial support to the Coalition.

The Task Force has signed up several countries to join the Coalition, including Mongolia, Georgia, Egypt, Iceland, Switzerland, the United States, Japan, Australia, and Rwanda. The hope is that all national elimination programs will eventually join the network.

Supporting Hepatitis Interventions

TEPHINET, a network of field epidemiology training programs based at The Task Force, works with countries in Europe and the Middle East to support the implementation of prevention and intervention strategies for viral hepatitis. TEPHINET manages and supports Infectious Disease Detection, Prevention, and Elimination projects, including providing Support for Hepatitis C Elimination in Georgia, developing Best Practices for Hepatitis C Virus Elimination, and Viral Hepatitis Prevention and Control in Pakistan.

Website: Viral Hepatitis - The Task Force for Global Health

EMCDDA

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is the leading authority on illicit drugs in the European Union. The Lisbon-based agency provides independent scientific evidence and analysis on all aspects of this constantly changing threat to individual lives and wider society. Its work contributes to EU and national policies to protect Europe's citizens from drug-related harms.

The agency does not make policy or recommendations. Its expertise helps to ensure that the decisions of EU and national policymakers, professionals and practitioners are based on objective and verified facts, not ideology or moral and value judgements. It frequently identifies important drug-related threats, helping EU countries be better prepared to handle them.

Website: EMCDDA home page | www.emcdda.europa.eu

CORRELATION NETWORK

Our Vision

C-EHRN envisions an inclusive and just Europe, in which people who use drugs (PWUD) and other related vulnerable, marginalised and underserved individuals and communities have equitable and universal access to social and healthcare services without being discriminated against and stigmatised.

Our Mission

The overall objective of C-EHRN is to improve access to and the quality of low-threshold, community-based and community-led health and harm reduction services for vulnerable, marginalised and underserved individuals and communities, and to enhance policy and practice to increase their social inclusion.

C-EHRN activities are targeted at people who use drugs, including related marginalized individuals and communities such as drug-using sex workers, people with a diverse sexual orientation, gender identity, expression and sex characteristics, (undocumented) migrants, people in prison, people experiencing homelessness and people living with HIV/AIDS and HCV.

Our Guiding Principles

The work of C-EHRN is guided by the principle that all members of society deserve equitable and appropriate access to health care and civil rights. C-EHRN supports marginalised and vulnerable communities in realising and advocating for their rights. Support is provided in an unprejudiced, unbiased and impartial way, striving towards a more diverse, equitable, just and inclusive Europe. As a European civil society initiative, C-EHRN aims to strengthen the important role of community-based and community-led harm reduction services as part of an evidence-based and integrated people-centred approach to drug use.

C-EHRN advocates for **human rights-based policies**, **services and practices to improve public health**. C-EHRN advocates for a **harm reduction approach that is based on solid evidence and on human rights principles**,

addressing both health and social aspects of drug use. We understand harm reduction in the broadest sense of the word, targeting policies and programmes that contribute to individual health, well-being, social justice, and public health in general – in line with the 'Health in all Policies' approach.

C-EHRN is convinced that civil society, and in particular people who use drugs, should play a vital role in the development and implementation of harm reduction interventions and policies. We acknowledge and respond to the direct and negative impact of stigma, marginalisation and criminalisation on people's access to health and social services. All our activities are therefore inevitably connected to the reduction of social and health inequalities.

C-EHRN gives specific attention to the **prevention, treatment and care of infectious diseases**, including HIV/AIDS, viral hepatitis and COVID19 among the individuals.

C-EHRN works with all relevant stakeholders in the field: health professionals, social and community workers, peer workers, researchers, policymakers, activists, and others. Most of all, we cooperate closely with affected communities and make sure that their voices are heard and their experiences are incorporated in policy and practice. To achieve our goals, our activities promote expert collaboration and networking, community-based monitoring and data collection, capacity building, training and knowledge exchange, information dissemination, awareness-raising and advocacy.

In line with the European Union's competencies and policies in the field of drugs, as reflected in the EU Drug Strategy 2021-2025, C-EHRN's activities aim to **support EU actions to protect and improve the well-being of society and the individual and to protect and promote public health in regard to illicit drug use**. C-EHRN particularly embraces the EU approach to drug policy at a national, regional and international level, which takes into account an integrated, balanced and multidisciplinary approach, based on scientific evidence, human rights and best practices.

Finally, C-EHRN objectives and activities build on other relevant European and international policy and guidance documents, including the United Nations System Common Position on Drug Policy of 2018, the International Guidelines on Human Rights and Drug Policy, the European Convention on Human Rights and the EU Charter of Fundamental Rights.

Website: Correlation European Harm Reduction Network | (correlation-net.org)

INTERNATIONAL CENTRE FOR MIGRATION, HEALTH AND DEVELOPMENT

ICMHD's commitment to understanding and describing the dynamics of migration, health and development has prompted a strong investment in epidemiological and social research, situation assessments, monitoring and evaluation, training and education, and policy formulation and advocacy that takes into account the changing geopolitical nature of migration and its interaction with health and development.

Research

ICMHD's research focuses on communicable and non-communicable health challenges and increasingly on the interaction between them. In the area of communicable diseases, it is working on emerging issues in the fields of HIV, hepatitis B and C, and TB. In the field of non-communicable diseases it is working on emerging issues in the fields of diabetes, reproductive health, maternal and child health, and psychosocial health and wellbeing. In terms of the interactions between communicable and non-communicable diseases, ICMHD is looking at the links between diabetes, TB, and hepatitis C. It is also looking at the barriers to vaccination and the effective use of primary health care in situations of population displacement and resettlement.

Situation Assessments

ICMHD undertakes assessments of health and social conditions in natural and man-made crisis situations where people are displaced. It has evaluated the link between access to healthcare services and social integration of migrants and refugees in Geneva, the health condition and needs of Kosovar refugees in Albania and Macedonia,

the healthcare needs and response to tsunami survivors in Sri Lanka and the Maldives, HIV and viral hepatitis among migrants in Europe and refugees in Lebanon and Jordan, and diabetes and TB in Kuwait.

<u>Training</u>

As part of its commitment to institution strengthening, ICMHD develops training courses for Ministry of Health officials, UN personnel, peacekeeping personnel, military and police, humanitarian relief workers, and primary healthcare staff. Its training courses have covered issues such as preparing for sudden and massive influxes of migrants and refugees, sexual gender based violence in conflict and post-conflict situations, psychosocial needs of migrants and refugees and the humanitarian relief staff who work with them, HIV prevention and treatment, and diagnosis and treatment of viral hepatitis in migrant and refugee populations.

Policy Formulation and Advocacy

ICMHD formulates migration and health/welfare policy options based on real-time evidence and advocates for these policies on behalf of its stakeholders. It has worked with the Council of Europe, the Europe Centre for Disease Control, UNAIDS and WHO on policies related to issues such as screening and access to healthcare, the need for new responses to the threat of communicable and non-communicable disease challenges in sending, transit and receiving countries.

Website: ICMHD - International Center for Migration Health and Development

WORLD HEPATITIS ALLIANCE

We lead the fight against hepatitis. Throughout our history we have ran awareness raising campaigns, championed civil society and advocated and the highest levels to change the course of hepatitis.

We have put hepatitis on the global health agenda, through advocacy we made World Hepatitis Day an internationally recognised global health day, we had combatting hepatitis included in the Sustainable Development Goals and in United Nations political declaration on Universal Health Coverage and we have championed putting civil society at the heart of the hepatitis response. But we won't rest until hepatitis is eliminated. We run international campaigns, build the capacity of civil society through events and webinars and deliver programmes that will see the elimination of hepatitis by 2030.

Website: Home - World Hepatitis Alliance

EUROPEAN LIVER PATIENTS' ASSOCIATION (ELPA)

ELPA's aim is to promote the interests of people with liver disease and in particular: to highlight the size of the problem; to promote awareness and prevention; to address the low profile of liver disease; to share experience of successful initiatives; to work with professional bodies such as EASL and with the EU to ensure that treatment and care are harmonised across Europe to the highest standards.

Website: ELPA - European Liver Patients' Association (eu-patient.eu)

LIVER PATIENTS INTERNATIONAL (LPI)

Who we are

LPI is an international umbrella organization, founded in 2019, that represents and welcomes national liver patient support organizations that work in line with our:

- Vision
- Mission

Values

*We use World Health Organization's precedent for defining region

Our Vision

Liver Patients International (LPI) has a vision where all patients affected by liver disease, wherever they live in the world, have access to timely diagnosis, appropriate healthcare, the best possible quality of life, and that their voice is part of the decision-making process

Our Mission

LPI will keep patients at the center of all that it does. We work in a progressive and collaborative way, ensuring meaningful engagement and partnerships with other stakeholders. We represent and advocate for all patients affected by liver disease in both policy and operational contexts and promote equal access to effective areas of liver healthcare.

Our values

- Collaboration
- Transparency
- Equity
- Respect
- Integrity

LPI will hold these values to its very core in each and every transaction: internal and external

Website: Home - Liver Patients International

UNITE

UNITE is a non-profit, non-partisan, global network of current and former members of parliament from multinational, national, state, and regional Parliaments, Congresses, and Senates, committed towards the promotion of efficient and sustainable policies for improved global health systems, in alignment with the United Nations Sustainable Development Goals (SDGs).

Website: https://www.unitenetwork.org/

CDA FOUNDATION

Mission Eliminate suffering, adverse societal impact and mortality caused by preventable, treatable diseases.

Vision Accelerate hepatitis B and C elimination through verified epidemiological data, disease burden and economic impact modeling, intervention strategies, access to affordable diagnostics and treatments, innovative financing and knowledge-sharing partnerships.

Website: CDA Foundation – STUDY | MODEL | ELIMINATE

VACCINE JOURNAL

Vaccine is **unique** in publishing the highest quality science across **all disciplines** relevant to the field of vaccinology - all original article submissions across basic and clinical research, vaccine manufacturing, history,

public policy, behavioral science and ethics, social sciences, safety, and many other related areas are welcomed. The submission categories as given in the Guide for Authors indicate where we receive the most papers. Papers outside these major areas are also welcome and authors are encouraged to contact us with specific questions. We also invite authors to submit relevant basic science and clinical reviews, methodological articles, opinion and commentary pieces, visual pieces, and letters. Authors are required to consult the <u>Guide for Authors</u> as the submission guidelines are dynamic and therefore subject to change.

Website: Vaccine | Journal | ScienceDirect.com by Elsevier

EUROPEAN SOCIETY FOR CLINICAL VIROLOGY

The European Society for Clinical Virology (ESCV) is a non-profit organization founded in 1997. Since then, it has provided a forum for virologists, scientists and physicians interested in all aspects of Clinical Virology and human viral diseases.

Website: European Society for Clinical Virology (escv.eu)

EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)

Our vision

Many ways, one aim: beating liver disease

Our mission

The European Association for the Study of the Liver mission is to be the Home of Hepatology so that all who are involved with treating liver disease can realise their full potential to cure and prevent it. The purpose of the association is to promote communication between European professionals interested in the liver and its disorders. In particular, the association shall:

- 1. Promote research concerning the liver
- 2. Promote education of physicians, scientists and public awareness of liver diseases and their management
- 3. Act as an advisor to European and national health authorities concerning liver diseases, provision of clinical services and the need for research funding
- 4. Foster European multicentre controlled trials
- 5. Facilitate scientific exchange
- 6. Facilitate participation of Young Investigators at its meetings

Website: EASL | The Home of Hepatology

ACHIEVE

THE ELIMINATION OF VIRAL HEPATITIS B AND C IS AMONGST THE STATED GOALS OF THE UN AND THE WHO. HOWEVER, EUROPE IS YET TO MAKE SIGNIFICANT PROGRESS.

These viruses affect 28 million people in the WHO Europe region, most of whom are living without visible symptoms for decades before disease progression<u>i</u>. As many as 171,000 deaths<u>ii</u> annually in the WHO Europe region are caused by two infections – hepatitis B virus and hepatitis C virus. Experts warn that the number of individuals affected will continue to increase in many countries across Europe over the next 15 years<u>iii</u> unless action is taken to prevent, detect, and cure these diseases.

THE GOAL

Countries must move to prevent infection, improve diagnosis across the spectrum of risk groups and ensure that direct acting antiviral treatment is affordable and accessible. Spending money today to control viral hepatitis will reduce costs later from its complications. iv

WHAT TO DO

Effective tools exist today. Hepatitis B is preventable through a vaccine, and can be controlled with treatment. Although there is still no vaccine, hepatitis C is now curable with a short course of highly effective and safe medicine. Significant progress towards eliminating both diseases as public health threats in European countries is possible, provided decisive action is taken to expand surveillance, prevention, testing, treatment and care.

ABOUT ACHIEVE

The members of the ACHIEVE (Associations Collaborating on Hepatitis to Immunise and Eliminate the Viruses in Europe) coalition, representing patients and community, clinicians and researchers, have therefore decided to collaborate to advance the fight against these diseases in line with the WHO Global Health Sector Strategy, the WHO Europe Action Plan and the UN Sustainable Development Goals. The ACHIEVE coalition includes the following organisations: The European Liver Patients' Association (ELPA), the Viral Hepatitis Prevention Board, Hepatitis B and C Public Policy Association, European Aids Treatment Group (EATG), Correlation Network, the World Hepatitis Alliance and the Barcelona Institue for Global Health (ISGlobal).

Website: <u>ACHIEVE – ASSOCIATIONS COLLABORATING ON HEPATITIS TO IMMUNIZE AND ELIMINATE THE VIRUSES IN EUROPE (achievehepatitiselimination.eu)</u>

BARRIERS FOR REACHING THE WHO ELIMINATION GOALS

(2020). WHO Guidelines Approved by the Guidelines Review Committee. <u>Prevention of Mother-to-Child</u> <u>Transmission of Hepatitis B Virus: Guidelines on Antiviral Prophylaxis in Pregnancy</u>. Geneva, World Health Organization

© World Health Organization 2020.

WHO estimates that in 2015, 257 million people were living with chronic hepatitis B virus (HBV) infection worldwide, and that 900 000 had died from HBV infection, mostly as a result of cirrhosis or hepatocellular carcinoma. Most HBV-associated deaths among adults are secondary to infections acquired at birth or in the first five years of life. In May 2016, the World Health Assembly endorsed the Global health sector strategy on viral hepatitis, which calls for the elimination of viral hepatitis as a public health threat by 2030 (defined as a 90% reduction in incidence of new infections and a 65% reduction in mortality). Elimination of HBV infection as a public health threat requires a reduction in the prevalence of hepatitis B surface antigen (HBsAg) to below 0.1% in children 5 years of age. This can be achieved through universal immunization of newborns against hepatitis B and other interventions to prevent mother-to-child transmission of HBV. These guidelines provide evidence-based guidance on the use of peripartum antiviral prophylaxis in HBsAg-positive pregnant women for the prevention of mother-to-child transmission of HBV.

Abdel-Daim MM (2020). "Editorial: the road to elimination of viral hepatitis-another promising real-world experience." Aliment Pharmacol Ther **52**(2): 405-406.

Akiyama MJ (2020). "<u>Hepatitis C in the criminal justice system: opportunities for global action in the era of viral hepatitis elimination.</u>" <u>BMC Med</u> **18**(1): 208.

Busschots D, S Toghanian, R Bielen, S Salomonsson, M Koc Ö, G Hendrickx, M Jadoul, F Nevens, E Sokal, C Brixko, K Peerlinck, L Apers, G Robaeys and JV Lazarus (2020). "Eliminating viral hepatitis C in Belgium: the microelimination approach." BMC Infect Dis 20(1): 181.

BACKGROUND: Hepatitis C virus is one of the leading causes of chronic liver disease and liver-related deaths worldwide. The estimated prevalence of chronic hepatitis C viral infection among the general Belgian population was 0.57% (n = 64,000) in 2015. Although Belgium has had a 'Hepatitis C Plan' since 2014, elimination efforts are unclear. This study employs the best available data and modelling estimates to define the burden of hepatitis C viral infection among key subgroups in Belgium, identify information gaps and propose potential approaches to screening, linkage to care and treatment, and cure. METHODS: We examined the peer-reviewed and grey literature since 2012 for data on the prevalence of hepatitis C viral infection in Belgium in key subgroups identified by national experts and in the literature. Ultimately, this research is primarily based on data provided by the key stakeholders themselves due to a lack of reliable data in the literature. Based on this, we modelled the treatment rates required to reach elimination of hepatitis C in several subgroups. RESULTS: Eleven potential subgroups were identified. There were no data available for two subgroups: generational cohorts and men who have sex with men. In six subgroups, fewer than 3000 people were reported or estimated to have hepatitis C infection. Migrants and people who inject drugs were the most affected subgroups, and children were the least affected subgroup. Only two subgroups are on target to achieve elimination by 2030: patients living with haemophilia and transplant recipients. CONCLUSIONS: Removing Belgian treatment reimbursement restrictions in January 2019 was a big step towards eliminating HCV. In addition, increasing surveillance, including with a national registry, treatment prescription by other health-care providers and availability of treatment in local pharmacies are central to improving the current situation and getting on track to reach the 2030 WHO hepatitis C elimination targets in Belgium.

Cox AL, MH El-Sayed, JH Kao, JV Lazarus, M Lemoine, AS Lok and F Zoulim (2020). "Progress towards elimination goals for viral hepatitis." Nat Rev Gastroenterol Hepatol 17(9): 533-542.

The global burden of viral hepatitis is substantial; in terms of mortality, hepatitis B virus and hepatitis C virus infections are on a par with HIV, malaria and tuberculosis, among the top four global infectious diseases. In 2016, the 194 Member States of the World Health Organization committed to eliminating viral hepatitis as a public health threat by 2030, with a particular focus on hepatitis B virus and hepatitis C virus infection. With only 10 years to go until the 2030 deadline is reached, and although much progress

has been made towards elimination, there are still some important gaps in terms of policy and progress. In this Viewpoint, we asked a selection of scientists and clinicians working in the viral hepatitis field for their opinions on whether elimination of viral hepatitis by 2030 is feasible, what the key areas of progress are and what the focus for the next 10 years and beyond should be for viral hepatitis elimination.

Døssing A, BT Røge, LG Madsen, AL Laursen, JB Hansen, J Bukh and N Weis (2020). "[Elimination of hepatitis C virus in Denmark]." Ugeskr Laeger 182(9).

In Denmark, about 50% of patients with chronic hepatitis C virus (HCV) infection are undiagnosed. Since 2014, therapy containing direct-acting antivirals (DAA) has proven efficient and is available to all patients, who have a chronic HCV infection and a Danish personal identification number. The World Health Organization has a goal of elimination of viral hepatitis in 2030. Elimination of HCV in Denmark should focus on reducing HCV transmission, incidence and prevalence, combined with treatment with DAA of all infected patients. Micro-elimination strategies may play a major role, but a national strategy is lacking.

Dunn R, E Musabaev, H Razavi, S Sadirova, S Bakieva, K Razavi-Shearer, K Brigida, S Kamili, F Averhoff and M Nasrullah (2020). "Progress Toward Hepatitis B and Hepatitis C Elimination Using a Catalytic Funding Model - Tashkent, Uzbekistan, December 6, 2019-March 15, 2020." MMWR Morb Mortal Wkly Rep 69(34): 1161-1165. In 2016, the World Health Organization (WHO) set hepatitis elimination targets of 90% reduction in incidence and 65% reduction in mortality worldwide by 2030 (1). Hepatitis B virus (HBV) and hepatitis C virus (HCV) infection prevalences are high in Uzbekistan, which lacks funding for meeting WHO's targets. In the absence of large financial donor programs for eliminating HBV and HCV infections, insufficient funding is an important barrier to achieving those targets in Uzbekistan and other low- and middleincome countries. A pilot program using a catalytic funding model, including simplified test-and-treat strategies, was launched in Tashkent, Uzbekistan, in December 2019. Catalytic funding is a mechanism by which the total cost of a program is paid for by multiple funding sources but is begun with upfront capital that is considerably less than the total program cost. Ongoing costs, including those for testing and treatment, are covered by payments from 80% of the enrolled patients, who purchase medications at a small premium that subsidizes the 20% who cannot afford treatment and therefore receive free medication. The 1-year pilot program set a target of testing 250,000 adults for HBV and HCV infection and treating all patients who have active infection, including those who had a positive test result for hepatitis B surface antigen (HBsAq) and those who had a positive test result for HCV core antigen. During the first 3 months of the program, 24,821 persons were tested for HBV and HCV infections. Among those tested, 1,084 (4.4%) had positive test results for HBsAq, and 1,075 (4.3%) had positive test results for HCV antibody (anti-HCV). Among those infected, 275 (25.4%) initiated treatment for HBV, and 163 (15.2%) initiated treatment for HCV, of whom 86.5% paid for medications and 13.5% received medications at no cost. Early results demonstrate willingness of patients to pay for treatment if costs are low, which can offset elimination costs. However, improvements across the continuum of care are needed to recover the upfront investment. Lessons learned from this program, including the effectiveness of using simplified test-and-treat guidelines, general practitioners in lieu of specialist physicians, and innovative financing to reduce costs, can guide similar initiatives in other countries and help curb the global epidemic of viral hepatitis, especially among low- and middle-income countries.

