

TOWARDS THE GOAL OF HEPATITIS C ELIMINATION IN LATVIA — USING PATIENT SURVEY RESULTS

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The success of global strategies to eliminate hepatitis C as a public threat by 2030 depends on local country-wide activities of all involved stakeholders, the most important being general practitioners (GP) and the entire country population. The opinion of currently diagnosed patients can help stakeholders to plan further actions such as addressing new target groups. Our aim was to determine the experiences, opinions, and attitudes of viral hepatitis C (VHC) patients towards the hepatitis C virus (HCV) infection and corresponding healthcare services in Latvia. Questionnaires were distributed by nurses in hospitals of major cities in Latvia. The survey results highlighted the importance of the role of the general practitioner and time from diagnosis to specialist consultation. The majority of respondents were not aware of VHC symptoms, although they were informed about possible complications such as liver cirrhosis and hepatocellular carcinoma. The major VHC patient pool was not composed of drug users, but people who never used narcotics, highlighting the importance to increase VHC awareness in other risk groups and in the general population. Consequently, targeted VHC screening programmes are essential tools in achieving elimination of HCV infection as a public threat in Latvia. The action plans should be updated regularly aiming to strengthening of the GP role and shortening time to consultation with a specialist.

Keywords: chronic hepatitis C, HCV, eradication, HCV screening, general practitioners.

INTRODUCTION

On 10 October 2020, the Nobel Assembly at Karolinska Institute made the decision to award the 2020 Nobel Prize in Physiology or Medicine to three distinguished scientists — Harvey J. Alter, Michael Houghton, and Charles M. Rice for the discovery of hepatitis C virus (HCV). The discovery of HCV (Houghton, 2009) in 1988 made a significant contribution to the fight against viral hepatitis C, a major global health problem that causes liver cirrhosis and liver cancer.

The results of research enabled healthcare professionals to develop effective laboratory tests for detection of the virus and anti-HCV antibodies. Although the discovery of HCV occurred already more than 30 years ago, there is still no vaccine available to prevent HCV infection. However, there has been a major breakthrough in its treatment. After gradual and steady progress, there are highly effective direct-acting antiviral (DAA) medications available with cure rates, defined as sustained virological response (SVR), reaching 95–98% (Afdhal *et al.*, 2014; Balistreri *et al.*,

2017; Forns *et al.*, 2017; Wirth *et al.*, 2017; Pawlotsky *et al.*, 2018; Zeuzem *et al.*, 2018).

The current treatment efficacy using DAAs provides an opportunity to cure most of the patients suffering from chronic hepatitis C infections globally. This is a rather unique opportunity as elimination of HCV infection is possible even in the absence of an effective vaccine.

In 2016, the World Health Assembly adopted the Global Health Sector Strategy (GHSS) on viral hepatitis to eliminate hepatitis C as a public threat by 2030. The goal of the World Health Organisation (WHO) GHSS is to decrease viral hepatitis C incidence from 6–10 million cases to 0.9 million cases (World Health Organisation, 2016). In addition to that, a very important goal to be reached by 2030 is to reduce annual hepatitis deaths from 1.4 million to 0.5 million. Two targets will be measured: reduction of new infections by 90% and reduction of mortality by 65% (EASL, 2020). To achieve WHO targets in the European Union, according to a study by the European Union HCV Collaborators, considerable effort will be needed in terms of increasing unrestricted treatment from 150 000 patients in 2015 to 187 000 patients in 2025 and increasing diagnosis from 88 800 new cases annually in 2015 to 180 000 in 2025 (European Union HCV Collaborators, 2017).

The World Health Organisation estimates that 71 million people worldwide are chronically infected with hepatitis C virus (World Health Organisation. Global Hepatitis Report 2017). The analysis performed by the Polaris Observatory HCV Collaborators estimated the global prevalence of 71.1 million viraemic HCV patients in 2015, a decrease from 80 million in 2013 (Polaris Observatory HCV Collaborators, 2017). WHO estimates obtained from modelling suggest that in 2015 there were still 1.75 million new HCV infections worldwide (global incidence rate: 23.7 per 100 000). Unsafe health-care procedures and injection drug use were the leading causes of new HCV infections.

