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Assessment of the Viral Hepatitis Response in Kyrgyzstan

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Mission Report

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Contents

Abbreviations

HAV	hepatitis A virus
HBsAg	HBV surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HCW	health-care worker
IPC	infection prevention and control
MOH	Ministry of Health
NGO	nongovernmental organization
PCR	polymerase chain reaction
PWID	people who inject drugs
TTI	transfusion-transmissible infections

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Introduction

Kyrgyzstan is one of the focus countries for viral hepatitis in the WHO European Region, due to the high rates of infections, the commitment of national stakeholders and the interest of the Ministry of Health (MOH) to address viral Hepatitis. WHO estimates that around half a million people with chronic hepatitis B and nearly 100 000 people with chronic hepatitis C are living in Kyrgyzstan.[1,2]

The current assessment mission was conducted over a period of four days, with the aim to make a short review of hepatitis related surveillance, national policies and services. The result of this short review would inform the Ministry of Health and WHO identify specific areas for further technical cooperation. The report does not claim to be a comprehensive assessment of all aspects related to viral hepatitis prevention and control. This report could best be used to start a dialogue between WHO and the MOH for further technical support in the priority areas identified below.

The mission members included Dr Hande Harmanci, Medical Officer from WHO Headquarters, Global Hepatitis Programme, Geneva, Dr Antons Mozalevskis, Medical Officer from WHO Regional Office for Europe, Copenhagen, Dr Alexey Bobrik, Technical Officer from WHO Country Office in Ukraine and Ms Saliya Karymbaeva, National Professional Officer from WHO Country Office in Kyrgyzstan.

[1] Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet. 2015;386(10003):1546–55. doi: 10.1016/S0140-6736(15)61412-X.

[2] Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H. Global epidemiology and genotype distribution of the hepatitis C virus infection. Journal of Hepatology. 2014;61(1 Suppl):S45–57. doi: 10.1016/j.jhep.2014.07.027.

Summary of recommendations

The full list of recommendations is provided here for ease of reference. Please refer to the main body for a more detailed explanation.

Governance and programme management

- Set up an internal MOH hepatitis coordination body.
- Establish a national Strategic and Technical Advisory Group (STAG).
- Set up working groups for the development of the national programme (action plan) and updated clinical protocols.
- Build an investment case for hepatitis in Kyrgyzstan.

Awareness raising and promoting partnerships

- Observe World Hepatitis Day on 28 July to increase awareness among the general population and health-care workers (HCWs) about all types of hepatitis.
- Seek partnerships with nongovernmental organizations (NGOs) and relevant internal units (like Health Promotion) to develop and implement a communication strategy on all types of hepatitis.
- Join the NOhep campaign.

Data for policy and action

- Develop standardized surveillance case definitions for acute and chronic viral hepatitis based on new WHO guidance.
- Collect and critically appraise the available data in the country from all possible sources to estimate the burden of disease.
- Plan for a population-based sero-survey, representative of relevant age groups.
- Consider reviving the sentinel surveillance sites for monitoring trends in acute viral hepatitis, with aetiological diagnosis.
- Introduce an electronic registry of hepatitis patients, which would be the best approach to monitoring and evaluating a national programme for testing and treatment of viral hepatitis.

Prevention of transmission

Vaccination

- Set national targets for hepatitis B control through immunization, based on regional targets defined by the European Action Plan on Viral Hepatitis.
- Document the attainment of the national targets for hepatitis B control through immunization.
- Prioritize hepatitis B vaccination of HCWs and consider the feasibility of vaccinating other higher-risk groups and people born before the introduction of universal hepatitis B vaccination (2000).

Infection prevention and control

- Continue strengthening infection prevention and control (IPC) in all health-care facilities across the country.
- Consider a phased replacement of outdated sterilizing equipment.
- Enforce IPC and occupational safety standards.

- Provide strong leadership and supportive supervision for continued behaviour change among HCW.
- Continue staff training on IPC through graduate, post-graduate and on-the-job training.
- Address the punishment epidemiology approach applied to nosocomial infections.

Blood safety

- Promote strong leadership to reduce the number of blood donation sites.
- Organize blood delivery logistics to meet the requirements of restructured national blood service.
- Ensure that universal screening for transfusion-transmissible infections (TTIs) is in place throughout the country and is applied effectively and consistently in accordance with national standards.
- Consider centralized procurement of reagents and test kits with ensured quality.
- Consider promoting voluntary blood donations and phasing out paid donors completely.
- Include a representative of the blood service in the working group for the development of the national viral hepatitis programme.

Harm reduction

- Expand testing for hepatitis B and C to harm reduction clients and other people who inject drugs (PWID).
- Start planning domestic support for the long-term sustainability of harm reduction projects in the country.

Screening, treatment and care

Human resources for health

- Identify duties and responsibilities at all levels of the health-care system and build capacity to diagnose viral hepatitis, initiate treatment, follow up and monitor patients, and complete treatment. Use this to develop policies for task-shifting for hepatitis B and C treatment scale-up.
- Revise the current post-diploma education and develop a standardized curriculum for specialist training in viral hepatitis to be approved by the MOH.

Testing and diagnosis

- Develop and publish national viral hepatitis testing and diagnosis algorithms, including identifying groups at higher risk for hepatitis infection that need to be offered hepatitis testing, along with the national treatment protocols.
- Develop educational programmes for laboratory specialists on quality control for laboratory diagnostics.
- Ensure state control over the diagnostic test systems that are entering the market.
- Consider offering routine testing to populations at higher risk, including outreach and using rapid tests or dried blood spot tests.
- Consider the feasibility of using AIDS-centres for screening, linkage to care and treatment of hepatitis.

