

Viral Hepatitis Prevention Board

Prevention and control of viral hepatitis in the Russian Federation: lessons learnt and the way forward

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The Viral Hepatitis Prevention Board, with the co-sponsorship of the Sechenov University (Moscow, Russian Federation), organized a meeting with the following objectives:

- to review the epidemiological situation on viral hepatitis and burden of disease in the Russian Federation

- to provide an overview of surveillance systems for viral hepatitis and infectious diseases, current approaches to treatment of chronic viral hepatitis, current issues of organization of medical care and access to treatment for patients with viral hepatitis

- to identify achievements and challenges in prevention and the possible implementation of new national prevention strategies

- to discuss the development and implementation of a national plan of action to control viral hepatitis in Russia

- to evaluate what is still needed to achieve the viral hepatitis elimination goals defined by the WHO global health sector strategy on viral hepatitis and WHO's Regional office for Europe, identifying successes, issues and barriers to overcome, and the way forward.

The meeting, drawing participants from the four corners of the country, provided a welcome opportunity to share experience and find solutions.

Among VHPB's series of country meetings in the WHO European Region over the past 20 years or so, this was the most challenging, given that the country is by far and away the largest and most diverse in the Region: more than 17 million km², 11 time zones, a population of about 147 million (more than 80% ethnic Russians), and 85 constituent "subjects" (these entities are divided into eight Federal regions)^a. The average salary is currently the equivalent of €550 (42,000 rubles) a month¹ but the urban-rural divide is widening with poverty becoming a largely rural phenomenon.

^a Including Crimea and the city of Sevastopol. According to the Russian Constitution, the Russian Federation consists of republics, krais, oblasts, cities of federal importance, an autonomous oblast, and autonomous okrugs, all of which are equal subjects of the Russian Federation.

Context

In the 2030 Agenda for Sustainable Development, adopted in 2015, Goal 3 (ensure healthy lives and promote well-being for all at all times) includes a target “to combat viral hepatitis”. In 2016, the World Health Assembly adopted the global health sector strategy on viral hepatitis², and the WHO Regional Committee for Europe endorsed an action plan for the health sector response to viral hepatitis in the WHO European Region³.^b The Regional Action Plan set the goal of elimination of viral hepatitis as a public health threat by 2030: in other words, “reduce incidence and mortality by 90%”. It also sets interim hepatitis B control targets to be achieved by 2020. In support of these policy documents, WHO has issued numerous guidelines and recommendations, ranging from policy briefs to technical guides, and the WHO Regional Office for Europe has issued a publication on the United Nations common position on ending HIV, tuberculosis and viral hepatitis through intersectoral collaboration.⁴

For the past four years the WHO Regional Office for Europe has also been working with the Ministry of Health in the Russian Federation on a country cooperation strategy for strengthening the national health system and reinforcing health promotion and prevention.⁵ The strategy covers the years 2014-2020.

It is acknowledged that the Russian Federation has made good progress on preventing and controlling viral hepatitis in the past two decades, but nevertheless the diseases, especially hepatitis C, remain a serious public health problem.

Health care systems in the Russian Federation

The country’s Constitution (Article 41) guarantees “the right to health protection and medical aid ... rendered to individuals gratis”. Viral hepatitis is specifically covered by several specific federal laws and sanitary-epidemiological regulations⁶. It was observed, however, that guaranteed rights do not always correspond to reality.

Recent strategic documents (2015-2017) aim at the formulation of uniform policies and prioritization of funding. Presidential Decree 204 of May 2018 on national objectives and strategic tasks for the country’s development to 2024 identified health as a national health project to 2030⁷. Under this heading, two specific projects relate to cancer control, including liver cancer associated with viral hepatitis, and ensuring optimal access to primary health care (through which 60% of health care is delivered). Goals and expected results include increasing treatment, reducing mortality and educating the general population.

The **Ministry of Health** sets policies and the legal framework for health care and disease prevention. It delegates responsibilities for implementation through national medical centres, federal and regional health institutions, and inter-regional specialized care entities to facilities at district, municipality and community levels (including feldsher/midwife posts in remote areas), and oversees their operation. These total 81,000 in 156,000 communities. The Ministry is responsible for issuing clinical

^b Both documents are available in Russian.

recommendations and ensuring their incorporation into practice, and quality control criteria.

The Ministry of Health has constituted an expert group to draft a new law on public health and biosecurity. This law will include prevention and treatment among its priorities and build on healthy lifestyles and more access to good-quality health care. It will cover inter alia provision of treatment and care, better surveillance, and raising public awareness. It will also reflect clinical recommendations. It is under consideration by the federal Government. This draft federal law is expected to provide the legal basis for a more specific federal law on viral hepatitis in the Russian Federation, including prevention, care and treatment, and to set a clear framework for the Patient Registry. In addition, in 2019 programmes on prevention and treatment of “socially significant diseases”, including improvements in the regulatory framework, quality assurance of diagnosis and treatment, and surveillance, will be implemented.

Funding of health care derives from State and regional budgets (through tax levies) and insurance (mainly the Federal Compulsory Medical Insurance Fund). These sources are supplemented by patients’ out-of-pocket payments. A programme of State guarantees of free medical care determines the minimum volumes of medical care and the financial resources to ensure them; government funding is linked to identified needs and reflects costs of all relevant services rather than being related solely to numbers of patients as at present. Doubts were expressed that funding would increase much in the immediate future unless there were much greater pressure from experts and the community. State policy allows for voluntary (private) health insurance and this market is growing, particularly in large cities.

The mandatory health insurance programme covers the provision of medicines for primary care at day care facilities and in emergencies, as well as for all types of inpatient care. However, it does not cover the provision of medicines for outpatient care. Clinical guidelines have been produced as the basis for setting medical and economic standards in relation to diagnosis-related groups, but not all regions follow them. Presidential Decree 204 also sets the objective of implementing clinical guidelines and medical protocols and using them for setting payment rates. Although several international guidelines for the treatment of viral hepatitis have been published (such as those of the European Association for the Study of the Liver, EASL), existing Russian guidelines have been adapted to take into account international recommendations and the local context.