Giuliani R, V Casigliani, M Fornili, T Sebastiani, E Freo, G Arzilli, G Scardina, L Baglietto, L Tavoschi and R Ranieri (2020). "HCV micro-elimination in two prisons in Milan, Italy: A model of care." J Viral Hepat 27(12): 1444-1454.

People in prison represent a high-risk population for HCV infection control. With the advent of new direct antiviral agents (DAAs) HCV micro-elimination in prison setting became a feasible strategy. We assessed the impact of an intervention for HCV testing and treatment in 2017 and 2018 in a jail (San Vittore,SV) and a prison for sentenced individuals (Opera,OP). A dedicated protocol was applied and implemented over the two years. We collected data on demographics, HCV testing and treatment on all inmates present on 31 October 2017 and 2018. In the two facilities, there were 2,366 and 2,369 inmates in 2017 and 2018 respectively; the majority were men (95.6%; 96.4%) and Italians (57.0%; 61.9%) with a median age of 41 years. Prevalence of lifetime reported drug use remained high (46.5%; 44.2%). HCV screening coverage was 89% in both years, while HCV RNA test coverage increased (90.6%; 99.0%). HCV seroprevalence remained stable (10.1%; 9.2%). In 2017 among inmates with HCV chronic infection 90 (42.4%) individuals had started DAAs treatment and 106 (54.6%) in 2018; of whom 38 (17.9%) and 74 (38.1%) achieved the SVR. The viremic pool decreased significantly over time (SV,24.4%; 15.4%;OP, 16.1%; <1%). Among inmates with HCV-positive serology in 2018, 121 (81.0%) were never linked to care before

incarceration. Our study showed how a targeted and well-implemented HCV test-and-treat intervention in prison was feasible and effective in achieving micro-elimination. Viral hepatitis elimination agenda may help drawing interest onto this neglected population and bringing prison health higher up in the global public health agenda.

Hatzakis A, JV Lazarus, E Cholongitas, R Baptista-Leite, C Boucher, CS Busoi, S Deuffic-Burban, J Chhatwal, G Esmat, S Hutchinson, MM Malliori, M Maticic, A Mozalevskis, F Negro, GA Papandreou, GV Papatheodoridis, M Peck-Radosavljevic, H Razavi, T Reic, E Schatz, N Tozun, Z Younossi and MP Manns (2020). "Securing sustainable funding for viral hepatitis elimination plans." Liver Int 40(2): 260-270.

The majority of people infected with chronic hepatitis C virus (HCV) in the European Union (EU) remain undiagnosed and untreated. During recent years, immigration to EU has further increased HCV prevalence. It has been estimated that, out of the 4.2 million adults affected by HCV infection in the 31 EU/ European Economic Area (EEA) countries, as many as 580 000 are migrants. Additionally, HCV is highly prevalent and under addressed in Eastern Europe. In 2013, the introduction of highly effective treatments for HCV with direct-acting antivirals created an unprecedented opportunity to cure almost all patients, reduce HCV transmission and eliminate the disease. However, in many settings, HCV elimination poses a serious challenge for countries' health spending. On 6 June 2018, the Hepatitis B and C Public Policy Association held the 2nd EU HCV Policy summit. It was emphasized that key stakeholders should work collaboratively since only a few countries in the EU are on track to achieve HCV elimination by 2030. In particular, more effort is needed for universal screening. The micro-elimination approach in specific populations is less complex and less costly than country-wide elimination programmes and is an important first step in many settings. Preliminary data suggest that implementation of the World Health Organization (WHO) Global Health Sector Strategy on Viral Hepatitis can be cost saving. However, innovative financing mechanisms are needed to raise funds upfront for scaling up screening, treatment and harm reduction interventions that can lead to HCV elimination by 2030, the stated goal of the WHO.

Karimi-Sari H and MS Rezaee-Zavareh (2020). "COVID-19 and viral hepatitis elimination programs: Are we stepping backward?" Liver Int 40(8): 2042.

Kasai T (2020). "<u>Time to act to make elimination of viral hepatitis a reality.</u>" <u>Lancet Gastroenterol Hepatol</u> **5**(2): 102-103.

Krekulová L and R Honzák (2020). "Obstacles and problems in global elimination of viral hepatitis C." Cas Lek Cesk 159(6): 213-216.

The global elimination of viral hepatitis C (HCV) infection according to WHO plan 2016 is conditioned by controlling the HCV epidemic among people who inject drug (PWID). This high-risk subpopulation has no interest in prevention, diagnostic or treatment of HCV infection. The problem is not only the lack of interest in changing their behaviour pattern, but also inability of health care professionals to conduct efficient assistance to PWID. The key to any successful intervention or treatment is to master the communication with problem patients. Providing efficient care of PWID with HCV is the most important step to successful HCV elimination.

Lancaster K, T Rhodes and J Rance (2020). ""Towards eliminating viral hepatitis": Examining the productive capacity and constitutive effects of global policy on hepatitis C elimination." Int J Drug Policy 80: 102419.

In 2016 the World Health Organization published the first global health strategy to address viral hepatitis, setting a goal of eliminating viral hepatitis as a major public health threat by 2030. While the field has been motivated by this goal, to date there has been little critical attention paid to the productive capacity and constitutive effects of this policy. How is governing taking place through the mechanism of this global strategy, and how are its goals and targets shaping what is made thinkable (indeed, what is made as the real) about hepatitis C and its elimination? And with what effects? Taking the Global Health Sector Strategy on Viral Hepatitis, 2016-2021 as a text for analysis, we draw on poststructural thinking on problematisation and governmental technologies to examine how 'elimination' - as a proposal - constitutes the problem of hepatitis C. We critically consider the conceptual logics underpinning the elimination goal and targets, and the multiple material-discursive effects of this policy. We examine how governing takes place through numbers, by analysing 'target-setting' (and its accompanying practices of management, quantification and surveillance) as governmental technologies. We consider how the goal of elimination makes viral hepatitis visible and amenable to structuring, action and global management. Central to making viral hepatitis visible and manageable is quantification. Viral

hepatitis is made as a problem requiring urgent global health management not through the representation of its effects on bodies or situated communities but rather through centralising inscription practices and comparison of estimated rates. It is important to remain alert to the multiple makings of hepatitis C and draw attention to effects which might be obscured due to a primary focus on quantification and management. To do so is to recognise the ontopolitical effects of governmental technologies, especially for communities 'targeted' by these strategies (including people who inject drugs).

Lazarus JV, A Øvrehus, J Demant, L Krohn-Dehli and N Weis (2020). "<u>The Copenhagen test and treat hepatitis C in a mobile clinic study: a protocol for an intervention study to enhance the HCV cascade of care for people who inject drugs (T'N'T HepC).</u>" <u>BMJ Open</u> **10**(11): e039724.

INTRODUCTION: Injecting drug use is the primary driver of hepatitis C virus (HCV) infection in Europe. Despite the need for more engagement with care, people who inject drugs (PWID) are hard to reach with HCV testing and treatment. We initiated a study to evaluate the efficacy for testing and linkage to care among PWID consulting peer-based testing at a mobile clinic in Copenhagen, Denmark. METHODS AND ANALYSIS: In this intervention study, we will recruit participants at a single community-based, peer-run mobile clinic. In a single visit, we will first offer participants a point-of-care HCV antibody test, and if they test positive, then they will receive an HCV RNA test. If they are HCV-RNA+, we will administer facilitated referrals to designated 'fast-track' clinics at a hospital or an addiction centre for treatment. The primary outcomes for this study are the number of tested and treated individuals. Secondary outcomes include individuals lost at each step in the care cascade. ETHICS AND DISSEMINATION: The results of this study could provide a model for targeting PWID for HCV testing and treatment in Demark and other settings, which could help achieve WHO HCV elimination targets. The Health Research Ethics Committee of Denmark and the Danish Data Protection Agency confirmed (December 2018/January 2019) that this study did not require their approval. Study findings will be disseminated through peer-reviewed publications, conference presentations and social media.

Maticic M and MU Mondelli (2020). "<u>Elimination of viral hepatitis: where do we stand in the year 2020?</u>" <u>Clin Microbiol Infect</u> **26**(7): 816-817.

Mohanty P, P Jena and L Patnaik (2020). "<u>Vaccination against Hepatitis B: A Scoping Review</u>." <u>Asian Pac J Cancer Prev</u> **21**(12): 3453-3459.

OBJECTIVE: Elimination of viral hepatitis by 2030 as one of the international Sustainable Development Goals puts the hepatitis B vaccination on the forefront. However, barriers to vaccination reported in various studies are of concern. This study explores the global barriers for effective uptake of Hepatitis-B vaccination. METHODS: A scoping review of studies reporting hepatitis B vaccination barriers was done using PMC data base and Google scholar search engine. About 803 journal articles and reports on hepatitis B barriers were retrieved but only 36 most relevant items during last 10 years were identified, pile sorted, grouped and analyze. RESULTS: Overall 74 barriers have been identified for effective uptake of hepatitis-B vaccines. Most studies focused on non-zero dose of hepatitis B vaccine, One-third of the barriers are related to system issues, one-fourth of the barriers were related to caregiver education or awareness, fear of side effect, migration etc., one-fifth barriers were related to service provider issues like poor out-reach, home visits, poor communication and/relation with the caregivers, failure to identify unimmunized children etc., and other barriers were social-cultural issues. The review reveals limited availability and accessibility to health-facility based immunization, lack of awareness among caregivers, poor communication by the healthcare workers and negative relationships with the beneficiaries, cost of vaccine in private sector, inconvenience time and place of vaccination etc. as the major barriers for hepatitis B vaccination. Barriers varied from country to country. CONCLUSION: Myriad barriers for reduced hepatitis-B vaccine uptake need to be addressed contextually as countries are at different stages of hepatitis-B vaccination implementation.

Nakitanda AO and E Duffell (2020). <u>"Hospital discharges of hepatocellular carcinoma and non-alcohol related cirrhosis in the EU/EEA and United Kingdom: a descriptive analysis of 2004-2015 data.</u>" <u>Infect Dis (Lond)</u> **52**(11): 816-827.

BACKGROUND: Viral hepatitis is a leading cause of mortality globally, comparable to that of HIV and TB. Most hepatitis deaths are related to liver cirrhosis and hepatocellular carcinoma (HCC) associated with chronic hepatitis B and C infections. To examine the progress towards the elimination goals set in the global health sector strategy for viral hepatitis, we aimed to assess the impact of mortality-indicative

morbidity. METHODS: We retrieved inpatients and day cases hospital discharges data from the Eurostat hospital activities database, and analysed ICD-10 and ICD-9 specific codes related to primary HCC and non-alcohol related cirrhosis registered by European Union/European Economic Area (EU/EEA) countries and United Kingdom (UK) for 2004 to 2015. RESULTS: In 2015, 20 countries (45.7% of total EU/EEA/UK population) reported 13,236 (Range 0-6294) day cases and 36,012 (4-9097) inpatients discharges of HCC. Romania, Croatia, Luxembourg and UK reported increasing day cases discharge rates between 2004 and 2015; while HCC inpatients discharge rates increased overall during this period. There were 13,865 (0-5918) day cases and 56,176 (3-29,118) inpatients discharges reported for cirrhosis across the 20 countries in 2015. Over the 12 years, day cases discharge rates for cirrhosis increased in Romania, Croatia and UK. Though higher than for day cases, cirrhosis inpatients discharge rates remained stable. CONCLUSIONS: The hospital burden of HCC and cirrhosis is high, with considerable inpatient load including sustained increasing trends in HCC discharge rates. Further interpretation in light of local health system contexts, and more robust harmonised data are needed to better understand the impact of the viral hepatitis epidemic in the region.

Nguyen MH, G Wong, E Gane, JH Kao and G Dusheiko (2020). "<u>Hepatitis B Virus: Advances in Prevention,</u> <u>Diagnosis, and Therapy</u>." <u>Clin Microbiol Rev</u> **33**(2).

Currently, despite the use of a preventive vaccine for several decades as well as the use of effective and well-tolerated viral suppressive medications since 1998, approximately 250 million people remain infected with the virus that causes hepatitis B worldwide. Hepatitis C virus (HCV) and hepatitis B virus (HBV) are the leading causes of liver cancer and overall mortality globally, surpassing malaria and tuberculosis. Linkage to care is estimated to be very poor both in developing countries and in highincome countries, such as the United States, countries in Western Europe, and Japan. In the United States, by CDC estimates, only one-third of HBV-infected patients or less are aware of their infection. Some reasons for these low rates of surveillance, diagnosis, and treatment include the asymptomatic nature of chronic hepatitis B until the very late stages, a lack of curative therapy with a finite treatment duration, a complex natural history, and a lack of knowledge about the disease by both care providers and patients. In the last 5 years, more attention has been focused on the important topics of HBV screening, diagnosis of HBV infection, and appropriate linkage to care. There have also been rapid clinical developments toward a functional cure of HBV infection, with novel compounds currently being in various phases of progress. Despite this knowledge, many of the professional organizations provide quidelines focused only on specific questions related to the treatment of HBV infection. This focus leaves a gap for care providers on the other HBV-related issues, which include HBV's epidemiological profile, its natural history, how it interacts with other viral hepatitis diseases, treatments, and the areas that still need to be addressed in order to achieve HBV elimination by 2030. Thus, to fill these gaps and provide a more comprehensive and relevant document to regions worldwide, we have taken a global approach by using the findings of global experts on HBV as well as citing major guidelines and their various approaches to addressing HBV and its disease burden.

Palayew A, H Razavi, SJ Hutchinson, GS Cooke and JV Lazarus (2020). "Do the most heavily burdened countries have the right policies to eliminate viral hepatitis B and C?" Lancet Gastroenterol Hepatol 5(10): 948-953.

In 2019, a Lancet Gastroenterology & Hepatology Commission on accelerating the elimination of viral hepatitis reported on the status of 11 viral hepatitis policy indicators in 66 countries and territories with the heaviest burden by global region. Policies were reported as being either in place, in development, or not in place. This study uses the Commission findings to estimate hepatitis B virus (HBV) and hepatitis C virus (HCV) policy scores and rankings for these 66 countries and territories. We applied a multiple correspondence analysis technique to reduce data on policy indicators into a weighted summary for the HBV and HCV policies. We calculated HBV and HCV policy scores for each country. Countries and territories that received higher scores had more policies in place and in development than did countries with lower scores. The highest scoring country for HBV was Australia, whereas Somalia had the lowest score. For the HCV policy score, Australia and New Zealand had perfect scores, whereas Somalia, Sudan, and Yemen had the lowest scores, all having no policy indicators in place.

Perrett SE, A Plimmer, AG Shankar and N Craine (2020). "Prevalence of HCV in prisons in Wales, UK and the impact of moving to opt-out HCV testing.v" J Public Health (Oxf) 42(2): 423-428.

BACKGROUND: Viral hepatitis is a leading cause of death worldwide. The World Health Organisation introduced a target to reduce hepatitis C virus (HCV) as a public health threat by 2030. Testing and treatment of those at elevated risk of infection in prison is key to achieving disease elimination. An opt-

out testing policy for those in prison was introduced in Wales, UK, in 2016. METHODS: We analysed all Wales laboratory data where the testing site was a prison. We analysed numbers tested and positivity for a 14-month period before and after the introduction of opt-out testing policy. RESULTS: Between September 2015 and December 2017, 6949 HCV tests were from prison settings in Wales, equating to 29% of admissions to prison (P < 0.001). All but one prison increased testing following the introduction of opt-out policy. Percentage positivity for HCV remained at 11% before and after opt-out policy (P = 0.572). Short-stay prisons saw higher rates of HCV positivity than long stay. CONCLUSION: Data suggest implementation of opt-out policy improved uptake and diagnosis of HCV amongst those in prison; however, further effort is required to fully embed screening for all. Positivity remains high amongst those in prison, particularly in short-stay prisons. Laboratory data can support audit of opt-out policy.

Pluta M, M Pokorska-Śpiewak, M Aniszewska and M Marczyńska (2020). "On a straight path to HCV elimination in children - new prospects for hepatitis C treatment in Poland.v" Przegl Epidemiol **74**(4): 662-666.

Difficulties in achieving elimination targets of the World Health Organization's Global Strategy on viral hepatitis might be overcome through a new micro-elimination approach that allows for a quick, efficient targeting of treatment and prevention services. Particular focus on identification of high-risk and so far marginalized populations, such as children and adolescents, increases chances for HCV elimination on a country, and ultimately on a population level. Therefore, a broad access to safe and highly effective direct-acting antiviral drugs is of upmost importance in the pediatric population.

Sperle I, G Steffen, SA Leendertz, N Sarma, S Beermann, R Thamm, Y Simeonova, M Cornberg, H Wedemeyer, V Bremer, R Zimmermann and S Dudareva (2020). "Prevalence of Hepatitis B, C, and D in Germany: Results From a Scoping Reviewv." Front Public Health 8: 424.

Background: One of the five strategic directions in the World Health Organization global health sector strategy on viral hepatitis 2016-2021 is to generate strong strategic information for focused action to understand the viral hepatitis epidemic and focus the response. Knowledge of national prevalence is a cornerstone of strategic information. Germany is considered to be a low prevalence country for viral hepatitis B, C, and D, however the prevalence is likely to be higher among at-risk groups. Methods: The aim of this work was to give a detailed overview of the prevalence of viral hepatitis B (HBsAq, anti-HBc), C (anti-HCV, HCV RNA), and D (anti-HDV, HDV RNA) in different population groups in Germany. Therefore, we analyzed the results of a comprehensive literature search on various aspects of the epidemiological situation of hepatitis B, C, and D in Germany. Eligible publications including information on hepatitis B, C, and D prevalence were extracted from the overall spreadsheet table and summarized and analyzed based on virus and different population groups. A quality appraisal was performed using a checklist developed by Hoy et al. to assess risk of bias in prevalence studies. Results: Overall, 51 publications were identified through the literature search. The overall prevalence of HBsAg in the general (and proxy) population ranged from 0.3 to 1.6%. Among at-risk groups, including clinical populations and health care workers, the HBsAq prevalence ranged from 0.2% (among rheumatic patients) to 4.5% among HIV positive patients. The overall prevalence of anti-HCV in the general (and proxy) population ranged from 0.2 to 1.9%. Among at-risk groups, including clinical populations and health care workers, the anti-HCV prevalence ranged from 0.04% (among health care workers) to 68.0% among people who inject drugs. Conclusions: The hepatitis B and C prevalence in the general population in Germany is low. Prevalence is high to very high among at-risk populations, however for some groups evidence was incomplete or missing completely. To reach the elimination goals in Germany and implement a targeted response, more research among at-risk groups is needed.

Stasi C, C Silvestri and F Voller (2020). "<u>Update on Hepatitis C Epidemiology: Unaware and Untreated Infected Population Could Be the Key to Elimination.</u>" <u>SN Compr Clin Med</u> **2**(12): 2808-2815.

Globally, the World Health Organization (WHO) estimates that 71 million people have chronic hepatitis C virus (HCV) infection. A significant number of these will develop cirrhosis or liver cancer. Currently, during the COVID-19 outbreak, a high mortality rate has been found in patients with COVID-19 and cirrhosis. New direct-acting antiviral agents can cure more than 90% of HCV-infected patients. The new WHO strategy has introduced global goals against viral hepatitis, including a 30% reduction in new HCV cases and a 10% reduction in mortality by 2020. HCV transmission has changed considerably, reflecting both the evolution of medicine and health and social changes. The HCV is usually spread through blood-to-blood contact. After the discovery of HCV in 1989, antibody screening has drastically decreased the incidence of post-transfusion hepatitis. Nowadays, routine blood donor screening by nucleic acid

amplification testing for the presence of HCV RNA has been introduced in many countries. It is conceivable that HCV screening could be offered to people born between 1946 and 1964 in the developed world and to people at high risk for HCV infection such as those who have received blood transfusions, blood products or organ donations before the 1990s, prisoners, health care workers, drug users and infants born to HCV-infected women. To achieve HCV elimination, health programmes should include improvement to access to health care services, increased screening and new projects to identify a submerged portion of patients with HCV infection. Submerged people with HCV infection are both people who are unaware of their condition and people diagnosed with HCV but not yet treated. Based on these premises, this review will examine and discuss the epidemiological changes in contracting HCV, highlighting the ways in which to identify a submerged portion of patients with HCV infection.