Care and treatment

- Update national chronic hepatitis treatment protocols (including for cirrhosis and hepatocellular carcinoma (HCC)) in line with WHO guidelines.
- Include medicines recommended by WHO guidelines for treating hepatitis B and C infection in the National Essential Medicines List of Kyrgyzstan.
- Establish a centre of excellence for chronic viral hepatitis care and treatment (e.g. National Hepatology Centre) to implement the new protocols, follow up on treatment outcomes and serve as a centre for capacity-building.
- Provide publicly funded or co-funded treatment of chronic viral hepatitis, at least for higher risk patients (e.g. advanced liver disease, HCWs, people living with HIV, etc.).
- Take active measures to further reduce the price of chronic viral hepatitis medicines and diagnostics (e.g. by promoting generic competition, improving regulatory processes).
- Consider centralized procurement of medicines and single-use consumables (syringes, vacuum blood collection tubes etc.) with ensured quality and WHO pre-qualification.

Methodology of assessment

The assessment included the following activities:

- desk review of relevant publications and reports prior to arrival
- review of national policies and status of implementation
- field visits to:
  - MOH
  - Mandatory Health Insurance Fund
  - Republican Infectious Diseases Hospital
  - Republican Medical Information Centre
  - Scientific and Production Institute “Preventive Medicine”
  - National Hospital
  - Republican Blood Centre
  - Republican AIDS Centre
  - Partnership Network, NGO
  - Family Health Practitioners Centre of Chui Oblast
  - Bonetsky Laboratories
- key-informant interviews with the following people:
  - Talantbek Batyraliev, Minister of Health, MOH
  - Samat Toymatov, MOH
  - Nurgul Ibraeva, MOH
  - Baktygul Ismailova, MOH
  - Tolo Isakov, MOH
  - Sultan Suranchiev, MOH
  - Baktygul Kambaralieva, MOH
  - Lubov Komarevskaya, Mandatory Health Insurance Fund
  - Elmira Ibraimova, United States Agency for International Development, Defeat TB Project Director
  - Joldosh Kalilov, Republican Centre of Immunoprophylaxis
  - Ainagul Murzaeva, Republican Medical Information Centre
  - Gulnara Kokulova, Republican Medical Information Centre
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- Irina Kalinicheva, Bonetsky Laboratories
- Nazira Usmanova, United States Centers for Disease Control and Prevention, Central Asia Regional Office.

Findings and recommendations

The findings of the mission team and related recommendations are grouped under five main headings: (1) governance and programme management; (2) raising awareness and promoting partnerships; (3) data for policy and action; (4) prevention of transmission; and (5) screening, care and treatment.

1. Governance and programme management

Good governance and programme management are crucial for an effective and efficient national health programme. At each management level, staff should be provided with adequate authority for appropriate decision-making, along with responsibility and accountability. Effective human resource planning is also crucial, as are job definitions at each level. Care should be taken to ensure effective collaboration and communication between relevant health programmes. This could be a significant cost-saving measure as well as a means to increase programme effectiveness.

National planning process should be based on the best available data generated by strategic information systems. It should enable input from all key stakeholders – including civil society – on policy development, service planning and resource allocation, and should ensure coordination and alignment of the viral hepatitis response with the broader health sector. It should also advocate for political commitment for sustained financing and national ownership.

1.1. Findings

Viral hepatitis is listed under the staff job descriptions of two deputy ministers at the MOH (Medical Services and Public Health). Viral hepatitis related issues are addressed in several laws (on public health, public health protection, HIV, immunization and blood donation). Several normative regulations have been approved by the MOH on the surveillance, prevention, screening, care and treatment of viral hepatitis and on general IPC measures. The target programme, Prevention and Treatment of Viral Hepatitis in the Kyrgyz Republic for 2011–2015, has been implemented, though only to a limited extent, due to lack of funding.

In August 2015, at the invitation of the MOH, a working group was established for the development of the new Target Programme on Viral Hepatitis for 2016–2022, which has prepared an early draft of this programme.

Key priorities of the draft programme include:

- Improve surveillance systems for acute and chronic viral hepatitis, liver cirrhosis and HCC;
- Strengthen primary viral hepatitis prevention (vaccination against hepatitis A and B, prevention of hepatitis B virus (HBV) transmission from mother to child, water and food security, safety of medical procedures and blood safety);
- Improve diagnosis and treatment of viral hepatitis;
- Improve the capacity of staff responsible for viral hepatitis;
- Integrate control of viral hepatitis with other state strategies and programmes aimed at control and prevention of infections associated with health-care delivery and socially significant infections (HIV, tuberculosis, sexually transmitted infections, etc.);
- Promote scientific and innovative approaches to prevention of viral hepatitis;

- Involve communities in prevention of viral hepatitis;
- Monitor and evaluate measures and activities aimed at countering viral hepatitis.

Members of the working group indicated that due to insufficient leadership and lack of time and motivation among group members, the development of the national programme is being delayed.