The **Federal Service for Surveillance on Consumer Rights Protection and Human Well-being (Rospotrebnadzor)** is the executive body that is responsible for carrying out the federal state sanitary and epidemiological surveillance, as well as developing and approving the state sanitary and epidemiological guidelines. Rospotrebnadzor reports directly to the Government of the Russian Federation. It operates at federal, regional and municipal levels in close collaboration with the Ministry of Health. The Reference Centre for Viral Hepatitis serves as an expert body for Rospotrebnadzor in the relevant field.

Rospotrebnadzor’s planned future activities include updating the Sanitary and Epidemiological Rules for hepatitis B and C^c, making hepatitis D a notifiable disease at

^c The previous ones date from 2008 for prevention of hepatitis B and 2013 for prevention of hepatitis C.

the federal level, enhancing screening programmes for hepatitis B and C, and improving the recording of outcomes of chronic hepatitis in terms of cirrhosis and hepatocellular carcinoma.

Simultaneously with the meeting, Heads of State and Government adopted the Declaration of Astana, reaffirming their commitment to primary health care and attainment of the Sustainable Development Goals.⁸ In the Russian Federation 60% of health care is delivered through primary health care services.

Prevention – vaccination

Vaccination against **hepatitis A** is not included in the current immunization schedule in the Russian Federation. The Republic of Tyva^d introduced single-dose vaccination in 2012. Since then nearly 90% of children aged 3-8 years have been vaccinated. This preventive measure had a dramatic impact on incidence rates in both the entire population of the Republic and especially children, with no case in the latter since 2016. In 2018 the Republic's health ministry authorized mass vaccination of children and adolescents.

According to WHO, 16 countries in 2016 used hepatitis A in routine immunization of children. Some countries are looking at single-dose vaccination while others still practice full vaccination of risk groups, but it was commented that there was no alternative to universal vaccination.

Hepatitis B vaccine was first introduced into the Russian Federation in 1996 for vaccination of newborns, children and adults at high risk of infection with HBV. The following year the policy was expanded to universal vaccination of newborns, and in 2001 to all children at 13 years of age. Catch-up vaccination programmes began in 2006, for children aged 1-17 years and adults from 18-35 years, and in 2007 for adults aged 18-55 years. By 2004, coverage of 1-years-olds with three doses of vaccine was 96.1% and has remained above that level ever since. Data on timeliness of birth dose are not available as this information is not officially reportable. The rates for adults (84% of 36-55-year olds) in 2017 are approaching the targets, although some regions are lagging behind.

Both Russian-made vaccines and foreign-purchased vaccines are used. Some of the Russian products contain antigen constructed from *ay* HBV subtype, while others contain *ad* subtype antigen.

Since the campaign began, about 100 million people have been vaccinated. The incidence rate of acute hepatitis B significantly decreased and in 2017 reached 0.86 cases per 100,000 population.

With further data needed to confirm attainment of regional goals, future work aims at ensuring registration and improving record-keeping of the administration of the birth dose of vaccine. In addition, a serosurvey on HBsAg prevalence in vaccinated cohorts is needed in order to evaluate the effectiveness of the immunization programme.

^d An area in southern Siberia four times the size of Switzerland with a population of 320,000 people.

Surveillance

In 2016 WHO published a monitoring and evaluation framework for viral hepatitis B and C, with a special focus on acute and chronic disease, recommended indicators, a framework and a protocol for surveillance of sequelae.⁹ Also in 2016, it issued guidelines on surveillance of viral hepatitis¹⁰ and new recommendations for the screening, care and treatment of persons with chronic hepatitis C infection – a policy brief¹¹.

In the Russian Federation, Rospotrebnadzor collects, analyses and disseminates surveillance and epidemiological data and information, and its activities include forecasting and planning specific anti-epidemic actions and target setting for plans. Since 2011 a web-based information system drawing information on viral hepatitis from reference centres has been operating. The epidemiological pattern that appears shows considerable variations across the country; these are thought to be both real differences and reporting artefacts. The data for the Republics of Tyva and Sakha seem to be unique, but the overall picture may reflect poor access to diagnosis and treatment.

Although the Federal Registry of Viral Hepatitis Patients was established in 2012 to collect systematically uniform personal and epidemiological information on hepatitis B, C and D as well as on treatment and outcomes from national, regional and local levels, it is not yet implemented in 13 of the 85 constituent subjects of the country. The Registry allows disaggregation of data by age, sex, route of transmission (HCV), genotype, fibrosis stage and detection of temporal changes. Work is being undertaken or planned to fully implement it nationally and to improve it through the addition of modules on monitoring, clinical and laboratory data, antiviral treatment and statistics. With some 500,000 patients on record, it is a “living and evolving system”.

Most deaths in patients with viral hepatitis are due to late complications (cirrhosis and hepatocellular carcinoma), but in most cases the viral infection is not entered on the death certificate which requires a single underlying cause of death to be recorded. That means that the real burden of disease is underestimated; this problem is not restricted to the Russian Federation. Adoption of the multiple-causes-of-death approach would more fully describe the burden of disease associated with chronic viral hepatitis (and indeed other chronic diseases). Data on outcomes are vital for an appreciation of the true burden of chronic hepatitis. With that in mind a six-month study was undertaken of deaths recorded as having a viral hepatitis-related single underlying cause in Moscow in 2018: the results showed that HCV caused 7.4 times more deaths than HBV, whereas in Europe that ratio was less than 3.0.

Epidemiology

HAV and HEV

HAV. The changing epidemiology of hepatitis A seen in the Russian Federation, with declining incidence rates since 1977, mirrors global trends and reflects improved socioeconomic conditions (including a declining birth rate), better hygiene and sanitation, and fewer organized camps and activities for young people. The numbers of older susceptible people and cases of more serious disease are increasing; only 25% of all reported cases in 2017 were in children under 17 years of age. The national average

incidence rate in 2017 was 5.5/100,000 population¹² but the rates vary widely across the country with very varied patterns of HAV epidemiology.

Outbreaks still occur, mainly through contaminated water and food. Reported transmission routes, however, are changing, with more cases in people who inject drugs (PWIDs) and men who have sex with men (MSM). Lessons can be learnt from other countries with recent outbreaks (e.g. in homeless people and PWID in the USA), including determining the need for universal vaccination, especially for risk groups.

The national routine immunization schedule does not prescribe hepatitis A vaccination but allows divergent regional policies.

