

Original paper

How close are we to hepatitis C virus elimination in Central Europe?

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Abstract

Aim of the study: To collect and analyse data obtained from HCV opinion leaders/experts from central European countries, on factors which can affect the WHO target of HCV elimination by 2030.

Material and methods: Data were collected from opinion leaders/experts involved in management of HCV infections in Central European countries which participated in 9th Conference of the Central European Hepatologic Collaboration (Warsaw, 10-11 October 2019). A dedicated questionnaire collected current information related to HCV elimination in Bulgaria, Croatia, the Czech Republic, Hungary, Latvia, Lithuania, Poland and Slovakia.

Results: The HCV prevalence rate in particular countries varied from 0.2% to 1.7%. In most central European countries all the HCV infected population is eligible for reimbursement of treatment. However, in some countries there are still some limitations related to the stage of the disease and people who inject drugs. All countries have access to at least one pangenotypic regimen. The most common barrier to HCV elimination in all countries is insufficient political will to establish priority for HCV. None of the reporting countries has established a national screening programme.

Conclusions: Access to therapy for HCV is similar and the majority of patients in Central Europe can be treated according to the current guidelines. Unfortunately there are still some limitations and a lack of political will to implement national screening programmes. According to collected data HCV elimination will not be possible in the region by 2030.

Key words: therapy, liver, epidemiology, hepatitis C virus.

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Introduction

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease worldwide and according to World Health Organization (WHO) estimations affects approximately 71 million individuals [1]. Most Central European countries demonstrate relatively low prevalence of this infection, but some neighbouring countries in the region (Romania and Ukraine) are well known to have high HCV prevalence rates [2]. Until 2014 the effectiveness of HCV treatment based on interferon alfa was suboptimal because only about half of the patients were able to achieve a sustained virologic response (SVR). This rate was even much lower in patients with advanced liver diseases and a number of them were unable to complete therapy due to adverse events. Availability of direct acting antivirals (DAA) and treatment with their combinations improved the effectiveness significantly, with an SVR rate close to 100% irrespective of factors previously recognized as reducing risk of treatment effectiveness. However, some restrictions limited access to therapy in some populations [3]. Anyway new therapeutic options caused elimination of waiting lists for treatment and cure of the majority of patients who failed previous interferon-based therapy. Unfortunately, the large majority of HCV-infected patients remain still undiagnosed and therefore are at risk of development of cirrhosis and/or hepatocellular carcinoma [4]. In 2016, the WHO initiated a plan to eliminate viral hepatitis as a public health threat by diagnosing 90% of HCV-infected and treating 80% of all eligible patients by 2030 [5]. Based on recent estimations from the Centers of Disease Analysis this target will be difficult to achieve in the majority of countries [6], mostly due to the lack of national programmes of HCV elimination. Such programmes should include, in addition to unlimited access to highly efficient therapeutic options, also screening programmes which provide an opportunity to diagnose hidden cases of HCV infection in the general population as well as appropriate preventive measures. It is obvious that without a screening programme covering the whole population of entire country elimination or even significant reduction of HCV prevalence will not be possible.

The purpose of this study was to collect and analyse data obtained from HCV opinion leaders/experts of Central European countries on factors which potentially can affect the WHO target of HCV elimination.

Material and methods

Data were collected from opinion leaders/experts involved in management of HCV infections in Cen-

tral European countries, which participated in the 9th Conference of the Central European Hepatologic Collaboration (Warsaw, 10-11 October 2019). A dedicated questionnaire containing questions on epidemiology of HCV, access to therapy, barriers to HCV elimination and initiatives to remove them was mailed to experts to characterize the current situation in Bulgaria, Croatia, the Czech Republic, Hungary, Latvia, Lithuania, Poland and Slovakia. Answers were collected before the conference and the results were presented in lectures and posters. A scoring system was created for evaluation of factors affecting HCV elimination by the year 2030 according to targets set by the WHO [5].