1.2. Recommendations

- It is very important to set up an internal **MOH hepatitis coordination body** that should report to a higher level official at the MOH and involve all programmes with hepatitis-related functions. The main purposes of this group would be joint planning and goal-setting, preventing duplication of efforts, and more effective orientation and training of HCWs, among others. Initially the coordination body will need to include assigned staff from (i) the Public Health Department, (ii) the Medical Services Department, and (iii) the Surveillance Department. At a later stage, staff from departments responsible for financing and procurement of medicines and diagnostics could join the coordination body.
- A **national Strategic and Technical Advisory Group (STAG)** comprising internal and external stakeholders needs to be officially established. It should include policy-makers, implementers from different sectors (e.g. military, other ministries, etc.), patient groups, NGOs, national professional societies (e.g. of doctors and nurses) and the WHO Country Office. Its role would be to guide the MOH on development of the national strategy, clinical protocols and other normative documents. Such a STAG is essential to ensure intersectoral collaboration and stakeholder agreement.
- **Working groups for the development of the national viral hepatitis programme and updated clinical protocols** need to be formalized, terms of reference need to be revised and a strict working schedule needs to be established. Positive incentives can be considered for working group members to ensure motivation and commitment.
- In order to better understand the burden of viral hepatitis and estimate its cost to the Kyrgyz economy, as well as the relative cost of effective interventions, **disease burden modelling should be conducted, followed by economic analysis (the so-called investment case)**. WHO can support Kyrgyzstan by attracting an external expert team who will conduct this modelling work. The investment case will use data from the initial assessment, particularly the prevalence of chronic infection in various age groups, to evaluate various intervention scenarios. These scenarios may combine interventions in the field of prevention (e.g. immunization, blood and injection safety, harm reduction) and in the field of testing and treatment, so as to estimate cost, budget implications, epidemiological impact and cost effectiveness. Such economic analyses can take the form of an investment case for broader audiences or a cost-effectiveness analysis for a health sector audience.

2. Raising awareness and promoting partnerships

Raising awareness and changing behaviours in the general population and among targeted groups such as HCWs requires careful collaborative planning, persistent implementation and monitoring of results. Better informed populations are expected to make better informed choices. Technical programmes (the viral hepatitis programme in this case) should work closely with communication and social mobilization experts to craft the right approach and messages fit for purpose for the specific community.

2.1. Findings

The great majority of the population is unaware of the consequences of chronic hepatitis, and viral hepatitis is considered to be a stigmatizing disease, especially in the context of injection drug use.

The level of knowledge among HCWs is not sufficient, and some HCWs seem to be unaware of the importance of being vaccinated against hepatitis B. The stigma regarding viral hepatitis infection is also persistent among HCWs, and anecdotal evidence was reported of physicians being discriminated against and losing their job after disclosure of viral hepatitis infection. This may create unwillingness to test for viral hepatitis for fear of being stigmatized or discriminated against.

Wold Hepatitis Day has not yet been observed in Kyrgyzstan.

2.2. Recommendations

- Observe **World Hepatitis Day on 28 July** to increase awareness among the general population and HCWs about all types of hepatitis.
- Seek partnerships with NGOs and relevant internal units (like Health Promotion) to develop and **implement a communication strategy** on all types of hepatitis.
- Join the **NOhep campaign** at www.nohep.org. NOhep is a global movement aimed at uniting those working in the field of hepatitis and others from across the world around one common purpose: the elimination of viral hepatitis by 2030.

3. Data for policy and action

Accurate data enable policy-makers and decision-makers at all levels to understand the burden of disease caused by viral hepatitis and to develop prevention and control strategies accordingly. Key information required for policy and programme planning includes:

- the number of people living with viral hepatitis infection (prevalence) and the number of new infections (incidence) occurring each year;
- the characteristics of most-affected populations;
- the most relevant modes of transmission;
- the cost-effectiveness of different case-finding strategies (including testing of symptomatic cases, screening of asymptomatic populations, contact tracing, client-initiated testing, etc.);
- the coverage and impact of prevention interventions (vaccination, health education, testing and treatment, partner notification, etc.).

Viral hepatitis surveillance systems are needed to detect outbreaks; monitor trends in incidence and risk factors; assess the burden of chronic hepatitis and disease outcomes (e.g. liver cirrhosis and liver cancer), including deaths; monitor treatment coverage and its impact on chronic liver disease; and evaluate the efficacy of interventions to prevent, control and treat viral hepatitis. Implementing surveillance systems for viral hepatitis complies with International Health Regulations (2005)[3] to strengthen disease detection. Furthermore, a viral hepatitis surveillance system can improve country's overall performance in numerous other synergistic areas, such as water and sanitation, blood safety and injection safety.

[3] International Health Regulations (2005). Geneva: World Health Organization; 2005.

3.1. Findings

3.1.1.Country situation

Kyrgyzstan is considered to be a relatively high-burden country for viral hepatitis, similar to other Central Asian republics. No population-based nationally representative studies have been conducted to measure the prevalence of chronic hepatitis B or C. The best available data comes from the testing database compiled by the Republican AIDS Centre; however, this data is not representative and is based on a convenience sample of people who undergo testing for different reasons (Table 1).

Table 1. Prevalence of hepatitis B (HBsAg) and C (anti-HCV) in different population groups tested in Kyrgyzstan, 2013–2015

	HBV (%)			HCV (%)		
	2013	2014	2015	2013	2014	2015
Total number of Kyrgyzstan citizens	4.6	4.6	4.7	3.3	2.9	3.0
Partners of people living with HIV	2.7	7.8	6.0	15.4	11	13.5
PWID	1.9	8.2	4.9	31.9	40.4	35.2
STI patients	3.4	3.7	4.1	3.0	2.7	5.8
Prisoners	6.4	10.4	13.3	31.9	53.6	23.9
Pregnant women	4.2	3.9	3.7	1.0	1.4	1.6
Blood donors	4.4	4.5	4.4	2.6	1.8	2.0
Health workers	3.4	3.5	3.6	2.8	2.4	2.4
Tested due to clinical indications	6.8	7.0	7.8	5.6	5.7	6.2
Tested anonymously	6.1	4.5	4.2	5.9	19.1	33.3
People travelling abroad	7.2	6.1	6.5	2.4	18.4	2.2

HBV = hepatitis B virus; HCV = hepatitis C virus; PWID = people who inject drugs; STI = sexually transmitted infection.
Source: Republican AIDS Centre data

Analysis of surveillance data on acute viral hepatitis demonstrates that during the last 25 years, the incidence has remained high, with cyclic waves every 4–5 years. About 60–70% of acute viral hepatitis cases are caused by hepatitis A virus (HAV) infection. Routine testing for hepatitis E virus is not available in the country and a relatively high proportion of reported acute cases are of unknown aetiology (up to 25%).