HEV. Hepatitis E has been a notifiable disease in the Russian Federation since 2013. Only a few cases are seen, including some that are imported, but there is some serological evidence of infection and rising seroprevalence rates in the population. Highest rates are seen in the Central Federal Region, including the Belgorod region, a centre for pig breeding. The contribution of pig farms to HEV epidemiology through the presence of the virus in sewage has been confirmed in the country. Awareness among doctors and public about the virus and the disease remains very low.

HBV

The impact of hepatitis B vaccination has been dramatic:¹³ the incidence rate of acute hepatitis B had fallen in 2017 to 0.9/100,000 population and for chronic hepatitis B (including carriage of HBsAg) to 19.7/100,000. About 3.3 million people were immunized in 2017, giving a cumulative total of about 100 million people vaccinated. Vaccination coverage rates for children have reached targets and those for adults are approaching the targets. Screening of pregnant women is almost 100% with accurate data (showing an average seroprevalence rate of 0.2% but rising to 8% in some regions). This significant progress is widely acknowledged, but regional and local variations demand further attention.

Incidence rates of acute disease indicate large falls in most of the country, with a five-fold decrease since 2008 to a rate of 0.86/100,000 population in 2017.¹⁴ Nevertheless, pockets with rising rates are reported (for example, in the Rostov region), particularly in 30-39-year olds.

Rates of chronic disease vary across the country, but overall the rate is falling. Rates of newly diagnosed chronic HBV infection as high as 54/100,000 population have been reported in the Republic of Tyva in 2017, and high incidence rates are still seen in regions such as the Republic of Sakha (Yakutia) and in Saint Petersburg, Kaliningrad and Novgorod – the North-West Federal District generally has had a rate double that of the national average for two decades. The highest prevalence rates of chronic disease are found in people aged 30 to 60 years (from 258/100,000 in 50-60-year olds to 290/100,000 in 40-49-year olds). In 2017, some 28,900 cases of chronic HBV infection were newly identified.

The most common genotype of HBV is D, which is found in 85-90% of cases. Subgenotypes D1, D2 and D3 cocirculate in the majority of country regions. Genotype A is the second most frequent genotype and is represented only by subgenotype A2.

A survey is being undertaken to estimate the seroprevalence of HBsAg carriage and other markers of HBV infection among schoolchildren across the country. Some 12,000 children in eight federal districts will be covered by the survey.

HDV

Cases of hepatitis D are reported from all over the country. A high prevalence rate is seen in several regions of the country, one of which is Republic of Tyva (where a prevalence rate for HBsAg of 8.1% is reported and 28% of HBsAg-positive people are positive for anti-HDV, with the highest rate (75%) in those aged 40-49 years). The most common genotype seen throughout the country is 1. The unique genotype 2 found in substantial number of cases only in Republic of Sakha (Yakutia).

Intrafamilial transmission is reported. The data are, however, poor because the disease is not notifiable; all cases are reported in combined statistics with those for hepatitis B.

Treatment relies on pegylated interferon regimens, although new compounds with different modes of action are in clinical trials.

HCV

Nationally, the incidence of **acute hepatitis C** has fallen to low levels (1.2/100,000 population in 2017) but it was pointed out that relying on identification of symptoms was an insensitive indicator, as in most cases the infection is asymptomatic.

The estimated number of cases of hepatitis C infection in the country is put at 5.7 million, about the sixth highest total in the world, with about 51,000 new cases identified in 2017. In terms of the cascade of care, estimates show that, of the 5.7 million, 2.9 million (51%) have been diagnosed and, of those, 1.6 million cases (55%) have been confirmed by HCV RNA testing. In only about one third of those RNA-positive cases (about 600,000) have the patients been linked to the care system (although that figure is twice as high as in 2011) and only 29,600 (5%) of them treated. The cure rate is 72%.

The rate of newly diagnosed chronic hepatitis C cases (about 35/100,000 population in 2017) is highest in 30-39-year olds but declining, whereas it is increasing in older age groups. Similar patterns are seen for both men and women. A fall in rates between 2014 and 2017 may reflect a decline in the epidemic of injecting drug use that burst on the country in the 1990s. High recorded rates may reflect good screening and reporting practices. The argument for community screening was underlined.

The accepted algorithm for diagnosis of HCV infection specifies testing for anti-HCV antibodies, then, if positive, HCV RNA, followed by either monitoring and treatment of a current infection or repeat testing for IgG antibodies and HCV RNA in six months. In 2017, only 60% of diagnoses of hepatitis C were confirmed by an HCV RNA test. Testing

for HCV RNA is neither universally available nor covered by mandatory insurance. Testing for HCV antigen may be used as a confirmatory test to simplify the algorithm.

HCV contributes substantially to cirrhosis and liver cancer in the Russian Federation as in the rest of the world (globally chronic viral hepatitis is thought to cause 1.3 million deaths annually, comparable to the mortality due to HIV, tuberculosis or malaria). Viruses, HCV in about two-thirds of cases, account for at least 44% of cases of cirrhosis in the country and HCV and HBV together account for more than half the cases of hepatocellular carcinoma, although much better data are needed on the contribution of hepatitis viruses to morbidity and mortality due to liver disease.

Regional patterns

Reports were presented from six very different regions of the country.

The **Chelyabinsk Region** is a large industrial area in the **Ural Federal District** with most of the population of 3.5 million (83%) living in cities. Its viral hepatitis disease burden is high (an estimated 109,000 cases of chronic hepatitis C in 2017 - the rate of newly reported cases of 55/100,000 is among the 10 highest in the country). Funding to cope with that burden is insufficient. There is some access to direct-acting antiviral agents, but most patients make out-of-pocket payment for treatment. The Viral Hepatitis Registry is functioning, so helping to identify the extent of the problem of viral hepatitis and the associated needs. Mathematical modelling has been applied to project the epidemiological pattern of chronic HCV to 2030; the results showed a peaking of new infections in 2018 but rising numbers of primary and treated cases to 2030.

Numerous steps have recently been taken to improve the prevention and control of viral hepatitis. These include stronger links between health facilities at different levels, introduction of modern serological and molecular diagnoses, the use of transient elastometry, training of health care workers, collaboration with patients' associations, and adoption of a multidisciplinary approach.