Steffen G, I Sperle, SA Leendertz, N Sarma, S Beermann, R Thamm, V Bremer, R Zimmermann and S Dudareva (2020). "The epidemiology of Hepatitis B, C and D in Germany: A scoping review v." PLoS One 15(3): e0229166.

BACKGROUND: Germany is considered to be a low prevalence country for viral Hepatitis B, C and D (HBV, HCV, HDV). However, the burden of disease can be high among subpopulations. To meet the world Health Organization (WHO) viral hepatitis (VH) elimination goals, a national strategy was developed by the German government in 2016. We performed a scoping review to understand the baseline epidemiological situation in Germany regarding burden of disease, sequelae and care of HBV, HCV and HDV as a reference to monitor the progress of the national VH elimination and to identify further knowledge gaps and research needs. METHODS: The protocol of the systematic review was prepared following the PRISMA statement guidelines for scoping reviews. Relevant search terms were used to identify eligible studies according to the research questions. We searched six online databases for original work published between January 2005 and March 2017. Based on the identified references, a matrix was developed presenting the eligible literature by targeted population group and outcome category. RESULTS: 104 publications were eligible for extraction covering 299 outcome results. The population groups targeted in the identified studies included the general population and proxy populations, a range of clinical populations, people who inject drugs, men who have sex with men, healthcare workers, people in prisons and different migrant/mobile populations. Other vulnerable populations (e.g. sex workers) were not targeted. Overall, good evidence was found for HBV and HCV prevalence and HBV vaccination coverage in the GP and proxy populations. Evidence for these outcomes was weaker in populations at risk for VH. For HBV and HCV incidence and mortality, we identified large evidence gaps in all population groups. Outcomes on VH sequelae and care were mainly covered by studies in clinical populations of people living with viral hepatitis. For HDV the overall evidence available was scarce. CONCLUSIONS: We created a comprehensive evidence-based overview on the current epidemiological situation of viral hepatitis in Germany. We identified knowledge gaps for further research and established a baseline for future monitoring of viral hepatitis elimination goals in Germany.

Tordrup D, Y Hutin, K Stenberg, JA Lauer, DW Hutton, M Toy, N Scott, J Chhatwal and A Ball (2020). "Cost-Effectiveness of Testing and Treatment for Hepatitis B Virus and Hepatitis C Virus Infections: An Analysis by Scenarios, Regions, and Income." Value Health 23(12): 1552-1560.

OBJECTIVES: Testing and treatment for hepatitis B virus (HBV) and hepatitis C virus (HCV) infection are highly effective, high-impact interventions. This article aims to estimate the cost-effectiveness of scaling up these interventions by scenarios, regions, and income groups. METHODS: We modeled costs and impacts of hepatitis elimination in 67 low- and middle-income countries from 2016 to 2030. Costs included testing and treatment commodities, healthcare consultations, and future savings from cirrhosis and hepatocellular carcinomas averted. We modeled disease progression to estimate disability-adjusted life-years (DALYs) averted. We estimated incremental cost-effectiveness ratios (ICERs) by regions and World Bank income groups, according to 3 scenarios: flatline (status quo), progress (testing/treatment according to World Health Organization guidelines), and ambitious (elimination). RESULTS: Compared with no action, current levels of testing and treatment had an ICER of \$807/DALY for HBV and -\$62/DALY (cost-saving) for HCV. Scaling up to progress scenario, both interventions had ICERs less than the average gross domestic product/capita of countries (HBV: \$532/DALY; HCV: \$613/DALY). Scaling up from flatline to elimination led to higher ICERs across countries (HBV: \$927/DALY; HCV: \$2528/DALY, respectively) that remained lower than the average gross domestic product/capita. Sensitivity analysis indicated discount rates and commodity costs were main factors driving results. CONCLUSIONS: Scaling up testing and treatment for HBV and HCV infection as per World Health Organization guidelines is a cost-effective intervention. Elimination leads to a much larger impact though ICERs are higher. Price

reduction strategies are needed to achieve elimination given the substantial budget impact at current commodity prices.

van Dijk M and JPH Drenth (2020). "Loss to follow-up in the hepatitis C care cascade: A substantial problem but opportunity for micro-elimination." J Viral Hepat **27**(12): 1270-1283.

Since the advent of direct-acting antivirals, elimination of hepatitis C viral (HCV) infections seems within reach. However, studies on the HCV cascade of care show suboptimal progression through each step for all patient groups. Loss to follow-up (LTFU) is a major issue and is a barrier to HCV elimination. This review summarizes the scale of the LTFU problem and proposes a micro-elimination approach. Retrieving LTFU patients and re-engaging them with care again has shown to be feasible in the Netherlands. Micro-elimination through retrieval can contribute to reaching the World Health Organization's viral hepatitis elimination targets by 2030.

Polaris Observatory Collaborators (2021). "The case for simplifying and using absolute targets for viral hepatitis elimination goals." J Viral Hepat 28(1): 12-19.

The 69th World Health Assembly endorsed the Global Health Sector Strategy for Viral Hepatitis, embracing a goal to eliminate hepatitis infection as a public health threat by 2030. This was followed by the World Health Organization's (WHO) global targets for the care and management of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. These announcements and targets were important in raising awareness and calling for action; however, tracking countries' progress towards these elimination goals has provided insights to the limitations of these targets. The existing targets compare a country's progress relative to its 2015 values, penalizing countries who started their programmes prior to 2015, countries with a young population, or countries with a low prevalence. We recommend that (1) WHO simplify the hepatitis elimination targets, (2) change to absolute targets and (3) allow countries to achieve these disease targets with their own service coverage initiatives that will have the maximum impact. The recommended targets are as follows: reduce HCV new chronic cases to ≤5 per 100 000, reduce HBV prevalence among 1-year-olds to ≤0.1%, reduce HBV and HCV mortality to ≤5 per 100 000, and demonstrate HBV and HCV year-to-year decrease in new HCV- and HBV-related HCC cases. The objective of our recommendations is not to lower expectations or diminish the hepatitis elimination standards, but to provide clearer targets that recognize the past and current elimination efforts by countries, help measure progress towards true elimination, and motivate other countries to follow suit.

Blach S, LA Kondili, A Aghemo, Z Cai, E Dugan, C Estes, I Gamkrelidze, S Ma, JM Pawlotsky, D Razavi-Shearer, H Razavi, I Waked, S Zeuzem and A Craxi (2021). "Impact of COVID-19 on global HCV elimination efforts." J Hepatol 74(1): 31-36.

BACKGROUND & AIMS: Coronavirus disease 2019 (COVID-19) has placed a significant strain on national healthcare systems at a critical moment in the context of hepatitis elimination. Mathematical models can be used to evaluate the possible impact of programmatic delays on hepatitis disease burden. The objective of this analysis was to evaluate the incremental change in HCV liver-related deaths and liver cancer, following a 3-month, 6-month, or 1-year hiatus in hepatitis elimination programs. METHODS: Previously developed models were adapted for 110 countries to include a status quo or 'no delay' scenario and a '1-year delay' scenario assuming significant disruption in interventions (screening, diagnosis, and treatment) in the year 2020. Annual country-level model outcomes were extracted, and weighted averages were used to calculate regional (WHO and World Bank Income Group) and global estimates from 2020 to 2030. The incremental annual change in outcomes was calculated by subtracting the 'no-delay' estimates from the '1-year delay' estimates. RESULTS: The '1-year delay' scenario resulted in 44,800 (95% uncertainty interval [UI]: 43,800-49,300) excess hepatocellular carcinoma cases and 72,300 (95% UI: 70,600-79,400) excess liver-related deaths, relative to the 'no-delay' scenario globally, from 2020 to 2030. Most missed treatments would be in lower-middle income countries, whereas most excess hepatocellular carcinoma and liver-related deaths would be among high-income countries. CONCLUSIONS: The impact of COVID-19 extends beyond the direct morbidity and mortality associated with exposure and infection. To mitigate the impact on viral hepatitis programming and reduce excess mortality from delayed treatment, policy makers should prioritize hepatitis programs as soon as it becomes safe to do so. LAY SUMMARY: COVID-19 has resulted in many hepatitis elimination programs slowing or stopping altogether. A 1-year delay in hepatitis diagnosis and treatment could result in an additional 44,800 liver cancers and 72,300 deaths from HCV globally by 2030. Countries have committed to hepatitis elimination by 2030, so attention should shift back to hepatitis programming as soon as it becomes appropriate to do so.

Block TM, KM Chang and JT Guo (2021). "Prospects for the Global Elimination of Hepatitis B." Annu Rev Virol **8**(1): 437-458.

Chronic hepatitis B virus (HBV) infection is the leading cause of liver cirrhosis and hepatocellular carcinoma, estimated to be globally responsible for ~800,000 deaths annually. Although effective vaccines are available to prevent new HBV infection, treatment of existing chronic hepatitis B (CHB) is limited, as the current standard-of-care antiviral drugs can only suppress viral replication without achieving cure. In 2016, the World Health Organization called for the elimination of viral hepatitis as a global public health threat by 2030. The United States and other nations are working to meet this ambitious goal by developing strategies to cure CHB, as well as prevent HBV transmission. This review considers recent research progress in understanding HBV pathobiology and development of therapeutics for the cure of CHB, which is necessary for elimination of hepatitis B by 2030.

Busschots D, R Bielen, M Koc Ö, L Heyens, R Verrando, C de Galocsy, C Van Steenkiste, F Nevens, H Midgard, O Dalgard and G Robaeys (2021). "Hepatitis C reinfection in former and active injecting drug users in Belgium." Harm Reduct J 18(1): 102.

BACKGROUND: There is currently no systematic screening for hepatitis C (HCV) reinfection in people who inject drugs (PWID) after treatment in Belgium, However, in a recent meta-analysis, the overall HCV reinfection rate was 5.9/100 person-years (PY) among PWID. Accordingly, this study was undertaken to investigate the reinfection rate in former and active PWID who achieved the end of treatment response after direct-acting antiviral (DAA) treatment in Belgium. METHODS: This observational cross-sectional study recruited individuals with a history of injecting drug use who had achieved the end of treatment response to any DAA treatment between 2015 and 2020. Participants were offered a post-treatment HCV RNA test. RESULTS: Eighty-five potential participants were eligible to participate and contacted, of whom 60 participants were enrolled in the study with a median age of 51.0 (IQR 44.3-56.0) years; it was reported that 23.3% continued to inject drugs intravenously after DAA treatment. Liver cirrhosis was present in 12.9%. The majority had genotype 1a (51.7%) or genotype 3 (15.0%) infection. We detected no reinfections in this study population. The total time patients were followed up for reinfection in the study was 78.5 PY (median 1.0 years IQR 0.4-2.0), CONCLUSION: Reinfection after successful treatment with DAA initially appears to be very low in Belgian PWID. Therefore, efforts should be made to screen individuals with persistent risk behaviors for reinfection systematically. In addition, a national HCV registry should be established to accurately define the burden of HCV infection and reinfection in Belgium and support the elimination of viral hepatitis C in Europe. Trial registration clinicaltrials.gov NCT04251572, Registered 5 Feb 2020-Retrospectively registered, https://clinicaltrials.gov/ct2/show/NCT04251572.

Busschots D, C Kremer, R Bielen, M Koc Ö, L Heyens, E Dercon, R Verrando, T Windelinckx, G Maertens, S Bourgeois, N Hens, C Matheï and G Robaeys (2021). "Identification and treatment of viral hepatitis C in persons who use drugs: a prospective, multicenter outreach study in Flanders, Belgium." Harm Reduct J 18(1): 54.

BACKGROUND: Targeted screening for hepatitis C viral (HCV) infection is not yet widely executed in Belgium. When performed in people who use drugs (PWUD), it is mainly focused on those receiving opiate agonist therapy (OAT). We wanted to reach out to a population of difficult to reach PWUD not on centralized OAT, using non-invasive screening as a bridge to re-integration in medical care supported by facilitated referral to a specialist. METHODS: This was a prospective, multicenter cohort study in PWUD not enrolled in a centralized OAT program in a community-based facility in Limburg or OAT program in a community-based facility in Antwerp, Belgium, from October 2018 until October 2019. Two study teams recruited participants using an outreach method at 18 different locations. Participants were tested for HCV antibodies (Ab) by finger prick, and risk factors were assessed through a face-to-face questionnaire. Univariate analyses were used to assess the association between HCV Ab and each risk factor separately. A generalized linear mixed model was used to investigate the association between the different risk factors and HCV. RESULTS: In total, 425 PWUD were reached with a mean age of 41.6 ± 10.8, and 78.8% (335/425) were men. HCV Ab prevalence was 14.8% (63/425). Fifty-six (88.9%) PWUD were referred, of whom 37 (66.1%) were linked to care and tested for HCV RNA. Twenty-nine (78.4%) had a chronic HCV infection. Treatment was initiated in 17 (58.6%) patients. The adjusted odds for HCV Ab were highest in those with unstable housing 6 months before inclusion (p < .001, AOR 8.2 CI 95% 3.2-23.3) and in those who had ever shared paraphernalia for intravenous drug use (p < .001, AOR 6.2 CI 95% 2.5-16.0). CONCLUSIONS: An important part tested positive for HCV. Treatment could be started in more than half

of the chronically infected referred and tested positive for HCV-RNA. Micro-elimination is necessary to achieve the World Health Organization goals by 2030. However, it remains crucial to screen and link a broader group of PWUD to care than to focus solely on those who inject drugs. TRIAL REGISTRATION: clinicaltrials.gov NCT04363411, Registered 27 April 2020-Retrospectively registered. https://clinicaltrials.gov/ct2/show/NCT04363411?term=NCT04363411&draw=2&rank=1.

Cabezas J, S Llerena and J Crespo (2021). "<u>Telemedicine, time to change the paradigm of hepatitis C management: improve access and reduce costs In reference to: Chronic viral hepatitis C micro-elimination program using telemedicine. The Mexican experience, by Pérez Hernández et al." Rev Esp Enferm Dig 113(8): 623-624.</u>

Hepatitis C (HCV) management has dramatically changed with the advent of direct-acting antivirals. Their high efficacy and safety are changing the paradigm of detection and treatment of patients with an active HCV infection. Following the latest guidelines, the path to elimination of hepatitis C will be achieved by simplifying management.

Crespo J, JV Lazarus, P Iruzubieta, F García and J García-Samaniego (2021). "Let's leverage SARS-CoV2 vaccination to screen for hepatitis C in Spain, in Europe, around the world." J Hepatol **75**(1): 224-226.

Easterbrook P, N Luhmann, M Newman, N Walsh, O Lesi and M Doherty (2021). "New WHO guidance for country validation of viral hepatitis B and C elimination." Lancet Gastroenterol Hepatol 6(10): 778-780.

Feld JJ and JW Ward (2021). "Key Elements on the Pathway to HCV Elimination: Lessons Learned From the AASLD HCV Special Interest Group 2020." Hepatol Commun 5(6): 911-922.

With a decade left to reach the ambitious goals for viral hepatitis elimination set out by the World Health Organization, many challenges remain. Despite the remarkable improvements in therapy for hepatitis C virus (HCV) infection, most people living with the infection remain undiagnosed, and only a fraction have received curative therapy. Accordingly, the 2020 HCV Special Interest Group symposium at the annual American Association for the Study of Liver Diseases Liver Meeting examined policies and strategies for the scale-up of HCV testing and expanded access to HCV care and treatment outside the specialty setting, including primary care and drug treatment and settings for care of persons who inject drugs and other marginalized populations at risk for HCV infection. The importance of these paradigms in elimination efforts, including micro-elimination strategies, was explored, and the session also included discussion of hepatitis C vaccine development and other strategies to reduce mortality through the use of organs from HCV-infected organ donors for HCV-negative recipients. In this review, the key concepts raised at this important symposium are summarized.

Fouad Y, JV Lazarus, F Negro, M Peck-Radosavljevic, SK Sarin, P Ferenci, G Esmat, H Ghazinian, A Nakajima, M Silva, S Lee and M Colombo (2021). "MAFLD considerations as a part of the global hepatitis C elimination effort: an international perspective." Aliment Pharmacol Ther 53(10): 1080-1089.

BACKGROUND: The World Health Organization (WHO) set a goal to eliminate hepatitis *C* (HCV) infection globally by 2030, with specific targets to reduce new viral hepatitis infections by 80% and reduce related deaths by 65%. However, an overlooked aspect that may hinder these efforts is the impact other liver diseases could have by continuing to drive liver disease progression and offset the beneficial impact of DAAs on end-stage liver disease and hepatocellular carcinoma (HCC). In particular, the decrease in HCV prevalence has been countered by a marked increase in the prevalence of metabolic-associated fatty liver disease (MAFLD). AIMS: To review the potential interaction of HCV and MAFLD. METHODS: We have reviewed the literature relating to an arrange of interaction of HCV, metabolic dysfunction and MAFLD. RESULTS: In this viewpoint, international experts suggest a holistic and multidisciplinary approach for the management of the growing number of treated HCV patients who achieved SVR, taking into consideration the overlooked impact of MAFLD for reducing morbidity and mortality in people who have had HCV. CONCLUSIONS: This will strengthen and improve the continuum of care cascade for patients with liver disease(s) and holds the potential to alleviate the cost burden of disease; and increase quality of life for patients following DAAs treatment.

Gamkrelidze I, JM Pawlotsky, JV Lazarus, JJ Feld, S Zeuzem, Y Bao, A Gabriela Pires Dos Santos, Y Sanchez Gonzalez and H Razavi (2021). "Progress towards hepatitis C virus elimination in high-income countries: An updated analysis." Liver Int 41(3): 456-463.

BACKGROUND & AIMS: Elimination of HCV by 2030, as defined by the World Health Organization

(WHO), is attainable with the availability of highly efficacious therapies. This study reports progress made in the timing of HCV elimination in 45 high-income countries between 2017 and 2019. METHODS: Disease progression models of HCV infection for each country were updated with latest data on chronic HCV prevalence, and annual diagnosis and treatment levels, assumed to remain constant in the future. Modelled outcomes were analysed to determine the year in which each country would meet the WHO 2030 elimination targets. RESULTS: Of the 45 countries studied, 11 (Australia, Canada, France, Germany, Iceland, Italy, Japan, Spain, Sweden, Switzerland, and United Kingdom) are on track to meet WHO's elimination targets by 2030; five (Austria, Malta, Netherlands, New Zealand, and South Korea) by 2040; and two (Saudi Arabia and Taiwan) by 2050. The remaining 27 countries are not expected to achieve elimination before 2050. Compared to progress in 2017, South Korea is no longer on track to eliminate HCV by 2030, three (Canada, Germany, and Sweden) are now on track, and most countries (30) saw no change. CONCLUSIONS: Assuming high-income countries will maintain current levels of diagnosis and treatment, only 24% are on track to eliminate HCV by 2030, and 60% are off track by at least 20 years. If current levels of diagnosis and treatment continue falling, achieving WHO's 2030 targets will be more challenging. With less than ten years remaining, screening and treatment expansion is crucial to meet WHO's HCV elimination targets.

González Grande R, I Santaella Leiva, S López Ortega and M Jiménez Pérez (2021). "Present and future management of viral hepatitis." World J Gastroenterol **27**(47): 8081-8102.

Viral hepatitis can result in important morbidity and mortality, with its impact on health conditioned by the specific type of hepatitis, the geographical region of presentation and the development and access to new drugs, among other factors. Most acute presentation forms are self-limiting and may even go unnoticed, with just a small percentage of cases leading to acute liver failure that may necessitate transplantation or even cause the death of the patient. However, when they become chronic, as in the case of hepatitis B virus and C virus, unless they are diagnosed and treated adequately they may have severe consequences, like cirrhosis or hepatocarcinoma. Understanding of the mechanisms of transmission, the pathogenesis, the presence of vaccinations and the development over recent years of new highly-efficient, potent drugs have meant that we are now faced with a new scenario in the management of viral hepatitis, particularly hepatitis B virus and hepatitis C virus. The spectacular advances in hepatitis C virus treatment have led the World Health Organization to propose the objective of its eradication by 2030. The key aspect to achieving this goal is to ensure that these treatments reach all the more vulnerable population groups, in whom the different types of viral hepatitis have a high prevalence and constitute a niche that may perpetuate infection and hinder its eradication. Accordingly, micro-elimination programs assume special relevance at the present time.

