National Hepatitis C Virus Elimination Progress Report

Georgia, 2015-2017

MINISTRY OF LABOUR
HEALTH AND
SOCIAL AFFAIRS

NCDC

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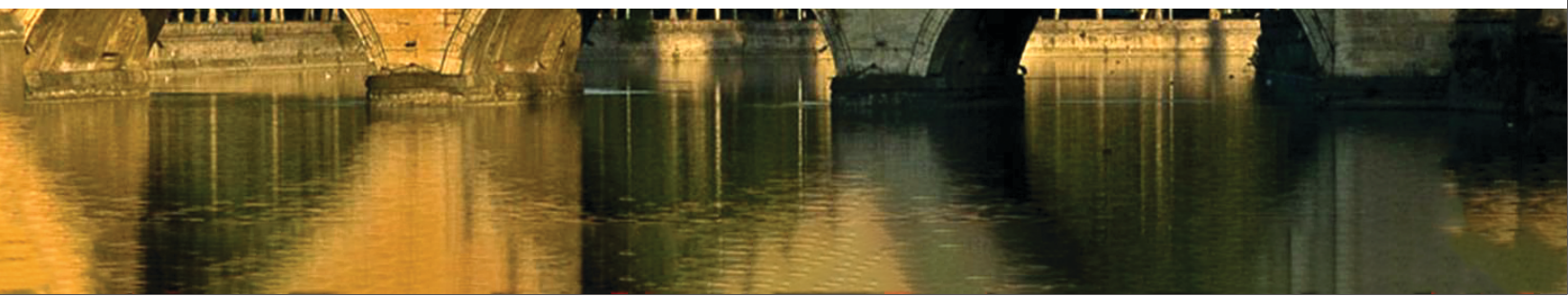

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LIST OF ABBREVIATIONS

AASLD	American Association for the Study of Liver Diseases
AMR	Antimicrobial resistance
BBSS	Bio-Behavioural Surveillance Survey
CME	Continuing medical education
DAA	Direct acting antivirals
DVH	Division of Viral Hepatitis
EASL	European Association for the Study of the Liver
ECHO	Extension for Community Healthcare Outcomes
ELISA	Enzyme linked immunoassay
EQA	External quality assessment
ESLD	End-stage liver disease
GFATM	Global Fund to Fight AIDS, Tuberculosis, and Malaria
GHRN	Georgia Harm Reduction Network
GMP	Good Manufacturing Practice
GSA	Georgian Stomatological Association
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HCW	Health-care workers
HRU	Health Research Union
IDACIRC	Infection Diseases, AIDS and Clinical Immunology Research Center
IDSA	Infectious Diseases Society of America
IDU	Injection-drug use
ILC	International Liver Conference
IPC	Infection prevention and control
KAP	Knowledge, attitudes, and practices
LED	Ledipasvir
LIFER	Liver Institute and Foundation for Education and Research
LSS	Laboratory surveillance stations
M&E	Monitoring and evaluation
MoLHSA	Ministry of Labour, Health, and Social Affairs
MOU	Memorandum of Understanding
NCDC	Georgia's National Center for Disease Control and Public Health
NSP	Needle and syringe program
OST	Opioid substitution treatment
PHC	Primary health centers
PSA	Public service announcement
PWID	Persons who inject drugs
QA/QC	Quality assurance/quality control
RAMA	Regulation Agency for Medical Activities
SC	Scientific Committee
SOF	Sofosbuvir
SOPs	Standard operating procedures

SVR	Sustained virologic response
TAG	Technical Advisory Group
TTI	Transfusion transmissible infections
U.S. CDC	United States Centers for Disease Control and Prevention
U.S. FDA	United States Food and Drug Administration
VCT	Voluntary counseling and testing
WHA	World Hepatitis Alliance
WHD	World Hepatitis Day
WHO	World Health Organization

EXECUTIVE SUMMARY*

Globally, an estimated 71 million persons are living with hepatitis C virus (HCV) [1]. Georgia has a high burden of HCV infection, with an estimated 5.4% of the adult population (150,000 people) living with HCV, with the greatest burden among men aged 30–59 years [2,3]. Risk factors associated with HCV infection in Georgia include receipt of contaminated blood products and injection-drug use [3]; HCV prevalence is highest among the estimated 50,000 persons who inject drugs (PWID) [4]. HCV efforts began in Georgia in 2011. At that time, a limited number of HCV-infected persons with HIV c-infection were offered treatment annually through the State HIV prevention program, funded by the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) [5]. In 2013, a program in the prison system also began offering screening and treatment services to a limited number of inmates annually. However, for most persons infected with HCV, treatment options were limited to all interferon-based regimens and costs were prohibitive, even though the government did obtain some discounted pricing (60%), resulting in a very small number receiving treatment through the private sector.

In 2013, Georgia engaged the United States Centers for Disease Control and Prevention (U.S. CDC) to embark on a path towards addressing the country's HCV epidemic. By the following year, Gilead Sciences and other partners had come on board. These efforts resulted in the conduct of a national seroprevalence survey in 2015, culminating in the launch of the world's first HCV Elimination Program in April of that same year. Elimination was deemed feasible in Georgia given the following:

- Georgia's strong political and financial commitment;
- active participation of civil society;
- an engaged and experienced medical community committed to high quality care and treatment of HCV infected persons;
- adherence to principles of evidence-based medicine for hepatitis C as evidenced by the availability of national guidelines for many years;
- existence of effective systems for implementing large-scale national and international health programs, including through multi-sectoral approaches;
- availability of logistic and control mechanisms within existing national HIV/AIDS, tuberculosis, and hepatitis C treatment programs that effectively prevent inadvertent provision of medicines to local and/or neighboring markets;
- best-practice experience in the field of HIV/AIDS that can be replicated for hepatitis C programs, namely achievement of universal access to antiretroviral therapy that has remained unique in the Eastern European region for more than a decade;
- large burden of disease;
- small country population;
- political stability;
- active engagement of U.S. CDC's in-country South Caucasus Office; and
- commitment by U.S. CDC's Division of Viral Hepatitis (DVH) to provide technical assistance and support.

* Data through 2016 are complete; this report includes provisional and incomplete data from 2017.

With strong stakeholder support, including partnership and technical assistance from U.S. CDC and commitment from Gilead Sciences to donate direct-acting antiviral HCV medications (DAAs), Georgia embarked on the world's first HCV elimination program on April 28, 2015. Georgia set an Elimination Program goal of reducing HCV prevalence by 90% by 2020, and to achieve this goal, the following 2020 targets were established:

1. Identify 90% of adults (≥18 years of age) infected with hepatitis C
2. Treat 95% of people with chronic HCV infection
3. Cure 95% of persons treated for their HCV infection

The program initially focused on providing treatment to 5,000 persons with severe liver disease (i.e., those with fibrosis levels of F3 or F4 by METAVIR scale [6] and/or FIB-4 score >3.25 [7]). In anticipation of the launch, key activities were undertaken, including assessment of clinical and laboratory capacity; drafting of HCV management and treatment guidelines to include regimens based on sofosbuvir (donated DAA) +/- pegylated interferon and ribavirin; development of an HCV Elimination Program treatment registry and database (STOP-C) based on the data system utilized when the program offered interferon treatment; and public service announcements to provide the public with general information about the program and details about where to present for determination of program eligibility.
This report chronicles the progress of Georgia's HCV Elimination Program from its April 2015 launch through December 31, 2016*. The following are highlights/accomplishments for this period.

- **Seroprevalence Survey**: From May through August 2015, a national house-to-house population seroprevalence survey was conducted to collect the following key information used to guide program development:
    - 7.7% of the adult population (i.e., persons ≥18 years of age) showed evidence of ever being infected with HCV (anti-HCV positive), and 5.4% tested positive for current infection (approximately 150,000 persons).
    - HCV RNA prevalence was higher in urban populations than those living in rural areas (6.6% vs. 3.7%, respectively) and among men (8.9% vs. 2.1% in women). Up to 20% of men aged 30–60 years had evidence of HCV infection.
    - Key risk factors identified among anti-HCV positive persons included history of injection-drug use (IDU) and history of receipt of blood products.
    - Nearly two thirds of those with evidence of HCV infection were unaware of their status, learning about their infection for the first time through this survey.
    - Genotype 1b was the most common HCV infection (40.5%), followed by genotype 3 (34.7%) and genotype 2 (23.6%).
- **Workshops:** Since 2014, an annual national HCV workshop has been jointly conducted by the Georgia National Center for Disease Control and Public Health (NCDC) and the U.S. CDC. These workshops have been key to reviewing progress and challenges, conducting program planning, and discussing the implementation steps needed to continuously improve the HCV elimination program.
- **European Association for the Study of the Liver (EASL) Side Meetings/Symposia:** Since 2014, the EASL meeting has included a sponsored symposium dedicated to discussion of Georgia's HCV Elimination Program. These symposia have been invaluable as a forum to present activities, progress, and challenges and solicit input and feedback from international experts, as well as to recruit organizations and individuals interested in becoming program partners.

- **Monitoring and Evaluation (M&E):** Data obtained through M&E activities facilitate important data-driven policy decisions and steer program direction by determining the effectiveness of current activities. During 2016, an M&E plan was developed jointly by the Ministry of Labour, Health, and Social Affairs (MoLHSA), the Georgia NCDC and U.S. CDC with critical input from key stakeholders.
- **State Committee:** In 2015, a special commission on HCV overseeing the overall coordination of Georgia's national HCV elimination initiative was established under MoLHSA. The commission includes members from governmental and non-governmental sectors, clinicians, and a representative from U.S. CDC.
- **Scientific Committee (SC):** Developed in 2016 and co-chaired by NCDC and U.S. CDC, this committee serves as the official forum of the elimination program to identify and propose key topics in need of additional scientific attention as well as to support data analysis and dissemination; members include representatives from key clinical partners and MOLHSA. A key role of the SC is to support priority activities and research and to assist in securing funding from partners. In its first year, the SC helped obtain funding for priority projects and fostered collaboration with Georgian and international researchers. A total of 35 research proposals have been reviewed as of October, 2017. The SC will report on progress annually and actively seek support for the research agenda in Georgia. Appendix 4 and 5 include the scientific publications highlighting the progress and research activities related to HCV Elimination Program.
- **Technical Advisory Group (TAG):** An independent TAG convened its first meeting in November 2015, with the second meeting held in October 2016. The TAG, an independent body consisting of international experts covering each Elimination Plan priority, is an invaluable program partner. TAG meetings bring the Government of Georgia together with key international partners to discuss program accomplishments and challenges in an open forum. TAG meets annually in Tbilisi, Georgia, the third TAG meeting was held November 30 and December 1, 2017.
- **Partnerships:** Partnerships were critical to realizing the launch of the HCV Elimination Program in 2015; founding partners include the Government of Georgia (MOLHSA and NCDC), Gilead Sciences, and U.S. CDC. A Memorandum of Understanding (MOU) was signed between the Government of Georgia and Gilead Sciences on April 21, 2015, with an additional MOU signed between the Government of Georgia and U.S. CDC in 2017. Additional domestic and international partners have become involved in Georgia's elimination effort. These include
    - **Domestic partners:** Clinicians and Georgian Harm Reduction Network (GHRN)
    - **International partners:** the CDC Foundation (CDCF), U.S. Embassy, World Health Organization (WHO) headquarters and the WHO Regional Office for Europe (WHO/Europe), University of New Mexico Health Sciences Center—Project of Extension for Community Healthcare Outcomes (ECHO), Liver Institute and Foundation for Education and Research (LIFER), World Hepatitis Alliance, Foundation for Innovative Diagnostics (FIND), Global Fund to Fight AIDS, Tuberculosis, and Malaria, Abbott, Bristol University, Emory University, Becton Dickinson (BD), and Georgia State University (GSU).
- **HCV Elimination Strategic Plan:** The 2016–2020 *Strategic Plan for the Elimination of Hepatitis C Virus in Georgia* was approved by the Georgian Government on August 18, 2016. An English language version of the Plan was published in March 2017; this version was organized by strategy for achieving elimination (Figure 1) and included specific activities needed to achieve

HCV elimination goals by 2020. Progress has been made towards reaching these goals, and substantial data have been collected towards measuring this progress (Appendix 1).