Results

As shown in Table 1, the HCV RNA prevalence rate in particular countries varied from 0.2% in Slovakia to 1.7% in Latvia, which resulted in an estimated total number of almost 410 thousand HCV-infected persons. In all countries the most frequently diagnosed was infection with genotype (G) 1b, followed by either G1a in southern (Bulgaria, Croatia, Czech Republic, Hungary) or G3 in northern countries (Latvia, Lithuania, Poland, Slovakia) of the region. In most countries all the HCV-infected population is eligible for reimbursement of treatment (Table 1). However, in Lithuania there are still some limitations related to the stage of the disease, and the major problem in Slovakia is the lack of reimbursement for people who inject drugs (PWID), which affects about half of the infected population. Despite these limitations there are no longer existing waiting lists for treatment. The number of treated patients is usually stable or increasing except in Poland and Hungary, which have already reached the highest volume of therapies and currently demonstrate a decreasing pattern due to a low diagnosis rate (Table 1).

As demonstrated in Table 2, all included countries have access to at least one “dual” pangenotypic regimen (GLE/PIB or SOV/VEL), and some have also access to a “triple” one (SOV/VEL/VOX). However, use of pangenotypic therapeutic options varies widely from 15% in Hungary to more than 80% in Croatia, the Czech Republic and Lithuania (Table 2). All interferon-free regimens, including OBV/PTV/r ±DSV, are still available in the Czech Republic and Hungary. On the other hand, in Lithuania there are only two therapeutic options available (GLE/PIB and GZR/EBR).

The most common barrier to HCV elimination in all countries is insufficient political will to establish priority for HCV (Table 3), which can be solved by creation of a national plan (Table 4). All countries have sufficient coverage of therapy for HCV. However,

Table 1. Characteristics of HCV infection in general population. It is not representative for incarcerated persons and PWID

	Bulgaria	Croatia	Czech Rep.	Hungary	Latvia	Lithuania	Poland	Slovakia
Estimated HCV RNA prevalence, n (%)	80,000 1.1%	20,000 0.6%	40,000 0.5%	40,000 0.4%	40,000 1.7%	25,500 0.9%	150,000 0.4%	10,000 0.2%
Genotypes								
1a	26%	30%	20%	5%	5%	11%	5%	16%
1b	59%	25%	41%	86%	52%	52%	75%	51%
2	1%	2%	0	0	2%	5%	0	0
3	14%	39%	37%	3%	37%	22%	13%	31%
4	0	4%	1%	0	0	0	6%	2%
other	0	0	1%	6%	4%	10%	1%	0
Population eligible for reimbursement	100%	100%	100%	97%	100%	90%	100%	50-60%*
Waiting list	No	No	No	No	No	No	No	No
Number of treated								
2016	720	179	622	916	486	966	8000	450
2017	1325	342	620	928	1173	998	11700	350
2018	1200	440	648	2446	1632	1164	7100	400
2019	1000	468	1360	1332	3000	1320	8500	400

*Treatment is not reimbursed for active IVDU with CHC; this group represents appr. 40-50% of all HCV-infected patients in Slovakia.

Table 2. Proportion of anti-HCV regimens prescribed in 2019

	Bulgaria	Croatia	Czech Rep.	Hungary	Latvia	Lithuania	Poland	Slovakia
GLE/PIB	40%	52%	57%	8%	27%	82%	40%	60%
SOF/LDV	16%	7%	2%	18%	0	0	7%	17%
SOF/VEL	32%	29%	26%	5%	10%	0	25%	7%
SOF/VEL/VOX	0	2%	5%	2%	0	0	0	2%
GZR/EBR	12%	10%	7%	40%	31%	18%	28%	14%
OBV/PTV/r ±DSV	0	0	3%	27%	28%	0	0	0
SOF + RBV ±PegIFN	0	0	0	0	0	0	0	0
Other	0	0	0	0	4%	0	0	0