3.1.2.Hepatitis surveillance

The case definitions for acute and chronic viral hepatitis used in Kyrgyzstan are not in line with WHO case definitions (e.g. the outdated term “virus carriage” is used and represents a significant share of the registered burden of disease).

Kyrgyzstan has an established case reporting system for hepatitis, which captures mostly acute cases. Chronic viral hepatitis has been a notifiable disease since 2010. Each case of acute or chronic hepatitis is required to be reported to the region or city centre of the State Sanitary Epidemiological Surveillance department through Form 1, which is eventually collected and analysed at the national level (see Annex 1).

Kyrgyzstan has a well-developed system of data collection on ambulatory (Form 12) and hospitalized (Form 14) cases. However, duplications within these systems are possible, with one person being counted more than once in a year and possibly in multiple health-care facilities. An automated information system is currently being developed, which will minimize the risk of duplications. No assessment has been made of the viral hepatitis surveillance system and it is not clear whether this surveillance system is adequate to monitor hepatitis trends in the country.

Recording and registration of chronic viral hepatitis in health-care facilities is not systematized, and no system is in place for the surveillance of viral hepatitis complications (e.g. cirrhosis and liver cancer registry). The country has no centralized viral hepatitis patient registry.

3.2. Recommendations

- Develop **standardized surveillance case definitions for acute and chronic viral hepatitis** based on new WHO guidance.
- Collect and critically appraise **the available data in the country from all possible sources** (including data available from the Mandatory Insurance Fund, Republican Medical Information Centre, Republican AIDS Centre and others) to estimate the burden of disease.
- Plan for a **population-based sero-survey**, representative of relevant age groups. This would provide an excellent estimate of hepatitis A, B and C prevalence rates, which in turn would allow estimates of hepatitis disease burden and costs to society. Such a sero-survey would also be useful to assess the effectiveness of hepatitis B immunization. Since sero-surveys are costly, consider adding a hepatitis component to any other population-based survey.
- Consider reviving the **sentinel surveillance sites** for monitoring trends in acute viral hepatitis, with aetiological diagnosis.
- Introduce an **electronic registry of hepatitis patients**, which would be the best approach to monitoring and evaluating a national programme for testing and treatment of viral hepatitis. A registry is a database of patients with certain characteristics. When a person is diagnosed (i.e. newly identified cases of chronic infection) their record is added to the database. This information is removed when the person is cured or dies. Setting up a national registry of patients with chronic HBV and HCV infections requires a system in which health-care providers can collect information on personal characteristics, diagnosis, treatment initiation or deferral, monitoring and viral suppression or cure. This system may be based on standardized patient cards, paper registers or an electronic data entry system. If data collection is paper-based, information then needs to be entered into a computer.

4. Prevention of transmission

Preventing new cases of disease remains the basis of any public health programme, including viral hepatitis, even in the presence of effective and accessible medication. Governments have the responsibility to prevent transmission of infection to populations using all available means, including

provision of vaccinations, ensuring safe injections and safe medical interventions, and providing safe blood and blood products, tissues and organs. Hepatitis B vaccine remains one of the most effective public health tools to prevent infection, and eventually millions of deaths due to liver cancer worldwide.

4.1. Findings

4.1.1.Vaccination

Immunization with hepatitis B birth-dose vaccine started in 1999 in Bishkek and was scaled up to the whole country on 1 January 2000. Up to 97% of births take place in health-care settings attended by trained HCWs. The birth dose (using monovalent vaccine) is administered within 24 hours of birth, in maternity clinics, followed by three more doses at 2, 3.5 and 5 months (as a part of the pentavalent vaccine from 2009).

Both third-dose coverage and birth-dose coverage were 97% in 2015.[4] The coverage rates for the HBV third-dose vaccine for 2002–2015 are provided in Table 2. Some national experts have expressed concern about the effectiveness and immunogenicity of hepatitis B vaccines, as there is some information on low anti-HBV surface antigen (HBsAg) titres in vaccinated children. No nationally representative sero-survey for HBV among vaccinated cohorts of children has been carried out; therefore data is insufficient to evaluate the effectiveness of the national immunization programme for hepatitis B.

Kyrgyzstan has no national strategy for routine hepatitis B vaccination of higher risk groups (e.g. HCWs, military personnel, commercial sex workers, PWID, men who have sex with men and people with HIV or chronic HCV). Vaccination of adults is provided in the private sector for self-purchase. Vaccination is recommended for HCWs; however, HCWs have reportedly insufficient awareness of the importance of a completed vaccination series.

Table 2. Reported hepatitis B birth-dose and third-dose vaccine coverage rates for Kyrgyzstan (2002–2015)

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
HBV birth-dose coverage (%)	99	99	99	99	97	98	99	98	99	73	94	96	99	97
HBV third-dose coverage (%)	99	99	99	97	90	94	97	96	96	96	96	97	96	97

HBV = hepatitis B virus.
Source: UNICEF-WHO

[4] World Health Organization (WHO). Immunization, Vaccines and Biologicals. Data, statistics and graphics. Geneva: WHO; Available from: http://www.who.int/immunization/monitoring_surveillance/data/en/

The country also lacks a national strategy for routine HAV vaccination of higher risk groups (e.g. travellers to areas of high-endemicity, military personnel, ecological and sanitary workers, people with HIV or chronic HBV or HCV infection). The HAV vaccine is available in the private sector for self-purchase. Some experts argue for the need to introduce hepatitis A vaccination to the infant immunization calendar; however, no proper assessment has been made of the feasibility of this measure and better age-specific data on HAV incidence and anti-HAV prevalence is needed.[5]

4.1.2.Infection prevention and control activities

Significant outbreaks of HIV infection among children were recorded in the 2000s. Investigation concluded that at least some cases were related to nosocomial transmission, presumably due to repeated use of injection equipment and unsafe blood transfusion. After the last outbreak, complex measures were undertaken in the country, such as strengthening the normative base for IPC, providing staff training, designating dedicated infection control officers in all health facilities, improving the supply of single-use consumables, providing personal protective and waste management equipment, and mandating exclusive use of auto-disable syringes for immunization.