Barriers to implementing the cascade of care include: poor definition of target groups with above-average incidence of HCV infection and difficulty of contacting hard-to-reach groups; long distances to travel to existing screening facilities; loss to follow-up after screening; lack of awareness among general practitioners, especially about the criteria for testing for HCV antibodies; and poor linkage to care. Limited access to treatment reduces motivation to be screened. Untreated subjects and patients who are treated privately are not included in the reporting system.

Krasnodar krai is part of the **Southern Federal District**, the southernmost area of the country. Chronic viral hepatitis is a public health problem, but the incidence rates are lower than the national average. The Viral Hepatitis Registry has been functional in the Krasnodar krai for more than one year. The region has a specialized hepatology centre that provides diagnosis, treatment and care, laboratory services and a liver transplant unit. Patients are referred from health facilities at the municipal level to the centre via four regional hospitals. Nevertheless, nearly two-thirds of patients with HCV infection are seen at a late stage of fibrosis.

Some 83% of 1554 patients seen in 2016-2017 paid for their treatment out of their own pockets, with only 11% being covered by the medical insurance fund and 6% by the federal drug coverage scheme. Direct-acting antiviral agents are available but expensive.

To reach the targets of WHO's strategy for chronic hepatitis C in 2030, it is projected that the number of treated cases will have to increase to 5060 with a sustained viral response and that the number of newly-diagnosed cases will plateau at just over 14,000 between 2022 and 2030. The rate of new cases of infection is expected to decline from a peak of 10,400 in 2018 to 1030 in 2030.

Future steps envisaged included: extension of an existing screening programme for chronic viral hepatitis; use of modern diagnostic methods; better monitoring and recording of patients; increased accessibility to treatment; training of health professionals; and increasing awareness among general population. The need for a national plan was stressed.

The **Far-East Federal District**, home to 6.2 million people, comprises eight regions, including the Primorskiy Region (1.9 million people), the Republic of Sakha (Yakutia) and the autonomous area of Chukhotka (see below).

In the Primorskiy Region, patients with chronic hepatitis B are referred from local health facilities to polyclinics providing ambulatory care and thence to the regional centre for confirmatory diagnosis and treatment. Most patients with chronic hepatitis B and C are diagnosed at early stages of fibrosis (F0 or F1) but increasing numbers of patients progressing to cirrhosis are being recorded. In 2018, the total number of cases of chronic hepatitis C recorded in the Registry was 13,200, of whom 639 have been treated, 29% with non-interferon-containing regimens. The highest prevalence rates of chronic viral hepatitis are seen in the 30-39-year age group with progressively lower rates in older age groups and some infections seen in 20-29-year olds. For HBV genotype D predominates (64%) and for HCV genotype 1 accounts for 55% of cases, followed by genotypes 3 then 2.

The **Republic of Sakha (Yakutia)** occupies some 18% of the territory of the Russian Federation, 40% of it lying above the Arctic Circle, with a very low population density and low-income communities outside the main centres of population. For some years, the Republic has had an incidence of chronic viral hepatitis (B and C) that is almost double the national average, a rate of hepatocellular carcinoma (20/100,000 in 2015) 4-5 times the national average and increasing mortality from cirrhosis; the rate of HBsAg carriers was 15/100,000 in 2017. The high prevalence of chronic hepatitis B, C and D and the number of cirrhotic patients explains the growing waiting list for liver transplants (for which a selection and procedural algorithm exists). More than 15,000 patients with chronic hepatitis have been recorded in the Viral Hepatitis Registry, about 6800 with hepatitis C, 6400 with hepatitis B and 1100 with hepatitis D.

The linkage to care starts with infectious disease surgeries and polyclinics in regional centres and cities, through regional hospitals to the main hospital in Yakutsk and the associated national medical centre. Over six years some 1013 patients have been treated, but funding for treatment is minimal. The health authorities have invested in

prevention, with a liver cancer prophylaxis and treatment surgery in Yakutsk, mobile outreach teams offering screening, introduction of telemedicine, education of the general population and people at risk, and continuing training for health workers including students.

In the extreme south-west of the country, the **North Caucasus Federal District** is a geographically and ethnically diverse constituent entity. The rate of annually reported cases of chronic hepatitis C in the District is less than half the national rate except in one Republic (Karachay-Cherkess), where it has recently risen. The rate of carriage of HBsAg has also declined significantly (especially so in the Dagestan Republic) over the past 10 years, with the rate for chronic hepatitis B generally following the downward trajectory to 1-5/100,000 population. Some 27,000 cases of chronic hepatitis B have been recorded in the Registry (although it is not operational in all areas). Follow-up of patients with chronic viral hepatitis is poor, and the dynamics of the disease are not clear. Only in one of the seven administrative subdivisions of the District are all patients with chronic hepatitis C routinely tested for stage of fibrosis, viral load and genotype.

The picture that emerges from across the District are that HCV genotypes 1b and 3 predominate equally, followed by genotypes 2 and 1a. Treatment is almost entirely with interferon-containing regimens and mostly (56%) at the patients' own expense, with 31% funded by the Essential Drugs Supply Programme. The overall picture of the cascade of care is also not clear, because of a lack of testing and follow-up. One positive experience is provided by the Kabarda Balkar Republic, whose health ministry has established a diagnostic and treatment centre for chronic viral hepatitis, defined the pathway for linkage to care, and allocated funds for biomolecular testing and transient elastography.

At the opposite end of the country is the **Chukotka Autonomous District**, described as "the end of the world": a population of only 49,000 people (52% ethnic Russians and the rest indigenous) spread across 700,000 km², with 70% living in towns, a severe climate, long distances between communities (served sometimes only by an air bridge), a traditional socio-cultural life-style with large movements of populations, and where prescriptive regulations are hard to apply. The incidence of acute hepatitis A has been practically zero for almost a decade and that for acute hepatitis B low (2/100,000); no case of acute hepatitis C has been seen since 2010. The incidence rates for chronic hepatitis B and C have been declining for 10 years to 10 and 12/100,000, respectively, in 2017, and no carrier of HBsAg has been detected in the past two years. The health authorities are conscious of the need to extend hepatitis B vaccination, to introduce better diagnostic methods and to aim to screen the entire population, especially people living in hard-to-reach places, to extend health education among health workers, and to raise awareness of the general population.