Latvia is considered as one of the countries of the European Union with relatively high prevalence of HCV infection. The prevalence of antibodies to HCV (anti-HCV) and HCV-RNA in Latvia was estimated at 2.4% and 1.7%, respectively (Tolmane *et al.*, 2011).

Consequently, WHO member countries, including Latvia, are now working on HCV infection control and elimination strategies and tactics. This is not an easy task as evaluation indicates that by the end of 2018 there were only 12 countries on track to achieve hepatitis C elimination targets (Waheed *et al.*, 2018).

There will be many obstacles on the way to reaching the targets, for example limited access to DAA medicines in many low- and middle-income countries due to relatively high costs (Chugh *et al.*, 2019), slow and gradual improvements in blood and injection safety, low hepatitis C awareness in the population, overloaded general practitioners, not able to focus on this problem, lack of political will and others. Con-

tinuous financing to support chronic hepatitis C programmes will be challenging, but nevertheless an achievable task.

Among the most important current tasks in Latvia is how to speed up diagnosis of HCV infection and find the missing thousands of people living with viral hepatitis C. Policy-makers, other authorities, health care professionals (general practitioners, hepatologists, infectious disease specialists, epidemiologists and others), and affected communities will have to reach defined patient target groups in the population (Stasi *et al.*, 2020) and secure adherence to treatment (Bonacini *et al.*, 2020).

One of the starting points in performing this task is to understand the opinions and beliefs of the patients who are currently infected by HCV or have been infected previously and cleared the virus naturally or have been cured. The results of a survey would help developing and updating country-specific HCV infection elimination action plans to be implemented during the upcoming years. Therefore, a survey of hepatitis C patients was performed in Latvia.

The aim of the survey was to determine characteristics of average hepatitis C patients in Latvia and to understand how HCV infection was diagnosed, obstacles encountered in diagnostic process as well as patients' opinion on the disease, possible ways to become infected and others.

MATERIALS AND METHODS

The targeted hepatitis C patient's survey was developed by the authors and performed by healthcare professionals and the Marketing and Public Opinion Research Centre SKDS.

The target group for the survey were hepatitis C patients. Inclusion criteria were: HCV-RNA positive adult patients.

The selected group very well represented the total hepatitis C patient population in Latvia, although the results cannot be extrapolated to the whole population of the country. Not all HCV-positive patients visit an infectious disease specialist. However, the study covered all three cities where HCV treatment is available. HCV/HIV co-infected patients were also included.

A written self-administered questionnaire was handed out to patients by nurses. The out-patient departments of the hospitals in the three biggest cities of Latvia (Riga, Daugavpils, and Liepāja) were included.

The questionnaire contained 20 questions on personal experience related to HCV infection management, medical procedures performed, possible risk factors for HCV infection, current health status, information sources used, beliefs, opinions and attitudes towards HCV infection, and healthcare in general. Basic demographic information was obtained from respondents as well.

Responses were analysed by public opinion research specialists and healthcare professionals. IBM SPSS Statistics

26 for Windows was used for statistical analyses. The Chi-Square (χ^2) test was used to determine statistically significant differences. Statistical differences and associations were considered significant when $p < 0.05$.

The study was conducted in accordance to the Declaration of Helsinki ethical standards. The de-personification took place in the patient-nurse-researcher phase. Data were analysed without personification. The questionnaires are stored at Riga East University Hospital, Latvian Centre of Infectious Diseases. The study was approved by the Scientific Research Ethics Committee of the Institute of Cardiology and Regenerative Medicine of the University of Latvia, 6 November 2019.