In general, all national stakeholders agree that the situation with injection safety and IPC standards has improved substantially over the past 5–10 years. However, many challenges still exist, and the key issues identified through interviews with national experts were as follows:

- insufficient procurement of single-use consumables, such as vacuum blood collection tubes and syringes, as well as of personal protective equipment (certain items HCWs have to buy with their own money);
- old sterilizing equipment that in most health facilities dates back to the 1960s and may not be fully reliable;
- insufficient knowledge and practical skills among medical personnel;
- difficulties with personnel capacity-building due to high staff turn-over; and
- overall lack of funding that limits further improvement of the situation.

Observations by the mission team at the health facilities visited also suggest a gap between the normative base and its implementation. It was observed that sometimes blood collection was conducted inappropriately and personal protective equipment was not properly used even when it was available in the laboratory.

Despite some improvements over the past years, in interviews some specialists repeatedly mentioned “punishment epidemiology” applied to investigation of potential intra-hospital outbreaks. This is of special concern as it can lead to hiding of an event and to significant underestimation of the real situation with nosocomial transmission of bloodborne infections in the country.

Another important issue is occupational safety, as according to official statistics up to 25% of hepatitis B and C cases in the country are registered among HCWs. Out of approximately 50 000 HCWs in Kyrgyzstan, about 16 000 conduct invasive procedures or have other types of professional contact with blood.

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[5] Whether or not the hepatitis A vaccine should be included in routine childhood immunizations depends on the local context, such as the proportion of susceptible people in the population and the level of exposure to the virus. Generally speaking, countries with intermediate endemicity will benefit the most from universal immunization of children. Countries with low endemicity may consider vaccinating high-risk adults. In countries with high endemicity, the use of vaccines is limited as most adults are naturally immune. More detailed information can be found in the WHO position paper on hepatitis A vaccination: http://www.who.int/wer/2012/wer8728_29.pdf.

4.1.3.Blood safety

As reported by the interviewed specialists, 23% of blood donations in the country are provided by voluntary donors, 75% by relatives and around 2% by paid donors. The proportion of paid donors may in fact be higher, as some paid donors might be presented by the patient as a relative.

Kyrgyzstan has 39 blood collection sites, which are methodologically but not administratively linked to a national blood centre. All blood is routinely tested for four TTIs – HIV, HBV, HCV and syphilis. Laboratory test procurement is largely decentralized, which might create risks for quality assurance and control.

After the last nosocomial HIV outbreak, the country developed a blood safety programme that has the following components:

- reduction of the number of blood-collection sites from 39 to 7 (1 national and 6 regional);
- renovation of facilities and upgrading of equipment at the seven sites to meet minimum international standards;
- centralization of management of the blood service;
- installation of a blood quarantine system with documentation of each donation;
- strengthening of the donor management system with information exchange between blood-collection sites and a national register of donors.

At the time of the mission, the blood safety improvement programme was being implemented: the renovation of the national blood centre was in the final stages and new modern equipment was mostly installed. As for the next steps, the specialists of the national blood centre would like to supplement serologic screening for TTIs with polymerase chain reaction (PCR) testing and install automated equipment for virus inactivation.

4.1.4.Harm reduction

Across the country, 35 needle and syringe programmes (NSP) and 31 opioid substitution therapy (OST) programmes are available, supported by the Global Fund to Fight AIDS, Tuberculosis and Malaria. It is especially noteworthy that they operate in the penitentiary sector as well (15 NSP and 8 OST programmes). Independent feedback from civil society is generally positive – harm reduction sites provide user-friendly services and do not meet serious obstacles in their operation. The prevailing psychoactive substances in the country are opiates; synthetic drugs are rare. Most drug users are of older age (40+) and the influx of younger people to this cohort is relatively limited. There is a general consensus among key national stakeholders (health professionals, NGOs, law enforcement) about the positive role and effectiveness of harm reduction programmes. The key identified risk is sustainability, as the national harm reduction programme is heavily dependent on the Global Fund.

4.1.5. Sanitation, clean water and food safety

It was not possible to meet with the relevant units within the MOH; therefore this report does not address national policies and guidance on water and sanitation, and food safety.

4.2. Recommendations

Vaccination

- Hepatitis B vaccination (both the birth-dose and three-dose vaccination) is a well-established programme with very high coverage rates. Therefore it is recommended to **set national targets for hepatitis B control through immunization**, based on regional targets defined by the European Action Plan on Viral Hepatitis.
- Document **the attainment of the national targets** for hepatitis B control through immunization.
- **Prioritize hepatitis B vaccination of HCWs** and consider the feasibility of vaccinating other high-risk groups born before the introduction of universal hepatitis B vaccination (2000):
    - higher risk groups such as men who have sex with men, PWID, sex workers, etc.;
    - incarcerated people;
    - people who need frequent blood transfusions, dialysis patients and patients with chronic liver diseases, including chronic HCV infection.

Infection prevention and control

- Continue **strengthening IPC in all health-care facilities** across the country.
- Consider a phased **replacement of outdated sterilizing equipment**.
- **Enforce IPC and occupational safety standards** (proper work algorithms, universal precautions, availability and consistent use of protective equipment, etc.).
- Provide **strong leadership and supportive supervision** for continued behaviour change among HCWs.
- Continue **staff training on IPC** through graduate, post-graduate and on-the-job training.
- **Address the "punishment epidemiology"** approach applied to nosocomial infections.