Haering C, B McMahon, A Harris, N Weis, J Lundberg Ederth, M Axelsson, S Olafsson, C Osiowy, K Tomas, S Bollerup, K Liitsola, C Archibald, H Blystad, M Bruce and L Nolen (2021). "Hepatitis B virus elimination status and strategies in circumpolar countries, 2020." Int J Circumpolar Health 80(1): 1986975.

Hepatitis B virus (HBV) infection remains a global health threat. The World Health Organization (WHO) established a goal to eliminate HBV infection as a public health threat by 2030, and defined targets for key interventions to achieve that goal. We evaluated HBV burden and relevant national recommendations for progress towards WHO targets in circumpolar countries. Viral hepatitis experts of circumpolar countries were surveyed regarding their country's burden of HBV, achievement of WHO targets and national public health authority recommendations for HBV prevention and control. Eight of nine circumpolar countries responded. All countries continue to see new HBV infections. Data about HBV prevalence and progress in reaching WHO 2030 elimination targets are lacking. No country was able to report data for all seven WHO target measures. All countries have recommendations targeting the prevention of mother-to-child transmission. Only the USA and Greenland recommend universal birth dose vaccination. Four countries have recommendations to screen persons at high risk for HBV. Existing recommendations largely address prevention; however, recommendations for universal birth dose vaccination have not been widely introduced. Opportunities remain for the development of trackable targets and national elimination planning to screen and treat for HBV to reduce incidence and mortality.

Hagymási K (2021). "The Nobel Prize in Physiology or Medicine-2020." Struct Chem 32(2): 909-913.

At the time of COVID-19 coronavirus pandemia, the Nobel Prize of Physiology or Medicine 2020 was awarded jointly to three researchers Harvey J. Alter, Charles M. Rice, and Michael Houghton for the discovery of Hepatitis C virus. Their works contributed to the isolation of the blood-borne virus, causing chronic hepatitis in 80% of infected person, resulting in cirrhosis, and in elevated risk of liver failure and

hepatocellular carcinoma formation. Their results created the basis of HCV screening of blood, and blood products, achieving more than 95% cure of infected people without nearly side effects with direct-acting antiviral agents, supporting the goal of the WHO targeting the elimination of viral hepatitis by 2030.

Howell J, A Pedrana, SE Schroeder, N Scott, L Aufegger, R Atun, R Baptista-Leite, G Hirnschall, E t Hoen, SJ Hutchinson, JV Lazarus, L Olufunmilayo, R Peck, M Sharma, AH Sohn, A Thompson, M Thursz, D Wilson and M Hellard (2021). "A global investment framework for the elimination of hepatitis Bv." J Hepatol 74(3): 535-549. BACKGROUND & AIMS: More than 292 million people are living with hepatitis B worldwide and are at risk of death from cirrhosis and liver cancer. The World Health Organization (WHO) has set global targets for the elimination of viral hepatitis as a public health threat by 2030. However, current levels of global investment in viral hepatitis elimination programmes are insufficient to achieve these goals. METHODS: To catalyse political commitment and to encourage domestic and international financing, we used published modelling data and key stakeholder interviews to develop an investment framework to demonstrate the return on investment for viral hepatitis elimination. RESULTS: The framework utilises a public health approach to identify evidence-based national activities that reduce viral hepatitis-related morbidity and mortality, as well as international activities and critical enablers that allow countries to achieve maximum impact on health outcomes from their investments - in the context of the WHO's 2030 viral elimination targets. CONCLUSION: Focusing on hepatitis B, this health policy paper employs the investment framework to estimate the substantial economic benefits of investing in the elimination of hepatitis B and demonstrates how such investments could be cost saving by 2030. LAY SUMMARY: Hepatitis B infection is a major cause of death from liver disease and liver cancer globally. To reduce deaths from hepatitis B infection, we need more people to be tested and treated for hepatitis B. In this paper, we outline a framework of activities to reduce hepatitis B-related deaths and discuss ways in which governments could pay for them.

Huiban L, C Stanciu, CM Muzica, T Cuciureanu, S Chiriac, S Zenovia, VM Burduloi, O Petrea, AM Sîngeap, I Gîrleanu, C Sfarti, C Cojocariu and A Trifan (2021). "Hepatitis C Virus Prevalence and Risk Factors in a Village in Northeastern Romania-A Population-Based Screening-The First Step to Viral Micro-Elimination." Healthcare (Basel) 9(6).

(1) Background: The World Health Organization adopted a strategy for the Global Health Sector on Viral Hepatitis in 2016, with the main objective of eliminating hepatitis C virus (HCV) by 2030. In this work, we aimed to evaluate the prevalence of HCV infection and risk factors in a Romanian village using population-based screening as part of the global C virus eradication program. (2) Methods: We conducted a prospective study from March 2019 to February 2020, based on a strategy as part of a project designed to educate, screen, treat and eliminate HCV infection in all adults in a village located in Northeastern Romania. (3) Results: In total, 3507 subjects were invited to be screened by rapid diagnostic orientation tests (RDOT). Overall, 2945 (84%) subjects were tested, out of whom 78 (2.64%) were found to have positive HCV antibodies and were scheduled for further evaluation in a tertiary center of gastroenterology/hepatology in order to be linked to care. In total, 66 (85%) subjects presented for evaluation and 55 (83%) had detectable HCV RNA. Of these, 54 (98%) completed antiviral treatment and 53 (99%) obtained a sustained virological response. (4) Conclusions: The elimination of hepatitis C worldwide has a higher chance of success if micro-elimination strategies based on mass screening are adopted.

Hüppe D, A Stoehr, P Buggisch, S Mauss, H Klinker, G Teuber, D Hidde, K Lohmann, M Bondin and H Wedemeyer (2021). "The changing characteristics of patients infected with chronic hepatitis C virus from 2014 to 2019: Real-world data from the German Hepatitis C-Registry (DHC-R)." J Viral Hepat 28(10): 1474-1483.

The number of patients diagnosed with hepatitis C virus (HCV) is markedly higher than the number initiating treatment indicating gaps in the care cascade, likely centred around reaching at-risk populations. Understanding changing characteristics of patients with HCV allows for targeted programs that increase linkage to care. We investigated changes in demographic and clinical characteristics of patients registered in the German Hepatitis C-Registry (DHC-R) from 1 January 2014 to 31 December 2019. The DHC-R is an ongoing, noninterventional, multicentre, prospective, observational cohort registry including 327 German centres. Patient characteristics were analysed over time in 7 phases for all patients completing a screening visit. Overall, 14,357 patients were enrolled. The percentage of treatment-naïve/non-cirrhotic patients increased from 34.4% in phase 1 (1 January-31 December 2014) to 68.2% in phase 7 (1 August-31 December 2019). The proportion of migrants, alcohol users, people who inject drugs, and those receiving opiate substitution therapy increased in later registry phases. Most patients

(60.1%) were receiving comedication at baseline. The most prescribed comedications were drugs used to treat opioid dependence which increased from 9.2% in phase 1 to 24.0% in phase 7. The patients' mean age decreased from 52.3 years in phase 1 to 48.7 years in phase 7. From 2014 to 2019, the proportion of at-risk patients enrolling in the registry increased. To eliminate viral hepatitis as a major public health threat, a continued commitment to engaging underserved populations into the HCV care cascade is needed.

Jachs M, T Binter, D Chromy, H Schalk, K Pichler, D Bauer, B Simbrunner, L Hartl, C Schmidbauer, F Mayer, R Strassl, M Mandorfer, M Gschwantler and T Reiberger (2021). "<u>Outcomes of an HCV elimination program targeting the Viennese MSM population</u>." <u>Wien Klin Wochenschr</u> **133**(13-14): 635-640.

BACKGROUND AND AIMS: Recent reports suggest an increasing incidence of hepatitis C virus (HCV) infections among MSM (men-who-have-sex-with-men). Early treatment with direct-acting antivirals (DAAs) achieves high cure rates and prevents further HCV transmission. We offered barrier-free HCV screening in the Viennese MSM population and immediate access to DAA treatment. METHODS: In collaboration with gay health specialists, we screened for HCV seropositivity in Viennese MSM between 2019 and 2020. Barrier-free HCV-RNA-PCR tests, transient elastography (TE) and immediate access to DAA treatment were offered. RESULTS: A total of 310 HCV-seropositive patients were identified. Of those, 145 could be contacted and 109 attended their appointment at our clinic. HIV-coinfection was highly prevalent in our cohort (n = 86/145; 78.9%), while pre-exposure prophylaxis (PrEP) was taken by 21.7% (n = 5/23) of non-HIV patients. Sexual risk behavior and (history of) intravenous drug use was reported by 32.1% and 13.8% of patients, respectively. Most MSM had already achieved sustained virological response (SVR) to previous antiviral treatment (n = 72, 66.1%) or experienced spontaneous clearance (n = 10, 9.2%). Advanced fibrosis was only detected in 3/109 (2.8%) patients. 30 MSM tested positive for HCV-RNA and DAA treatment was initiated in 29 patients - all achieved SVR. CONCLUSION: A targeted HCV test-and-treat program revealed a high prevalence of HCV seropositivity among Viennese MSM, potentially associated with high-risk sexual behavior and drug use. Early DAA treatment seems warranted in viremic HCV-MSM as SVR was 100%, which in turn prevents further HCV transmission.

Jaquet A, G Muula, DK Ekouevi and G Wandeler (2021). "Elimination of Viral Hepatitis in Low and Middle-Income Countries: Epidemiological Research Gaps." Curr Epidemiol Rep 8(3): 89-96.

PURPOSE OF REVIEW: The purpose of our review was to summarize current recommendations on testing strategies, antiviral therapy eligibility and monitoring, and prevention of mother-to-child transmission of chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, and to highlight major research gaps in low and middle-income countries (LMIC), with a particular focus on sub-Saharan Africa (SSA). RECENT FINDINGS: While data on the prevalence of HBV and HCV infections in LMIC are increasing, current knowledge on liver-related complications as well as on treatment outcomes remains limited. Furthermore, very little information is available on the feasibility and cost-effectiveness of large-scale testing and management strategies in high-prevalence settings. The availability of policy-relevant data is particularly scarce in SSA, which accounts for a significant part of the global burden of chronic viral hepatitis. SUMMARY: Current recommendations on the management and monitoring of chronic viral hepatitis rely mainly on data from high-income settings. The global elimination of viral hepatitis will only be achieved if prevention, testing, and treatment strategies tailored to specific LMIC are implemented. In order to inform scalable and cost-effective interventions, dedicated research initiatives have to be undertaken. Future studies will have to include the evaluation of innovative testing strategies, the validation of simplified methods to diagnose liver cirrhosis and hepatocellular carcinoma, and the monitoring of long-term treatment outcomes and toxicity. In addition, national plans to achieve the elimination of HBV mother-to-child transmission are urgently needed, including effective ways to test pregnant women, treat those who are eligible, and ensure birth dose vaccination is given to all newborns.

Kim JU, P Ingiliz, Y Shimakawa and M Lemoine (2021). "Improving care of migrants is key for viral hepatitis elimination in Europe." Bull World Health Organ **99**(4): 280-286.

By 2040, deaths from chronic viral hepatitis worldwide are projected to exceed those from human immunodeficiency virus infection, tuberculosis and malaria combined. The burden of this disease is predominantly carried by low-resource countries in Africa and Asia. In resource-rich countries, the epidemiological spread of viral hepatitis is partially driven by migrant movements from areas of high endemicity. In the last decade, Member States of the European Union and the European Economic Area have experienced an unprecedented influx of migrants, which has resulted in the polarization of political views about migration. In addition, the coronavirus disease 2019 pandemic has worsened the economic

and health conditions of migrants and contributed to hostility to ensuring their health rights. Moreover, the implementation of hostile laws in some host nations has increased the vulnerability of marginalized migrant subgroups, such as asylum seekers and undocumented individuals. These developments have complicated the historical challenge of identifying high-risk migrant groups for screening and treatment. However, if European countries can apply the simplified assessment tools and diagnostic tests for viral hepatitis that have been used for decentralized screening and monitoring in resource-poor countries, the uptake of care by migrants could be dramatically increased. Given the global calls for the elimination of viral hepatitis, European nations should recognize the importance of treating this vulnerable migrant population. Political and health strategies need to be adapted to meet this challenge and help eliminate viral hepatitis globally.

Krekulova L, R Honzák and LW Riley (2021). "Viral hepatitis C pandemic: Challenges and threats to its elimination." J Viral Hepat 28(5): 694-698.

Under the WHO plan, the global elimination of the HCV pandemic is scheduled for 2030. The burden of HCV infection in developed countries is largely borne by people who inject drugs (PWID): new infections and reinfections are related to their risky behaviour. Although safe and sensitive hepatitis C diagnostic tools and directly acting antiviral medication are widely used, major challenges to disease elimination still remain in developed countries, where the WHO plan is in progress. The challenge is in the involvement and engagement of infected PWID. There is a strong need to change our uptake and treatment strategies to address all patients from the risk groups, connect them with the healthcare system and cure them with the vision to eliminate this HCV pandemic.

Krekulová L and L Vavrinčíková (2021). "Experience with viral hepatitis C treatment among people who inject drugs and participate in a methadone substitution treatment program." Epidemiol Mikrobiol Imunol 70(1): 18-25.

OBJECTIVES: Long-term monitoring of the mutual effects of chronic viral hepatitis C (VHC) treatment and tailored addiction treatment. In 2016, the World Health Organization (WHO) published an action plan to eliminate viral hepatitis C globally by 2030. People who inject drugs (PWID) are a key population that needs increased attention and care. Two decades before the announcement of the WHO plan for the global elimination of HCV (hepatitis C virus), the Remedis Medical Facility, where the study was conducted, established a "Comprehensive Care Program for patients with substance use disorders and addictive behaviour". METHODS: We evaluated all patients who were in the methadone program as of 1 March 2020, regardless of OST duration, OST dosage, age or gender. Their epidemiological and demographic data obtained during a structured clinical interview and laboratory test results were analysed. RESULTS: Of 24 patients on methadone substitution therapy, 12 (50%) were anti-HCV negative before starting OST. None of them became newly infected with hepatitis C virus (HCV) during OST. The remaining 12 of the study patients were anti-HCV positive. Ten of them have already undergone successful treatment for viral hepatitis. Two patients were re-infected with HCV. CONCLUSION: The presented work confirms the high efficacy of chronic VHC treatment among PWID in inducing suitable conditions. We consider combination of HCV infection treatment and targeted tailored addiction treatment as a starting point for achieving control over the HCV epidemic in the Czech Republic, with a possible positive impact on other blood-borne infections related to risky behaviour.

Lazarus JV, CA Picchio, D Guy, S Aleman, C James, FA Nava, A Øvrehus, J Turnes, JW Ward and A Ustianowski (2021). "Hepatitis C standards of care: A review of good practices since the advent of direct-acting antiviral therapy." Clin Res Hepatol Gastroenterol 45(2): 101564.

Significant steps must be taken to reduce the global incidence and prevalence of hepatitis C virus (HCV) and mortality from HCV infection to achieve the WHO goal of eliminating viral hepatitis as a public health threat by 2030. Proper epidemiological surveillance of the full continuum of care is essential for monitoring progress and identifying gaps that need to be addressed. The tools required for elimination have largely been established, and the issue at hand is more how they should best be implemented in different settings around the world. Documenting good practices allows for knowledge exchange to prevent transmission and improve health outcomes for people with HCV. This review found 13 well documented HCV good practices that have become the standard of care or that should become the standard of care as soon as possible. In 2013, highly effective direct-acting antiviral therapy became available, which has cure rates of over 95%. Together with this new therapy, evidence-based good practices can help countries eliminate viral hepatitis C.

Lemoine M, GS Cooke, M Thursz and PC Matthews (2021). "Cuts to UK official development assistance budget jeopardise global viral hepatitis elimination goals." Lancet Gastroenterol Hepatol 6(7): 527-528.

Pérez Hernández JL, R Lehmann Mendoza, J Luna Martínez, JF Torres Roldán, PA Chaidez Rosales, HA Martinez Arredondo, V Rebollar González, L De la Cruz Silva, D Santana Vargas, MF Higuera de la Tijera and CA Arce Salinas (2021). "Chronic viral hepatitis C micro-elimination program using telemedicine. The Mexican experience."

Rev Esp Enferm Dig 113(6): 432-435.

BACKGROUND: hepatitis C virus (HCV) infection is a global health problem. Chronic infection induces the development of fibrosis and cirrhosis together with all the related complications. The use of direct-acting antiviral (DAA) drugs has proven highly effective. Telemedicine is a present-day resource that brings treatment closer to distant areas and may result in cost savings. OBJECTIVE: to implement a microelimination program for HCV using DAAs with the support of a telemedicine program to minimize expenses. PATIENTS AND METHODS: the program was developed at the Medical Services department of Petróleos Mexicanos (SMPM) with a national coverage; patients diagnosed with chronic hepatitis C were included. These were classified into locals and outsiders. Treatment for foreign patients was indicated, monitored and completed via telemedicine. Thus, avoiding their travel to the country's capital city, in order to save on transportation costs and travel allowances. RESULTS: a total of 136 patients, 74 locals and 62 outsiders, participated in the study. Transfer was avoided for 62 patients (45.5 %), which meant that telemedicine resulted in savings of 3,176.20 USD per patient, with overall savings of 196,924.40 USD from cost minimization. A total of 30 patients remained untreated due to lack of medication, hence the coverage amounted to 86 %. Sustained virological response (SVR) was achieved in 99 % of cases. Only two patients had treatment failure. Adverse events included headache and fatigue in 5 % of the cohort. CONCLUSIONS: with the aid of a telemedicine approach, significant savings were achieved by minimizing costs, since nearly half of patients were outsiders. Coverage reached 86 % and treatment with DAAs was successful for 99 % of our cases.

Pinon M, L Giugliano, E Nicastro, O Kakaa, A Coscia, C Carbonara, L D'Antiga and PL Calvo (2021). "<u>Timely Birth</u> <u>Dose Vaccine to Prevent Vertical Transmission of Hepatitis B: A Single Center Experience on the Road to the WHO Elimination Goals in Italy.</u>" <u>Vaccines (Basel)</u> **9**(7).

Italy was one of the first industrialized countries to implement a program of routine vaccination against hepatitis B virus (HBV) infection. However, currently, no HBV vaccine is administered at birth if the screened mother is HBsAq negative, whilst babies born to HBsAq positive mothers are given vaccine and hepatitis B immunoglobulin, within 12-24 post-delivery hours. A single center retrospective analysis of policies and practices to prevent mother-to-child transmission of HBV was carried out, to evaluate their adherence to HBV care guidelines. Paired maternal-infant medical records for consecutive live births, between January 2015 and December 2019, were reviewed at the AOU Città della Salute e Scienza di Torino, where a total of 235/35,506 babies (0.7%) were born to HBsAg positive mothers. Markers of active viral replication, i.e., HBV DNA level and/or HBeAg, were reported in only 66/235 (28%) of the mothers' medical records. All newborns had immunoprophylaxis at birth: 61% at <12 h, 31% between 12 and 24 h, 7% between 24 and 36 h and 1% at >36 h. In 2019, two cases of vertical HBV transmission occurred, despite timely immunoprophylaxis, as their mothers' viral load was detected too late for antiviral prophylaxis. Missed early identification of pregnant women with high viremia levels or late vaccinations may contribute to perinatal HBV infection. Immunoprophylaxis should be given to babies born to HBsAg positive mothers at the latest within 12 h. In Italy, policies aimed at achieving the WHO 2030 goal of eliminating viral hepatitis should be further implemented.

Piselli P, D Serraino, M Fusco, E Girardi, A Pirozzi, F Toffolutti, C Cimaglia and M Taborelli (2021). "Hepatitis C virus infection and risk of liver-related and non-liver-related deaths: a population-based cohort study in Naples, southern Italy." BMC Infect Dis 21(1): 667.