RESULTS

Study sample characteristics. The total number of respondents was 624. The survey was performed from January 2020 till July 2020. The majority (54.8%, $n = 342$) of respondents — where males were compared to female (44.2%, $n = 282$). A minority of respondents (22%) lived in rural areas. From all patients, the majority (87.2%) were treated in Riga. Most patients were above 40 years old, with secondary education and increased body mass index (Table 1).

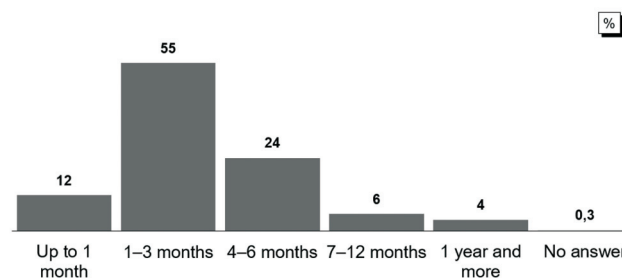
Role of general practitioner. More than a half of the hepatitis C patients surveyed (58%) indicated that initially they had been referred for an anti-HCV test by a GP. One-fifth of the respondents (20%) asked for the test themselves, 7% of the respondents had this test referred by a medical specialist before surgery or for other reasons, while 5% of the respondents — by a medical specialist during pregnancy. The remaining 10% of respondents indicated that the first anti-HCV test was referred by an infectious disease specialist, dermatologist or in an anonymous clinic/test point. An overwhelming majority (93%) of the respondents were referred to a hepatologist and/or infectious disease specialist for further clarification of the diagnosis by a GP, and only 6% — by another specialist.

Waiting time till specialist's consultation. For the majority (55%) of hepatitis C patients it took 1 to 3 months to see a hepatologist and/or infectologist. A quarter of respondents (24%) indicated that 4–6 months passed until consultation, while 12% of respondents waited up to 1 month, 6% of respondents even 7–12 months, and 4% more than a year (Fig. 1). The majority (83%) of the respondents indicated that the major obstacle was waiting time until availability of specialist consultation. A relatively lower proportion of respondents indicated the following reasons of delay: waiting time to receive GP's referral (13%); financial problems (12%); did not consider it an urgent matter (9%) and "health problems" (7%).

There was a statistically significant relationship between the patient's gender and reasons, which prevented him/her from getting to the specialist faster. Men more often than women

Table 1. Demographic characteristics of respondents

	Characteristics	n	%
Respondents	All	624	100
Gender	Male	342	54.8
	Female	282	45.2
Age	18–29 years	79	12.7
	30–39 years	129	20.7
	40–49 years	158	25.3
	50–59 years	105	16.8
	> 60 years	150	24
	No answer	3	0.5
Education	No education	8	1.3
	Basic education	129	20.7
	Secondary or secondary professional education	360	57.7
	Higher education	126	20.2
	No answer	1	0.2
Occupation*	Senior or middle manager	51	8.2
	Specialist, official, not in manual work	127	20.4
	Working manual work	208	33.3
	Owner of enterprise, individual work	88	14.1
	Retired	101	16.2
	Pupil, student	15	2.4
	Housewife, parental leave	32	5.1
	Unemployed	89	14.3
	No answer	1	0.2
Body weight	Insufficient body weight	4	0.6
	Normal body weight	152	24.4
	Excess body weight	223	35.7
	Obesity	240	38.5
	No answer	5	0.8



Base: all respondents, $n=624$

Fig. 1. Time to a specialist's consultation for HCV patients.

mentioned financial problems, $\chi^2(1, n = 624) = 4214, p < 0.04$ and the fact that they did not consider the situation being urgent, $\chi^2(1, n = 624) = 17757, p < 0.001$.

Hepatitis C disease awareness. The majority (90%) of hepatitis C patients were unaware of the symptoms of acute and chronic hepatitis C. From the remaining 10% of patients, the majority indicated weakness and fatigue as predominant symptoms followed by upper right quadrant pain and nausea. Hepatitis C patients most often obtained information on how to treat and prevent hepatitis C from healthcare professionals (90%). This was followed by information

sources like social networks/internet (28%), relatives and acquaintances (19%), media/press (6%) and scientific literature (4%). Information through social networks/internet was more often obtained by women, as well as by the younger age respondents. The majority of respondents (84%) believed that untreated chronic hepatitis C was a dangerous infection due to potential development of cirrhosis and 32% indicated liver cancer as a threat.