it needs to be approved every year, causing an unstable financing situation (Table 3). The solution to this problem is different in each country (Table 4). As shown in Table 3, there are still some restrictions in access to treatment-related uninsured patients (Bulgaria, Hungary, Slovakia), active alcohol and drug users (Croatia, Czech Republic, Poland), prisoners (Bulgaria, Slovakia), failures to respond to DAA (Latvia) and the difficult reimbursement process of pangenotypic regimens (Hungary). Poor linkage to care in all countries is caused by a number of out-patient visits between diagnosis and the beginning of treatment and it can be solved by fast track referrals to treating centres and removal of administrative barriers (Tables 3 and 4). A growing problem seems to be insufficient staff in all countries (Tables 3 and 4).

None of the reporting countries has established a national screening programme (Table 3); therefore the WHO 2030 target is recognized as impossible or at least difficult to achieve without screening of a sufficient number of patients (Table 4). According to subjective expert opinions, the WHO 2030 target can be reached in Croatia, Latvia, and Lithuania. Representatives of other countries are considering such an opportunity with some conditions (Hungary, Slovakia) or do not consider the WHO 2030 target to be realistic (Bulgaria, Czech Republic, Poland) (Table 5). As shown in Table 5, the highest score (31) among all factors that can affect HCV elimination was obtained by financial coverage of therapy, meaning basically no limitation, whereas the lowest was presence of national screening programmes, representing the most relevant barrier.

Table 3. The biggest barrier to HCV elimination

	Bulgaria	Croatia	Czech Rep.	Hungary	Latvia	Lithuania	Poland	Slovakia
Political will	HCV not a health policy priority	HCV is of moderate health policy priority	HCV not a health policy priority	HCV is of moderate health policy priority	HCV is of moderate health policy priority	HCV not a health policy priority	HCV not a health policy priority	HCV not a health policy priority
Financial coverage of therapy	HCV treatment budget needs to be approved every year again	HCV treatment budget needs to be approved every year again	HCV treatment budget needs to be approved every year again	HCV treatment budget needs to be approved every year	HCV treatment budget needs to be approved every year again	HCV treatment budget needs to be approved every year again	HCV treatment budget needs to be approved every year again	No reimbursement of HCV treatment for PWID and prisoners
Treatment restrictions	No reimbursement for health uninsured people	Limitations related to active alcohol and drug abuse	Some limitations related to alcohol and drug addicts	Some limitations in access to pangenotypic regimens	Some limitations in treatment access for DAA failures	Access to treatment limited by degree of inflammation or fibrosis	Some limitations related to active alcohol and drug abusers	No reimbursement for active PWID, prisoners and health uninsured people
Medical staff capacity	Insufficient staff in some treating centres	Sufficient staff in all treating centres	Insufficient opening hours in some treating centres	Shortage of non-medical staff	Insufficient staff in all treating centres, waiting lists to infectologists	Sufficient staff in all treating centres	Insufficient staff in some treating centres	Sufficient staff in all treating centres
National screening programme	No screening policy and reimbursement, but expected shortly	No national screening programme, mandatory screening in some risk groups	No screening policy and reimbursement, but expected in 2020	No screening policy and reimbursement	No screening policy and reimbursement	No screening policy and reimbursement	No screening policy and reimbursement, disregard of screening in prisons	No screening policy and reimbursement
Linkage to care	Too many visits needed for final diagnosis and start of the treatment	Too many visits needed for final diagnosis and start of the treatment	Too many visits needed for final diagnosis and start of the treatment	Too many visits needed for final diagnosis and start of the treatment Underserved populations are not linked to care	Too many visits needed for final diagnosis and start of the treatment	Too many visits needed for final diagnosis and start of the treatment	Too many visits needed for final diagnosis and start of the treatment	Too many visits needed for final diagnosis and start of the treatment
Barrier to achieve WHO 2030 target?	Insufficient number of diagnosed and treated patients annually	Insufficient number of diagnosed and treated patients annually	Insufficient number of diagnosed and treated patients annually political will to include PWID	Insufficient number of diagnosed and treated patients annually	Insufficient number of diagnosed and treated patients annually	Insufficient number of diagnosed and treated patients annually	Insufficient number of diagnosed and treated patients annually. No will to screen prisoners	Insufficient number of diagnosed and treated patients annually especially PWID and prisoners