BACKGROUND: Hepatitis C virus (HCV) infection represents a global health issue with severe implications on morbidity and mortality. This study aimed to evaluate the impact of HCV infection on all-cause, liver-related, and non-liver-related mortality in a population living in an area with a high prevalence of HCV infection before the advent of Direct-Acting Antiviral (DAA) therapies, and to identify factors associated with cause-specific mortality among HCV-infected individuals. METHODS: We conducted a cohort study on 4492 individuals enrolled between 2003 and 2006 in a population-based seroprevalence survey on viral hepatitis infections in the province of Naples, southern Italy. Study participants provided serum for antibodies to HCV (anti-HCV) and HCV RNA testing. Information on vital status to December 2017 and cause of death were retrieved through record-linkage with the mortality database. Hazard ratios (HRs) for

cause-specific mortality and 95% confidence intervals (CIs) were estimated using Fine-Grey regression models. RESULTS: Out of 626 deceased people, 20 (3.2%) died from non-natural causes, 56 (8.9%) from liver-related conditions, 550 (87.9%) from non-liver-related causes. Anti-HCV positive people were at higher risk of death from all causes (HR = 1.38, 95% CI: 1.12-1.70) and liver-related causes (HR = 5.90, 95% CI: 3.00-11.59) than anti-HCV negative ones. Individuals with chronic HCV infection reported an elevated risk of death due to liver-related conditions (HR = 6.61, 95% CI: 3.29-13.27) and to any cause (HR = 1.51, 95% CI: 1.18-1.94). The death risk of anti-HCV seropositive people with negative HCV RNA was similar to that of anti-HCV seronegative ones. Among anti-HCV positive people, liver-related mortality was associated with a high FIB-4 index score (HR = 39.96, 95% CI: 4.73-337.54). CONCLUSIONS: These findings show the detrimental impact of HCV infection on all-cause mortality and, particularly, liver-related mortality. This effect emerged among individuals with chronic infection while those with cleared infection had the same risk of uninfected ones. These results underline the need to identify through screening all people with chronic HCV infection notably in areas with a high prevalence of HCV infection, and promptly provide them with DAAs treatment to achieve progressive HCV elimination and reduce HCV-related mortality.

Pley CM, AL McNaughton, PC Matthews and J Lourenço (2021). "The global impact of the COVID-19 pandemic on the prevention, diagnosis and treatment of hepatitis B virus (HBV) infection." BMJ Glob Health 6(1).

The COVID-19 pandemic caused by the SARS-CoV-2 virus has resulted in a myriad of interventions with the urgent aim of reducing the public health impact of this virus. However, a wealth of evidence both from high-income and low-income countries is accruing on the broader consequences of such interventions on economic and public health inequalities, as well as on pre-existing programmes targeting endemic pathogens. We provide an overview of the impact of the ongoing COVID-19 pandemic on hepatitis B virus (HBV) programmes globally, focusing on the possible consequences for prevention, diagnosis and treatment. Ongoing disruptions to infrastructure, supply chains, services and interventions for HBV are likely to contribute disproportionately to the short-term incidence of chronic hepatitis B, providing a long-term source of onward transmission to future generations that threatens progress towards the 2030 elimination goals.

Pol S, L Lair-Mehiri and A Vallet-Pichard (2021). "<u>Is elimination of HCV realistic by 2030: France.</u>" <u>Liver Int</u> **41 Suppl 1**: 45-49.

The World Health Organization (WHO) has proposed a plan for the elimination of viral hepatitis with a goal of reducing new hepatitis infections by 30% and 90% in 2020 and 2030, and associated mortality by 10% and 65% respectively. Actions and targets to reach these goals include improving hepatitis B virus (HBV) vaccination programs, the prevention of mother-to-child transmission of HBV, improving the safety of blood products and injections, risk reduction policies and optimizing the diagnosis and treatment of hepatitis. The goal of eliminating hepatitis C virus (HCV) by 2030 is based on three main actions: increased screening, strengthening access to care and the prevention of infections and reinfections. But, can this goal be reached? The answer to this question is yes in some countries, perhaps in others and no in most countries. Success will be limited by a "diagnosis burn-out" with 5 times more new viral infections than diagnoses in 2016 and a "treatment burn-out" with cure rates that are 5 times lower than the number of new infections. Nevertheless, France, like 10 other countries, is on track to achieve the WHO elimination plan by 2030. In France, the prioritization of oral antivirals in 2013-2014 which was extended to high-risk populations in 2015 (HIV-infected patients) and 2016 (men who have sex with men, dialyzed or kidney transplant recipients), then in 2017 to universal treatment with full coverage by French national healthcare (10 to 15 000 treatments per year) has resulted in half of the 120 000 patients needed to be treated by 2022 have been treated. Renewed efforts should make it possible to reach the target announced by the French Minister of Health in May 2018 by 2025.

Queiroz IT, S Couras and D Cabral (2021). "MICRO-ELIMINATION OF HEPATITIS C IN THE INCARCERATED POPULATION: IS IT REALLY POSSIBLE?" Arq Gastroenterol 58(3): 399-401.

According to the World Health Organization, 71 million people live with chronic hepatitis C. The treatment of this disease requires assistance from specialized physicians and a highly complex health care system. The prison population has been recognized as being at a high risk of acquiring confinement-related infections, including viral hepatitis. Hepatitis C virus (HCV) infection is a primary cause of death owing to liver disease among liberty-deprived individuals. Generally, prisons do not have adequate isolation wards for persons with communicable diseases, and overcrowding is a risk factor for this population. Besides prison overcrowding, violence, poor sanitary conditions, low socioeconomic

status, social isolation, and emotional instability are factors that can lead detainees to adopt unhealthy habits that make them more susceptible to infections, including HCV, and complicate effective treatment. The Criminal Execution Law 7, 210 of July 11, 1984, in Article 14, grants preventive and curative medical, dental, and pharmacological healthcare to detainees. However, adequate hepatitis C treatment is rarely provided at prisons owing to social stigma and lack of knowledge on the severity of this condition or because most detainees are unaware of their condition. Given the multiple limitations imposed by the prison system model, implementing measures to treat diseases effectively is challenging. However, it is possible to eliminate hepatitis C in prisons in the long term through the coordinated action of public health institutions and the prison system.

Rastogi A, S Chauhan, A Ramalingam, M Verma, S Babu, S Ahwal and A Bansal (2021). "Capacity building of healthcare workers: Key step towards elimination of viral hepatitis in developing countries." PLoS One 16(6): e0253539.

BACKGROUND: Lack of awareness about viral hepatitis (VH) potentially predisposes the healthcare workers (HCWs) to a higher risk of infection and may in turn increase the risk of transmission of the infection to their families and in the community. Thus, combating VH, requires adequate and updated training to the HCWs. With this objective, Project PRAKASH designed a meticulously planned training program, aimed to assess the effect of a one-day training on VH among in-service nurses. METHODS AND MATERIAL: The content and schedule of scientific sessions of the training program were decided by subject experts to improve knowledge, attitude and practice(KAP) related to VH among in-service nurses. A 54-item questionnaire divided into four domains: Transmission and Risk Factors; Prevention; Treatment; Pathophysiology and Disease Progression were used to assess the KAP related to VH. The questionnaire consisted of four sections: demographic details, knowledge(30-items), attitude(12-items) and practice(12-itmes) with a total score of 30, 60 and 24 respectively in each section. The pre-post knowledge assessment was done and impact assessment survey was undertaken among the participants who completed six months post-training period. Paired-t-test was used to assess the effect of training on knowledge using SPSSv-22. RESULTS: A total of 5253 HCWs were trained through 32 one-day trainings, however data for 4474 HCWs was included in final pre-post knowledge analysis after removing the missing/incomplete data. Mean age of participants was 33.7±8.4 with median experience of 8(IQR: 3-13). Mean improvement in knowledge score was found to be significant (p<0.001) with mean knowledge score of 19.3±4.4 in pre-test and 25.7±3.9 in the post-test out of 30. Impact assessment survey suggested change in attitude and practice of HCWs. CONCLUSION: The one-day training programs helped the in-service nurses to enhance their knowledge related to viral hepatitis. The study provided a roadmap to combating viral hepatitis through health education among HCWs about viral hepatitis.

Rehman ST, H Rehman and S Abid (2021). "Impact of coronavirus disease 2019 on prevention and elimination strategies for hepatitis B and hepatitis C." World J Hepatol 13(7): 781-789.

The coronavirus disease 2019 (COVID-19) pandemic has resulted in significant morbidity and mortality since its first case was discovered in December 2019. Since then, multiple countries have witnessed a healthcare system collapse due to the overwhelming demand for COVID-19 care. Drastic measures have been taken globally in order to curb the spread of the virus. However, those measures have led to the disruption of other aspects of healthcare, increasing the burden due to other medical conditions. We have also stepped back in achieving the ambitious goal set in place by World Health Organization to eliminate viral hepatitis as a public threat by 2030. Hepatitis B and C are chronic conditions with a significant worldwide burden, and COVID-19 has resulted in many hepatitis elimination programs slowing or stopping altogether. In this review, we elucidate the impact of the ongoing COVID-19 pandemic on the interventions targeted towards the elimination of hepatitis B virus and hepatitis C virus. Some of the salient features that we have covered in this review include hindrance to screening and diagnostic tests, neonatal vaccinations, the transmission dynamics affecting hepatitis B virus and hepatitis C virus, role of limited awareness, restrictions to treatment accessibility, and disparity in healthcare services. We have highlighted the major issues and provided recommendations in order to tackle those challenges.

Schmit N, S Nayagam, MR Thursz and TB Hallett (2021). "<u>The global burden of chronic hepatitis B virus infection: comparison of country-level prevalence estimates from four research groups.</u>" <u>Int J Epidemiol</u> **50**(2): 560-569.

BACKGROUND: Progress towards viral hepatitis elimination goals relies on accurate estimates of chronic hepatitis B virus (HBV)-infection prevalence. We compared existing sources of country-level estimates

from 2013 to 2017 to investigate the extent and underlying drivers of differences between them. METHODS: The four commonly cited sources of global-prevalence estimates, i.e. the Institute for Health Metrics and Evaluation, Schweitzer et al., the World Health Organization (WHO) and the CDA Foundation, were compared by calculating pairwise differences between sets of estimates and assessing their withincountry variation. Differences in underlying empirical data and modelling methods were investigated as contributors to differences in sub-Saharan African estimates. RESULTS: The four sets of estimates across all ages were comparable overall and agreed on the global distribution of HBV burden. The WHO and the CDA produced the most similar estimates, differing by a median of 0.8 percentage points. Larger discrepancies were seen in estimates of prevalence in children under 5 years of age and in sub-Saharan African countries, where the median pairwise differences were 2.7 percentage and 2.4 percentage points for all-age prevalence and in children, respectively. Recency and representativeness of included data, and different modelling assumptions of the age distribution of HBV burden, seemed to contribute to these differences. CONCLUSION: Current prevalence estimates, particularly those from the WHO and the CDA based on more recent empirical data, provide a useful resource to assess the population-level burden of chronic HBV-infection. However, further seroprevalence data in young children are needed particularly in sub-Saharan Africa. This is a priority, as monitoring progress towards elimination depends on improved knowledge of prevalence in this age group.

Sowah L and C Chiou (2021). "Impact of Coronavirus Disease 2019 Pandemic on Viral Hepatitis Elimination: What Is the Price?" AIDS Res Hum Retroviruses 37(8): 585-588.

In 2016, the World Health Organization developed a plan for viral hepatitis elimination by 2030. Globally, control of hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most challenging aspects of viral hepatitis elimination. In many developed countries elimination of HBV could be targeted to special populations mostly immigrants from low resource settings. Elimination of HCV, however, remains a challenge globally. Barriers to HCV elimination include high cost of medications and the ability to engage specific at-risk populations as well as individuals who are out of medical care. In the context of the coronavirus disease 2019 (COVID-19) pandemic, treatment access and screening have been further negatively impacted by social distancing rules and COVID-19-related anxieties. This threatens to throw most countries off course in their elimination efforts. Before the pandemic, some states in the United States had scaled up their elimination efforts with plans to ramp up testing and treatment using Netflixlike payment models for HCV direct acting antiviral drugs. Most of these efforts have stalled on account of the health system's focus on COVID-19 control. To prevent further delays in achieving elimination targets, programs would need to explore new models of care that address COVID-19-related access hurdles. Systems that leverage technologies such as telemedicine and self-testing could help maintain treatment levels. Mathematical models estimate that COVID-19-related delays in 2020 could lead to 44,800 hepatocellular cancers and 72,300 liver-related deaths for the next decade.

Sperle I, S Nielsen, V Bremer, M Gassowski, H Brummer-Korvenkontio, R Bruni, AR Ciccaglione, E Kaneva, K Liitsola, Z Naneva, T Perchemlieva, E Spada, SE Toikkanen, AJ Amato-Gauci, E Duffell and R Zimmermann (2021).

"Developing and Piloting a Standardized European Protocol for Hepatitis C Prevalence Surveys in the General Population (2016-2019)." Front Public Health 9: 568524.

Background: A robust estimate of the number of people with chronic hepatitis C virus (HCV) infection is essential for an appropriate public health response and for monitoring progress toward the WHO goal of eliminating viral hepatitis. Existing HCV prevalence studies in the European Union (EU)/European Economic Area (EEA) countries are heterogeneous and often of poor quality due to non-probability based sampling methods, small sample sizes and lack of standardization, leading to poor national representativeness. This project aimed to develop and pilot standardized protocols for undertaking nationally representative HCV prevalence surveys in the general adult population. Methods: From 2016 to 2019 a team from the Robert Koch-Institute contracted by the European Centre for Disease Prevention and Control synthesized evidence on existing HCV prevalence surveys and survey methodology and drafted a protocol. The methodological elements of the protocol were piloted and evaluated in Bulgaria, Finland and Italy, and lessons learnt from the pilots were integrated in the final protocol. An international multidisciplinary expert group was consulted regularly. Results: The protocol includes three alternative study approaches: a stand-alone survey; a "nested" survey within an existing health survey; and a retrospective testing survey approach. A decision algorithm advising which approach to use was developed. The protocol was piloted and finalized covering minimum and gold standards for all steps to be implemented from sampling, data protection and ethical issues, recruitment, specimen collection and laboratory testing options, staff training, data management and analysis and budget considerations.

Through piloting, the survey approaches were effectively implemented to produce HCV prevalence estimates and the pilots highlighted the strengths and limitations of each approach and key lessons learnt were used to improve the protocol. Conclusions: An evidence-based protocol for undertaking HCV prevalence serosurveys in the general population reflecting the different needs, resources and epidemiological situations has been developed, effectively implemented and refined through piloting. This technical guidance supports EU/EEA countries in their efforts to estimate their national hepatitis C burden as part of monitoring progress toward the elimination targets.

Steffen G, I Sperle, T Harder, N Sarma, S Beermann, R Thamm, V Bremer, R Zimmermann and S Dudareva (2021). "Hepatitis B vaccination coverage in Germany: systematic review." BMC Infect Dis 21(1): 817.

BACKGROUND: Despite being considered as a low prevalence country for hepatitis B (HBV), some populations in Germany are at higher risk of infection. In the context of the World Health Organization's (WHO) viral hepatitis elimination goals, a valid epidemiological data base is needed to plan and monitor the national response. Prevention strategies include general and targeted HBV vaccination programmes. OBJECTIVE: The aim of this work was to estimate the HBV vaccination coverage (VC) in the general population (GP) and different population groups in Germany from available evidence and to identify current evidence gaps for future research. METHODS: We conducted a systematic review on HBV VC in the general population and populations at high risk of HBV exposure or severe infection in Germany. We included eligible publications (01/01/2017 to 06/06/2020) from databases Embase, Pubmed and Livivo, from a previous scoping review (including data published 01/01/2005-17/03/2017), from the national surveillance system and screened the reference lists of all publications at full text level. Risk of bias was assessed using the Hoy et al. tool. RESULTS: We included 68 publications of 67 studies and assigned them to one or more suitable population groups. Twenty-one studies contained data among children/adolescents and three among adults from the GP (VC 65.8-90.5% and 22.9-52.1%, respectively), one among travelers (VC 89.0%), 13 among immunocompromised populations (VC 7.8-89.0%), 16 among populations with occupational risk and 16 with non-occupational risk of HBV exposure (VC 63.6-96.5% and 4.4-84.5%, respectively). CONCLUSION: Comprehensive evidence at low risk of bias was identified for children/adolescents. However, 25 years after including HBV in the national immunisation schedule, VC in Germany is still below the 95%-goal defined by WHO. For people at occupational risk of HBV exposure, VC was mostly reported to be over the WHO goal of 80%, but quality of evidence was heterogenous and should be improved. For people at non-occupational risk of HBV exposure, evidence was sparse and of low quality. The low VC highlights the need for future research to plan vaccination programmes targeting these populations.

van Dijk M, FM van Agt and JPH Drenth (2021). "Legal and Ethical Challenges in Developing a Dutch Nationwide Hepatitis C Retrieval Project (CELINE)." Int J Health Policy Manag 10(3): 113-117.

In 2016 the World Health Organization (WHO) called upon nations worldwide to eliminate viral hepatitis. Due to suboptimal hepatitis C virus (HCV) therapies in the past, many patients could not be treated or cured. With the current options, all patients can be treated and >90% is cured. However, these developments have not reached all patients, especially those who were lost to follow-up (LTFU) in previous years, an estimated 30% in the Netherlands. Retrieving these patients can contribute to HCV elimination. In light of this, we aimed to develop a nationwide retrieval strategy. During development we identified four major challenges. The first challenge is ethical and arises from the aim of the project: should physicians retrieve LTFU patients? We argue that the arguments in favour outweigh those against. The three other challenges are methodological and mainly legal in nature. Firstly, how far back are we allowed to trace LTFU patients? In the Netherlands, patient files should be kept for a minimum of fifteen years, but in chronic disease they may be archived longer. Secondly, which professional should identify the LTFU patients? Ideally this would be the treating physician, but we describe the circumstances that allow inclusion of assistance. Lastly, what is the proper way to invite the LTFU patients? We found that we can often request current address information from municipalities, and explain this process in detail. The offered solutions are feasible and translatable to other healthcare environments. We hope to take away any insecurities people may have about the ethical and legal nature of such a retrieval project and hope to inspire others to follow in our footsteps.

van Santen DK, RA Coutinho, A van den Hoek, G van Brussel, M Buster and M Prins (2021). "<u>Lessons learned from the Amsterdam Cohort Studies among people who use drugs: a historical perspective.</u>" <u>Harm Reduct J</u> **18**(1): 2.

The Netherlands is well known for its early adoption of harm reduction (HR) programs at the height of its

heroin crisis in the 1970s/1980s, including the implementation of the first needle and syringe program worldwide. In this manuscript, we describe how the Amsterdam Cohort Studies (ACS) among people who use drugs (PWUD) was conceived within the context of the Dutch HR approach, including the challenges scientists faced while establishing this cohort. This required striking a balance between public health and individual benefit, solving research dilemmas in the face of uncertainty, developing controversial innovative and cutting-edge interventions, which changed the prevention landscape for PWUD, and using longitudinal cohort data to provide unique insights. Studies from the ACS covering follow-up between 1985 and 2016 revealed that participation in both opioid agonist therapy and needle and syringe programs led to a major decrease in the risk of HIV and hepatitis B and C infection acquisition. ACS data have shown that the observed decrease in incidence also likely included shifts in drug markets and drug culture over time, selective mortality among those with the highest levels of risk behaviour, demographic changes of the PWUD population, and progression of the HIV and HCV epidemics. Moreover, HR programs in the Netherlands provided services beyond care for drug use, such as social support and welfare services, likely contributing to its success in curbing the HIV and viral hepatitis epidemics, increasing access and retention to HIV and HCV care and ultimately decreases in overdose mortality over time. Given the low coverage of HR programs in certain regions, it is unsurprising that continued HIV and HCV outbreaks occur and that transmission is ongoing in many countries worldwide. If we aim to reach the World Health Organization viral hepatitis and HIV elimination targets in 2030, as well as to improve the life of PWUD beyond infection risk, comprehensive HR programs need to be integrated as a part of prevention services, as in the Netherlands. We should use the evidence generated by longstanding cohorts, including the ACS, as a basis for which implementation and improved coverage of integrated HR services can be achieved for PWUD worldwide.

Waheed Y (2021). "Progress on global hepatitis elimination targets." World J Gastroenterol **27**(47): 8199-8200. In 2016, the World Health Assembly adopted a Global Health Sector Strategy on viral hepatitis, with targets set for the years 2020 and 2030 to achieve hepatitis elimination. The main target of hepatitis elimination strategy is to reduce the incidence of hepatitis B virus (HBV) and hepatitis C virus (HCV) by 90% and mortality by 65% in 2030. In last 5 years, the number of people receiving HCV treatment has increased from 1 million to 9.4 million; however, this number is far from the 2030 target of 40 million people receiving HCV treatment. HBV and HCV incidence rates are down from 1.4 million to 1.1 million annual deaths but this is far from the 2030 target of < 0.5 million deaths. The coronavirus disease 2019 pandemic has severely affected the efforts in the fight against hepatitis. No major donor has committed to investing in the fight against hepatitis. Time is running out. There is a need to speed up efforts in the fight against hepatitis to achieve hepatitis elimination by 2030.