Risk groups

Hepatitis B and C continue to be occupational diseases of **health care workers**, but the prevalence of these chronic diseases is generally lower among them than in the general population. The risk increases with poor training, non-compliance with infection control procedures, a high proportion of viral hepatitis patients in a health care facility (for example, higher rates were found in health care workers in a tuberculosis hospital and a

centre for PWID), and, for hepatitis B, lack of vaccination (even though vaccination of medical students is not only free but mandatory). Infections were most frequently found in nurses and laboratory staff, and attributable to poor handling practices with sharps, but sputum was identified as a high-risk vehicle for transmission of both HBV and HCV. It was noted that health care workers were screened annually for anti-HCV and HBsAg, and hepatitis B vaccination was provided as necessary. The practices in private clinics might be different.

The necessity to observe universal precautions was emphasized, and the further development of prevention strategies was encouraged. Regulations call for a booster dose of hepatitis B vaccine for vaccinated health care workers every five years, and every three years (with a double dose of antigen) for patients on dialysis. For HCV infection, transmission should be confirmed by biomolecular analysis of the virus (genotype and sequencing) from patient and health care worker.

In discussion of provisions for infected health care workers exposed to risk-prone procedures^e, it was urged that recommendations be formulated, especially for surgeons, and treatment be offered. Based on results of screening of health care workers, exposure-prone procedures for HBsAg-positive subjects with a viral load ≤ 2000 IU/ml should be restricted until they are treated with an antiviral agent; thereafter there should be annual follow-up.

The early results of a study of HBV and HCV in **PWID** in Saint Petersburg by Humanitarian Action, a charitable organization whose initial focus was on HIV, indicated the value of outreach services in improving access to care and the need for trusted counsellors. First operating small vans for outreach service provision, it expanded its operations to a bus for outreach. In a political environment where there are no targeted or low-threshold programmes (i.e. programmes with no or low barriers to entry and retention), the organization provides drop-in advice and counselling and harm-reduction services, offering testing not only for HIV but HBV, HCV and other infections. It found, though, that many PWID shared a belief that the risk of infection did not apply to them. Treatment guidelines for viral hepatitis in the country do not mention risk groups such as PWID, MSM or commercial sex workers, in contrast to those for HIV infection. Costs of treatment were high (more than €2500 for a course of sofosbuvir and even more than €500 for illegally imported generics); no PWID could afford testing and treatment costs for HCV, let alone co- or multiple infections. This would seem to negate the concept of treatment as prevention.

Little attention seems to be being paid to the risks facing prisoners, MSM and commercial sex workers or to preventive action or care for them, although recent outbreaks of hepatitis A in MSM is drawing public health attention. It was reported that Russian prisons had had some successes in delivering health care: screening and access to treatment were generally better than for the general population. Funding for those activities comes from the justice ministry. Further work was needed to make harm-reduction programmes politically acceptable and to improve them. For haemophiliacs the charity "United against Hepatitis" reported poor government support.

^e Defined as "medical procedures where there is no contact between the eyes and the fingers tip of the performer".

Role of civil society

Presentations from nongovernmental organizations sketched a broad range of activities and interests. The charity United Against Hepatitis has conducted a survey of website users which indicated that, despite each constituent subject of the State having to create its own care programme, special viral hepatitis programmes existed in only 14 of the 56 regions that responded. It also showed low levels of awareness and that patients generally received poor, inaccurate or no information.

The organizations work towards ensuring access to combinations of all-oral, pan-genotype direct-acting antiviral agents. One provides data on prices, volumes of drug supply and demand, reviews of guidelines, and translated up-to-date information on a website; this activity could be expanded.

Numerous concerns were expressed. These ranged broadly: the perceived insufficiency (or absence) of provision of prevention and care services for viral hepatitis in the country, the lack of a unified approach to prevention and treatment, the costs of testing and treatment, the paucity of infectious disease physicians able to deal with viral hepatitis and the fact that the average age of those in post is about 50 years, with the associated need for continuing education of all medical professionals. At least half the patients responding to a survey only became aware of their chronic viral hepatitis during medical examinations such as during pregnancy or before surgery. There is also the need to raise public awareness and for more work to be undertaken on the economic impact of viral hepatitis and the economic benefits of treatment for both patients and the State.

The Ministry of Health acknowledged such concerns and welcomed the healthy discussion of the issues. That in itself was progress: a similar meeting years ago with representatives of patient groups would have been unthinkable. Many of the concerns were actively being dealt with. For instance, continuing medical education of professionals had been mandated in 2017.

According to the International Treatment Preparedness Coalition in Russia, specific activities for civil society in improving access to the most efficacious and safe treatment of viral hepatitis included continuing monitoring and analysis of access to care and dialogue with stakeholders on the findings, provision of support to patients in face of obstacles to access, disseminating information about treatment options, and opposition to patents (based on experience with HIV medicines). A recent success has been the reduction in price of sofosbuvir, and its inclusion in the national essential medicines list and in guidelines for procurement.

A considerable body of experience existed in countries in Europe and Central Asia on ways to improve access to antiviral treatment, with several having national programmes for treatment of chronic hepatitis C with direct-acting antiviral agents (with Kazakhstan ambitiously aiming to treat more than 18,000 people) and some having elimination programmes or plans. In the Russian Federation the International Treatment Preparedness Coalition publishes detailed HCV drug-procurement reports on its website, and the Government was urged to learn valuable lessons from the

various approaches taken. At the same time, the community had a valuable role in advocacy and engaging with pharmaceutical companies, other stakeholders and patients in improving access to treatment.

Treatment of chronic viral hepatitises

Clinical guidelines and guidance for the treatment of chronic hepatitis B (2014) and C (2017) have been issued in the Russian Federation by the Russian Gastroenterological Association and the Russian Society for the Study of Liver Diseases on Diagnosis and Treatment of Adult Patients with Hepatitis. These are being revised into a single document in the light of the previous clinical guidelines of the European Association for the Study of the Liver (EASL) and other national and international guidelines and guidance. The Russian guidelines recommend that all patients with cirrhosis and detectable HBV DNA should be treated, regardless of alanine aminotransferase activity, and detail those who should be, may be and can be treated. New biomarkers are being looked at as predictors for stopping direct-acting antiviral treatment, including quantitative HBsAg, HBsAg kinetics and quantitative HBV core-related antigen.