- As of September 2017, over 1,200,000 HCV screening tests were performed across the country; screening data from 712,534 unique individuals were incorporated into the national screening registry. Among registered persons, more than 8% (N=58,339) had anti-HCV positive results.
- During 2015–2016 the highest rate of HCV-antibody-positive screening tests (45.0%) was among persons who attended programs providing services for PWID.
- By September 2017, a total of 31 health facilities in different cities across Georgia, including one center in a penitentiary system, were providing diagnostic and treatment services to HCV Elimination Program beneficiaries.
- From April 28, 2015 through October 31, 2017, a total of 49,624 persons with evidence of HCV infection (i.e., persons with reactive rapid test on HCV antibody) were enrolled in the HCV program to seek confirmation of active HCV infection by HCV RNA testing. Overall, 40,420 persons initiated treatment either with the sobosbuvir-based (without ledipasvir) regimen (N=7,342) or with a combination of sofosbuvir/ledipasvir (N=33,078). A total of 36,012 patients have completed treatment. Among those with sustained virologic response (SVR) results available, the overall cure rate was 98.2%.

Elimination of hepatitis C in Georgia is feasible. To achieve this goal, existing gaps revealed through M&E efforts must be closed. Improvements in HCV testing, diagnosis, and care require a multi-sectoral approach, including cooperation of various agencies, stakeholders, and private-sector organizations. These partnerships are also critical to successful implementation of strategies for preventing new infections (i.e., improving safety of the blood supply, ensuring infection control in health-care settings, and providing PWID with harm-reduction services). The M&E data obtained through Georgia's Elimination Program will ensure that the strategies outlined in the national strategic plan for HCV elimination are fully implemented and, if needed, resources redirected in a timely manner.

INTRODUCTION

The global burden of viral hepatitis is substantial with an estimated 71 million persons living with HCV, and approximately 400,000 dying from HCV each year largely due to the sequelae associated with chronic infection (e.g., cirrhosis and HCC) [1]. Georgia has a high burden of HCV infection. According to the national seroprevalence survey conducted in 2015 by Georgia's NCDC with support from the U.S. CDC, an estimated 5.4% of Georgia's adult population (approximately 150,000 people) are living with HCV [3]. The burden is greatest among men aged 30–50 years, and both injection-drug use and receipt of blood products have been identified as risk factors [3]. Given that an estimated 50,000 Georgians inject drugs, among whom HCV prevalence is high [4], this behavioral risk factor contributes substantially to the current HCV epidemic.

Efforts to combat HCV infection began in Georgia in 2011 when the country began offering treatment to a limited number of HCV-HIV co-infected persons each year through the Georgia HIV Program (funded by GFATM). A program in the prison system also began offering screening and treatment services in 2014. All treatments provided through these programs were interferon-based. Although a reduced cost program funded by the government also launched in 2014, for most persons with hepatitis C, treatment options were limited and costs prohibitive, resulting in a very limited number receiving treatment through the private sector.

In 2013, Georgia engaged the U.S. CDC and embarked on a path towards addressing their growing HCV epidemic. In 2014 the concept of HCV elimination in Georgia was first conceptualized, and Gilead Sciences became engaged; that same year, representatives of Gilead conducted an assessment of Georgia's clinical and logistic capacity to determine whether introduction of a large-scale treatment program was feasible. Early in 2015, a Georgian delegation visited Egypt to learn about that country's experience in similar large-scale public health programs involving treatment of patients with new DAAs. These efforts resulted in development of an action plan that described immediate, urgent measures for initiating the program, culminating in the launch of the world's first HCV Elimination Program in April 2015. Several key considerations contributed to this collaborative launch of the elimination program, including Georgia's political and financial commitment; active participation of civil society; engagement of an experienced medical community committed to high quality care and treatment for HCV-infected persons; large burden of disease; small population; and political stability. The U.S. CDC's commitment to providing technical assistance and support to the program, along with active engagement of their South Caucasus-based office, facilitated program implementation. Gilead Sciences took these factors into consideration before committing to donate DAAs to treat all HCV-infected Georgians as part of the elimination effort.

The National HCV Elimination Program was launched on April 28, 2015. On this day, the Government of Georgia committed to eliminating HCV in the country (i.e., reducing infection prevalence by 90%) by the year 2020. To achieve its elimination goal, the country of Georgia set forth the following 2020 targets.

1. Identify 90% of adults (≥18 years of age) infected with hepatitis C
2. Treat 95% of people with chronic HCV infection
3. Cure 95% of persons treated for their HCV infection

The initial focus of the program was treatment of 5,000 persons with known and severe liver disease (i.e., those with a liver fibrosis level of F3 or F4 by METAVIR scale [6] and/or FIB-4 score >3.25 [7]). In anticipation of the launch, key activities were undertaken. Assessment of clinical and laboratory capacity was conducted to ensure quality; management and treatment guidelines were drafted (including for sofosbuvir [donated DAA] +/-

pegylated interferon and ribavirin regimens); an HCV Elimination Program treatment registry and database (STOP-C) were developed based on the data system used during the time interferon was offered through the program; and public service announcements were created and disseminated to inform the public about the program and instruct people where to present to learn their enrollment eligibility. Beginning June 10, 2016, inclusion criteria were removed to allow every person infected with HCV to enroll in the program and start treatment with new DAAs, regardless of liver-disease severity.

This Annual Report chronicles progress of the National HCV Elimination Program since its launch in April 2015 through December 31, 2016, and available data and select findings through 2017. Designed to mirror the six elimination strategies presented in the larger 2016-2020 *Strategic Plan for the Elimination of Hepatitis C Virus in Georgia* (Figure 1), it presents strategy-specific, qualitative information about milestones met towards reaching elimination goals and quantitative M&E data. The Annual Report will be updated each year to reflect current HCV elimination program progress and can be used to inform modifications and enhancements to existing activities to ensure program effectiveness.

Figure 1. PROGRAM STRATEGIES FOR HEPATITIS C ELIMINATION IN GEORGIA

Strategy 1: Promote advocacy, awareness and education, and partnerships for HCV-associated resource mobilization	•Educate the public and high-risk groups about viral hepatitis and the importance of testing •Reduce stigma and discrimination associated with hepatitis in healthcare settings and among the general public
Strategy 2: Prevent HCV transmission	•Decrease HCV incidence among PWID by promoting harm reduction •Prevent healthcare-related transmission of viral hepatitis by improving blood safety •Prevent healthcare-associated transmission of viral hepatitis by improving infection control •Prevent HCV in non-traditional healthcare and other community settings
Strategy 3: Identify Persons Infected with HCV	•Increase the number of HCV diagnoses through expanded screening and testing •Expand HCV testing to better reach high-risk populations
Strategy 4: Improve HCV Laboratory Diagnostics	•Improve laboratory detection of HCV infection
Strategy 5: Provide HCV Care and Treatment	•Promote universal access to HCV care and treatment
Strategy 6: Improve HCV Surveillance	•Estimate the national burden of chronic viral hepatitis

STRATEGY 1:

PROMOTE ADVOCACY, AWARENESS AND EDUCATION, AND PARTNERSHIPS FOR HCV-ASSOCIATED RESOURCE MOBILIZATION

Introduction

The HCV Elimination Program in Georgia receives strong support from the national government. Georgia has also successfully established local partnerships (e.g., governmental organizations; Infectious Disease, AIDS and Clinical Immunology Research [IDACIRC]; and Ministry of Corrections and Legal Assistance [MCLA]) and international collaborations to help with the overall program implementation. Also providing advocacy and assistance are private-sector representatives (e.g., private clinics delivering HCV-associated health services) and non-governmental and community-based organizations that are actively involved in HCV service delivery (e.g., testing and referral), policy dialogue, and long-term elimination planning. Partnerships can play a pivotal role in promoting HCV-related communication and education in the community at large.

The first nationally representative seroprevalence survey of adults aged ≥18 years was conducted in 2015 in six major cities (MoLHSA, unpublished data, 2016). A total of 6,331 respondents were interviewed using a structured questionnaire, which included questions pertaining to the knowledge of HCV in addition to demographics, medical history, and lifestyle. This seroprevalence survey revealed low knowledge about hepatitis C, with approximately 60% of the general population knowing the transmission routes for this infection. When participants were asked about specific modes of transmission, 52% cited sharing needle/syringes, 44% reported sharing household objects that have had contact with blood, and 32% cited sexual contact. Only 57% of respondents were aware that HCV infection can be asymptomatic. More than 70% knew that HCV infection can be treated, and 8% erroneously believed that HCV is a vaccine-preventable infection. HCV-related knowledge was higher among participants who were anti-HCV positive and highest among anti-HCV positive PWID in particular (MoLHSA, unpublished data, 2016). This data helped Georgia prioritize activities to increase public awareness of the natural history of HCV, transmission routes, and the importance of testing and treatment.

Hepatitis C not only causes serious liver damage, but is also associated with mental, psychological, and social consequences and stigma [8]. Data is available that suggests that diagnosis with hepatitis C has a profound impact on social functioning [9]. As such, any campaign to improve public awareness of HCV must be accompanied by a solid understanding of the societal factors that drive stigma in particular communities and populations; only through such knowledge can appropriate, culturally sensitive messages be developed, eliminating stigma as a barrier to patient acceptance of HCV testing and treatment.

Progress and Program Outcomes

To raise awareness of hepatitis C and prevent its spread among at-risk groups, since the launch of the HCV elimination initiative, NCDC's Health Promotion National Program has implemented an extensive program of diverse activities, involving development of educational materials. Two national educational social media campaigns targeting adults aged ≥18 years were conducted from 2015 through 2016. These campaigns used a variety of media strategies to increase knowledge of the benefits of HCV diagnoses, treatment, and prevention and to garner community support for the HCV elimination effort, with the ultimate goal of a) encouraging persons at high risk of HCV exposure to seek counseling about high-risk behaviors and b) providing the public with relevant information about local facilities providing HCV prevention services. Specific campaign components are as follows:

- Social digital advertisements highlighted the importance of HCV prevention and provided education on the modes of virus transmission. Social internet advertisements generated more than 1 million views (video clip: 1,000,000 views; web banner: 4,000,000 views); this represents substantial coverage given Georgia's total population of 3.7 million.

- Social media platforms such as the Health Promotion Facebook page (https://www.facebook.com/HealthPromotionGeorgia/) and NCDC blogs (https://ncdcgeorgia.wordpress.com/) were an effective means of communicating awareness on hepatitis C and disseminating campaign messages through posts, visual materials, and online surveys.