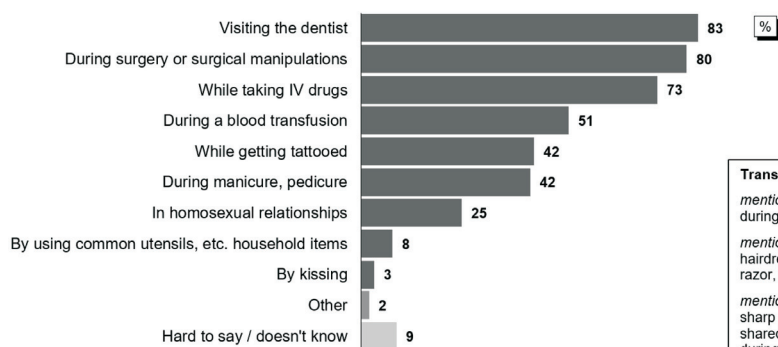
Beliefs and opinions about HCV. Respondents most often believed that people can become infected with hepatitis C by visiting a dentist (83%). Almost as many (80%) respondents believed that they can become infected during surgery or surgical manipulations. Other risks mentioned by respondents are IV drug use, blood transfusion, performing tattoos, manicures, pedicures and in men having sex with men (Fig. 2). When asked where they got infected, almost half of the respondents (46%) replied that happened during the visit to a dentist and/or hygienist. A smaller proportion of respondents (19%) indicated the hospital as the place of infection. Almost as many (18%) believed that they were infected through sexual contact (Fig. 3). Women believed that they most likely had been infected by visiting a dentist, $\chi^2(1, n = 624) = 11\ 296, p = 0.001$, in hospital, or during a manicure/pedicure procedure, while men believed they were infected through sexual contact.

There were discrepancies between believed ways of HCV transmission in the society and patients' opinions concerning how they got infected. While 51% of respondents mentioned blood transfusion as an important factor in acquiring HCV infection, only 1% thought that they were infected that way. Regarding the importance of IV drug use, 72.8% of respondents believed it was an important factor in gen-

eral while only 5.1% thought that it was the way of their own infection. No in-depth analysis of the reasons for these discrepancies was performed in this study.

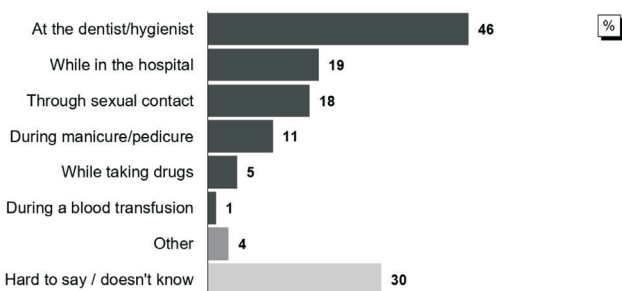
Regarding the time of infection, respondents most often believed that they became infected with hepatitis C two to five years before (34%), 26% thought they were infected 6–10 years before, the same number (26%) — 11 years or more before, and 14% — up to one year before.

Life, lifestyle, and habits. 28% of respondents used alcohol regularly (21% of respondents 1–2 times a week while 7% — 3–4 times a week or more). Almost half of the respondents (48%) used alcohol rarely, and one-fifth of respondents (22%) did not drink alcohol at all. The older-age respondents, as well as women, used alcohol less compared to other groups. 6% of hepatitis C patients surveyed currently used (1% of total) or had used intra-venous drugs in the past (5% of total). The most commonly used drug was amphetamine. One-third of the respondents (33%) had tattoos or piercings (other site than ears). Tattoos and piercings were more common in men and in respondents under the age of 50. One-third of the respondents (33%) tended to have manicures and pedicures (24% regularly and 9% rarely). Manicures and pedicures were more common among women and younger-age respondents. Regarding the number of sexual partners, 42% indicated that they had up to five sexual partners, 16% had 6–10 while 15% — more than eleven partners. 11% of respondents had been imprisoned during their lifetime. Men had been imprisoned more often than women, as well as respondents aged 30 to 49 years. Of all respondents, 4% of hepatitis C patients had a blood transfusion. Excess body weight was indicated by 223 respondents (35.7%).