Blood safety

- Promote strong leadership to **reduce the number of blood donation sites** only to those meeting minimum international quality standards as soon as possible.
- **Organize blood delivery logistics** to meet the requirements of the new organization of the national blood service.
- Ensure that universal screening for TTIs is in place throughout the country and is applied effectively and consistently in accordance with national standards. Disparities in the standards and **quality of screening across the country should be resolved** before consideration is given to the introduction of any new technology.[6]
- Consider **centralized procurement of reagents** and test kits with ensured quality.

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[6] Although the risk of transfusing a blood unit collected during the window period may be decreased with the addition to the screening algorithm of nucleic acid amplification technology assays (PCR) the incremental gain is minimal as the number of donors in the window period at the point of donation is generally low. In addition, before any new technology (like additional PCR testing or automated devices for viral inactivation) is introduced into a blood screening programme its feasibility should be fully considered, including the requirements for infrastructure, costs of reagents and consumables financing, staffing levels, training and quality systems. Since the overall costs of implementation may far outweigh any potential benefit in terms of increased blood safety, a cost-benefit analysis should be performed.

- Fully utilize additional cost-effective opportunities for improved blood safety in the areas of **donor selection and counselling** as well as the sensitivity of the serological screening undertaken.
- Consider **promoting voluntary blood donations** and phasing out paid donors completely.
- Include a representative of the **blood service in the working group for the development of the national viral hepatitis programme**.

Harm reduction

- Start planning **domestic support for long-term sustainability** of harm reduction projects in the country.
- Expand **testing for hepatitis B and C** to harm reduction clients and other PWID.

5. Diagnosis, treatment and care

Early diagnosis of hepatitis infection is critical for effective treatment and care; yet, the majority of people living with viral hepatitis are not aware of their infection. Testing services and reliable diagnostics that are appropriate for the setting are not sufficiently available, and laboratory capacity is often weak. Increasing early diagnosis requires overcoming those shortcomings, using effective testing approaches and quality-assured diagnostics, and linking the results of testing to treatment and care services.

Effective clinical management of viral hepatitis reduces the individual, social and health burden related to the infection. Effective antiviral agents against viral hepatitis B and C have the potential to dramatically reduce morbidity and mortality, including among people co-infected with HIV. Direct-acting antivirals for the treatment of chronic HCV infection have cure rates exceeding 95%, with pan-genotypic regimens becoming available. Effective treatment is available for chronic HBV infection.

WHO has published and will regularly update guidelines for the care and treatment of people with hepatitis B and C. It is important that countries develop or adapt clinical treatment guidelines for these infections.

5.1. Findings

5.1.1. Infrastructure and human resources for health

Viral hepatitis patients can be managed in outpatient facilities (e.g. family medicine practices) by general practitioners and infectious disease doctors who practice in the outpatient medical centres. Informants mentioned that a lack of specialists (especially in the regions) is an issue, which results in HCWs without sufficient qualifications getting involved in patient management and treatment, providing suboptimal care, including with alternative and unproven methods not aligned with international standards.

If hospitalization is required, patients with acute viral hepatitis are usually hospitalized in the infectious disease wards of territorial hospitals or the Republican Infectious Disease Hospital in Bishkek (which has 400 beds in total and 40 beds in the viral hepatitis ward). Chronic hepatitis patients, when requiring hospitalization due to disease exacerbation or complications, are usually treated by gastroenterologists either in territorial hospitals or in the National Hospital (which has 1070 beds in total and 45 beds for patients with gastroenterological pathology including chronic hepatitis). HCC patients are referred to oncologists.

Kyrgyzstan has no officially recognised speciality of hepatology. Specific viral hepatitis treatment can be prescribed by infectious disease doctors, gastroenterologists and internists. A considerable number of privately practicing physicians also offer viral hepatitis treatment, and some concerns about their competency have been raised.

Specialists who will be treating viral hepatitis are trained in the Kyrgyz State Medical Academy (6 years of general medicine, followed by 2 years of residency in infectious disease speciality). Two other higher medical education institutions also provide post-diploma training of specialists who can treat viral hepatitis: the Kyrgyz State Post-Graduate Medical Institute and the Kyrgyz-Russian Slavic University. These institutions offer internships, residencies or shorter courses for changing the specialty.

5.1.2.Diagnosis

All major testing options are available in Bishkek, including serology (ELISA), viral load and genotyping (PCR); however, quality assurance is an issue in some laboratories. Access to high-quality laboratory tests in the regions is limited. Viral load and genotyping tests are available in the Department of Disease Prevention, the State Sanitary Epidemiological Surveillance department and in some private laboratories.

Rapid tests for viral hepatitis are not used in Kyrgyzstan, except in some private laboratories.

The reference laboratory for viral hepatitis of the Scientific and Production Institute “Preventive Medicine” conducted an external quality assessment of viral hepatitis diagnostics (anti-HCV and HBsAg) in 2015 among 57 national, regional and private laboratories. It showed that many different test systems are in use in the country, with differing quality. The most significant reasons for diagnostic failure included: lack of knowledge and skills in quality management among laboratory specialists, insufficient implementation of internal laboratory quality control and poor quality of test systems used.

FibroScan is available in the Government Hospital, the Republican Clinical Hospital and in two private medical centres, but APRI scoring (recommended by WHO) is reportedly used more commonly for staging liver fibrosis. Almost all these tests must be paid for by the patient and no standardized testing algorithm is in place; selection of tests change according to physician and the patient’s ability to pay.