    - ✓ In total, 40 Facebook posts and six blogposts were released, resulting in more than 1,000 unique user views for each. The Facebook page has garnered around 9,000 "Likes." The top five most viewed Facebook posts are listed in decreasing order:

        -Hepatitis C prevention and control measures (4,991 reaches)

        -Hepatitis C complications and high-risk populations (3,827 reaches)

        -HCV transmission and measures undertaken by the Government of Georgia to prevent the disease (3,014 reaches)

        -HCV Elimination Program progress, statistics, and treatment outcomes (2,871 reaches)

        -Infographic about why the hepatitis C elimination program is a unique opportunity for Georgia (2,556 reaches)

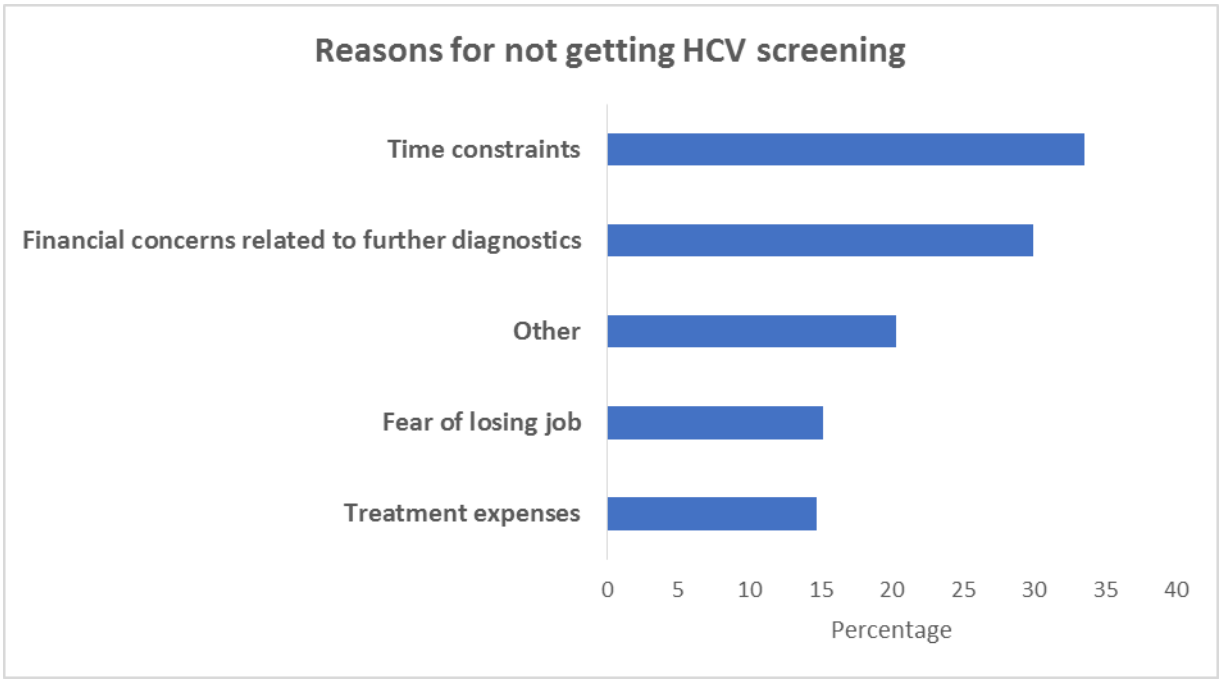
    - ✓ Three main topics (i.e., screening acceptance, HCV transmission routes, and HCV high-risk groups) were included in a series of three online surveys and placed on the Facebook page.

    - ✓ A total of 360 unique users have completed the Facebook surveys. Analysis of the hepatitis C Facebook page indicated:

        - >66% of responders (185/278) did not undergo free HCV screening for various reasons.

- 15% identified social stigma (e.g., potential job loss if the employer becomes aware of an employee's HCV status) as the reason for their reluctance to be screened for HCV (Figure 1.1).
- Risk behaviors and transmission modes were correctly identified by 89% (326/362) of Facebook visitors to the site.

Figure 1.1 Reasons for not being screened for HCV infection according to Facebook survey, November–December 2016, (N=220)



- Public education materials in the form of posters, infographics, flyers, and booklets were developed and disseminated (Figure 1.2); all public and private partners (including non-governmental organizations) were actively involved with the development and dissemination of these materials to ensure maximum coverage among the general population and those subpopulations at increased risk for HCV. In total, 7,000 posters, 30,000 booklets (15,000 targeting the general population and 15,000 targeting risk groups), and 17,000 flyers (8,500 for the general population and 8,500 for beneficiaries enrolled in the treatment program) were disseminated throughout the country. All posters and booklets were translated into Armenian and Azeri languages.

- To accelerate prevention and control of HCV infection, six articles were published in print and through online media.*

- Television public service announcements (PSAs) aired six times per day for 2 months on both central and regional TV channels covering seven regions of Georgia: Kakheti, Imereti, Adjara, Samegrelo-Zemo Svaneti, Kvemo Kartli, Shida Kartli, and Samtskhe-Javakheti.
- Web banners featuring a hotline number to encourage persons to get tested for HCV garnered 4 million views (http://openx.palitra.ge/baner/c_heapatiti/hepatiti.html).

Figure 1.2 Poster for the 2016 communication campaign "Hepatitis C Prevention, Population Education, and Promotion"

- In 2016, a television media campaign aired for 6 months on one of the seven top-rated TV broadcasts. Additionally, TV shows with invited guests (e.g., hepatitis experts, clinicians, and MoHLSA leadership) helped boost awareness of the HCV elimination program.

* http://www.kvirispalitra.ge/medicina/31695-30000-ze-meti-narkomomkhmarebeli-c-hepatitithaa-daavadebuli.html http://www.ipress.ge/new/49744-giorgi-bakhturidze-6-tveshi-ertkhel-chaitaret-C-hepatitze-gamokvleva http://www.ipress.ge/new/49740-C-hepatitis-eliminaciis-programis-farglebshi-pacientebs-24-samedicino-datsesebuleba-moemsakhureba http://liberali.ge/news/view/25666/2015-tslis-kvlevit-C-hepatitis-aqtiuri-formit-daavadebulia-mosakhleobis-54 http://www.ambebi.ge/sazogadoeba/185793-ra-bedi-elis-c-hepatitis-eliminaciis-proeqts-qqmsoflios-nebismier-qveyanashi-inatreben-sastsauls-rac-aq-khdebaq.html

- Vitally important to Elimination Program success were efforts by HCV patients who became beneficiaries of the HCV program (i.e., those diagnosed with hepatitis C infection and cured of their infection) to raise public awareness of all aspects of HCV, reducing patient-driven stigma, empowering their local communities, and serving as Elimination Program "success stories."

- To improve HCV-associated communication, over the past 3 years the Government of Georgia began participating in international meetings (e.g., EASL), arranging for media coverage of annual TAG meetings, holding a National workshop on Hepatitis C, and commemorating World Hepatitis Day (WHD). These activities not only helped Georgians feel personally connected to the elimination effort and understand their role in elimination, but called Georgians to action and inspired behavioral change.

- To support WHO's hepatitis elimination strategy launched on WHD 2016, Georgia joined the NOhep worldwide movement (see Program-Related Scientific Activities, Events and Meetings).

- To engage the media in efforts to eliminate HCV-related stigma and discrimination and promote social responsibility of the general public, a media seminar was convened for 26 popular TV, social, and print-media journalists. Clinicians involved in the program joined representatives from NCDC to present data on the HCV elimination program in Georgia, including information about HCV-related epidemiology, screening, prevention, and treatment.

- In October 2016, a qualitative study was conducted to assess hepatitis C-related awareness, stereotypes, stigma, and discrimination and to test and discuss communication campaign messages among the general population, HCV program beneficiaries, and populations at high risk for HCV infection.

    - ✓ Seven focus-group discussions took place in Tbilisi (Georgia's capital city) and Zugdidi (a city in one of the Western regions with a high HCV prevalence as identified by the hepatitis C seroprevalence survey). Four of these discussions aimed to study knowledge, attitudes, and practices (KAP), while the objective of the remaining three focus-group discussions was to test communication materials. In addition, eight in-depth interviews with PWID were conducted in the same cities. A total of 6-7 participants were recruited for each focus group, for a total of 52 participants. Recruitment of participants was conducted using convenience sampling and snowball sampling methodology with informational fliers; recruitment for HCV program beneficiaries and most-at-risk groups was conducted through treatment and harm-reduction service providers. The following information was gathered from these discussions.

        - All respondents participating in the KAP focus-group discussions and in-depth interviews (N=34) stated they knew how people contracted hepatitis C, what parts of the body it affected, and how transmission could be prevented.
        - Most HCV patients that became program beneficiaries (12 of 14) had disclosed their serostatus to family members and close friends.
        - Although most HCV-infected persons did not experience stigma, they reported that healthcare workers lack awareness of the stigma experienced by hepatitis C patients.
        - Education campaign messages were broadly understood by the 18 participants in the three groups focused on testing current communication materials, but many

participants noted that the video advertisements did not encourage a specific call-to-action, such as "get tested for hepatitis C;" rather, advertisements focused on providing prevention measures.

Challenges

- Activities to raise awareness and educate the public play a key role in reaching the 2020 HCV elimination goals and must be enhanced to promote screening and prevention; these activities must be modified based on community feedback.
- Hepatitis C not only causes serious liver damage, but is also associated with mental, psychological, and social consequences and with stigma. Although HCV education campaigns can reduce the stigma associated with an HCV diagnosis, gaps in knowledge exist regarding the societal factors that drive stigma.
- Critical to successful messaging is strong collaboration between patient advocacy groups and government, including law enforcement.

TAG 2016 Recommendations[§]

1. **Promote Advocacy, Awareness, and Education and Partnerships for HCV-Associated Resource Mobilization**

1.1. Revise public-awareness campaigns to reflect changes in screening recommendations and locations of treatment facilities.

1.2. Incorporate campaign messages recognizing the synergistic effect of alcohol and hepatitis C infection on liver damage.

1.3. Incorporate messages that help PWID recognize their risk for HCV infection and accept harm reduction, testing, and treatment services. This requires elimination of the social stigma and threat of incarceration associated with injection-drug use. Mass media campaigns should incorporate messages to improve public understanding of injection-drug use and addiction.

1.4. Remove legislation that penalizes drug use by encouraging collaborations between government agencies; drug addiction should be addressed as a health issue, not as a crime.

1.5. Educate health-care providers and other professionals about how to reduce or eliminate the stigma related to drug use and HCV infection.

[§]The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring & Evaluation: Advocacy, Awareness and Education, and Partnerships 2015–2016

Objective	Indicator name	Measurement	Data Source	Value/Result	Remarks
1.1. Educate the public and high-risk groups about viral hepatitis and the importance of testing	1. Levels of awareness among the general public regarding a) HCV transmission and prevention b) potential health outcomes c) testing and diagnosis d) treatment	**High Awareness** All or most participants aware **Medium Awareness** Some participants aware **Low Awareness** A few or no participants aware	Qualitative Survey 2016 (KAP)	a) High b)Medium c) High d) Medium	
	2. Levels of awareness among PWID regarding a) HCV transmission and prevention b) potential health outcomes c) testing and diagnosis d) treatment	**High Awareness** All or most participants aware **Medium Awareness** Some participants aware **Low Awareness** A few or no participants aware	Qualitative Survey 2016 (KAP)	a) High b)Medium c) High d) Medium	
	3. Implementation and breadth of STOP-C media campaigns		Qualitative survey 2016 Social media analytics		Data not available

Objective	Indicator name	Measurement	Data Source	Value/Result	Remarks
1.2 Reduce community-level stigma and discrimination associated with HCV infection	4. Level of perceived HCV-related stigma and discrimination experienced among HCV patients in health-care and other settings (e.g., work, housing, school, corrections, and law enforcement)		Qualitative survey among beneficiaries		Data not available
	How well training on HCV-related stigma/discrimination for professionals who have frequent interactions with persons with HCV (e.g., health professionals, social workers, law enforcement) were implemented and changed participants' attitudes		Qualitative and quantitative assessment (pre- and post-tests)		Data not available

STRATEGY 2:

PREVENT HCV TRANSMISSION

No vaccine is available to protect persons from HCV infection, and although there are curative treatments, the importance of prevention is critical to achieve HCV Elimination in Georgia. Strategy 2 of the Georgia National Elimination Plan comprises three priority prevention areas: a) harm reduction; b) blood safety; and c) infection control in health-care settings and in non-traditional health-care and other community settings.

A. Harm Reduction

Introduction

With an estimated 49,700 people who inject drugs (PWID) currently living in the country, Georgia faces an epidemic of injection-drug use [10]. Based on the 2014 Bio-Behavioural Surveillance Survey (BBSS) conducted across seven cities, >66% PWID are infected with HCV [4]. The prevalence of risk behavior is high among PWID, with only 80.4% of PWID reporting use of sterile injecting equipment[*] during last injection. The 2015 seroprevalence survey identified injection-drug use as a major risk factor for HCV; 40% of HCV-infected persons acknowledged using injection drugs in the past.

Strengthening HCV prevention by increasing access to needle and syringe programs (NSP) remains a top priority at the national level. With support from the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) and coordinated by a network of 27 community-based and non-governmental organizations known as the Georgian Harm Reduction Network (GHRN)[†], 14 NSP drop-in centers have operated in 11 cities across Georgia since 2006. Geographic coverage for programs serving PWID has increased with the addition of six mobile vans that provide services to PWID (Figure 2.1). The basic package of services provided to PWID at any of these settings includes distribution of sterile injection equipment; voluntary counseling and testing (VCT) for HIV, HCV, HBV, and syphilis; distribution of condoms and safe sex information; and drug overdose prevention (i.e., distribution of naloxone).