Transcript of the answer «Other»:
 mentioned 5 times:
 during sex;
 mentioned 2 times:
 hairdressing services;
 razor, toothbrush;
 mentioned 1 time:
 sharp objects / through the blood;
 shared syringes;
 during permanent make-up.

Fig. 2. Beliefs of respondents about possible ways to acquire HCV infection. Question: Are you aware of how you can become infected with hepatitis C?'



Transcript of the answer «Other»:
 mentioned 10 times:
 while getting tattooed;
 mentioned 3 times:
 while getting tattooed in prison;
 mentioned 2 times:
 during surgery;
 mentioned 1 time:
 alcohol;
 about 7 years ago, when I started going on various IV systems — vitamins in a vein — in polyclinics; in Central prison;
 it turned out that the husband is a carrier of the «B» virus; inherited from mother;
 permanent make-up;
 at the gynecologist.

Fig. 3. Respondents' opinion about the way they got infected with HCV. Question: Where do you think you got hepatitis C?'

Concomitant diseases and healthcare interventions. 27% of respondents indicated that they had concomitant chronic illness. The most common chronic diseases were: HIV/AIDS (17%), hypertension (12%), asthma (11%), and other cardiovascular diseases (10%). Almost a quarter of respondents (23%) had had surgery. The history of surgery was more common in women than in men.

DISCUSSION

There were more men than women among the respondents, which coincides with the epidemiological data indicating that the prevalence of HCV infection was higher among men.

Regarding discrepancies between respondents' believed ways to acquire HCV infection and their opinion on how they got infected, re-grouping of the options and additional analysis using cross-tabulation (available on request) yielded no meaningful results. These discrepancies could be used as a basis for further decisions for searching and addressing society groups with higher risk of HCV infection.

The role of GPs is crucial in securing success of an HCV elimination programme. This is clearly reinforced by patients in the study who indicated that GPs play the most important role in initial examinations targeted to detect liver function and possible HCV infection.

Three months of waiting time till a specialist's consultation is not considered to be a big harm from a medical point of view, because cirrhosis does develop in a much longer period. At the same time, epidemiologically, these patients would continue spreading infection during this time because they would not be aware of infection. Therefore, the problem of a long waiting time should be addressed to healthcare authorities.

Additional factors contributing to a prolonged time until consultation were lower education level and insufficient body mass index. Due to very small groups, it was not possible to draw conclusions about this finding. The underlying specific reasons could be studied further in the light of adjusting the national policy of HCV elimination.

Patients would rather harm themselves by considering their HCV infection as a minor health problem not requiring immediate attention, consequently not visiting GP at all. This issue is closely related to awareness and health education of population.

Acquiring HCV infection in a healthcare institution should still be considered to be a problem. In recent years, stricter legislation and controls have been introduced for dentistry and beauty salons, educational campaigns are under way, and the control of infections in medical facilities is improving, which could reduce the number of new infections.

Regarding lifestyle, it is important to note that many patients had never used intra-venous narcotic drugs in their lives, so they had become infected in other ways.

Excess body weight in one-third of respondents indicated that lifestyle was not very healthy for HCV patients, which may have led to non-alcoholic fatty liver disease. Increased body weight along with regular alcohol intake may also contribute to the development of cirrhosis.

The following actions should be prioritised as reinforced by survey results in this study.