Overall, the proportion of patients with chronic hepatitis in the country being treated with interferon-free regimens is only 15%. To reach 100% will be a major challenge.

Several issues remain unresolved, including when to start and stop therapy, what criteria should apply for restarting treatment after discontinuation of direct-acting antivirals, and the residual risk of developing hepatocellular carcinoma in patients on long-term direct-acting antiviral treatments. Novel endpoints to define cure of HBV infection are needed.

EASL's guidelines for the treatment of hepatitis C (2018) have to be seen through a Russian lens, with Russian guidelines reflecting the realities of the hepatitis situation in the country. EASL recommends routine voluntary testing, harm-reduction activities and treatment without delay of people at risk of transmitting HCV, including PWID, MSM and incarcerated individuals: these are not covered by the Russian guidelines. EASL also recommends treatment with velpatasvir, voxilaprevir and ledipasvir; none of these is registered in the Russian Federation. The recommendations also cover the use of generics (provided that they meet quality control standards); doctors who acted on this recommendation the Russian Federation could be in a difficult position as the national criminal code penalizes the circulation of counterfeit, substandard and unregistered medicines with imprisonment.¹⁵

Physicians in the country are not familiar with co-infections (HBV and HCV). The meeting was told that further work on harmonizing guidelines for treatment of hepatitis C would continue so that HCV infection in the Russian Federation can be properly controlled.

A further challenge is to translate guidelines into practice across the country, given: the limited availability of antiviral agents and poor access for vulnerable groups; the constrained ability of people to pay; and the need to optimize data, especially collecting data on outcomes (in particular for hepatitis C), so that authorities can appreciate the seriousness of the disease.

Currently no guidelines are available for hepatitis D treatment, although some new antivirals (for hepatitis B as well as hepatitis D) are in the R&D pipeline.

Outpatient treatment of chronic hepatitis C is not covered by mandatory health insurance. Inpatient and day-care treatment at the expense of mandatory health insurance is possible, but the tariffs are too low and do not cover the use of interferon-free regimens. Taking into account the average income, only 5% of the population was considered to be able to afford to pay for their own treatment.

A study based on 500,000 patients with chronic hepatitis C in the country put the total medical costs and social losses due to hepatitis C for 2010 at 0.1% of the gross domestic product; most of the costs and losses were due to liver disease (cirrhosis and hepatocellular carcinoma) which could have been prevented by early treatment.¹⁶ The cost of treatment currently ranges between the equivalent of €1600 and €13,000 (120,000-1,000,000 rubles).

Several main issues were identified as hindering better access to treatment. The concept of treatment as prevention is not widely recognized. National guidelines need to be updated and set in a legal framework that allows the use of modern direct-acting antivirals and generics. Medicines need to be affordable (through funding and negotiated prices). Some of the new antivirals should be classified as essential medicines, a move that would lower their cost. Inadequacies in reporting may also be the consequence of poor access to diagnosis and treatment.

Themes and observations

Much attention is being paid to the cascade of care, although more needs to be done to reach the objectives set out in WHO's strategies. The factors affecting access range from availability of diagnostics and medicines and the regulatory framework (including registration of medicines such as generics or specified as essential medicines) to the interest of public health authorities, recognition of the health economic implications, and general awareness of viral hepatitis. These areas were generally recognized as needing much more work. The regulatory framework, for instance, is out of date, in particular concerning modern antiviral medicines and generics.

On the positive side, several operational models of the cascade of care with possible positive outcomes were described. The value of mobile outreach and telemedicine was remarked upon. There clearly exists a motivated cadre of health care workers trying to improve prevention, care and control of viral hepatitis.

Norms and standards for screening are lacking or not well disseminated, and doctors and public health professionals generally have poor awareness of criteria for screening. Poor access to care and difficulties in being treated with efficacious modern medicines are disincentives for people to consider being screened. The crucial role of health

practitioners and the need for their continuing education as well as better access to care was repeatedly underlined.

The capacity to detect and diagnose chronic hepatitis C clearly does exist in the country. Across the various regions and territories and despite the different prevalence rates of chronic viral hepatitis, the burden of disease was recognized as significant, with many patients presenting at late stage of disease. The list of tests for diagnosis of infection and choice of treatment is long and their cost varies across the country. Figures quoted for pre-treatment costs ranged from the equivalent of €130 to €160 in Novosibirsk to €200-260 in Moscow.

A common refrain was the scarcity of funds. Not only was that a severe hindrance to treating patients, but it made it difficult for health authorities to project financing and plan or sustain programmes. The financing mechanisms for treatment programmes need to be improved, given that it makes better economic sense to treat viral hepatitis early than to treat its consequences.

Relevant clinical guidelines were used in 13 of 56 regions responding to a survey. Furthermore, the costs of treatment are high (see above), even in comparison with other upper-middle-income countries, and there is no national programme for treatment. Costs of antiviral treatment were covered by regional budgets in 29 regions and mandatory health insurance funds in 22 regions. Out-of-pocket payments were an economic burden for those paying for their own treatment, not just for patients living in low-income communities outside the main centres but across the country where 40% of the population were said to describe themselves as poor. Even generics could sometimes be obtained but they were difficult to afford; a major problem is that many effective generics are not registered in the Russian Federation and their use may contravene the criminal code. Paying for their own treatment would be inconceivable for people such as PWID.

For those patients fortunate enough to be treated, follow-up is poor and outcomes are often not recorded.

[How to achieve the goal of eliminating viral hepatitis in the Russian Federation by 2030?](#)

[National action plan](#)

Many references were made to the need for a national plan, and indeed the national health authorities are preparing a national action plan to eliminate viral hepatitis as a public health threat in the Russian Federation by 2030, with strategic directions, priorities and targets in line with WHO's global health sector strategies. It will cover diagnostics, preventive therapy and vaccination while encouraging the development of new diagnostic tests, new vaccines and improved treatment coverage.

Speakers argued strongly that the national plan should be based on objective data on the current epidemiological situation, including burden of disease, affected age groups, frequency of adverse outcomes and associated mortality. In early 2018 a plan on creating a national plan was published in the medical press in order to raise awareness.

A pilot study is being conducted in three regions with different prevalence rates to derive up-to-date data and to identify needs and essential actions in an attempt to change the mindset of regional governments and authorities.