Opioid substitution treatment (OST) was introduced in 2005. Overall, 22 OST service points have been established in 10 cities, 15 of which are supported by the State and the remainder funded by GFATM (including two sites located in penitentiaries).

[*] No needle/syringe previously used by another, no needle/syringe left at a place of gathering, no syringe prefilled by someone else without the user's presence, no shared equipment, no drug solution from shared container prepared without his/her presence.

[†] Only 10 of 27 GHRN member organizations have been providing harm reduction services to PWID.

Figure 2.1. Georgian Harm Reduction Network Coverage, 2017

Progress and Program Outcomes

- Over the past 4 years, the number of PWID accessing at least one harm-reduction intervention (including distribution of sterile injecting equipment, condoms, IEC material and risk reduction behavior counselling) in addition to sterile needles/syringes has increased significantly (Figure 2.2). More than 60% (30,330) of the estimated PWID population had received services offered by NSPs by the end of 2016, exceeding targets set for this prevention strategy (28,329 [57%]) [11].
- One in every five opioid-dependent PWID in the country (4,435 of 22,000) was enrolled in the opioid substitution therapy program in 2016, exceeding the target of 3,150 persons. In July 2017, the GFATM-supported OST program was fully transitioned to state-based funding. Optimization of the State OST program after this transition resulted in abolishment of co-payment requirements for patients and a considerable increase the number of PWIDs enrolled in OST (5,228 by November 1, 2017).[§]
- HCV screening efforts at NSP sites have increased the total number of PWID aware of their HCV infection status from 13,736 in 2014 (baseline) to 23,969 in 2016, exceeding the 2016 target of 21,000 (Figure 2.3).
- Most (97%) screened PWID were male. A substantial (2-fold) increase in the number of screened male PWID was observed over the past 2 years (12,761 in 2014 compared with 23,132 in 2016), whereas the number of women PWID tested for HCV antibody decreased from 1,325 in 2015 to 837 in 2016 (Figure 2.4).

[§] State OST Program Data

- The proportion of PWID testing positive for anti-HCV remained relatively stable during 2014–2016 (47% in 2014, 50% in 2015, and 44% in 2016) (Figure 2.3). The same patterns were seen across gender (Figure 2.4). Rates of HCV RNA-positive PWID are not currently available.
- In 2016, NSP sites provided screening to 1,362 sexual partners of PWID; 167 (12%) tested HCV-antibody positive.
- In 2016, about two-thirds of HCV antibody-positive results were from PWID aged 30–49 years (Table 1). However, over the past 3 years, the percentage of anti-HCV positive PWID slightly declined among 18–29 year-olds (5%) and among persons aged 30–39 years (5%) (Figure 2.5).

Figure 2.2 Uptake of at least two harm-reduction services among people who inject drugs, 2013–2016

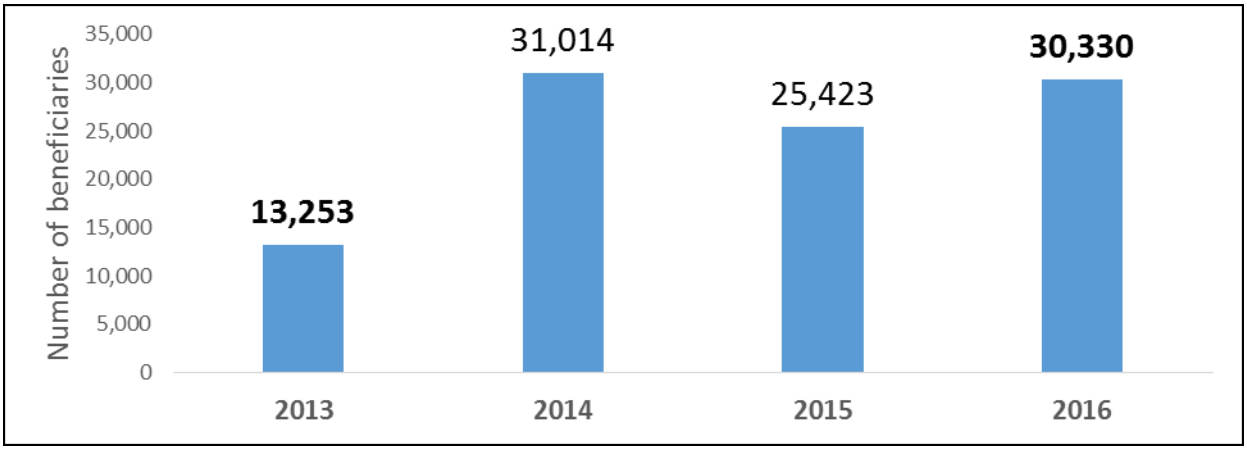


Figure 2.3 Number of people injecting drugs screened for HCV, and number and percent testing positive in Georgia, 2014–2016

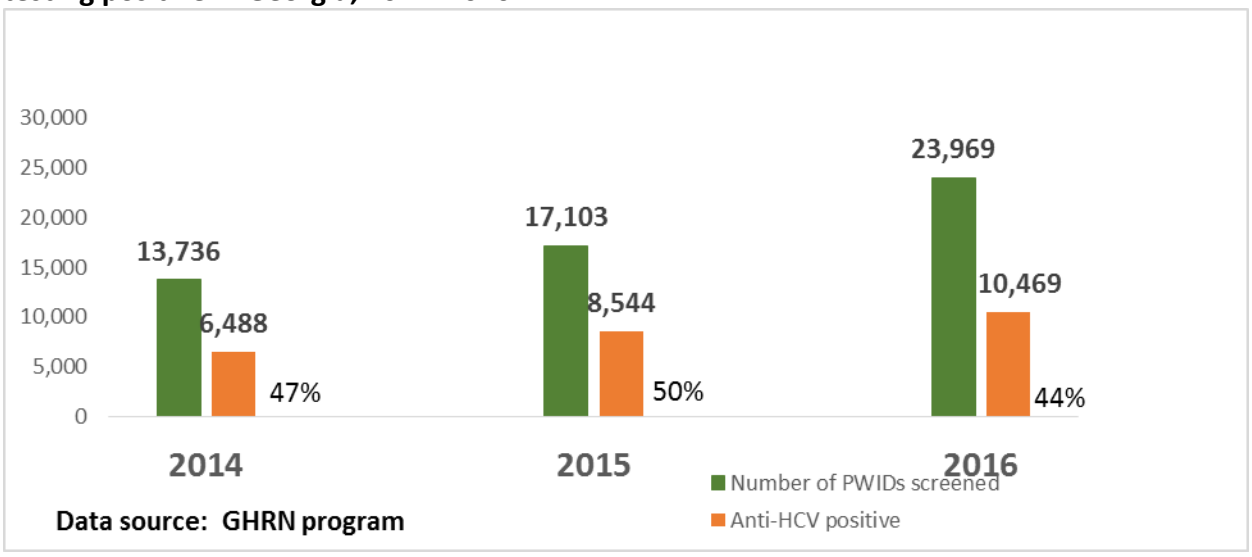


Figure 2.4 Number of people who inject drugs screened for HCV and percent testing positive in Georgia, by sex, 2014–2016

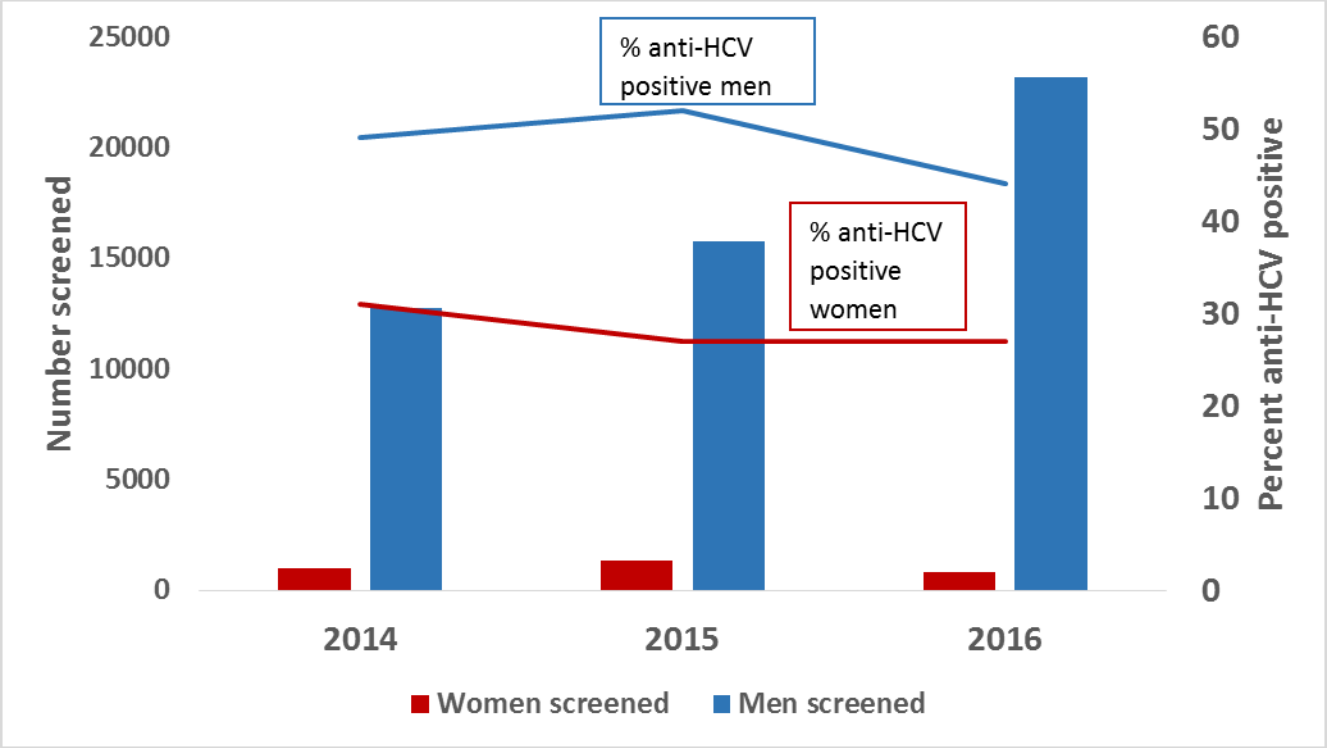


Figure 2.5 Distribution of anti-HCV positive people who inject drugs, by age group, 2014–2016

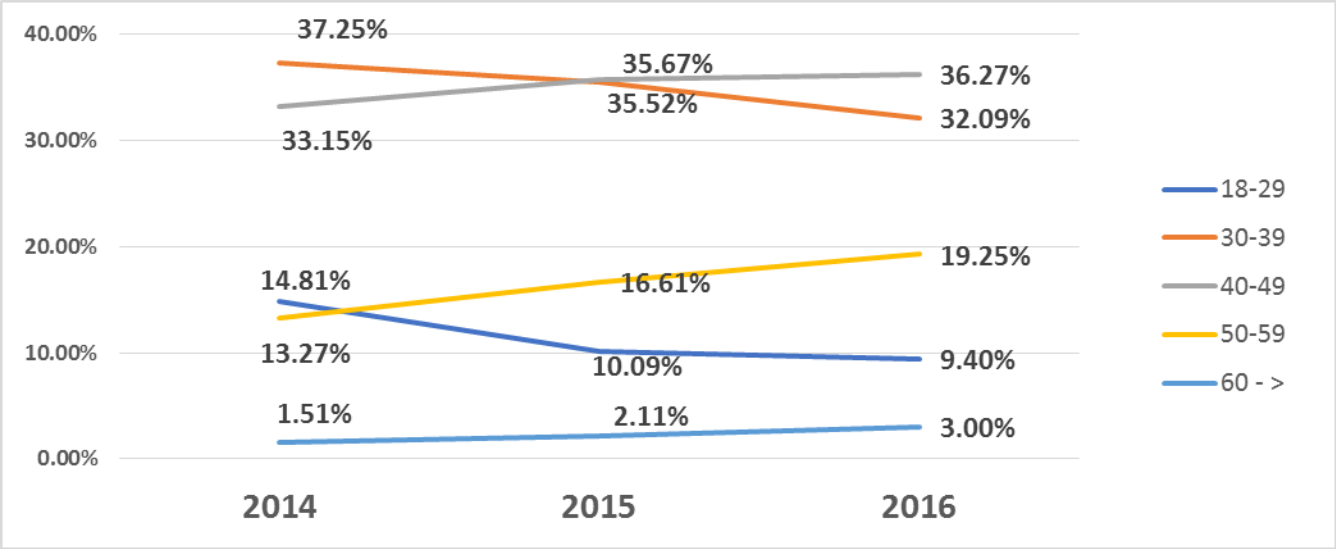


Table 1. Annual number of people who inject drugs screened for HCV and number of those tested anti-HCV positive, by age group, 2014–2016