Firstly, GPs should receive regular updates on their role in the country-wide HCV elimination programme and be encouraged to raise HCV infection awareness, ensure appropriate HCV preventive measures, assess liver health by offering testing not only in evident hepatitis C risk group patients, but also wider group, for example family members, close contacts and others. GPs would highly benefit from HCV elimination project reports showing the progress of the HCV infection elimination programme in the country. It is very important to reach out to the group of patients who never see a GP. Such an activity would be beneficial not only in terms of monitoring liver health, but also regarding information on other metrics, among which immunisation status would be a major one. The healthcare authorities and HCPs should focus more towards diagnosing HCV in patients who have not registered with a GP or decline from visits for a long time. These patients are usually young and healthy. The homeless people should be approached as well. For patients who never visit a GP and in whom a primary anti-HCV screening test is positive, there should be clearly defined possibility to visit an infectious diseases specialist directly without a family doctor referral. Healthcare authorities may consider implementing such an option in strategic documents. For those patients visiting a GP, the authorities should include detection of ALT in cardiovascular screening.

Secondly, as highlighted by survey results — time from diagnosis to a specialist consultation is an issue. All newly diagnosed patients should be linked to treatment and care as soon as possible. The waiting time to a specialist's consultation and prescription should be shortened, either by allocating additional resources or by changing prescribing conditions allowing GPs to prescribe particular DAA regimens in the future. This is also very closely linked to readiness of GPs to manage HCV patients. Currently, there are effective recommendations for family doctors indicating clearly which examinations to perform before a patient visits an infectious diseases specialist. This activity shortens the time from the first visit to an infectious disease specialist till initiation of DAA treatment.

Thirdly, as patients are involved more in their own personal and family healthcare decisions, stakeholders such as hepatologists, infectious diseases specialists, public health institutions and the authorities should organise regular campaigns with the aim to increase awareness and reach out to

the whole population in Latvia, encouraging them to monitor liver health regularly by attending GP and having a liver function test on yearly basis. The ultimate goal would be that every person in the country is tested for anti-HCV at least once in a lifetime.

Another important issue to address is continued population screening. Targeted cost-effective population screening should be performed using proper timing and criteria relevant for the target population. Inappropriate timing and non-relevant criteria would lead to low response, as observed in the case of oncological screening.

Similar to global trends, also in Latvia there is a lower incidence of diagnosed new acute or chronic HCV infections in recent years as well as improved injection and other invasive healthcare procedures, safety leading to lower risk of acquiring infection. As a consequence of safer healthcare, injection drug use may account for a substantial proportion of new infections. At the same time, as the survey indicates that currently drug addicts or HIV-infected are not the main group of hepatitis C patients, coverage of the wider population is needed. Also, it is important to consider the possibility of reinfection among HIV-infected MSM in whom it was successfully cured in previous years. It is estimated that the majority of patients from the following risk groups are diagnosed and treated — intravenous drug users, those who received blood transfusions before 1992, haemophiliacs and renal replacement therapy patients. All HIV-infected and prisoners are being treated provided if compliance is secured.

Screening is planned or underway for psychiatric patients, the homeless and people residing in long-term social care facilities. These actions, which are reinforced by data from patients' survey, will help to achieve goals of eradicating HCV infection set by the WHO.

Until 2016, only six to eight hundred chronic hepatitis C patients had been treated in Latvia with interferon-based regimens. Starting from 2016 when DAAs became available, there were almost 3000 patients treated in 2019. The estimated number of treated patients during 2020 was less due to the Covid-19 pandemic and was assumed to be about 2300 patients. In 2020, all chronic hepatitis C patients in Latvia had access to DAA medicines. The only limitations were according to genotypes — 1 and 4 genotype patients have 100% reimbursement for elbasvir/grazoprevir or ombitasvir/paritaprevir/ritonavir/dasabuvir. In the case of genotypes 2 and 3 — there is reimbursement for glecaprevir, pibrentasvir or sofosbuvir/ velpatasvir (www.vmnvd.gov.lv).