With the drafting of new national laws on public health and biological safety, now is the time to construct the legal framework for action to prevent and control viral hepatitis in line with WHO's goals and objectives. Patients and all stakeholders should be included at all levels of policy-making and implementation, and civil society organizations recognized and supported. A crucial step is to create a more coordinated approach, by designating a leader and a national body to bring stakeholders from all regions around the same table.

The way forward: conclusions and recommendations

Through four working groups and a general discussion, participants concluded with the following conclusions and recommendations.

General issues included how to translate the legal framework of public health (existing and future) into action at the patients' level. One particular issue related to funding: sustained funding was needed for the implementation of viral hepatitis policies and programmes. New thinking was needed about the funding of treatment through the mandatory health insurance system; it is cheaper to treat with antiviral agents than to provide care in hospitals for the consequences of chronic hepatitis. Further, treatment had to be affordable to those who needed it. Health economic studies on the potential cost benefits and savings of prevention and treatment would provide valuable input into policy-making and prioritization.

Epidemiology. Given questions about the existence and accuracy of data and reporting processes, several actions on data are vital. The Federal Viral Hepatitis Registry should be fully implemented nationwide. The burden of disease must be determined more accurately. The quality of data – including those on mortality, attributable fractions of liver cancer and cirrhosis to HBV and HCV, chronic cases, and registration of cases – needs to be verified and improved. HDV should be included in the list of notifiable diseases, and, in areas where hepatitis D is endemic, the epidemiological situation and trends should be evaluated, and all subjects positive for HBsAg should be tested for anti-HDV antibodies.

Other recommendations included the creation of new guidelines for recording deaths in cirrhotic and HCC patients, updating existing regulations on notification of infectious diseases, introducing a birth cohort screening approach, improving screening algorithms, investigating the efficiency of hepatitis B vaccination, including data on coverage of the birth dose in statistical reporting forms (the joint reporting form), and paying more attention to risk groups.

Screening. Broader screening programmes for HBV and HCV infections and disease were advocated. Viral hepatitis is not included in the national health check programme that is offered to all citizens and paid for by the health insurance fund; its inclusion could help to improve the link between screening and care. More attention, in terms of

everything from legal status, improved outreach and access to care to preventive and curative services, needs to be paid to neglected groups (e.g. PWID and other marginalized groups such as commercial sex workers and men who have sex with men, and prisoners – all drivers of the epidemics of chronic hepatitis B and C: a recent study shows that recent incarceration is strongly associated with HCV acquisition¹⁷).

For diagnosis, quality control of diagnostic tools was recommended as well as the establishment of an accreditation programme for validation of the methods used by various diagnostic laboratories country-wide.

Although cases are registered, existing links to care are poor and need to be strengthened and built upon in order to improve access to care, diagnosis and treatment. Information about outcomes needs to be captured in linked electronic databases. As funding for treatment varies between regions, treatment depends on a lottery of home location. There is no national strategy for viral hepatitis as there is for HIV/AIDS; the challenge is to increase pressure for a “silent disease”. There is no federal budget line for treatment or mandatory health insurance reimbursement; solutions are for the Federal Government to create such a budget line and secure willingness to pay.

Prevention. The issue of whether to introduce hepatitis A vaccination into routine immunization schedules needs consideration.

For hepatitis B, although the coverage rates of screening of pregnant women and of infant vaccination against hepatitis B are very good, vigilance is needed. In rare instances, cases of infection in pregnant women still escape detection and cases of maternal transmission do still occur. Anti-vaccine groups are active. The population needs to be educated and informed, and the media has a positive role in supporting vaccination activities. Fortunately, the media are supportive of public health activities against viral hepatitis, and educational and informational activities for the population are organized and supported by several professional and civil society organizations.

Vaccination of health care workers and medical students against hepatitis B is mandatory (and free of charge). Annual testing of all health care workers for HBV and HCV status is also mandatory. Guidelines should be issued for repeat vaccination if the HBV immunological status of health-care workers and medical and nursing students after vaccination so warrants it. Further recommended actions included better and continuing medical education of health care providers about viral hepatitis, and, vitally, ensuring strict observance of infection control and universal precautions including promotion of safe-injection practices. All health care workers who perform exposure-prone procedures should be screened. A list of all exposure-prone procedures should be established, and recommendations formulated for restriction of exposure-prone procedures for HBsAg-positive subjects and regular follow-up.

Treatment. Although patients co-infected with HIV get federal funding for treatment, patients with single hepatitis virus infections do not. Treatment regimens in many regions are still based on interferon and ribavirin, even though direct-acting antiviral agents are much more effective and better tolerated (but more expensive). Regional disparities need to be corrected. The issue of unregistered medicines needs solutions. Best treatment results depend on determining viral load and information on stage of

fibrosis: steps need to be taken to overcome the absence of such information. A central negotiating agency is needed in order to obtain new medicines at lower prices. Difficult issues remain relating to standardization and equal access.

The country's clinical guidelines of 2017 need to be updated and prioritized to reflect the much better treatment options with direct-acting antiviral agents. Meanwhile the valuable guidance provided by international guidelines should be accorded legal recognition. A huge community effort will be needed to update clinical guidelines in a timely manner. Registration of both newer antiviral agents for viral hepatitis recommended by EASL and generics should be accelerated, as should the inclusion of such drugs in national essential medicines lists. Overall, the coverage of antiviral treatments needs to be expanded. In particular, interferon-free treatments need to be introduced across the country.

Several countries have shown that the cost of newer antivirals is open to negotiation, with the size of the market and the competition from generics weighing considerably on the manufacturers' decision to lower prices. An accurate estimate of the actual burden of disease in the Russian Federation would be a strong argument in negotiating reductions in the price of medicines. One central agency or person needs to be nominated to negotiate with industry on prices.