	2014		2015		2016	
	Number screened	Number anti-HCV positive	Number screened	Number anti-HCV positive	Number screened	Number anti-HCV positive
18-29	3,273	961	3,271	862	4,410	984
30-39	4,955	2,417	6,130	3,035	7,872	3,359
40-49	3,780	2,151	5,037	3,048	7,078	3,797
50-59	1,519	861	2,259	1,419	3,789	2,015
60 >	209	98	406	180	820	314
OVERALL	13,736	6,488	17,103	8,544	23,969	10,469

- Regional variation of HCV screening coverage among PWID largely remained stable from 2014–2016; a slight increase was observed (3% in 2014 to 7% in 2016) in the Kakheti region. Of PWID tested for HCV antibody each year, one third were screened in Tbilisi.
- According to 2016 data, among PWID who screened antibody positive, the greatest proportion was located in Tbilisi (30%), followed by Imereti (16%) and Kvemo Kartli (14%) regions.
- Of PWID screened for HCV, 43% (10,304 of 23,969) received testing at mobile vans/laboratories. The substantial increase of HCV testing among PWID overall is likely attributed to improved geographic coverage using mobile vans/ambulatories, highlighting the effectiveness of this approach and suggesting the benefit of expanding the number as well as capacity of mobile teams across the country to better reach underserved and hard-to-reach PWID population.
- Based on available data from GFTAM, 836 persons were screened for hepatitis C infection at OST sites, of which 394 (47%) were HCV-positive. As part of the HCV Elimination Program and with technical support of Medicins du Monde (MDM, France), a pilot project was implemented in two harm-reduction sites: Tbilisi (New Vector) (2015–2016) and Zugdidi (Qsenoni) (at the end of 2016). This program is a peer-support intervention aimed at facilitating access to and retention of PWID in the national treatment program, preventing HCV reinfection after treatment, and overcoming treatment-related barriers and concerns identified by providers and PWID. The project's performance indicators showed that
  - ✓ 98% completed antiviral therapy and
  - ✓ treatment adherence reached 81%, with only 3.4% of patients failing to present for medical services after being screened at the harm-reduction center and referred for care.
- A thematic analysis of the qualitative research implemented by GHRN in 2016 (http://hrn.ge/home/content?content_id=325) identified three key domains affecting HCV treatment access for PWID: social structural factors (e.g., HCV stigma and lack of psychological support), financial concerns, and non-integrated care. This analysis also revealed the following:

- ✓ Persons were most likely to discontinue daily supervised OST service because of antiviral-treatment-associated side effects, and perceptions that they could not be trusted to take medication independently.
- ✓ Difficult venous access among PWID proved to be another challenge to HCV testing and treatment monitoring.
- ✓ Many PWID identified financial barriers and geographic accessibility as barriers to screening and treatment; another barrier was perceived lack of equity pertaining to the co-payment system in place for urban versus rural residents. Financial incentives (e.g., transportation reimbursement) may facilitate access and create demand for HCV treatment and improve treatment completion rates in this population.

Challenges

- Poor coverage of harm reduction services is a barrier to PWID being enrolled in treatment, and preventing infection in this population. Harm-reduction services (including NSPs and OST) in Georgia will continue operating with the goal of achieving 80% NSP coverage and providing services to 10,000 OST patients per year by 2020. Although data suggest that NSP services are being accessed by many PWID across Georgia, linking PWID found to be HCV-antibody positive to HCV care and treatment remains problematic.
- Stigma related to drug use, social factors, and economic factors that affect access to HCV care and treatment remain significant challenges to achieving HCV elimination goals.
- In the absence of an effective HCV vaccine, reaching elimination goals for transmission will require increased availability of HCV testing, and treatment integration at harm-reduction sites.

TAG 2016 Recommendations¶

2A Prevent HCV Transmission: Harm Reduction

2A.1 Guided by modeling, expand coverage and improve quality of NSPs and OST, and develop measurable targets for expanding access to these services. (Progress towards these targets will be discussed at the 2017 TAG meeting.)

2A.2 Develop a target for the number of persons who are currently using drugs to be treated and cured per year (i.e., at least 5,000 PWID by October 2017), and monitor successfully treated patients to assess rates of reinfection.

2A.3 Include NSP and OST sites in the screening and treatment monitoring and evaluation system, incorporating use of a unique identifier to facilitate monitoring, evaluation, and linkage to care.

2A.4 Develop a realistic, orderly, and achievable transition plan for the GFATM to ensure continuous support for harm-reduction services in Georgia.

[¶]The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring & Evaluation: Harm Reduction, 2015–2016

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
2A.a Decrease HCV incidence among PWID by promoting harm reduction	1. Number and percentage of PWID reached with preventive counseling (basic service combination)	**Numerator** Number of current PWID reached with preventive counseling **(N=30,330)**	Harm reduction program records	61%	BBSS 2014
		Denominator Estimated number of current PWID **(N=49,700)**	BBSS		
	2. Number and percentage of PWID enrolled in OST	**Numerator** Number of PWID enrolled in OST **(N=4,435)**	Harm reduction program records	20%	BBSS 2014
		Denominator Estimated number of opioid user PWID **(N=22,000)**	BBSS		
	3. Number and percentage of current PWID screened for HCV infection at: a. NSP sites b. OST service centers c. mobile ambulatories	**Numerator** Number of current PWID screened for HCV infection **a. N=23,969** **b. N/A** **c. N=10,304**	Harm reduction program records *Possible alternative*: new screening database	a. 48% b. n/a c. 2%	BBSS 2014

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
		Denominator Estimated number of current PWID **(N=49,700)**	BBSS		
	4. Number and percentage of current PWID with presence of anti-HCV antibodies	**Numerator** Number of current PWID with anti-HCV positivity **(N=10,469)**	Harm reduction program records OR Unified screening database	44%	
		Denominator Number of current PWID tested for HCV infection **(N=23,969)**			
	5. Number and percentage of PWID testing positive on rapid tests who undergo HCV RNA testing	**Numerator** Number of PWID tested for HCV RNA or HCV core antigen testing	Treatment database		Data not available Current database doesn't allow tracking of these data
		Denominator Number of current PWID with anti-HCV positive results	a) Harm reduction program records b)Unified screening database		
	6. Number and percentage of PWID diagnosed with active HCV infection	**Numerator** Number of PWID diagnosed with chronic HCV infection based on virologic biomarker testing (*HCV*			Data not available

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
		RNA or HCV core antigen assays)			
		Denominator Number of PWID who were tested for HCV RNA or HCV core antigen testing			
	7. Percentage of PWID living with HCV infection	**Numerator** Estimated number of current PWID living with HCV infection	BBSS	66.2%	Value is pooled estimate from BBSS 2014. Actual numerator unknown.
		Denominator Estimated number of current PWID **(N=49,700)**			
	8. Number and percentage of current PWID with positive HCV RNA test enrolled in HCV treatment and care	**Numerator** Number of current PWID enrolled in HCV care and treatment	Treatment database		Data cannot be assessed
		Denominator Number of PWID with diagnosed HCV infection			
	9. Number and percentage of current PWID living with HCV infection enrolled in HCV	**Numerator** Number of current PWID enrolled in HCV care	Treatment database		Data cannot be assessed

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
	treatment and care	**Denominator** Estimated number of current PWID living with hepatitis C	BBSS		BBSS 2014
	10. Number and percentage of current PWID enrolled in treatment program who completed treatment	**Numerator** Number of current PWID completed antiviral treatment	Treatment database		Data cannot be assessed
		Denominator Number of current PWID enrolled in HCV care and treatment			
	11. Number and percentage of current PWID completing treatment who achieved sustained virologic response (SVR)	**Numerator** Number of current PWID who achieved SVR	Treatment database		Data cannot be assessed
		Denominator Number of current PWID assessed for SVR at 12-24 weeks after the end of treatment			

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
	12. Percentage of current PWID reporting use of sterile injecting equipment the last time they injected	**Numerator** Number of current PWID reporting use of sterile injecting equipment the last time they injected	BBSS	80.4%	Value is estimate from BBSS 2014. Actual numerator unknown.
		Denominator Estimated number of current PWID **(N=49,700)**			

B. Blood Safety

Introduction

To prevent transfusion transmissible infections (TTI), Georgia launched its State Safe Blood Program in 1997. This program aimed to ensure the safety of blood and blood components through high-quality testing of donor blood for HCV, HBV, HIV, and syphilis and increasing the proportion of voluntary, non-remunerated donations. Yet only 12 of 20 blood banks in Georgia currently participate in the Program. Further, blood transfusion services in Georgia are not meeting international standards, and the 2015 seroprevalence survey revealed receipt of blood as a risk factor for HCV infection. About one-fifth of survey respondents with anti-HCV positive tests had at least one blood transfusion event in their lifetime [12].

In 2011, a Memorandum of Understanding (MoU) was signed between NCDC, Global Healing (GH)[§], and the Jo Ann Medical Center Blood Bank to establish the National Blood Safety Reform Program in Georgia. Objectives of this collaborative program included strengthening the health-care infrastructure, improving the quality of blood products, and developing a culture of voluntary blood donations. Because blood safety in Georgia is also compromised by lack of an effective mechanism for enforcing quality assurance standards at all blood banks in the country, the Blood Safety Reform Program also aimed to assist the Georgian medical community with establishing a national regulatory framework. Through a GH-supported distance learning initiative, a series of nine educational webinars (English language with Georgian subtitles) were created for blood-bank personnel throughout Georgia. These videos cover a wide range of topics dealing with the quality management of blood banks, audits, donor recruitment, and donor selection.

Although progress is being made towards promoting voluntary blood donations in Georgia, the Georgian profit-based model continues to raise safety and ethical concerns. Only two facilities remain non-profit legal entities, one of which is a public nonprofit organization, functioning under the authority of the Ministry of Defense of Georgia and the other a private, nonprofit blood bank affiliated with a hospital.

Progress and Program Outcome

- Given the importance of high-quality screening of donated blood in preventing TTI (including HCV), beginning in 2011, blood banks involved in the State Safe Blood Program were required to undergo routine external quality-control testing, for which randomly selected aliquots from 5% of all donations are rechecked for TTI by NCDC's Richard Lugar Center for Public Health Research (Lugar Center).
- During the first 6 months of 2016, a total of 12 blood banks submitted 1,492 aliquots for retesting to the Lugar Center; six (0.4%) of these samples were found to have discrepant HCV antibody testing results. Some of the blood samples sent to the Lugar Center for quality control were of inadequate volume, making it difficult to perform confirmatory testing after antibody testing revealed discrepant results.
- The National Blood Registry was upgraded in 2016 with the administrative, technical, and financial support of the State Safe Blood Program.
    - ✓ Manuals for data entry and operation have been developed for all staff working with the donor database, including blood banks, hospitals, and program administrators at NCDC.

[§] Global Healing is a U.S.-based nonprofit organization dedicated to providing modern medical equipment, training, and supplies to the developing world.

- ✓ Blood-bank personnel were provided training in data entry and operation of the updated donor database.