It is important to develop convenient HCV elimination project follow-up tools that will help to determine whether the number of HCV-infected persons is likely to increase or decrease in the country. As recommended by the WHO, the number of new HCV infections needs to be compared with the number of HCV-infected persons who die and those who are cured. The basis for developing local follow-up tools would be reliable data sourcing that would enable to

estimate the number of infections, healthcare interventions and results. At the same time, comparison with overall European Union data such as the European Union HCV Collaborators study may provide additional data for developing reliable local estimations.

While general population statistical data are available, numbers reflecting healthcare performance remain to be improved. The population in Latvia (<https://www.csb.gov.lv>) has been decreasing due to emigration and negative natural growth. We estimated some key figures for 2015 and 2020 based on reliable local sources as well as estimated and published European Union data. The number of viraemic HCV infections in Latvia in 2020 could be about 30–35 thousand. The number of newly diagnosed HCV infections is estimated to be about 1250 patients per year. To achieve WHO targets in Latvia, there is a need to diagnose at least 1000 new cases and provide 3000 unrestricted HCV treatments per year starting from 2021 but not later than in 2025. The pool of undiagnosed patients should shrink in the future, providing a solid base for achieving the target of elimination of HCV infection as a public threat by 2030.

Because of experience in communicating with patients and general population, healthcare professionals are in a better position to recognise actual ways of HCV acquisition. At the same time, no one can tell the exact route of infection for each individual hepatitis C patient. The most common routes of infection are known — IV drug use, cosmetology, dentistry, and medicine in general. Specialists can assume the most probable route of infection, but often it is impossible to prove it using current methods. As there are no extensive studies performed on actual HCV transmission ways with respect to socio-demographic profile in Latvia so far, this would be an important next step in uncovering new target groups for screening.

In order to improve outreach to the remaining undiagnosed HCV-infected patients, the stakeholders have to regularly update the local comprehensive hepatitis C national strategy and action plan, increasing the awareness throughout the whole population and target groups.

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CELĀ UZ C HEPATĪTA IZSKAUŠANU LATVIJĀ — PACIENTU APTAUJAS REZULTĀTU PIELIETOJUMS

C hepatīta izskaušanas līdz 2030. gadam stratēģijas veiksmē ir atkarīga no veselības aprūpes organizatoru, infektologu, it sevišķi ģimenes ārstu un visu valsts iedzīvotāju iesaistīšanās. Aptaujāto C vīrushepatīta (VHC) pacientu viedoklis palīdz plānot turpmākās darbības, piemēram, jaunu mērķa grupu uzrunāšanu un testēšanu. Mūsu mērķis bija ar aptaujas palīdzību uzzināt VHC pacientu pieredzi, viedokli un attieksmi pret C hepatītu (HCV) un ar to saistītajiem veselības aprūpes pakalpojumiem Latvijā. Aptaujas metode — medicīnas māsu izdalītas anketas Rīgas, Daugavpils un Liepājas slimnīcu ambulatorajās nodaļās. Aptaujas rezultāti pārliciecināši norādīja uz ģimenes ārstu lomu savlaicīgas diagnozes noteikšanā, kā arī ilgu gaidīšanas laiku līdz hepatologa vai infektologa konsultācijai. Lielākā daļa respondentu nebija informēti, kā simptomātiski izpaužas VHC, lai gan zināja par iespējamām komplikācijām, piemēram, aknu cirozi un aknu vēzi. Vairums VHC pacientu nav narkotiku lietotāji, bet cilvēki, kuri nekad nav lietojuši narkotikas, tāpēc ir svarīgi palielināt informētību un izpratni par VHC citās riska grupās un sabiedrībā kopumā. Lai veicinātu stratēģiskā mērķa sasniegšanu — VHC izskaušanu, papildus citiem pasākumiem, piemēram, ģimenes ārstu efektīvākai iesaistei, gaidīšanas laika līdz speciālista konsultācijai saīsināšanai, ir jāveic precīzi plānots HCV skrīnings konkrētās riska grupās, kā arī populācijā kopumā.