Table 4. Projects or initiatives aimed to remove the barriers for HCV elimination

	Bulgaria	Croatia	Czech Rep.	Hungary	Latvia	Lithuania	Poland	Slovakia
Political will	National hepatitis elimination plan – evidence-based and financially secured	National action plan for prevention and control of viral hepatitis finalized in July 2019 at the Ministry of Health, still not adopted by the Government	Creation of the HCV in IVDUs Eradication Committee supported by national Monitoring Centre for Drugs and Addiction	Creation of the National Hepatitis Committee, to form a national elimination programme. Universal screening for health care workers by June 2020	Creation of the HCV Eradication Committee at Ministry of Health in 2017, regular update of local recommendations and setting of treatment priorities	Attempt to form a national elimination programme	Approval by Health Ministry or National Health Fund of one of several screening programmes already submitted by expert groups	Screening programme, especially for high risk populations (PWID, prisoners)
Financial coverage of therapy	HCV included as national health priority in state budget and financing also treatment for health uninsured people	Special budget for HCV therapy at national health insurance fund to avoid burden of hospital budgets	HCV included as national health priority for health care payers with an annual increase of treatment budget by 30%	HCV included in national insurance fund budget to allow treatment of all diagnosed	HCV included in state budget as one of priorities	HCV treatment included as one of priorities in state budget with stable financing since 2018	HCV included as national health priority in state budget to assure screening and treatment budget for next 3 years	HCV included as national health priority in state budget, reimbursement of HCV treatment for PWID and prisoners
Treatment restrictions	Increase of treatment rate among vulnerable and hard to engage and retain risk populations	Removal of restrictions for active alcohol and PWID For patients at OST-psychiatrist consultation recommended	No treatment restrictions in the high prevalence groups (PWID)	Access to pangenotypic drugs	Removal of limitations for DAA failures	Removal of any limitations related to inflammation or fibrosis	Removal of limitation for active alcohol and drug abusers	Removal of all limitations from the therapeutic programme
Medical staff capacity	Increasing staff in treating centres, education of GPs and addiction specialists	Education of GPs and addiction specialists, and general population is needed	Increasing staff in HCV centres, education of GPs, and harm-reduction centre workers	Sufficient medical staff. Increase of non-medical support is not foreseen	Education of GPs, for proper examination before sending to specialist	No need of additional staff	Staff requirements established by National Health Fund to apply pressure on the hospital administration	Medical staff capacity is adequate, no need of additional staff
National screening programme	National screening programme created according to expert recommendations	National screening programme created according to National Action plan recommendations mainly aiming at screening of populations at risk	National screening programme “under construction” supported by Ministry of Health	Preparation of HCV screening programme is ongoing. General HCV screening of pregnant women is planned for 2020 (HBV is already screened)	National screening programmes – donors, dialysis pts, pregnant women	National screening programme is on preparation, but date of possible implementation is still undetermined	Several experts proposals ignored by Health Ministry. Ongoing preparation submitted to National Health Fund	National screening programme created according to expert recommendations, especially in IVDU and prisoners
Linkage to care programmes	Fast track referral for HCV diagnosed patients to treating centres	fast track referral for HCV diagnosed patients to treating centres	fast track referral for HCV diagnosed patients to treatment centres	Logistics for underserved populations (PWID, MSM)	Recommendations for GPs for max examination and fast track referral for HCV diagnosed patients to treating centres	fast track referral for HCV diagnosed patients to treating centres	fast track referral for HCV diagnosed patients to treating centres	Fast track referral for HCV diagnosed patients to treating centres, removal of administrative barriers
How to achieve WHO 2030 target?	National plan for elimination of viral hepatitis – covering all stages from screening, diagnosis, linkage to care and treatment	Need to screen at least 100,000 people annually in order to diagnose and treat 500-600 annually in order meet WHO targets at reducing mortality by 65%	Need to screen enough patients to treat 6000 patients annually	Need to screen enough patients (0,4-0,5 million) to treat 4000 annually	Need to screen enough patients to treat ~3000 annually	Need to screen enough patients to treat 2400 annually. Special attention to PWID and prisoners	Need to screen 3 million patients, to treat 12,000 annually	Need to screen enough patients, especially in risk groups