5.1.3.Treatment

National clinical protocols for diagnosis, treatment and prophylaxis of hepatitis B and C were developed in 2014, however these are not aligned with the current WHO guidelines, and for example do not include direct-acting antivirals (DAAs) for the treatment of chronic HCV infection.

For chronic HBV infection, standard treatment includes pegylated interferon and lamivudine, but treatment duration varies from 6–24 weeks, depending on the viral load and the patient’s ability to pay. Frequent interruption and retreatment take place.

Kyrgyzstan is one of four countries in the WHO European Region that was included in the Gilead HCV Treatment Access Programme, which allows registration and import of generic DAAs produced under voluntary licence agreement. Also, in 2015 the Patent Law of the Kyrgyz Republic was

amended to allow use of most of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities. Several generic versions of sofosbuvir have already been registered and are available on the market. In June 2016, a generic version of sofosbuvir/ledipasvir was registered and generic daclatasvir was awaiting registration. Prices for generic sofosbuvir are US$ 260–450 per package, which is still too expensive for most patients. Informants reported that people are resorting to the black market by purchasing from outside the country, which raises issues of dosage, monitoring, drug–drug interaction and quality. All viral hepatitis-specific treatment must be paid for by patients.

To summarize, the mission team identified the following challenges related to viral hepatitis treatment:

- lack of up-to-date treatment protocols;
- use of non-evidence based treatment regimens;
- use of black market medicines (raising quality and safety issues);
- lack of standardized and up-to-date physician training in viral hepatitis;
- limited access to treatment, which is unaffordable for most citizens;
- frequent treatment interruptions (increasing the potential for HBV resistance).

5.2. Recommendations

Human resources for health

- Identify **duties and responsibilities at all levels of the health-care system** and build capacity to:
    - test and diagnose viral hepatitis;
    - initiate treatment;
    - follow up and monitor patients;
    - complete treatment.

  Use this to develop policies for task-shifting for hepatitis B and C treatment scale-up.
- Revise the current **post-diploma education** and develop a standardized curriculum for specialist training in viral hepatitis to be approved by the MOH.

Testing and diagnosis

- Develop and publish **national viral hepatitis testing and diagnosis algorithms**, including identifying groups at higher risk for hepatitis infection that need to be offered hepatitis testing at different levels of the health-care system, along with the national treatment protocols.
- Develop **educational programmes for laboratory specialists** on quality control for laboratory diagnostics.
- Ensure state **control over the diagnostic test systems** that are entering the market.
- Consider offering **routine testing to populations at higher risk**, including outreach and using rapid tests or dried blood spot tests.
- Consider the feasibility of **using AIDS centres and drug treatment services** for screening, linkage to care and treatment of patients with chronic viral hepatitis.

Treatment and care

- Update **national chronic hepatitis treatment protocols** (including for cirrhosis and HCC) in line with WHO guidelines. This will ensure state-of-the-art treatment for patients and also will shape the pharmaceutical market.
- Include modern, safe and effective medicines recommended in WHO guidelines for treating hepatitis B and C, and included in the latest WHO Essential Medicines List, in the **National Essential Medicines List of Kyrgyzstan**.
- Establish a **centre of excellence** for chronic viral hepatitis care and treatment (e.g. National Hepatology Centre) to:
    - implement the new protocols;
    - follow up on treatment outcomes;
    - serve as a centre for capacity-building.
- Provide publicly funded or co-funded treatment of chronic viral hepatitis at least for higher risk patients (e.g. advanced liver disease, HCWs, people living with HIV, etc.).
- Take active measures to further **reduce prices of chronic viral hepatitis medicines and diagnostics** (e.g. by promoting generic competition and improving regulatory processes).
- Consider **centralized procurement of medicines and single-use consumables** (syringes, vacuum blood collection tubes, etc.) ensured quality and WHO pre-qualification.

Conclusions and next steps

The mission team recognized Kyrgyzstan's achievements in controlling hepatitis B through universal birth-dose vaccination, and the work done on normative guidance on blood safety and infection control. The team also acknowledged the commitment of national stakeholders and the interest of the MOH in continued collaboration with WHO in order to improve and scale up the response to viral hepatitis in Kyrgyzstan.

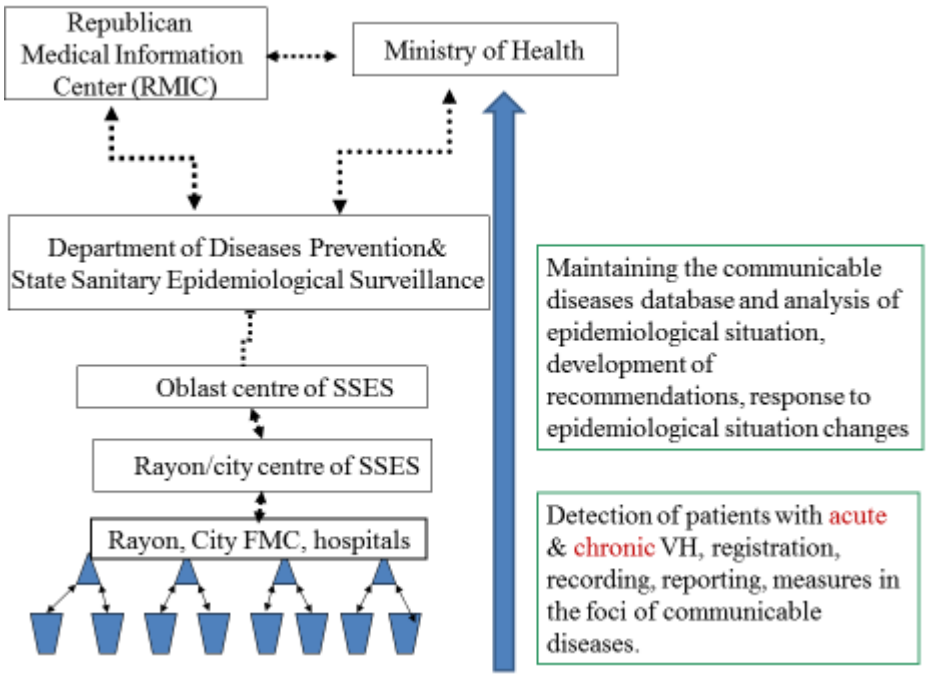
WHO is ready to provide further technical support within the framework of the biennial collaborative agreement covering 2016/2017 between the MOH and WHO, and suggests the following next steps to be discussed with national counterparts:

- The clinical protocols for diagnosis, treatment and care of viral hepatitis need to be updated and aligned with the latest WHO hepatitis guidelines as soon as possible. WHO has translated its latest guidelines into Russian and will be ready to review and provide comments on the draft national clinical protocols if necessary.
- The new national programme (national action plan) on viral hepatitis control for 2017–2022 should be finalized. It is recommended that it be aligned with the European Action Plan on Viral Hepatitis, endorsed by the WHO Regional Committee for Europe in September 2016. WHO would provide technical support in the development of the new national programme.
- The viral hepatitis surveillance system in Kyrgyzstan needs to be reviewed and aligned with WHO recommendations, including adopting WHO case definitions, creating a centralized registry of patients with chronic viral hepatitis. WHO has translated its guidance on viral hepatitis

surveillance and will be willing to provide technical support in updating and improving the national surveillance system.

- In order to better understand the burden of viral hepatitis and estimate its cost to the Kyrgyz economy, as well as the relative cost of effective interventions, disease burden modelling should be conducted, followed by economic analysis (the so called investment case). WHO can support Kyrgyzstan by attracting an external expert team who will conduct this modelling work. The investment case will use data from the initial assessment, particularly the prevalence of chronic infection in various age groups, to evaluate various intervention scenarios. These scenarios may combine interventions in the field of prevention (e.g. immunization, blood and injection safety, and harm reduction) and in the field of testing and treatment, so as to estimate cost, budget implications, epidemiological impact and cost effectiveness. Such economic analyses can take the form of an investment case for broader audiences or a cost-effectiveness analysis for a health sector audience.

Annex 1. Surveillance of viral hepatitis in Kyrgyzstan



SSES = State Sanitary Epidemiological Surveillance, FMS = Family Medicine Practice, VH = viral hepatitis

Annex 2. Detailed agenda of the WHO viral hepatitis mission to Kyrgyzstan, 11–15 July 2016

	11 July	12 July	13 July	14 July	15 July
Goal	*Advocacy and awareness raising; gathering information from MOH officials*	*In-depth information from MOH technical leads*	*In-depth information from academia and civil society*	*Getting missing information and preparing the report*	*Preparing and delivering the exit presentation*
Morning 1	8.00–9.00 Talantbek Batyraliev, Minister of Health (Confirmed)	9.00–10.00 Baktygul Ismailova, acting Head of Public Health Unit/Ministry of Health (MOH) & Department of Diseases Prevention and State Sanitary Epidemiological Surveillance	9.00–10.00 Visit to Republican Infectious Diseases Hospital	9.00–10.00 Visit to Family Health Practitioners Centre and interview with infectious disease specialist 9.00–10.00 Visit to Republican AIDS Centre	Preparing the exit briefing and report
Morning 2	9.00–10.00 Internal MOH meeting with heads of relevant programmes: Samat Toymatov, Head of Main Department of Organization of Health Service; Baktygul Ismailova, acting Head of Public Health Unit; Nurgul Ibraeva, Hepatitis Focal Point in MOH. 10.00–11.00 Bermet Barktabasova, Consultant, Evidence Based Medicine Centre, MOH and Working Group on Hepatitis Clinical Protocols	10.00–11.00 Anara Djumagulova, Head, Infectious Diseases Unit, Kyrgyz State Medical Academy and Working Group on National Hepatitis Strategy	10.10–11.10 Anara Djumagulova, Head, Infectious Diseases Unit, Kyrgyz State Medical Academy Rakhat Kadyrova, Head, Paediatric Infectious Diseases Unit, Kyrgyz State Medical Academy Kalys Nogoybaeva, Infectious Diseases Unit, State Post-graduate Medical Institute Elena Radchenko, Kyrgyz–Russian Slavic University	10.30–11.30 Visit to private laboratory	(continued)

Afternoon 1	13.00–16.00 National hepatitis stakeholders meeting to discuss the national/local epidemic and response (Mandatory Health Insurance Fund, infection control, drug supply, immunization, tuberculosis, HIV, harm reduction, hepatitis treatment, public health, academia, United Nations, international and local nongovernmental organizations	13.00–14.00 Larisa Murzakarimova, Head, Republican Medical Information Centre	13.00–14.00 Dinara Saginbaeva, Chief Doctor and Elmira Junushbaeva, Gastroenterologist, National Hospital Bakyt Karabaev, Director, Republican Blood Centre	Preparing the exit briefing	14.30–15.30 Exit briefing to Jarno Habicht, WHO Country Office in Kyrgyzstan
Afternoon 2		14.15–16.00 Omor Kasymov, Director; Zuridin Nurmatov, Deputy Director; Gulmira Suranbaeva, Clinician, Scientific and Production Institute “Preventive Medicine”	14.30–15.30 Site visit and interviews with civil society representative Aibar Sultangaziev	(continued)	16.00–17.00 Exit briefing to Talantbek Batyraliev, Minister of Health and MOH officials (to be confirmed)
Evening	Mission team meeting	Mission team meeting	Mission team meeting	Mission team meeting	Mission team meeting for follow-up actions

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