Zimmermann R, W Külper-Schiek, G Steffen, S Gillesberg Lassen, V Bremer and S Dudareva (2021). "[How to assess the elimination of viral hepatitis B, C, and D in Germany? Outcomes of an interdisciplinary workshop]." Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 64(1): 77-90.

BACKGROUND: In 2016, the World Health Organization (WHO) released a strategy to eliminate hepatitis B, C, and D and defined indicators to monitor the progress. The Robert Koch Institute organized an interdisciplinary working meeting in 2019 to identify data sources and gaps. OBJECTIVES: The objectives were to network, to create an overview of the data sources available in Germany on hepatitis B and C, and to discuss how to construct indicators. MATERIALS AND METHODS: We extracted the WHO indicators relevant for Germany and determined how they can be constructed on the basis of available data. Stakeholders from public health services, clinics, laboratories, health insurance companies, research institutes, data holders, and registries attended a workshop and discussed methods of constructing the indicators for which data are lacking. Data sources and data were evaluated and prioritized with regard to their quality and completeness. RESULTS: Indicators on prevalence, incidence, prevention, testing and diagnosis, treatment, cure, burden of sequelae, and mortality for the general population can be constructed using secondary data such as diagnosis, health service, and registry data, data from laboratories and hospitals as well as population-based studies. Data sources for vulnerable groups are limited to studies among drug users, men who have sex with men, and about HIV coinfected patients. Data for migrants, prisoners, and sex workers are largely lacking as well as data on burden of disease from chronic viral hepatitis in the general population. CONCLUSIONS: We identified data sources, their limitations, and methods for construction for all selected indicators. The next step is to convert the ideas developed into concrete projects with individual stakeholders.

GBD 2019 Hepatitis B Collaborators (2022). "Global, regional, and national burden of hepatitis B, 1990-2019: a

systematic analysis for the Global Burden of Disease Study 2019." Lancet Gastroenterol Hepatol 7(9): 796-829.

BACKGROUND: Combating viral hepatitis is part of the UN Sustainable Development Goals (SDGs), and WHO has put forth hepatitis B elimination targets in its Global Health Sector Strategy on Viral Hepatitis (WHO-GHSS) and Interim Guidance for Country Validation of Viral Hepatitis Elimination (WHO Interim Guidance). We estimated the global, regional, and national prevalence of hepatitis B virus (HBV), as well as mortality and disability-adjusted life-years (DALYs) due to HBV, as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019. This included estimates for 194 WHO member states, for which we compared our estimates to WHO elimination targets. METHODS: The primary data sources were population-based serosurveys, claims and hospital discharges, cancer registries, vital registration systems, and published case series. We estimated chronic HBV infection and the burden of HBV-related diseases, defined as an aggregate of cirrhosis due to hepatitis B, liver cancer due to hepatitis B, and acute hepatitis B. We used DisMod-MR 2.1, a Bayesian mixed-effects meta-regression tool, to estimate the prevalence of chronic HBV infection, cirrhosis, and aetiological proportions of cirrhosis. We used mortality-to-incidence ratios modelled with spatiotemporal Gaussian process regression to estimate the incidence of liver cancer. We used the Cause of Death Ensemble modelling (CODEm) model, a tool that selects models and covariates on the basis of out-of-sample performance, to estimate mortality due to cirrhosis, liver cancer, and acute hepatitis B. FINDINGS: In 2019, the estimated global, all-age prevalence of chronic HBV infection was 4.1% (95% uncertainty interval [UII 3.7 to 4.5), corresponding to 316 million (284 to 351) infected people. There was a 31.3% (29.0 to 33.9) decline in all-age prevalence between 1990 and 2019, with a more marked decline of 76.8% (76.2 to 77.5) in prevalence in children younger than 5 years. HBV-related diseases resulted in 555 000 global deaths (487 000 to 630 000) in 2019. The number of HBV-related deaths increased between 1990 and 2019 (by 5.9% [-5.6 to 19.2]) and between 2015 and 2019 (by 2.9% [-5.9 to 11.3]). By contrast, all-age and age-standardised death rates due to HBV-related diseases decreased during these periods. We compared estimates for 2019 in 194 WHO locations to WHO-GHSS 2020 targets, and found that four countries achieved a 10% reduction in deaths, 15 countries achieved a 30% reduction in new cases, and 147 countries achieved a 1% prevalence in children younger than 5 years. As of 2019, 68 of 194 countries had already achieved the 2030 target proposed in WHO Interim Guidance of an all-age HBV-related death rate of four per 100 000. INTERPRETATION: The prevalence of chronic HBV infection declined over time, particularly in children younger than 5 years, since the introduction of hepatitis B vaccination. HBV-related death rates also decreased, but HBV-related death counts increased as a result of population growth, ageing, and cohort effects. By 2019, many countries had met the interim seroprevalence target for children younger than 5 years, but few countries had met the WHO-GHSS interim targets for deaths and new cases. Progress according to all indicators must be accelerated to meet 2030 targets, and there are marked disparities in burden and progress across the world. HBV interventions, such as vaccination, testing, and treatment, must be strategically supported and scaled up to achieve elimination. FUNDING: Bill & Melinda Gates Foundation.

Artenie A, N Luhmann, AG Lim, H Fraser, Z Ward, J Stone, L MacGregor, JG Walker, A Trickey, LK Marquez, LJ Abu-Raddad, HH Ayoub, N Walsh, M Hickman, NK Martin, P Easterbrook and P Vickerman (2022). "Methods and indicators to validate country reductions in incidence of hepatitis C virus infection to elimination levels set by WHO" 2022 Lancet Gastroenterol Hepatol 7(4): 353-366.

One of the main goals of the 2016 Global Health Sector Strategy on viral hepatitis is the elimination of hepatitis C virus (HCV) as a public health problem by 2030, defined as an 80% reduction in incidence and 65% reduction in mortality relative to 2015. Although monitoring HCV incidence is key to validating HCV elimination, use of the gold-standard method, which involves prospective HCV retesting of people at risk, can be prohibitively resource-intensive. Additionally, few countries collected quality data in 2015 to enable an 80% decrease by 2030 to be calculated. Here, we first review different methods of monitoring HCV incidence and discuss their resource implications and applicability to various populations. Second, using mathematical models developed for various global settings, we assess whether trends in HCV chronic prevalence or HCV antibody prevalence or scale-up levels for HCV testing, treatment, and preventative interventions can be used as reliable alternative indicators to validate the HCV incidence target. Third, we discuss the advantages and disadvantages of an absolute HCV incidence target and suggest a suitable threshold. Finally, we propose three options that countries can use to validate the HCV incidence target, depending on the available surveillance infrastructure.

Barreira Díaz A, A Rando, A Feliu-Prius, A Palom, F Rodríguez-Frías, E Vargas-Accarino, J Vico-Romero, N Palomo, M Riveiro-Barciela, R Esteban and M Buti (2022). "LINK-B: study protocol of a retrospective and prospective project for identification and linkage to care of people living with hepatitis B in a large health area of Barcelona" BMJ Open 12(12): e062680.

INTRODUCTION: An estimated 290 million people are living with hepatitis B virus (HBV) worldwide; in Spain, the prevalence of hepatitis B virus surface antigen (HBsAq) is 0.4%. In our setting, many HBsAqpositive individuals are not linked to care, which implies a barrier to receiving treatment and controlling the infection. The main objective of this project is to evaluate the performance of a programme designed to achieve appropriate linkage to specialist care of HBsAg-positive individuals, newly tested or previously tested and lost to follow-up. METHODS AND ANALYSIS: This is a retrospective and prospective study in which all HBsAq-positive cases recorded in the microbiology database will be identified. The retrospective phase will include cases detected between 2018 and 2020, and the prospective phase will run from January 2021 to June 2022. The project will be carried out in a tertiary university hospital covering the northern health area of Barcelona with a catchment population of 450 000 inhabitants and 16 affiliated primary care centres. The central laboratory detects approximately 1200 HBsAg-positive individuals every year; therefore, we expect to identify around 4000 patients over the duration of the project. The medical records of HBsAq-positive individuals will be consulted to identify and retrieve those who have not been appropriately linked to care. Candidates will be contacted to offer specialist disease assessment and follow-up. A website will be created to provide HBV-related information to primary care physicians, and a mobile phone application will be available to patients to improve the linkage circuits and ensure follow-up continuity. ETHICS AND DISSEMINATION: The Vall d'Hebrón Hospital Ethics Committee (PR(AG)201/2021) and the Spanish Agency of Medicines and Medical Devices approved this study. The findings will be disseminated through peer-reviewed publications and conference presentations. This programme could increase the number of HBsAq-positive individuals properly linked to care and achieve better HBV monitoring, which will have a positive impact on WHO's viral hepatitis elimination goals.

Bihl F, P Bruggmann, E Castro Batänjer, JF Dufour, D Lavanchy, B Müllhaupt, F Negro, H Razavi, C Scheidegger, D Semela, N Semmo and S Blach (2022). "HCV disease burden and population segments in Switzerland." Liver Int 42(2): 330-339.

BACKGROUND: Switzerland has made strides towards hepatitis C virus elimination, but as of 2019, elimination was not guaranteed. However, political interest in viral hepatitis has been increasing. We sought to develop a better understanding of Switzerland's progress towards HCV elimination and the profile of remaining HCV-RNA-positive patients. METHODS: A previously described Markov model was updated with recent diagnosis and treatment data and run to generate new forecasts for HCV disease burden. Two scenarios were developed to evaluate HCV morbidity and mortality under the status quo and a scenario that achieves the Swiss Hepatitis Strategy Elimination targets. Next, an analysis was conducted to identify population segments bearing a high burden of disease, where future elimination efforts could be directed. RESULTS: At the beginning of 2020, an estimated 32 100 viremic infections remained in Switzerland (0.37% viremic prevalence). Adult (≥18 years of age) permanent residents born abroad represented the largest subpopulation, accounting for 56% of HCV infections. Thirteen countries accounted for ≥60% of viremic infections amongst permanent residents born abroad, with most people currently residing in Zurich, Vaud, Geneva, Bern, Aargau and Ticino. Amongst Swiss-born HCV-RNApositive persons, two-thirds had a history of IDU, corresponding to 33% of total infections. CONCLUSIONS: In Switzerland, extra efforts for diagnosis and linkage to care are warranted in foreignborn populations and people with a history of drug use. Population-level measures (eg increasing the number of providers, increase screening) can identify patients who may have otherwise fallen through the gaps or avoided care because of stigma.

Brakenhoff SM, RA de Man, RJ de Knegt, PJE Bindels and EIT de Schepper (2022). "Epidemiology and management of hepatitis B and C in primary care in the Netherlands: data from the Rijnmond Primary Care database." Fam Pract.

BACKGROUND: The Dutch guideline for general practitioners (GPs) advises biannual surveillance of hepatitis B (HBV) patients and referral of every hepatitis C (HCV) patient. We aimed to study the prevalence, incidence, and the management of hepatitis B and C in primary care. METHODS: This is a retrospective cohort study using the Rijnmond Primary Care database (RPCD), including health care data of medical records of GPs of approximately 200,000 patients in the area of Rotterdam, the Netherlands. Patient records were selected based on laboratory results, International Classification of Primary Care

(ICPC) codes, and free-text words. RESULTS: In total, 977 patients were included: 717 HBV, 252 HCV, and 8 HBV/HCV coinfected patients. Between 2013 and 2019, the prevalence of HBV and HCV declined from 5.21 to 2.99/1,000 person-years (PYs) and 1.50 to 0.70/1,000 PYs, respectively. We observed that the majority of the patients had been referred to a medical specialist at least once (71% HBV and 89% HCV patients). However, among chronic patients, we observed that 36.2% of the HBV patients did not receive adequate surveillance by their GP (≥2 alanine aminotransferase checks within 3 years) or a medical specialist. In addition, 44.4% of the HCV patients had no record about successful antiviral treatment. CONCLUSIONS: This study demonstrated a declining prevalence in viral hepatitis B and C in primary care in the Netherlands. However, a substantial part of the patients did not receive adequate surveillance or antiviral therapy. It is therefore crucial to involve GPs in case finding and in follow-up after treatment.

Buti M, A Craxi, GR Foster, M Maticic, F Negro, S Zeuzem and F Zoulim (2022). "Viral hepatitis elimination: Towards a hepatitis-free world." J Hepatol 77(5): 1444-1447.

Advances in diagnostics and therapeutics have brought the elimination of chronic viral hepatitis into focus. The World Health Organization has defined the targets for elimination, but it is unclear how these can be achieved and how they should be measured. The goal of this special conference was to examine current efforts and metrics to assess progress towards elimination.

Cao G, W Jing, J Liu and M Liu (2022). "Countdown on hepatitis B elimination by 2030: the global burden of liver disease related to hepatitis B and association with socioeconomic status." Hepatol Int 16(6): 1282-1296. BACKGROUND AND PURPOSE: Hepatitis B virus (HBV) infection causes both acute and chronic liver disease, performing the key driver toward the global elimination of viral hepatitis by 2030. We used data from Global Burden of Disease (GBD) study to quantify the burden of liver disease due to hepatitis B at the global, regional and national levels. METHODS: Annual incident cases and age-standardized incidence rates (ASIRs) of liver disease due to hepatitis B between 1990 and 2019 were collected from GBD study 2019. Percentage changes of incident cases and estimated annual percentage changes (EAPCs) of ASIRs were calculated to quantify their temporal trends. Correlations between EAPC and socio-demographic index (SDI) and universal health coverage index (UHCI) were evaluated by Pearson correlation analyses. RESULTS: Globally, the incident cases of liver disease due to hepatitis B decreased by 4.51% from 84.45 million in 1990 to 80.65 million in 2019 and ASIR decreased by an average of 1.52% (95%CI - 1.66%, - 1.37%) per year in this period. For the spectrum of liver disease due to hepatitis B, ASIR of cirrhosis and other chronic liver diseases increased by an average of 0.13% (95%CI 0.04%, 0.22%) per year in low SDI region and 0.24% (95%CI 0.04%, 0.34%) per year in low-middle SDI region, and ASIR of liver cancer increased by an average of 0.91% (95%CI 0.37%, 1.46%) per year in high SDI region in 1990-2019. Positive correlations of EAPC in ASIR of liver cancer with SDI and UHCI were observed in nations with SDI ≥ 0.7 or UHCI ≥ 70. CONCLUSION: HBV infection remains a global health problem, causing low and low-middle SDI regions with an increasing trend of cirrhosis and other chronic liver diseases, and high SDI region with an increasing trend of liver cancer. Efforts to eliminate hepatitis B by 2030 needs to focus on not only developing regions but also developed regions.

Colombe S, M Axelsson, S Aleman, AS Duberg, J Lundberg Ederth and V Dahl (2022). "Monitoring the progress towards the elimination of hepatitis B and C in Sweden: estimation of core indicators for 2015 and 2018." BMC Infect Dis 22(1): 885.

INTRODUCTION: To monitor Sweden's progress towards the WHO goal of eliminating viral hepatitis, we estimated the prevalence, notification rate, and liver-related morbidity and mortality for diagnosed hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in 2015 and 2018. METHODS: We identified cases of hepatitis B and C within the National System for Notifiable Diseases and obtained data on treatment and whether the case was deceased or not. We calculated prevalence, notification rates per 100,000, and proportion of newly diagnosed cases of hepatitis with liver disease at the time of diagnosis, and proportion of all deceased cases who died from liver disease. We calculated Poisson 95% confidence intervals (Cls) around the notification rates and Wilson 95% Cls around prevalence and mortality estimates. RESULTS: In 2015 and 2018, the prevalence of diagnosed HBV infections was 0.20% [95% Cl: 0.19-0.20] and 0.21% [0.20-0.21]. Notification rates per 100,000 for HBV infections were 13.02 [12.32-13.76] and 7.71 [7.18-8.27]. HBV liver-related morbidity was 2.65% [1.90-3.68] and 2.16% [1.35-3.43]. HBV liver-related mortality was 20.00% [14.81-26.44] and 17.95% [13.20-23.94]. In 2015 and 2018, the prevalence of diagnosed HCV-infections was 0.24% [0.24-0.25] and 0.18% [0.18-0.19]. Notification rates per 100,000 for HCV infections were 15.92 [15.14-16.73] and 13.05 [12.36-13.77]. HCV liver-related morbidity was 8.14% [6.89-9.60] and 3.90% [2.99-5.08]. HCV liver-related mortality was 27.08% [24.54-

29.77] and 26.90% [24.12-29.88]. CONCLUSIONS: All indicators decreased or remained stable between 2015 and 2018, indicating progress in the elimination of viral hepatitis, especially for HCV infection.

Colucci G, S Uceda Renteria, G Lunghi, F Ceriotti, E Sguazzini, S Spalenza, C Regazzo, P Lampertico and M Colombo (2022). "<u>Italian migrants study: An HCV and HBV micro-elimination pilot project</u>." <u>Clin Res Hepatol Gastroenterol</u> **46**(3): 101852.

BACKGROUND: Migrants represent a key target population for viral hepatitis micro-elimination programs and are important targets for specific prevention, screening and treatment programs. AIMS: To raise awareness on viral hepatitis among migrants and key stakeholders, assess the prevalence of HBV and HCV among migrants, and determine an optimal and scalable viral hepatitis screening and treatment protocol. MATERIAL AND METHODS: Unselected, consecutive migrants reaching the costs of Italy were screened for HBV, HCV, HDV and HIV markers. Anagraphic and anamnestic information were used to identify viral hepatitis endemic hotspots in the countries of birth or transit. Personal data, including migration route, test results and treatment, were collected and stored in a dedicated database RESULTS: 362 patients were recruited in 2019; median age was 28 years, 71% were male. Most of the patients were African (54%) or Asian (40%). 49% positive for at least one HBV marker: 2.2% HBsAg (asymptomatic carriers with low viremia); 10.6% anti-HBs; 28.5% anti-HBs and anti-HBc, 1.7% anti-HCV, 0.6% anti-HIV, with low or undetectable viral load. Libya was the nexus shared by most of the positive, reactive cases. HCV and HIV markers were only found in migrants already resident in Italy for more than 6-12 months. CONCLUSION: Low to moderate prevalence of hepatitis B markers were observed in African and Asian first arrival migrants. Migrants positive for HCV and HIV likely acquired the infection after arrival in Italy, suggesting migrants are at risk of contracting viral infections once in Italy, highlighting the importance of ensuring access to prevention for migrant communities.

Crespo J, J Cabezas, A Aguilera, M Berenguer, M Buti, X Forns, F García, J García-Samaniego, M Hernández-Guerra, F Jorquera, JV Lazarus, S Lens, E Martró, JA Pineda, M Prieto, F Rodríguez-Frías, M Rodríguez, M Serra, J Turnes, R Domínguez-Hernández, M Casado and JL Calleja (2022). "Recommendations for the integral diagnosis of chronic viral hepatitis in a single analytical extraction." Gastroenterol Hepatol.

The Spanish Society of Digestive Pathology (SEPD), the Spanish Association for the Study of the Liver (AEEH), the Spanish Society of Infections and Clinical Microbiology (SEIMC) and its Viral Hepatitis Study Group (GEHEP), and with the endorsement of the Alliance for the Elimination of Viral Hepatitis in Spain (AEHVE), have agreed on a document to carry out a comprehensive diagnosis of viral hepatitis (B, C and D), from a single blood sample; that is, a comprehensive diagnosis, in the hospital and/or at the point of care of the patient. We propose an algorithm, so that the positive result in a viral hepatitis serology (B, C and D), as well as human immunodeficiency virus (HIV), would trigger the analysis of the rest of the virus, including the viral load when necessary, in the same blood draw. In addition, we make two additional recommendations. First, the need to rule out a previous hepatitis A virus (VHA) infection, to proceed with its vaccination in cases where IgG-type studies against this virus are negative and the vaccine is indicated. Second, the determination of the HIV serology. Finally, in case of a positive result for any of the viruses analyzed, there must be an automated alerts and initiate epidemiological monitoring.

de Almeida NAA and VS de Paula (2022). "Occult Hepatitis B virus (HBV) infection and challenges for hepatitis elimination: A literature review." J Appl Microbiol 132(3): 1616-1635.