Table 5. How close to HCV elimination? Score for particular factors affecting HCV elimination, from 0 (minimal) to 4 (maximal)

	Bulgaria	Croatia	Czech Rep.	Hungary	Latvia	Lithuania	Poland	Slovakia	Total score
Political will	1	3	3	3	2	2	1	1	16
Financial coverage of therapy	4	4	4	4	4	4	4	3	31
No treatment restrictions	4	3	3	3	3	2	3	1	22
Medical staff capacity	3	3	3	3	2	3	3	3	23
National screening programme	2	2	0	1	2	1	1	2	11
Linkage to care programmes	2	3	3	2	3	2	1	1	17
Is WHO 2030 realistic?	No	Yes	No	Maybe	Yes	Yes	No	No*	

*WHO 2030 target could be realistic, if DAA therapy were reimbursed for active IVDU CHC patients.

Discussion

In 2016, the WHO initiated an ambitious plan to eliminate viral hepatitis as a public health threat by diagnosing 90% of HCV infections and treating 80% of all eligible patients by 2030. The goal of the WHO is reduction by 90% in HCV incidence and 65% in HCV-related mortality [5].

DAA treatment has been reimbursed in Bulgaria since 2016 for a selected groups of patients, but all restrictions were removed in 2017 for all patients with health insurance. Health insurance is not available for 12% of the general population and more that 50% of marginalised populations (PWID) [7]. Intravenous drug use is a leading cause of the spread of HCV infection in Bulgaria currently, with constantly increasing HCV prevalence, which in 2017 was reported to be 76.8% [8]. Existing measures in the field of harm reduction and treatment are not sufficient to limit and to control HCV infection among PWID. High seroprevalence is also reported among prisoners (26%), among the Roma community (24.6%) and sex workers (11%), but the diagnostic and treatment rates in these populations are not available [9-11]. Lack of a national screening programme is the main reason for the low diagnostic and treatment rates. The Ministry of Health is working on the plan and strategy for viral hepatitis elimination. The diagnostic and treatment rates in Bulgaria are not sufficient to achieve the WHO 2030 targets, so previous modelling studies need to be reassessed and scaled up.

The major HCV-related problem in Croatia is the currently high (up to 35%) prevalence of the infection among PWID. The first available interferon-free combination was ombitasvir/paritaprevir/ritonavir ±dasabuvir (OPrD) in 2015. Access to DAA-based therapy was initially limited to advanced liver disease,

but since 2018 it is available irrespective of fibrosis. Unfortunately it is still not reimbursed for active intravenous drug users and alcohol abusers [12, 13]. Screening is mandatory for blood or organ donors and dialysed patients. In PWID, HIV-infected persons and some other groups it is recommended only. In 2019 HCV elimination was achieved in liver transplant patients. A plan for prevention and control of viral hepatitis is ready and waiting for the final approval by the Ministry of Health, so Croatian experts are optimistic regarding HCV elimination by 2030 [14, 15].