- The number of donors has gradually increased during the past 10 years, whereas HCV prevalence among the donor population has decreased (from 3.9% in 2006 to 1.8% in 2016) (Figure 2.6).
- In 2016, a total of 51,731 donors and 86,608 donations were registered in the National Blood Registry, including 80,370 donations made at blood banks participating in the State Safe Blood Program. A total of 912 (1.8%) donors tested HCV positive, with highest prevalence among males in age groups 40–49 (3.97%) and 50–65 (4.01%) (Figure 2.7).

Figure 2.6. Number of HCV seroreactive donors, by year, 2006–2016

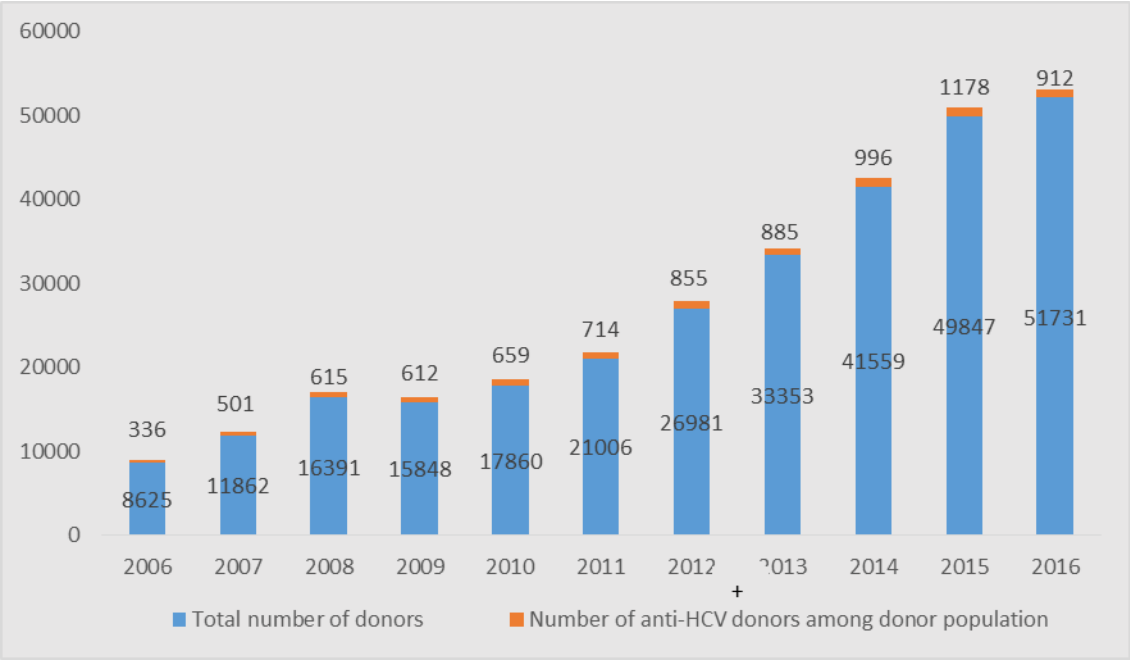
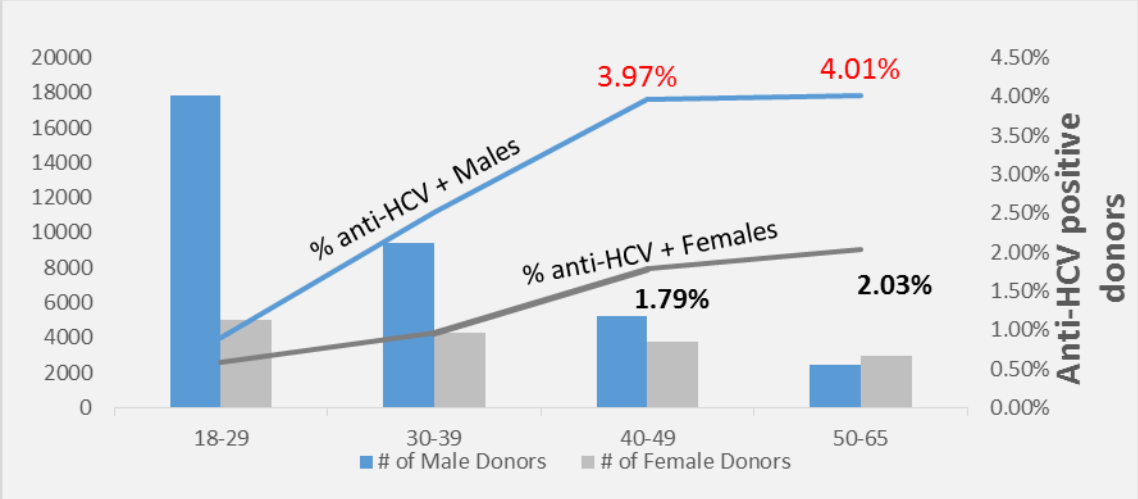


Figure 2.7 Age and gender distribution of anti-HCV positive blood donors, 2016



- Voluntary blood donation comprises approximately 30% (26,379 donations) of total donations in Georgia, falling short of the 2016 target of 35% [13]. An electronic National Blood Registry ("donor database") was launched in 2005. Georgia's blood banks have shown steady progress in the overall number of blood units collected, increasing from 40,900 donations in 2012 to 68,398 in 2015 and representing a 67% increase in available blood. However, much of this growth is the result of a corresponding rise in the number of paid donations, which also increased by 59% during the same time period.
- In collaboration with NCDC, a local NGO, "Artinfo Georgia," has been actively involved in campaigns to raise awareness about the importance of voluntary blood donations across Georgia since 2015. A total of 60 seminars, 32 events and 3 online surveys were conducted, about 20,000 SMS were sent to the targeted population (adults 18 to 45 years old) and a dedicated website (http://donori.ncdc.ge/) was established to promote social responsibility, share success stories, and highlight the importance of obtaining blood products from the low-risk donor population.

d

Blood Donor Day has been celebrated annually in Georgia since 2011 to raise awareness of the need for a safe and available blood supply provided by volunteer blood donors. Award ceremonies were held each year to thank blood donors for their voluntary, life-saving gifts of blood.

Challenges

- The blood system in Georgia has become more robust, and blood products have become safer over the past several years. However, the continued lack of standardized quality management, national guidelines, and standard operating procedures (SOPs) for blood production procedures (including donor selection, blood collection, and preparation) is hindering sustainable progress towards improving blood safety in Georgia.
  - ✓ Legislation regarding blood donations in Georgia fails to comply with European Union regulations and WHO standards.
  - ✓ No management body has been identified at the national level to monitor and oversee blood transfusion practices.
  - ✓ No external quality-control mechanisms are established for the blood banks that do not participate in the Safe Blood Program.

- ✓ No regulation exists requiring blood banks (those not participating in the State Safe Blood Program) to conduct Enzyme linked immunoassay (ELISA) testing for blood borne infections; few blood banks still use rapid tests to screen blood. Some of the blood samples sent to the Lugar Center for quality control were of inadequate volume, making it difficult to perform confirmatory testing after antibody testing revealed discrepant results.
- ✓ No procedures are in place for conducting HCV RNA testing among HCV antibody negative blood units donated; therefore, there is risk of infection from an acutely infected donor if he/she donates during the "window period" that follows acute infection, when individuals can be viremic but levels of HCV antibodies too low to be detected through routine anti-HCV testing. Blood donated during the window period poses a major challenge to Georgia's effort to improve blood safety among its blood centers and blood industry.

- The proportion of remunerated donations remains high, compromising blood safety.
- No data are available regarding referral and linkage to confirmatory testing and care for persons testing HCV-positive upon donating blood.

TAG 2016 Recommendations[‡]

2B Prevent HCV Transmission: Blood Safety

2B.1 Establish a task force consisting of local and international experts and technical advisors to align national regulations with European directives.

2B.2 Establish a governmental agency or board to provide the required oversight to ensure that national regulations are followed to provide safe blood transfusion services in Georgia (e.g., validation of methods used in processing blood products and testing and regular inspections and audits of blood banks).

2B.3 Mandate that all blood banks participate in the donor database, state quality-control system, and Safe Blood Program.

2B.4 Develop national, universal SOPs and guidelines for the manufacture of blood products, to include standards for donor selection and blood testing for TTI with validation of all TTI screening assays and quality assurance/quality control (QA/QC) of tests performed in blood banks.

2B.5 Consider future expansion of the current donor database to include more information (e.g., name of hospital receiving blood, transfusion recipients, adverse reactions, and assays used to screen donations) and enable linkage to a treatment database.

2B.6 Increase voluntary blood donations to reduce the demand for donations from family-recruited and paid donors. Prioritize recruitment of repeat HCV seronegative, low-risk, volunteer donors.

2B.7 Conduct nucleic acid testing on all anti-HCV negative donations, and where not possible, HCV core antigen testing.

2B.8 Guided by European standards, develop a centralized repository beginning with specimens from all HCV-positive blood donations at the Lugar Center.

2B.9 Incorporate training in transfusion medicine into the medical education and training curricula.

2B. 10 Consider conducting HBV, HCV, and HIV testing on repositories of seronegative blood donations in storage at the Lugar Center to estimate the rate of false-negative donations and determine the window period for positive donations that have already been transfused.

[‡]The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring and Evaluation: Blood Safety, 2015–2016

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
2B.a Prevent health-care-related transmission of viral hepatitis by improving blood safety	1. Number and percentage of all blood banks participating and operating in the National Blood Registry	**Numerator** Number of blood banks participating and operating in the National Blood Registry **(N=18)**	State Safe Blood Program	90%	
		Denominator Total number of blood banks **(N=20)**	State programs department at NCDC		
	2. Lead agency is established at central level to oversee and coordinate blood service in the country			Not established	
	3. Licensing regulations for the blood banks are established, approved, and published			Not established	
	4. Degree to which blood banks are complying with updated TTI prevention regulations		Quantitative and qualitative data collection methods		Data not available
	5. Percentage of all blood banks that have obtained Good Manufacturing Practice (GMP) and/or ISO certificates	**Numerator** Number of blood banks that have obtained GMP and/or ISO certificates			Data not available
		Denominator Total number of blood banks **(N=20)**			

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
	6. Percentage of blood donations tested for HCV by NAT and/or other sensitive tests at centralized TTI laboratories	**Numerator** Number of donated units tested for HCV N=0	State Safe Blood Program	0	
		Denominator Number of donated blood units **(N=86,608)**	Lead agency (when established)		
	7. Number and percentage of voluntary donations among all blood donors	**Numerator** Number of voluntary donations **(N=26,379)**	State Safe Blood Program	30.5%	
		Denominator Total number of blood donations **(N=86,608)**	State Safe Blood Program		
	8. Percentage of voluntary blood donations performed by mobile drives	**Numerator** Number of voluntary donations performed by mobile drives	State Safe Blood Program		Data not available
		Denominator Number of voluntary donations	State Safe Blood Program		
	9. Number of mobile blood collection units operating in the country	Total number of mobile blood collection units operating in the country	State Safe Blood Program Lead agency (when established)		Data not available
	10. Proportion of blood banks that have operating mobile blood collection units	**Numerator** Number of blood banks that have an operating mobile blood collection unit	Lead agency (when established)		Data not available

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
		Denominator Total number of blood banks			
	11. Percentage of anti-HCV reactive persons among blood donors	**Numerator** Number of blood donors with anti-HCV positive results **(N=912)**	State Safe Blood Program	1.8%	
		Denominator Total number of blood donors **(N=51,731)**	State Safe Blood Program		

C. Infection Control

Introduction

Inadequate infection prevention and control (IPC) likely contributes substantially to HCV transmission in Georgia, as suggested by data from the 2015 national HCV seroprevalence survey indicating that approximately 40% of persons with HCV infection did not report "other" known risk factors for HCV transmission (i.e., risk factors other than injection-drug use and receipt of blood products) [12]. Furthermore, many medical staff remain unfamiliar with existing national IPC regulations and standards: a survey conducted in 2014 by NCDC demonstrated that many medical personnel did not follow safe injection procedures due to lack of knowledge and practice. Equipment was not properly sterilized in many hospitals in Georgia, likely as a result of misperceived importance, inappropriate monitoring of sterilization procedures, and absence of SOPs (MoLHSA, unpublished data, 2015).