Occult hepatitis B infection (OBI) is characterized by the detection of hepatitis B virus (HBV) DNA in serum or liver but negativity for hepatitis B surface antigen. OBI, which is thought to be maintained by host, immunological, viral and/or epigenetic factors, is one of the most challenging clinical features in the study of viral hepatitis. Currently, there is no validated detection test for OBI. It is believed that OBI is widely distributed throughout the world, with a higher prevalence in populations at high-risk HBV, but the detailed worldwide prevalence patterns are unknown. We conducted a survey of recently published studies on OBI rates across all continents. High prevalence rates of OBI are observed in some specific groups, including patients with hepatitis C virus, human immunodeficiency virus co-infection or hepatocellular carcinoma. In 2016, the World Health Organization adopted strategies to eliminate viral hepatitis by 2030, but the difficulties in detecting and treating OBI currently challenge this goal. Subjects with OBI can transmit HBV, and episodes of reactivation can occur. Further studies to understanding the mechanisms that drive the development of OBI are needed and can contribute to efforts at eliminating viral hepatitis.

Dichtl A, H Stöver and D Schäffer (2022). "[HIV/HCV Among Drug Users in Germany: Elimination Targets in the Mirror of Practice]." Gesundheitswesen.

BACKGROUND: In 2016, the World Health Organization presented the first strategy for the elimination of viral hepatitis by 2030, following the goals of the Agenda 2030. Ending Acquired Immune Deficiency Syndrome (AIDS) by 2030 was also formulated as one of the Sustainable Development Goals and subsequently included and elaborated in the Joint United Nations Programme on HIV/AIDS (UNAIDS) strategy. People who inject drugs (PWID) are among the most vulnerable groups in terms of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection. Following the objectives of the WHO and the UN, the German Federal Ministry of Health (BMG) has presented the first integrated overall strategy for HIV and Hepatitis C (as well as Hepatitis B and other sexually transmitted infections).

OBJECTIVES AND METHODS: Six years after the adoption of the German government's BIS 2030 strategy this article discusses the role of PWID in Germany in relation to the elimination targets on HIV and HCV based on currently available data and in light of recent responses and efforts from the field. RESULTS: Although there are multiple positive practice approaches, the WHO elimination targets have not yet been achieved with regard to HCV and HIV in PWID. CONCLUSION: In order not to fail the elimination targets 2030, Germany will have to substantially improve the situation of PWID as a key group and in particular advance the implementation of diagnostics and treatment as well as evidence-based harm reduction measures

Dunn R, A Wetten, S McPherson and MC Donnelly (2022). "Viral hepatitis in 2021: The challenges remaining and how we should tackle them." World J Gastroenterol 28(1): 76-95.

Viral hepatitis results in 1.4 million deaths annually. The World Health Organization (WHO) set an ambitious target to eliminate viral hepatitis by 2030, but significant challenges remain. These include inequalities in access to healthcare, reaching at risk populations and providing access to screening and effective treatment. Stigma around viral hepatitis persists and must be addressed. The WHO goal of global elimination by 2030 is a worthy aim, but remains ambitious and the coronavirus 2019 pandemic undoubtedly has set back progress. This review article will focus on hepatitis A to E, highlighting problems that have been resolved in the field over the past decade, those that remain to be resolved and suggest directions for future problem solving and research.

Fiore V, A De Vito, A Colpani, V Manca, I Maida, G Madeddu and S Babudieri (2022). "Viral Hepatitis C New Microelimination Pathways Objective: Psychiatric Communities HCV Free." Life (Basel) 12(11).

BACKGROUND: People with psychiatric disorders have a high prevalence of HCV. For this reason, tailored interventions should be developed to reach this population. METHODS: We performed a retrospective study on patients treated for HCV infection in psychiatric nursing homes, approached with a quick diagnosis, staging and treatment. RESULTS: We included data on 586 people screened for HCV with quick tests. High HCV seroprevalence was found in this population (231; 39.4%). Among people who tested positive, there were high rates of active infection (220; 95.2%). Out of the 220 patients with active infection, 95.9% were male, 85.5% were Italian, median age was 43 (IQR = 35-52) years old. In the majority of cases (162; 73.6%), the risk factor was unknown. The most common genotype was 3a (98; 44.5%), and patients mostly had a low fibrosis, according with FIB-4 value (142; 64.5%). Of them, one (0.45%) categorically refused the treatment, and one (0.45%) had liver cirrhosis and advanced hepatocellular carcinoma. Overall, 218 patients underwent eligibility for DAAs. The most prescribed treatment was glecaprevir/pibrentasvir (GLE/PIB (172; 78.2%)). The others practiced sofosbuvir/velpatasvir (SOF/VEL). All patients reached the end of treatment. One (0.45%) was lost to follow up, and all the others reached the SVR12. CONCLUSIONS: The point-of-care testing and pangenotypic DAAs' availability represent one of the most important steps for a fast diagnostic and therapeutical option. Tailored microelimination pathways for every difficult-to-reach/to-treat populations are needed. This would allow us to move more easily towards HCV elimination.

Fiore V, E Rastrelli, G Madeddu, R Ranieri, A De Vito, R Giuliani, G Di Mizio, M Bolcato, G De Matteis, AM Ialungo, S Dell'Isola, G Starnini and S Babudieri (2022). "HCV spread among female incarcerated population and treatment pathways to viral elimination in Italian prison settings: clinical perspectives and medico legal aspects." BMC Infect Dis 22(1): 601.

BACKGROUND: Hepatitis C virus (HCV) infection is more frequent among incarcerated people than in general population. In the DAAs era, the short schedules and the low risk of adverse reactions, increased the number of HCV treatments. However, the most part of literature reports lack of incarcerated women inclusion in studies on field. Our aim is to assess the screening execution, HCV prevalence, and DAAs

treatment among incarcerated women. A focused insight on guick vs standard diagnosis and staging approach will be also provided. METHODS: Incarcerated women from 4 Italian regions' penitentiary institutes were included. HCV screening was executed with HCV saliva test (QuickOral Test(®)) or phlebotomy. Stage of liver fibrosis was evaluated with FIB-4 value or fibroscan(®), based on physicians' decision. Treatment prescription followed national protocols. RESULTS: We included 156 women, 89 (57%) were Italian, mean age was 41 ± 10 years, and 28 (17.9%) were people who inject drugs (PWIDs). Overall, the HCV seroprevalence was 20.5%. Being PWID and on opioid substitution therapy (OST) were significantly associated with serological status (p-value < 0.001). Of them, the 75.5% of patients had active infection, the most frequent genotype was 3a (50%). Among them, 4 (16.6%) and 6 (25%) had psychosis or alcohol abuse history. The 62.5%, 25% and 12.5% had low, intermediate, and advanced fibrosis, respectively. Out of the 24 HCV-RNA positive patients, the 75% underwent to DAAs treatment. The sustained virological response (SVR12) was achieved in 88.8% of cases. When evaluating the influence of quick diagnosis and staging methods vs standard phlebotomy and fibroscan(®) on SVR12, FIB-4 use showed higher performance for retainment in treatment during prison staying (p = 0.015), while the use of quick saliva test had no influence on the outcome (p = 0.22). CONCLUSION: HCV seroprevalence and active infections are very high among incarcerated women. More tailored interventions should be focused on HCV diagnosis and treatment in female prison population. The use of quick staging methods (FIB-4) is useful to increase SVR12 achievement without delays caused by the fibroscan(®) awaiting.

Flisiak R, D Zarębska-Michaluk, E Ciupkeviciene, S Drazilova, S Frankova, I Grgurevic, B Hunyady, P Jarcuska, L Kupčinskas, M Makara, G Saulite-Vanaga, M Simonova, J Sperl, I Tolmane and A Vince (2022). "HCV Elimination in Central Europe with Particular Emphasis on Microelimination in Prisons." Viruses 14(3).

In 2016, the WHO announced a plan to eliminate viral hepatitis as a public health threat by 2030. In this narrative review, experts from Bulgaria, Croatia, the Czech Republic, Hungary, Latvia, Lithuania, Poland and Slovakia assessed the feasibility of achieving the WHO 2030 target for HCV infections in Central Europe. They focused mainly on HCV micro-elimination in prisons, where the highest incidence of HCV infections is usually observed, and the impact of the COVID-19 pandemic on the detection and treatment of HCV infections. According to the presented estimates, almost 400,000 people remain infected with HCV in the analyzed countries. Interferon-free therapies are available ad libitum, but the number of patients treated annually in the last two years has halved compared to 2017-2019, mainly due to the COVID-19 pandemic. None of the countries analyzed had implemented a national HCV screening program or a prison screening program. The main reason is a lack of will at governmental and prison levels. None of the countries analyzed see any chance of meeting the WHO targets for removing viral hepatitis from the public threat list by 2030, unless barriers such as a lack of political will and a lack of screening programs are removed quickly.

Fursa O, A Mocroft, JV Lazarus, S Amele, J Lundgren, R Matulionyte, LD Rasmussen, JK Rockstroh, M Parczewski, D Jilich, S Moreno, A Vassilenko, K Lacombe, G Wandeler, E Borodulina, J Brännström, L Wiese, C Orkin, GMN Behrens, K Mansinho, JJ Portu and L Peters (2022). "The hepatitis C cascade of care in HIV/hepatitis C virus coinfected individuals in Europe: regional and intra-regional differences." Aids 36(3): 423-435.

BACKGROUND: Following the introduction of direct-acting antiviral therapy in 2013, WHO launched the first Global Health Sector Strategy on Viral Hepatitis. We describe a hepatitis C virus (HCV) cascade of care in people with HIV (PWH) across Europe in terms of reaching the WHO elimination targets of diagnosing 90% and treating 80% of HCV-infected individuals. METHODS: HIV/HCV-coinfected participants in the EuroSIDA cohort under prospective follow-up at October 1, 2019, were described using a nine-stage cascade of care. Care cascades were constructed across Europe, on a regional (n = 5) and country (n = 21) level. RESULTS: Of 4773 anti-HCV positive PWH, 4446 [93.1%, 95% confidence interval (CI) 92.4-93.9)] were ever tested for HCV RNA, and 19.0% (95% CI 16.4-21.6) were currently HCV RNA positive, with the highest prevalence in Eastern and Central-Eastern Europe (33.7 and 29.6%, respectively). In Eastern Europe, 78.1% of the estimated number of chronic infections have been diagnosed, whereas this proportion was above 95% in the other four regions. Overall, 3116 persons have ever started treatment (72.5% of the ever chronically infected, 95% CI 70.9-74.0) and 2404 individuals (55.9% of the ever chronically infected, 95% CI 53.9-57.9) were cured. Cure proportion ranged from 11.2% in Belarus to 87.2% in Austria. CONCLUSION: In all regions except Eastern Europe, more than 90% of the study participants have been tested for HCV-RNA. In Southern and Central-Western regions, more than 80% ever chronically HCV-infected PWH received treatment. The proportion with cured HCV infection did not exceed 80% in any region, with significant heterogeneity between countries. SUMMARY: In a pan-European cohort of PWH, all regions except Eastern Europe achieved the WHO target of diagnosing 90% of chronic HCV infections, while the target of treating 80% of eligible persons was achieved in none of the five regions.

Isfordink CJ, M van Dijk, SM Brakenhoff, PAM Kracht, JE Arends, RJ de Knegt, M van der Valk and JPH Drenth (2022). "Hepatitis C Elimination in the Netherlands (CELINE): How nationwide retrieval of lost to follow-up hepatitis C patients contributes to micro-elimination." Eur J Intern Med **101**: 93-97.

BACKGROUND & AIMS: The number of chronic hepatitis C virus (HCV)-infected patients who have been lost to follow-up (LTFU) is high and threatens HCV elimination. Micro-elimination focusing on the LTFU population is a promising strategy for low-endemic countries like the Netherlands (HCV prevalence 0.16%). We therefore initiated a nationwide retrieval project in the Netherlands targeting LTFU HCV patients. METHODS: LTFU HCV-infected patients were identified using laboratory and patient records. Subsequently, the Municipal Personal Records database was queried to identify individuals eligible for retrieval, defined as being alive and with a known address in the Netherlands. These individuals were invited for re-evaluation. The primary endpoint was the number of patients successfully re-linked to care. RESULTS: Retrieval was implemented in 45 sites in the Netherlands. Of 20,183 ever-diagnosed patients, 13,198 (65%) were known to be cured or still in care and 1,537 (8%) were LTFU and eligible for retrieval. Contact was established with 888/1,537 (58%) invited individuals: 369 (24%) had received prior successful treatment elsewhere, 131 (9%) refused re-evaluation and 251 (16%) were referred for re-evaluation. Finally, 219 (14%) were re-evaluated, of whom 172 (79%) approved additional data collection. HCV-RNA was positive in 143/172 (83%), of whom 38/143 (27%) had advanced fibrosis or cirrhosis and 123/143 (86%) commenced antiviral treatment, CONCLUSION: Our nationwide micro-elimination strategy accurately mapped the ever-diagnosed HCV population in the Netherlands and indicates that 27% of LTFU HCV-infected patients re-linked to care have advanced fibrosis or cirrhosis. This emphasizes the potential value of systematic retrieval for HCV elimination.

Khetsuriani N, O Lesi, S Desai, PA Armstrong and RA Tohme (2022). "Progress Toward the Elimination of Mother-to-Child Transmission of Hepatitis B Virus - Worldwide, 2016-2021." MMWR Morb Mortal Wkly Rep 71(30): 958-963.

Mother-to-child transmission (MTCT) of hepatitis B virus (HBV) often results in chronic HBV infection, the leading cause of cirrhosis and liver cancer (1). If not vaccinated, nine in 10 children infected at birth will become chronically infected. Globally, an estimated 6.4 million (range = 4.4-10.8 million) children aged ≤5 years are living with chronic HBV infection (2). In 2016, the World Health Assembly endorsed the goal to eliminate viral hepatitis as a public health threat by 2030, including the elimination of MTCT of HBV (3). Elimination of MTCT of HBV can be validated by demonstrating ≤0.1% prevalence of HBV surface antigen (HBsAg) among children aged ≤5 years, as well as ≥90% coverage with hepatitis B birth dose (HepB-BD) and 3 doses of hepatitis B vaccine (HepB3) (4,5). This report describes global progress toward elimination of MTCT of HBV during 2016-2021. By December 2020, 190 (98%) of 194 World Health Organization (WHO) member states* had introduced universal infant vaccination with hepatitis B vaccine (HepB), and 110 (57%) countries provided HepB-BD to all newborns. During 2016-2020, global HepB3 coverage remained between 82% and 85%, whereas HepB-BD coverage increased from 37% to 43%. In 2020, among the 99 countries reporting both HepB3 and HepB-BD coverage, 41 (41%) achieved ≥90% coverage with both. By December 2021, serosurveys documented ≤0.1% HBsAg prevalence among children in 11 countries. Accelerating HepB-BD introduction, increasing HepB3 coverage, and monitoring programmatic and impact indicators are essential for elimination of MTCT of HBV.

Kmet NG, M Poljak, B Zakotnik and M Matičič (2022). "<u>Hepatitis B Elimination in Children of Slovenian Origin</u>

<u>Born in Slovenia After the Introduction of Preventive Strategies: the Results of a National Study</u>." <u>Zdr Varst</u>

61(2): 109-114.

INTRODUCTION: In Slovenia national strategies to prevent hepatitis B virus (HBV) infection in children were introduced in the mid-nineties. The aim of the present study was to analyze the epidemiological characteristics of chronic hepatitis B infection in children in Slovenia after the introduction of mandatory HBV vaccination of children and mandatory screening of pregnant women for HBV surface antigen (HBsAg) with consecutive active and passive immunization of newborns of HBsAg-positive mothers. METHODS: Children from all regions of Slovenia whose blood samples tested positive for HBsAg at the national reference laboratory for viral hepatitis between January 1997 and December 2010 were included. Demographic, epidemiological and virological data were reviewed retrospectively. Statistical evaluation of the patients' characteristics was performed and possible trends during the observation period

determined. RESULTS: Among 52 HBsAg-positive children, there were 22 (42.3%) girls and 30 (57.7%) boys. Among 40 children tested for HBeAg, 17 were positive (42.5%). The most frequent risk factor for acquiring HBV infection was "presence of HBV infection within the family" (24/35; 68.8%). A significant association between the presence of HBeAg and a viral load of >20,000 IU/ml was found (p=0.001). The difference in the proportion of children of Slovenian origin born before 1994 and after was statistically significant (p=0.039). A statistically significant negative linear trend of the number of diagnosed children in the observed period was found (p=0.006). CONCLUSIONS: Prevention strategies adopted in the midnineties have resulted in the elimination of chronic hepatitis B in children of Slovenian origin born in Slovenia.

Kondili LA, M Buti, M Riveiro-Barciela, M Maticic, F Negro, T Berg and A Craxì (2022). "Impact of the COVID-19 pandemic on hepatitis B and C elimination: An EASL survey." JHEP Rep 4(9): 100531.

BACKGROUND & AIMS: The World Health Organization (WHO) HBV and HCV elimination targets, set in 2016 and based on projections to 2030, were unable to consider the impact of intervening factors. To evaluate the impact of the COVID-19 pandemic on viral hepatitis elimination programs, the European Association for the Study of the Liver (EASL) conducted a survey in liver centers worldwide in 2021. METHODS: A web-based questionnaire was distributed (May-July 2021) to all EASL members representing clinical units providing HBV and HCV hepatitis care. Results are expressed as absolute numbers and reduction rates for each care activity. RESULTS: Data were collected from 32 European and 12 non-European clinical centers. Between January 2019 (pre-pandemic) and December 2020 (during the pandemic), chronic HBV consultations decreased by 32% and 26%, new referrals by 38% and 39%, HBV testing rates by 39% and 21% (for HBsAg detection) and 30% and 22% (for HBV DNA detection), and new HBV treatments by 20% and 44% (p = 0.328) in European and non-European centers, respectively. With regard to HCV during the same time frame, the overall reductions were 39% and 50% for consultations, 49% and 49% for new referrals, 11% and 38% for HCV RNA detection, and 51% and 54% for new HCV antiviral treatments for European and non-European Centers, respectively (p = 0.071). CONCLUSIONS: All steps in the viral hepatitis care cascade have been hampered by the COVID-19 pandemic, with a comparable impact across different centers. These data reaffirm the pandemic's major effect on global viral hepatitis elimination programs and suggest that actions to achieve the WHO 2030 targets should be reconsidered and revised to account for each country's progress relative to prepandemic values. LAY SUMMARY: The EASL multinational survey conclusively shows that viral hepatitis elimination programs, expected to provide control of hepatitis B and hepatitis C worldwide by 2030, have been held back by the COVID-19 pandemic in clinical centers from several European and non-European countries, with a comparable impact across centers. Limitations in the cascade of care for both HBV and HCV were linked to limited access to screening, consultations, specific testing, and actual treatment. As restrictions for COVID-19 begin to lift, efforts to diagnose and provide treatment for viral hepatitis should remain high on the list of priorities for public health officials to maintain the WHO elimination efforts. Measures that have been put in place to control the COVID-19 pandemic could be transferred to increasing the diagnosis and linkage to care of people with hepatitis.

Kraef C, A Bentzon, A Skrahina, A Mocroft, L Peters, JD Lundgren, N Chkhartishvili, D Podlekareva and O Kirk (2022). "Improving healthcare for patients with HIV, tuberculosis and hepatitis C in eastern Europe: a review of current challenges and important next steps." HIV Med 23(1): 48-59.

OBJECTIVES: In some eastern European countries, serious challenges exist to meet the HIV-, tuberculosis (TB)- and hepatitis-related target of the United Nations Sustainable Development Goals. Some of the highest incidence rates for HIV and the highest proportion of multi-drug-resistant (MDR) tuberculosis worldwide are found in the region. The purpose of this article is to review the challenges and important next steps to improve healthcare for people living with TB, HIV and hepatitis C (HCV) in eastern Europe. METHODS: References for this narrative review were identified through systematic searches of PubMed using pre-idientified key word for articles published in English from January 2000 to August 2020. After screening of titles and abstracts 37 articles were identified as relevant for this review. Thirty-eight further articles and sources were identified through searches in the authors' personal files and in Google Scholar. RESULTS: Up to 50% of HIV/MDR-TB-coinfected individuals in the region die within 2 years of treatment initiation. Antiretroviral therapy (ART) coverage for people living with HIV (PLHIV) and the proportion virological suppressed are far below the UNAIDS 90% targets. In theory, access to various diagnostic tests and treatment of drug-resistant TB exists, but real-life data point towards inadequate testing and treatment. New treatments could provide elimination of viral HCV in high-risk populations but few countries have national programmes. CONCLUSION: Some eastern European countries face serious

challenges to achieve the sustainable development goal-related target of 3.3 by 2030, among others, to end the epidemics of AIDS and tuberculosis. Better integration of healthcare systems, standardization of health care, unrestricted substitution therapy for all people who inject drugs, widespread access to drug susceptibility testing, affordable medicines and a sufficiently sized, well-trained health workforce could address some of those challenges.