In the Czech Republic prevalence of anti-HCV in PWID is 58.6% according to recent data. There is no screening programme in the Czech Republic, but some populations, such as blood donors, healthcare workers, patients on maintenance haemodialysis, prisoners and drug users, are screened on a regular basis. DAA-based regimens became available in 2014 and currently there is no restrictions in access to therapy. HCV elimination has already been achieved in all solid organ transplant recipients and in haemodialyzed patients. A national action plan of elimination of viral hepatitis C in PWID was approved by the Government Council for Drug Policy Coordination in August 2019, and guidance for prevention and control of viral hepatitis in the Czech Republic endorsed by the Ministry of Health and the Czech Society of Hepatology (written according to WHO guidelines) will be launched in March 2020 [16, 17].

Interferon-free regimens became available in Hungary in 2015 for the highest priority HCV-infected patients (F3-F4 and special conditions) based on a priority scoring system. Access was expanded to a wider variety of patients in the following years, but there is still limited access to pangenotypic regimens, which seems to be the major HCV-related problem in Hungary. HCV prevalence and genotype distribution are different in prisons compared to the general popula-

tion [18]. A national screening programme is not approved and the therapeutic programme should be simplified to improve linkage to care.

Due to the high proportion of unknown transmission and undefined risk factors, the biggest challenge in Latvia is to develop the best screening approach to achieve WHO targets. An interesting observation in Latvia is higher HCV prevalence in males (3%) than in females (1%) and lower prevalence in health care professionals (1.2%) compared to the general population (1.7%) [19, 20]. DAA-based therapy has been reimbursed since 2016 and the first was OPrD. The pangenotypic SOF/VEL regimen became available in 2018. There is still discussion on the possible national screening strategy, but without a decision at the ministry level up to now. Anyway, experts from Latvia still believe that WHO targets of HCV elimination are achievable.

Serious obstacles for HCV elimination in Lithuania are the lack of a screening programme and high prevalence of HCV infection among PWID, which can reach up to 80% [21]. Access to OPrD combination started in 2015 and the first pangenotypic regimen GLE/PIB became available in 2018. Moreover, there are still some restrictions in access to DAA-based therapy, related to hepatic fibrosis. Confirmed viraemic prevalence is about 0.9%, and the rate of anti-HCV according to different studies is between 1.2 and 2.8% [22, 23, and Kupcinskas – unpublished data]. Despite all these facts, experts in Lithuania are optimistic to achieve the WHO target by 2030.

Access to DAA-based therapy in Poland started in 2015 and from the beginning it was available for all patients irrespective of fibrosis [24, 25]. Waiting lists for treatment were cleared and currently the major problem is the lack of political will to support a national screening programme. Moreover, testing of prisoners is still blocked by prisons administration despite the well-known higher prevalence of HCV infections in this population. According to the most recent estimations to achieve targets of the WHO programme it is essential to screen about 3 million and cure 12 thousand inhabitants annually [26]. Unfortunately the number of treated is falling due to lack of a national screening programme, so achievement of the WHO 2030 target is unlikely.

Sofosbuvir monotherapy in Slovakia became available in 2014, whereas SOV/LDV and OPrD became available in 2015. Prevalence of HCV infection declined significantly in Slovakia in the last two decades from 0.67% to 0.1% [27-29]. Since half of infected patients are from high risk groups (PWID and prisoners) the only way to reach the WHO target is screening and

treatment in these populations. Unfortunately at this moment treatment of HCV in high risk groups is not a health policy priority in Slovakia.

According to collected data and expert opinions it can be concluded that access to therapy for HCV is similar and the majority of patients in Central Europe can be treated according to the current international guidelines. Unfortunately there are still some limitations in access to treatment, particularly in PWID and prisoners. Apart from Croatia and the Czech Republic there is a universal problem of no political will to implement national screening programmes, which will be crucial to achieve the WHO 2030 target. The majority of experts are pessimistic regarding HCV elimination according to the WHO programme, but on the other hand Lithuania and Latvia consider it possible despite the lack of a national screening programme. Answering the title question, we can assume that HCV elimination will not be possible in the region by 2030. However, significant reduction of HCV infection will be achievable and a subsequent decrease of HCC and cirrhosis cases should be observed in the next decades.

Disclosure

The authors report no conflict of interest.

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