Infection control is believed particularly problematic in dental clinics. Although MoLHSA issued a legal decree regulating health-care waste management in January 2014 (Decree N64: Technical Regulation – Approval of Sanitary Regulations on Waste Collection, Storage and Disposal in Medical-prophylactic Facilities), implementation of this decree has not been effectively implemented in most dental facilities. To monitor infection-control practices in dental settings, in early 2015 the State Regulation Agency for Medical Activities (RAMA) visited 778 (59.7%) of the 1,304 dental clinics officially registered in Georgia; of those visited, 544 (69.9%) were located in Tbilisi and 234 (30.1%) were in the regions). An analysis of data obtained from these visits revealed poor practices relative to several IPC measures (including infection control, hand hygiene, and disinfection and sterilization of equipment), signaling the need for immediate attention. Only 10% of dental clinics provided staff with IPC training, and several clinics lacked running water in procedure rooms, not allowing for simple handwashing, overall the non-compliance rate was 14%. Only half (50%?) of the 778 monitored sites properly separated dental instruments according to their designation as critical, semi-critical, and non-critical, and slightly more than half (53%) separated clean from soiled instruments. Further, use of dedicated containers for sharps disposal was documented in only 53% of clinics, and waste was properly segregated in 64% of clinics. These data reflect an inadequate understanding of the risk of infection and necessary preventive measures in these clinics.

Non-traditional and community settings may also pose a risk for HCV transmission, however, the extent of this risk remains unknown in Georgia. An observational assessment of 2,133 acupuncture clinics and beauty, tattoo, and piercing salons conducted by NCDC in 2015 revealed substandard infection-control practices. Single-use instruments were discarded in sharps containers after a single use in only 21% of settings, and single-use sharp instruments for performing invasive procedures were used in 38% of facilities observed. For reusable instruments, cleaning, disinfection, and/sterilization immediately following each procedure was observed in only 64% of non-medical settings.

Progress and Program Outcomes

- Surveillance, prevention, and control of nosocomial infections is currently regulated by MoLHSA legislation (Decree N01-38/n, 7 September 2015[§§]) and enforced by RAMA; this legislation requires compliance in sterilization and disinfection standards as well as injection safety.
- In September 2015, MoLHSA developed a self-assessment tool to help health departments identify deficiencies in infection-control practices and guide quality improvement activities. In March 2016, an assessment team comprised of MoLHSA, NCDC, and RAMA representatives began assessing infection-control programs in 10 major hospitals and nine cardiology clinics located in Tbilisi using a structured observational checklist; the complete results of this assessment are not available at this time, but will be included in the next HCV Elimination Annual Report. Preliminary findings revealed that:

    - ✓ health-care personnel in five of 19 (26%) facilities provided annual IPC training using a standardized curriculum;
    - ✓ all 19 surveyed facilities have an appointed IPC point-of-contact, but only 14 (74%) have active IPC committees in place[¶¶];
    - ✓ only 40% of medical facilities were in compliance with all requirements for medical waste management; and
    - ✓ educational materials to promote IPC awareness were developed and distributed in only eight (42%) of 19 surveyed facilities.

- A collaborative agreement with U.S. CDC was established in July 2017 to provide supplemental funding to support antimicrobial resistance (AMR) surveillance. This agreement aims to promote development and validation of National IPC Policy and National IPC Technical Guidelines (including needle-stick injury and other related programs), to include updates to existing guidance.
- National IPC guidelines are being updated and are expected to be finalized by the end of 2017.
- During 2015–2016 more than 500 physicians and nurses attended trainings (each lasting 2–3 hours) on infection-control policies in Georgia and key IPC precautions.
- With strong support from the U.S. CDC, best practices for IPC programs were introduced in five hospitals (two each in Tbilisi and Kutaisi and one in Batumi). More than 15 chief nurses and IPC nurses attended these trainings of trainers (ToTs) focused on improving hand hygiene, safe injection practices, medical waste management, and sterilization and disinfection. These "master trainers" then used ToT materials to educate more than 1,650 health-care staff.
- During 2015, several audits were undertaken by RAMA in 422 dental clinics to monitor compliance with the Governmental Decree on Technical Regulations for High-Risk Healthcare Service Providers. Lack of compliance with established requirements for disinfection and sterilization was documented in 29% of dental clinics.
- The findings of the 2015 observational assessment of acupuncture clinics and beauty, tattoo, and piercing salons have informed policy changes. IPC oversight of settings that perform aesthetic and cosmetic procedures became the responsibility of municipal public health authorities and is now regulated in accordance with Governmental decree N473 (September

[§§] *https://matsne.gov.ge/ka/document/view/2958903*

[¶¶] IPC committee must include chief doctor or deputy chief doctor, an epidemiologist, an ID specialist, chief nurse, head of intensive care unit

14th, 2015), "Technical Regulation – Approval of Sanitary Norms of Infection Prevention and Control During Aesthetic and Cosmetic Procedures in Facilities of Public Importance."

- The Georgian Stomatological Association (GSA) has actively supported national HCV elimination initiatives since inception of the elimination program and has organized a series of events to raise awareness about the urgent need to reduce HCV incidence associated with high-risk health-care services, including dental care. In January 2015, GSA convened "Stomatology in Hepatitis C Elimination Program," a conference attended by more than 500 stomatologists.
- Tbilisi State Medical University Faculty of Stomatology, in collaboration with GSA and NCDC, designed a Continuing Medical Education (CME) short course that was accredited by the Professional Development Council at MOLHSA in March 2015. Since 2014, 40 health-care providers have received this 5-day training course based on a 2009 national IPC guideline.
- Informed by international guidelines, the national protocol "Infection Prevention and Control in Dentistry" was approved by GSA and published in 2016[**].
- During 2015–2016, GSA collaborated with NCDC to deliver educational presentations and conduct seminars for dental clinic personnel covering basic information about appropriate infection-control and waste-management procedures. Of the estimated 9,000 dentists in Georgia, more than 3,000 have received such training, along with more than 1,200 additional dental clinic staff (e.g., nurses and staff responsible for disinfection and sterilization); this educational program is expected to be expanded in 2017 to include dental clinic managers. These training courses resulted in substantial improvements (80% compliance) in IPC as documented by follow-up audits in 143 facilities.
- As of December 30, 2016, a total of 50 staff members from non-medical facilities (e.g., beauty salons, tattoo salons, and other facilities performing cosmetic procedures or providing non-traditional health-care services) have received on-the-job IPC training. Plans are in place to expand this educational program in 2017.

Challenges

- Although regulations are in place to mandate IPC in health-care facilities, these regulations are not well enforced. A total of 60% of medical settings lack an IPC action plan, and half of surveyed hospitals are unable to implement surveillance for nosocomial infections.
- IPC committees have been active only in a limited number of medical facilities.
- Most hospitals (90%) have no internal policy on hepatitis B vaccination for high-risk groups of healthcare workers.
- No SOPs have been developed to guide management of healthcare workers exposed to infectious material.
- To date, only one medical school (Tbilisi State Medical University) has implemented the 2009 IPC curriculum that was accredited by the Professional Development Council at MOLHSA in March 2014.

TAG 2016 Recommendations[***]

2C Prevent HCV Transmission: Infection Control

[**] https://www.gsa.ge/files/infekciebis_kontroli_new_new.pdf

2C.1 Continue to strengthen regulations aimed at improving infection control in health-care settings. To educate providers in infection control and enforce these regulations, launch a model infection control program in a large clinical setting by October 2017 that includes an evaluation plan to track program results.

2C.2 Continue to strengthen regulations aimed at improving infection control in non-traditional health-care and community settings with the potential for HCV transmission.

2C.3 Assess health-care settings and providers to better understand HCV transmission risks in community settings.

2C.4 Collect surveillance data (including laboratory test results from large inpatient settings) to better understand where HCV transmission is occurring.

2C.5 Consider requiring every HCW with direct patient contact to take a web-based course on infection-control practices; the ECHO care model can facilitate such courses.

***The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring and Evaluation: Infection Control, 2015–2016

Objectives	Indicator name	Measurement	Data source	Value/Result	Remarks
2C.a Prevent health-care-associated transmission of viral hepatitis by improving infection control in health-care facilities	1. National guidelines on injection safety developed and published online	N/A	Published guidelines	1	**Scale indicator:** 0 = not started; 1 = under development; 2 = draft complete; 3 = published.
	2. Policies on needle-stick injuries developed and published online	N/A	Published guidelines	1	(see 2C.a.1)
	3. National sterilization and disinfection guidelines developed and published online	N/A		1	(see 2C.a.1)
	4. National waste management guidelines revised and published online	N/A	Ministerial decree	1	(see 2C.a.1)
	5. National Essential Medicine Policy reviewed and includes rational use of injections		Essential Medicine Policy review	0	Yes/No 0=no 1=yes
	6. Number of medical universities and nursing colleges with IPC curriculum introduced into training program		Survey conducted by NCDC/Ministry	1	
			Ministry of Education		

Objectives	Indicator name	Measurement	Data source	Value/Result	Remarks
	7. Percentage of health-care facilities provided training with an IPC curriculum	**Numerator:** Number of health-care facilities receiving IPC training **(N=5)**	Survey conducted by NCDC/Ministry	26.3%	
		Denominator: Number of health-care facilities surveyed **(N=19)**	Survey conducted by NCDC/Ministry		
	8. Degree to which facilities follow national IPC guidelines, needle-stick policies, guidelines on injection safety, national sterilization guidelines, and national waste-management guidelines	**Numerator:** Number of health-care facilities compliant with national guidelines **(N=5)**	Survey conducted by NCDC/Ministry	26.3%	
		Denominator: Number of health-care facilities surveyed **(N=19)**	Survey conducted by NCDC/Ministry		

Objectives	Indicator name	Measurement	Data source	Value/Result	Remarks
	9. Percentage of health-care facilities with an appointed IPC focal person	**Numerator:** Number of health-care facilities with appointed IPC focal person **(N=19)**	Survey conducted by NCDC/Ministry	100%	
		Denominator: Number of health-care facilities surveyed **(N=19)**	Survey conducted by NCDC/Ministry		
	10. Percentage of health-care facilities with functional IPC committees	**Numerator:** Number of health-care facilities with active IPC committees **(N=14)**	Survey conducted by NCDC/Ministry	73.7%	
		Denominator: Number of health-care facilities surveyed **(N=19)**	Survey conducted by NCDC/Ministry		

Objectives	Indicator name	Measurement	Data source	Value/Result	Remarks
	11. Percentage of health-care facilities that received IPC awareness materials (posters, flyers, observation checklists)	**Numerator**: Number of health-care facilities received IPC awareness resources	Ministry/NCDC		Data not available
		Denominator: Total number of surveyed health-care facilities			
	12. Percentage of health-care facilities displaying IPC awareness materials	**Numerator:** Number of health-care facilities displaying awareness materials **(N=8)**	Survey conducted by NCDC/Ministry	42.1%	
		Denominator: Health-care facilities where the survey was conducted **(N=19)**	Ministry/NCDC Training records		

Objectives	Indicator name	Measurement	Data source	Value/Result	Remarks
2C.b Prevent HCV transmission in non-traditional health-care and other community settings	1. State regulations and policies of IPC in non-medical facilities are updated and published online		Published State regulations	3	**Scale indicator:** 0 = not started; 1 = under development; 2 = draft complete; 3 = published.
	2. Percentage of non-medical facilities where SOPs are available	N**umerator:** Number of non-medical facilities where SOPs are available	Survey conducted by NCDC/Ministry		Data not available Survey planned for 2017
		Denominator: Total number of sampled surveyed non-medical facilities	Ministry/NCDC Training records		
	3. Number of non-medical facility staff trained in IPC		Ministry/NCDC Training records	50	
	4. Degree to which sterilization, disinfection, and waste management SOPs are followed		Survey conducted by NCDC/Ministry		Data not available Survey planned for 2017

STRATEGY 3:

IDENTIFY PERSONS INFECTED WITH HCV

Introduction

The road to HCV elimination in Georgia by the year 2020 requires a comprehensive scale-up of high-quality HCV screening and linkage to treatment services. Challenges to HCV testing on a global scale include limited access to healthcare, limited laboratory capabilities, and lack of national guidelines and testing policies [14]. Unlike other countries, rather than recommending HCV screening only for specific populations with high prevalence (e.g., a specific birth cohort) or for those who engage in "at-risk" activities [15], Georgia employed both a targeted and universal screening strategy. The program is intended to improve HCV case-finding by screening the general population, conducting targeted screening of high-risk populations, and enhanced screening in regions with known high HCV prevalence. Two goals were established to prioritize HCV testing activities in Georgia: a) increase the number of people diagnosed with HCV infection through expanded HCV testing and b) expand HCV testing to better reach high-risk populations. Georgia is using results from the national serologic survey conducted in 2015 [16] to define the size and epidemiology of the population; these data can guide screening and linkage to care efforts to meet elimination goals. Beginning with the launch of the Elimination Program in 2015, screening for hepatitis C has been offered to Georgians free-of-charge through several Governmental programs across the country. Currently, no-cost HCV antibody testing is offered at the following sites:

- NCDC headquarters and its regional centers;
- blood banks (mandatory screening);
- antenatal clinics;
- hospitals (offering screening to all admissions/inpatients);
- outpatient facilities, including village doctors;
- HCV management center in Tbilisi (administered by Social Service Agency at MoLHSA);
- Georgian Harm Reduction Network sites;
- national screening center operated by the municipality of Tbilisi;
- prisons; and
- military enlistment locations.