Table

Some incidence and prevalence rates for chronic viral hepatitis B and C in varied constituent subjects in the Russian Federation in 2017

Federal subject	Population (million)	Area (km ²)	Chronic VH incidence	Chronic HBV incidence	Chronic HCV incidence	HCV genotype	Fibrosis stage at presentation	Estimated number of patients with CHC
Russian Federation ^f	147	17.2 million	44.4/10 ⁵ [78% HCV]	19.7/10 ⁵	34.6/10 ⁵	1 > 3 > 2	42% F0	4,7/10 ⁶ [3,3% of population] ¹⁷
Chelyabinsk Region	3.5	88,500	30/10 ⁵ [78% HCV]	14.9/10 ⁵	55.4/10 ⁵	1 > 3 > 2	61% F0	21,790
Krasnodar krai	5.6	76,000	36/10 ⁵ [79% HCV]	8.8/10 ⁵	30.4/10 ⁵	1 = 3 > 1b, 2	62% ≥F2	10,390
Far-East Federal District	6.2	6.9 million	51.2/10 ⁵	7.6/10 ⁵ (Primorskiy krai)	33/10 ⁵ (Primorskiy krai)	1 > 3 > 2	61% F0/F1	29,000 (out of a total of 37,000)

^f Including Crimea.

								chronic VH)
Republic of Sakha	0.95	3.1 millio n	86/10 ⁵	49.9/10 ⁵	52/10 ⁵	1 > 3 > 2	53% FO/F1 ^g	6,781
North Caucasus Federal District	9.8	170,0 00	15/10 ⁵	8.2/10 ⁵	11/10 ⁵	1 > 3 > 2 ^g	70% ≥F2 ^g	5,675
Chukotka Autonom ous Area	0.049	721,5 00	22/10 ⁵	10/10 ⁵	12/10 ⁵	1 > 3 > 2 ^g	No data	675

¹ See <https://tradingeconomics.com/russia/wages> (accessed 8 November 2018).

² Global health sector strategy on viral hepatitis 2016-2021 (<http://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/>, accessed 30 October 2018), adopted in resolution WHA69.22.

³ <http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/publications/2017/action-plan-for-the-health-sector-response-to-viral-hepatitis-in-the-who-european-region-2017> (accessed 30 October 2018).

⁴ See for example: Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva: World Health Organization; 2015 (<http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/publications/2016/guidelines-for-the-prevention,-care-and-treatment-of-persons-with-chronic-hepatitis-b-infection-2015>, accessed 30 October 2018); Guidelines for the screening, care and treatment of persons with chronic hepatitis C infection. Geneva: World Health Organization; Updated version, April 2016 (<http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/publications/2016/guidelines-for-the-screening,-care-and-treatment-of-persons-with-chronic-hepatitis-c-infection-updated-version,-april-2016>, accessed 30 October 2018); and United Nations common position on ending HIV, TB and viral hepatitis through intersectoral collaboration (2018) (<http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/publications/2018/united-nations-common-position-on-ending-hiv,-tb-and-viral-hepatitis-through-intersectoral-collaboration-2018>, accessed 30 October 2018).

⁵ Country cooperation strategy for the World Health Organization and the Ministry of Health of the Russian Federation 2014–2020. Copenhagen: WHO Regional Office for Europe; 2014 (<http://www.euro.who.int/en/countries/russian-federation/publications/country-cooperation-strategy-for-the-world-health-organization-and-the-ministry-of-health-of-the-russian-federation-20142020-2014>, accessed 30 October 2018).

⁶ Including Sanitary and Epidemiological Regulations SP 3.1.2341-08 on prevention of hepatitis B (<http://gostrf.com/normadata/1/4293831/4293831337.pdf>) and SP 3.1.3112-13 on prevention of hepatitis C (see link in http://rospotrebnadzor.ru/documents/details.php?ELEMENT_ID=3555) – texts in Russian only.

⁷ For original version in Russian see <http://publication.pravo.gov.ru/Document/View/0001201805070038>; for a translated text in English see <https://thesaker.is/presidential-decree-on-national-objectives-and-strategic-tasks-of-russian-federations-development-in-the-period-up-to-2024/> (accessed 8 November 2018).

⁸ Global Conference on Primary Health Care; from Alma-Ata towards universal health care and the Sustainable Development Goals (Astana, 25-26 October 2018) (<http://www.saluteinternazionale.info/wp-content/uploads/2018/10/gcphc-declaration.pdf>, accessed 30 October 2018).

^g Data from the national register.

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- ⁹ WHO. Monitoring and evaluation for viral hepatitis B and C: recommended indicators and framework Technical report. Geneva: World Health Organization ; 2016 (<https://www.who.int/hepatitis/publications/hep-b-c-monitoring-evaluation/en/>, accessed 30 October 2018).
- ¹⁰ WHO. Technical considerations and case definitions to improve surveillance for viral hepatitis: technical report. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/handle/10665/204501/9789241549547_eng.pdf?sequence=1, accessed 30 October 2018).
- ¹¹ WHO. New recommendations in the updated WHO guidelines for the screening, care and treatment of persons with chronic hepatitis C infection - Policy brief. Geneva: World Health Organization; 2016 (<http://www.who.int/hepatitis/publications/hepatitis-c-guidelines-policy/en/>, accessed 30 October 2018).
- ¹² State Report "On the state of the sanitary epidemiological well-being of the population In Russian Federation in 2017" (http://www.rospotrebnadzor.ru/upload/iblock/c51/gd_2017_seb.pdf, accessed 3 November 2018) [Russian language only], p.202.
- ¹³ See also an earlier report: Klushkina VV, Kyuregyan KK, Kozhanova TV, Popova OE, Dubrovina PG, Isaeva OV et al. Impact of universal hepatitis B vaccination on prevalence, infection-associated morbidity and mortality, and circulation of immune escape variants in Russia. PLOS One, 2016; 11(6):e0157161 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4900554/>, accessed 7 November 2018).
- ¹⁴ State Report "On the state of the sanitary epidemiological well-being of the population In Russian Federation in 2017" (http://www.rospotrebnadzor.ru/upload/iblock/c51/gd_2017_seb.pdf, accessed 3 November 2018) [Russian language only], p.130.
- ¹⁵ Criminal Code of the Russian Federation, Article 238.1.
- ¹⁶ Yushchuk ND, Znoyko OO, Yakushechkina NA et al. Assessment of the socio-economic burden of hepatitis C in the Russian Federation. Epidemiology and Vaccinal Prevention, 2013, 2(69). (For Russian text, see <https://cyberleninka.ru/article/n/otsenka-sotsialno-ekonomicheskogo-bremeni-gepatita-s-v-rossiyskoy-federatsii>, accessed 8 November 2018).
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