Krekulová L, T Damajka, Z Krumphanslová and V Řehák (2022). "Pilot Outreach Program in Remedis-The Promising Step toward HCV Elimination among People Who Inject Drugs." Int J Environ Res Public Health **20**(1).

The global effort to eliminate HCV infection requires new approaches to accessing and testing the affected population in a setting with as low of a threshold as possible. The focus should be on socially marginalized people who inject drugs (PWIDs) and who are not willing or able to visit standard medical services. With this vision, we established an outreach service-a testing point in an ambulance in the park in front of the Main Railway Station of the capital city of Prague-to provide bloodborne disease testing and treatment. The service was available every week on Wednesday afternoon. Over the initial two years of our experience, 168 unique people were tested. Of them, 82 (49%) were diagnosed with chronic HCV infection and were eligible for treatment with antivirals. Of these, 24 (29%) initiated antiviral treatment over the study period, and 17 (71%) of these individuals achieved a documented sustained virological response. Offering medical services in PWIDs' neighborhoods helps overcome barriers and increase the chances that they will become patients and begin HCV treatment. The described outcomes appear promising for reaching the vision of linkage to the care of such a hard-to-reach population and can serve as a feasible model of care for further expansion.

Krekulova L, Z Oktabec and LW Riley (2022). "Key Role of Multidisciplinary Collaboration towards Global Elimination of HCV Infection." Int J Environ Res Public Health 19(7).

The elimination of HCV (hepatitis C virus) infection is, according to WHO (World Health Organization), of international interest. With new diagnostic tools and treatment possibilities, one major challenge for the elimination is to involve infected patients, especially those from socially excluded subpopulations, into HCV infection-treatment programs. The key question is how to help people who inject drugs (PWID) to engage in HCV infection-treatment programs and improve communication between PWID and hepatologists or other medical professionals involved in the treatment of chronic HCV infection. Furthermore, the medical professionals have to accept the changing spectrum of patients with chronic viral hepatitis. Without close interdisciplinary cooperation, it would be extremely difficult to achieve the WHO goal of global viral hepatitis C elimination. Here, we try to encourage our colleagues as well as addictologists and social workers to play their crucial part in the viral hepatitis C eradication process. It is extremely important for the healthcare providers to be able to communicate with addicted clients, inform PWID about the latest developments in the diagnosis and HCV infection treatment, and get them motivated to engage with specialized treatment programs.

Nevola R, V Rosato, V Conturso, P Perillo, T Le Pera, F Del Vecchio, D Mastrocinque, A Pappalardo, S Imbriani, A Delle Femine, A Piacevole and E Claar (2022). "Can Telemedicine Optimize the HCV Care Cascade in People Who Use Drugs? Features of an Innovative Decentralization Model and Comparison with Other Micro-Elimination Strategies." Biology (Basel) 11(6).

People who use drugs (PWUDs) are a crucial population in the global fight against viral hepatitis. The difficulties in linkage to care, the low adherence to therapy, the frequent loss to follow-up and the high risk of re-infection make the eradication process of the hepatitis C virus (HCV) really hard in this viral reservoir. Several management and treatment models have been tested with the aim of optimizing the HCV care cascade in PWUDs. Models of decentralization of the care process and integration of services seem to provide the highest success rates. Giving this, telemedicine could favor the decentralization of diagnostic-therapeutic management, key for the implementation of linkage to care, reduction of waiting times, optimization of adherence and results and reduction of the costs. The purpose of this literature review is to examine the role and possible impact of telemedicine in optimizing the HCV care cascade, comparing the different care models that have shown to improve the linkage to care and therapeutic adherence in this special population.

Pourkarim M, S Nayebzadeh, SM Alavian and SH Hataminasab (2022). "<u>Digital Marketing: A Unique Multidisciplinary Approach towards the Elimination of Viral Hepatitis</u>." <u>Pathogens</u> **11**(6).

New technologies are supported by the global implementation of the internet. These improvements have deeply affected various disciplines of sciences and consequently changed services such as daily business, particularly health sectors. Innovative digital marketing strategies utilize the channels of social media and retrieved user data to analyze and improve relevant services. These multidisciplinary innovations can assist specialists, physicians and researchers in diagnostic, prophylaxis and treatment issues in the health sector. Accordingly, compared to recent decades, health decision makers are more accurate and trustful in defining new strategies. Interestingly, using social media and mobile health apps in current pandemics of SARS-CoV-2 could be an important instance of the key role of these platforms at the local and global level of health policies. These digital technologies provide platforms to connect public health sectors and health politicians for communicating and spreading relevant information. Adding influencers and campaigns to this toolbox strengthens the implementation of public health programs. In 2016, the WHO adopted a global program to eliminate viral hepatitis by 2030. Recent constructive measures that have been used in the battle against COVID-19 could be adopted for the elimination of viral hepatitis program. The presented evidence in our narrative review demonstrates that the application of digital marketing tools to create campaigns on social media, armed with professional influencers, can efficiently consolidate this program. The application of different strategies in using these popular tools will raise the public awareness about viral hepatitis. Subsequently, the availability of an effective vaccine for HBV and antiviral medication for HCV can motivate the audience to take steps towards prophylaxis and screening methods against these infectious illnesses. The encouragement of health policy makers to apply digital communication technologies and comprehensive roadmaps to implement this global program will certainly decrease the burden of viral hepatitis worldwide.

Pourkarim MR (2022). "World Hepatitis Day in 2022: Challenges of Viral Hepatitis Elimination in Elongated COVID-19 Pandemic." Pathogens 11(9).

Recently, the World Hepatitis Day (WHD) of 2022 was observed to raise awareness of the global burden of viral hepatitis [...].

Razavi H (2022). "Polaris Observatory-supporting informed decision-making at the national, regional, and global levels to eliminate viral hepatitis." Antivir Ther **27**(2): 13596535221083179.

Background: Tools to eliminate Hepatitis B and C have been available and in 2016, the World Health Assembly endorsed the Global Health Sector Strategy for Viral Hepatitis. However, the adoption of hepatitis elimination programs has remained slow. Research design: The Center for Disease Analysis created a universal registry, the Polaris Observatory, to support informed decision-making at the national, regional, and global level for HCV and HBV elimination. The observatory covers 110 countries for HCV and 135 countries for HBV and provides decision analytics, disease burden modeling, economic impact assessments, and training to help countries with their national hepatitis elimination programs. Results: By providing reliable and up-to-date country specific data and analyses, demonstrating the impact of decisions, and providing costing estimates of national programs, our collaborating countries are making informed decisions. Our economic impact analyses also helped countries fund their elimination programs and negotiate prices. Polaris Observatory is an example of impactful private-public partnership where funding by the John C. Martin Foundation allowed support for informed decisionmaking by public agencies and national governments who would not/could not support such programs on their own. Conclusions: The catalytic funding allowed the Polaris Observatory to demonstrate the utility of such a program resulting in other donors to support this work. The Polaris Observatory is now supported through a portfolio of funders while our work and outputs remain independent to continue support for viral hepatitis elimination by year 2030.

Sagnelli C, M Macera, C Camaioni, A Salvati, N Coppola and E Sagnelli (2022). "SARS-CoV-2 infection: a hurricane that does not ignore chronic hepatitis." Infection **50**(4): 849-858.

BACKGROUND: The COVID-19 pandemic significantly compromised screening, laboratory controls, clinical surveillance and treatment of chronic hepatitis patients and worsened their outcome, as evidenced by its significant correlation with advanced cirrhosis, liver decompensation and mortality. RESULTS: This pandemic significantly impaired also the sector of liver transplantation, whose wards, operating rooms, outpatients' facilities, and healthcare personnel have been dedicated to patients with COVID-19. In addition, screening and treatment for HBV infection have been delayed or suspended in in most countries, with an increased risk of viral reactivation. Similar delay or suspension have also occurred

for universal hepatitis B vaccination programs in many countries. Likewise, COVID-19 pandemic has made unreachable the goal of elimination of HCV infection as a worldwide public-health issue predicted for 2030 by the WHO. CONCLUSION: This review article demonstrates how COVID-19 pandemic is causing serious damage to the sector of liver disease, which has quickly lost the beneficial effects of years of study, research, and clinical and technological application, as well as considerable financial investments.

Sintusek P, K Thanapirom, P Komolmit and Y Poovorawan (2022). "Eliminating viral hepatitis in children after liver transplants: How to reach the goal by 2030." World J Gastroenterol 28(3): 290-309.

Viral hepatitis infections are a great burden in children who have received liver transplant. Hepatotropic viruses can cause liver inflammation that can develop into liver graft fibrosis and cirrhosis over the long term. Immunological reactions due to viral hepatitis infections are associated with or can mimic graft rejection, rendering the condition difficult to manage. Prevention strategies using vaccinations are agreeable to patients, safe, cost-effective and practical. Hence, strategies to eliminate viral hepatitis A and B focus mainly on immunization programmes for children who have received a liver transplant. Although a vaccine has been developed to prevent hepatitis C and E viruses, its use is not licensed worldwide. Consequently, eliminating hepatitis C and E viruses mainly involves early detection in children with suspected cases and effective treatment with antiviral therapy. Good hygiene and sanitation are also important to prevent hepatitis A and E infections. Donor blood products and liver grafts should be screened for hepatitis B, C and E in children who are undergoing liver transplantation. Future research on early detection of viral hepatitis infections should include molecular techniques for detecting hepatitis B and E. Moreover, novel antiviral drugs for eradicating viral hepatitis that are highly effective and safe are needed for children who have undergone liver transplantation.

Strebe J, NE Rich, L Wang, AG Singal, J McBryde, M Silva, V Jackson, H Fullington, DL Villarreal, S Reyes, B Flores and MK Jain (2022). "Patient Navigation Increases Linkage to Care and Receipt of Direct-acting Antiviral Therapy in Patients with Hepatitis C." Clin Gastroenterol Hepatol.

BACKGROUND & AIMS: Patient navigation interventions can improve health outcomes in underserved, low-income, and racial and ethnic minority groups, who often experience health disparities. We examined the effectiveness of patient navigation to improve linkage to hepatitis C virus (HCV) treatment receipt in a socioeconomically disadvantaged, racially diverse patient population. METHODS: We performed a pre-post analysis evaluating the effectiveness of a patient navigation program among baby boomers who tested positive for HCV in a safety-net health system. The usual care group (June 2013 to May 2015) and patient navigation group (January 2016 to December 2017) were balanced using a stabilized inverse probability of treatment weighting approach. We used logistic regression analyses to evaluate associations between patient navigation and linkage to care for HCV treatment evaluation, treatment initiation, and sustained virologic response. RESULTS: Among 1353 patients (62% black, 61% uninsured, 16% homeless), 769 were in the usual care group, and 584 were in the patient navigation group. The patient navigation group had significantly higher odds of linkage to care (odds ratio [OR], 3.7; 95% confidence interval [CI], 2.9-4.8) and treatment initiation (OR, 3.2; 95% CI, 2.3-4.2) within 6 months. The patient navigation group continued to have increased linkage to care (OR, 3.4; 95% CI, 2.7-4.3) and treatment initiation (OR 2.3; 95% CI, 1.7-3.0) at 12 months. However, there was no significant difference in sustained virologic response between the groups (86.9% vs 86.1%; P = .78). CONCLUSIONS: Patient navigation was associated with significantly increased linkage to care and treatment initiation among patients with HCV infection. Patient navigation programs can be used to promote HCV elimination among traditionally difficult-to-reach patient populations.

The Lancet (2022). "Viral hepatitis elimination: a challenge, but within reach." Lancet 400(10348): 251.

Tian F, JJ Feld, Z Feng, B Sander and WWL Wong (2022). "Feasibility of hepatitis B elimination in high-income countries with ongoing immigration." J Hepatol 77(4): 947-956.

BACKGROUND & AIMS: Addressing HBV is vital to meeting the World Health Organization (WHO)'s viral hepatitis elimination goals, as 47% of viral hepatitis complications can be attributed to HBV. The objective of this study is to develop an agent-based model determining which integrated strategies involving vaccination, screening, and treatment would achieve the WHO's goals. METHODS: We developed an agent-based model to characterize the HBV epidemic in a high-income country with ongoing immigration. The spread of HBV was simulated through sexual networks and perinatal transmission. Model parameters were estimated from the literature and calibrated against historical HBV

data. Sensitivity analyses were performed to assess the uncertainty. RESULTS: We predict that under the current strategies, the incidence of acute hepatitis B, and HBV-attributable decompensated cirrhosis and hepatocellular carcinoma would decrease by 64.5%, 9.4%, and 10.5% between 2015-2030, respectively. However, the incidence of chronic hepatitis B and liver-related deaths would increase by 26.6% and 1.0% between 2015-2030, respectively. Results were sensitive to the number of immigrants and HBV prevalence in immigrants. CONCLUSIONS: The results suggest that the current vaccination, screening, and treatment strategies will be inadequate to achieve WHO elimination goals. Even with extensive integrated scale-up in vaccination, screening, and treatment, the morbidity and mortality targets may not be reachable, highlighting the need for a re-evaluation of the global strategy for HBV, the importance of developing curative therapy for HBV, and of establishing tailored strategies to prevent long-term sequelae and improve health in immigrants. LAY SUMMARY: We have developed a model that reflects the dynamics of hepatitis B virus (HBV) transmission in a high-income country with ongoing immigration, which enabled us to forecast the epidemiology of HBV for policy-level decision making. Our analysis suggests that current vaccination, screening, and treatment strategies are inadequate to achieve the WHO goals of eliminating chronic hepatitis B. Even with extensive integrated scale-up in vaccination, screening, and treatment, the morbidity and mortality targets may not be reachable.

Von den Hoff DW, FAC Berden, F Atsma, AFA Schellekens and JPH Drenth (2022). "<u>Against All Odds? Addiction</u> <u>History Associated with Better Viral Hepatitis Care: A Dutch Nationwide Claims Data Study</u>." J Clin Med **11**(4).

The elimination of viral hepatitis in target populations is crucial in reaching WHO viral hepatitis elimination goals. Several barriers for the treatment of viral hepatitis in people with addictive disorders have been identified, yet nationwide data on hepatitis healthcare utilization (HCU) in these patients are limited. We investigated whether a history of addictive disorder is associated with suboptimal hepatitis HCU, indicating failure to receive diagnostic care or treatment. We identified all newly referred viral hepatitis patients in the Netherlands between 2014 and 2019 by query of the Dutch national hospital claims database. Each patient's first year of HBV or HCV care activities was collected and clustered in two categories, 'optimal' or 'suboptimal' hepatitis HCU. Optimal HCU includes antiviral therapy. We tested the association between addiction history and HCU, adjusted for sex, age, migrant status, and comorbidity. In secondary analyses, we explored additional factors affecting hepatitis HCU. We included 10,513 incident HBV and HCV patients, with 13% having an addiction history. Only 47% of all patients achieved optimal hepatitis HCU. Addiction history was associated with less suboptimal HCU (adjusted OR = 0.73, 95% CI = 0.64-0.82). Migration background was associated with suboptimal HCU (OR = 1.62, 95% CI = 1.50-1.76). This study shows that addiction history is associated with higher viral hepatitis HCU; thus, this population performs better compared to non-addicted patients. However, less than 50% of all patients received optimal hepatitis care. This study highlights the need to improve hepatitis HCU in all patients, with a focus on migrant populations. Linkage to care in the addicted patients is not studied here and may be a remaining obstacle to be studied and improved to reach WHO viral hepatitis elimination goals.

Walker C, J Ou and S Foung (2022). "Editorial overview: Engineering elimination of chronic viral hepatitis." Curr Opin Virol **52**: 57-59.

Zhang C, Y Liu, H Zhao and G Wang (2022). "Global Patterns and Trends in Total Burden of Hepatitis B from 1990 to 2019 and Predictions to 2030." Clin Epidemiol 14: 1519-1533.

BACKGROUND AND AIMS: Despite widespread vaccination against hepatitis B and availability of antiviral drugs, hepatitis B remained a major global public health problem. Therefore, an improved understanding of the burden of hepatitis B was required to help design strategies for global intervention. METHODS: Data on hepatitis B was collected by the Global Burden of Disease (GBD) 2019 database from 1990 to 2019. Age-standardized incidence rates (ASIR), mortality rates (ASMR) and disability-adjusted life year rates (ASDR) for hepatitis B were extracted from GBD 2019 and stratified by age, level of regionals and country. Estimated annual percentage changes (EAPC) of ASIR, ASMR and ASDR were calculated to quantify the temporal trends in hepatitis B. RESULTS: Globally, ASIR showed a continuous downward trend, from 1552.2 in 1990 to 1010.0 per 100,000 persons in 2019, with an annual decrease of 1.52% (95% CI -1.66--1.38). ASMR showed a persistent decline, declining by nearly half in 2019 compared to 1990 (6.7 vs 12.4 per 100,000 persons), with an annual decrease of 2.55% (95% CI -2.74--2.35). ASDR showed a continuing downward trend, and the EAPC was -2.55% (95% CI -2.74--2.35). This decreasing pattern was heterogeneous across regions and countries. Hepatitis B related deaths increased significantly in high socio-demographic index countries such as UK, USA, and Canada. The ARIMA model

estimates a 36.14% and 6.00% decrease in ASIR and ASMR, respectively, by 2030 compared to 2015. CONCLUSION: Global hepatitis B morbidity and mortality rates decreased significantly from 1990 to 2019, but with a high degree of heterogeneity among regions and countries. It was still far from achieving the WHO goal of elimination of viral hepatitis by 2030, especially mortality rate.

Elgalib A, R Lau, Z Al-Habsi, S Shah, B Al-Rawahi, ZA Memish, SS Lee and S Al-Abri (2023). "Elimination of mother-to-child transmission of HIV, syphilis and viral hepatitis B: A call for renewed global focus." Int J Infect Dis 127: 33-35.

Hiebert L, Ward JW. Strategic information to guide elimination of viral hepatitis. Lancet Gastroenterol Hepatol. 2023 Feb 7:S2468-1253(22)00433-2. doi: 10.1016/S2468-1253(22)00433-2. Epub ahead of print. PMID: 36764321.

Musabaev E, C Estes, S Sadirova, S Bakieva, K Brigida, R Dunn, S Kottilil, P Mathur, A Abutaleb, K Razavi-Shearer, T Anstiss, B Yusupaliev and H Razavi (2023). "Viral hepatitis elimination challenges in low- and middle-income countries-Uzbekistan Hepatitis Elimination Program (UHEP)." Liver Int.

BACKGROUND & AIMS: Chronic infection with hepatitis B and C viruses (HBV & HCV) is a major contributor to liver disease and liver-related mortality in Uzbekistan. There is a need to demonstrate the feasibility of large-scale simplified testing and treatment to implement a national viral hepatitis elimination program. METHODS: Thirteen polyclinics were utilized to screen, conduct follow-up biochemical measures and treat chronic HBV and HCV infection in the general adult population. Task shifting and motivational interviewing training allowed nurses to provide rapid screening and general practitioners (GPs) to treat individuals on-site. An electronic medical system tracked individuals through the cascade of care. RESULTS: The use of rapid tests allowed for screening of 60 769 people for HCV and HBV over 6 months and permitted outdoor testing during the COVID-19 pandemic along with COVID testing. 13%-14% of individuals were lost to follow-up after the rapid test, and another 62%-66% failed to come in for their consultation. One stop testing and treatment did not result in a statistically increase in retention and lack of patient awareness of viral hepatitis was identified as a key factor. Despite training, there were large differences between GPs and patients initiating treatment. CONCLUSIONS: The current study demonstrated the feasibility of large-scale general population screening and task shifting in low- and middle-income countries. However, such programs need to be proceeded by awareness campaign to minimize loss to follow up. In addition, multiple trainings are needed for GPs to bolster their skills to talk to patients about treatment.

O'Ferrall AM, A MacElhinney-West, MS Bell, MP Haslam, G Walker, D Norton, SA Burns, G Ferrier and NJW Easom (2023). "Geographically targeted chronic infection screening: lessons from a hepatitis B pilot study in the UK." Trans R Soc Trop Med Hyg.

Chronic hepatitis B (CHB) most commonly occurs following infection in early childhood. Prevalence varies markedly around the globe. Country of birth is therefore a strong predictor of CHB risk in adults. We used country of birth census data to predict CHB risk and carry out geographically targeted screening in East Yorkshire, UK. Despite engaging individuals born in high-prevalence countries with testing, we observed lower than expected prevalence in targeted highest-risk areas, which may indicate barriers to testing for people with undiagnosed CHB. Improved strategies for engagement with high-risk groups will be key for viral hepatitis elimination.

PARTICIPANTS LIST

Will be included in the final version that will be available on the website www.vhpb.org after the meeting.