HCV screening performed as part of Georgia's HCV Elimination Program consists of a rapid HCV test (with the exception of blood banks that participate in the safe blood program [see Strategy 2. Prevent HCV Transmission: Blood Safety], where most anti-HCV testing is performed by enzyme linked immunoassay [ELISA]). Data from various screening programs, including the percentage testing positive by site, have been analyzed (Table 2).

Table 2. Number of screening tests for hepatitis C virus and percentage testing positive by screening programs, 2015–2016

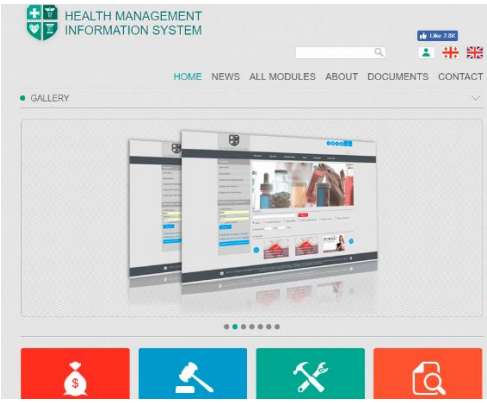
Group screened/Location of screening	No. screening tests	% HCV positive
Harm reduction centers	44,410	45.0
Prisoners ◊◊	14,053	37.4
HCV management center	2,453	31.4
Persons living with HIV	1,790	24.9
NCDC	83,910	17.5
Tbilisi citizens	26,159	13.8
Outpatients ◊	18,900	7.4
Hospitalized patients ◊	48,025	4.9
Military recruits ◊◊	11,217	1.5
Blood banks	168,121	1.3
Antenatal clinics	53,852	0.4
Total	**472,890**	**10.8**

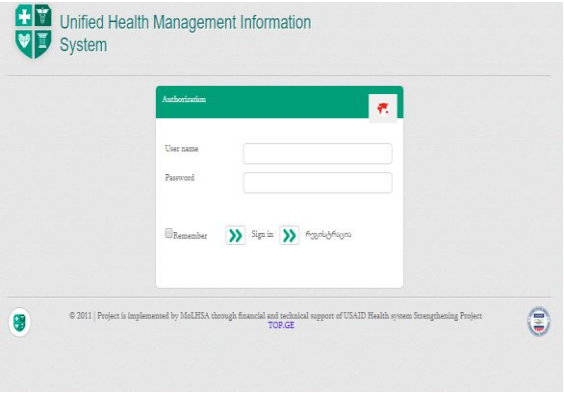
◊ Data from November and December 2016 only; ◊◊ Data are available through September 30, 2016

Progress and Program Outcomes

- A national screening protocol was developed based on U.S. and international guidelines, including WHO's *Guidelines on Screening, Care, and Treatment of Persons Infected with Chronic Hepatitis C* [14]. The protocol was approved by MoLHSA on April 6, 2017*
- Georgia is developing a comprehensive screening implementation plan that will increase access to testing at locations throughout the country; as of September 2017, screening was offered at the following sites: NCDC headquarters and its nine regional centers; antenatal clinics (N=296); blood banks (N=20); the GHRN (N=14 stationary and six mobile vans); screening centers operated by the City of Tbilisi (N=2); prisons (N=4); military accession centers (N=1); an HCV management center in Tbilisi (N=1); Infection disease, AIDS, and clinical immunology research center (IDACIRC); hospitals (N=273); and outpatient service providers (N=572, including 392 village doctors). The implementation plan will also strive to ensure that patients are informed of their test results, provided with confirmatory testing (if HCV-antibody positive on screening), and linked to care and treatment services (if chronically infected).
- Starting in 2015, Georgia's government purchased HCV rapid tests (manufactured by InTec Products Inc.; Toyo) to improve access to free HCV testing in the country. As of September 2017, a total of 572 primary-care facilities, including outpatient clinics and village doctors, had received free test-kits from NCDC and had begun offering free HCV screening.
- During 2015–2016, a total of 472,890 screening tests were conducted, of which 11% were positive; due to limitations related to screening-data quality, tests results were not analyzed by region or by participants' gender or age. More screening tests (35.6%) were performed at blood banks (N=168,121) compared to other sites. The highest rates of positive tests (45%) were obtained from screening programs that targeted PWID (Table 2).
- Informational meetings intended to educate and facilitate discussions about the logistics of testing and reporting of results were conducted for outpatient service providers offering HCV testing. Providers at these outpatient clinics were instructed to use the tests provided by NCDC for health-care workers and patients with hospital stays of <24 hours.
- In May 2017, an electronic module designed to capture results from all screening programs and compatible with the nationwide health management information system (HMIS) was launched. Before the launch of the electronic screening module, information about HCV screening coverage was collected through various systems and using different formats, such as Excel spreadsheets; hardcopies; the birth registry; and the blood donor registry. The new module is available at MoLHSA's web-site: http://stop-c.moh.gov.ge.

* http://www.moh.gov.ge/uploads/guidelines/2017/05/08/01e820305307903f4a0e082fae8e9b48.pdf



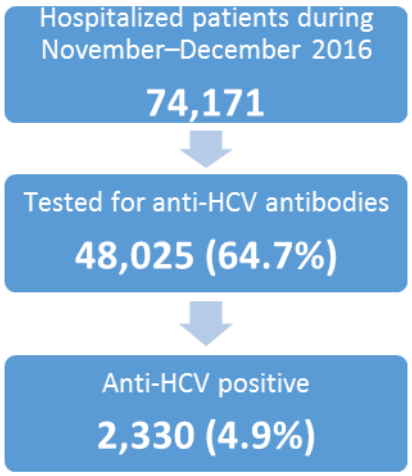


- ✓ An instructional video manual was created to describe all features of the screening registry and to help users during the data registration process.
- ✓ Ministerial Order N01-45/ნ (July 17, 2017) requires all HCV screening providers to submit their screening data within 72 hours after the test is performed.
- ✓ The number of system users is growing: since September 2017, over 400 facilities have registered HCV screening data in the electronic module.

- The unified web-based screening registry is being refined. Historical data have been validated and imported into the system, with most screening data (92%; 712,534 of 772,530) having been successfully incorporated into the screening module by September 2017. Since 2006, among registered persons, >8% (N=58,339) have anti-HCV positive results; given there are estimated to be >150,000 HCV infected adults in Georgia, an estimated 100,000 persons remain unaware of their HCV infection.
- NCDC has developed an educational booklet for people with newly diagnosed and confirmed HCV infection. The booklet was designed to help HCV infected persons learn more about hepatitis C and facilitate linkage to care by providing information about where patients can receive HCV care throughout Georgia.
- An educational video highlighting the importance of a timely screening and diagnosis of hepatitis C, demonstrating the algorithm of testing for HCV, and describing the interpretation of test results was made available free-of-charge to the public and health-care providers.
- With GFATM support, free HCV testing has been integrated into routine harm-reduction services at all NSP sites (for more details, see Strategy 2. Prevent HCV Transmission: Harm Reduction).
- According to the new governmental decree N445 (issued September 16, 2016 and enacted November 1, 2016)[†], all inpatient medical facilities are mandated to provide and report the results of anti-HCV testing for all hospitalized patients, with the following exceptions:
  - patients already registered in the HCV elimination program;
  - patients with documentation of completed antiviral treatment either before or as part of the elimination program; and
  - patients with documentation of a positive result on any HCV laboratory diagnosis (including anti-HCV test) within the last 6 months.

[†] https://www.matsne.gov.ge/ka/document/view/3398688

- As of December 31, 2016, a total of 273 hospitals participated in the program, and 48,025 (64.7%) of 74,171 patients hospitalized during the 2 months following enactment of the decree were tested for HCV (32 hospitals screened no patients). Of these, 2,330 patients (4.9%) tested positive, most of whom (N=1,558; 67%) were male. Because the information system does not allow for collection of data regarding testing eligibility or testing date, no determinations can be made regarding patient refusal, previous screening status, or previous antiviral treatment.



- Through December, most hospitalizations and anti-HCV screening testing occurred among persons aged >60 years, although among women, the highest rates of screening were among those aged 18–39 years (Figure 3.1).
- Males aged 30–50 years had the highest positive anti-HCV test result rate (Figure 3.2); these results mirrored findings from the national seroprevalence survey, where men aged 30–49 had the highest rates of HCV infection (MoLHSA, unpublished data, 2016). However, when analyzing numbers rather than percentage of anti-HCV positives, the number of men in these age groups hospitalized (2,844 in the 30–39-year age group and 3,375 in 40–49-year age group) and the number receiving anti-HCV testing were among the lowest (1,683 and 2,051, respectively) of any age and sex groups.

Figure 3.1 Hospitalized patients tested for HCV, by age and sex in Georgia, November–December 2016

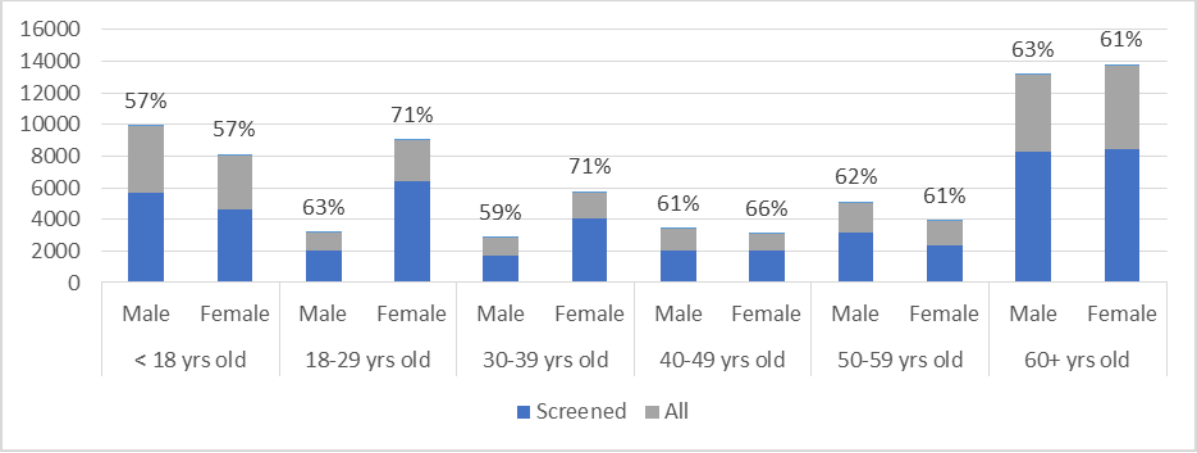
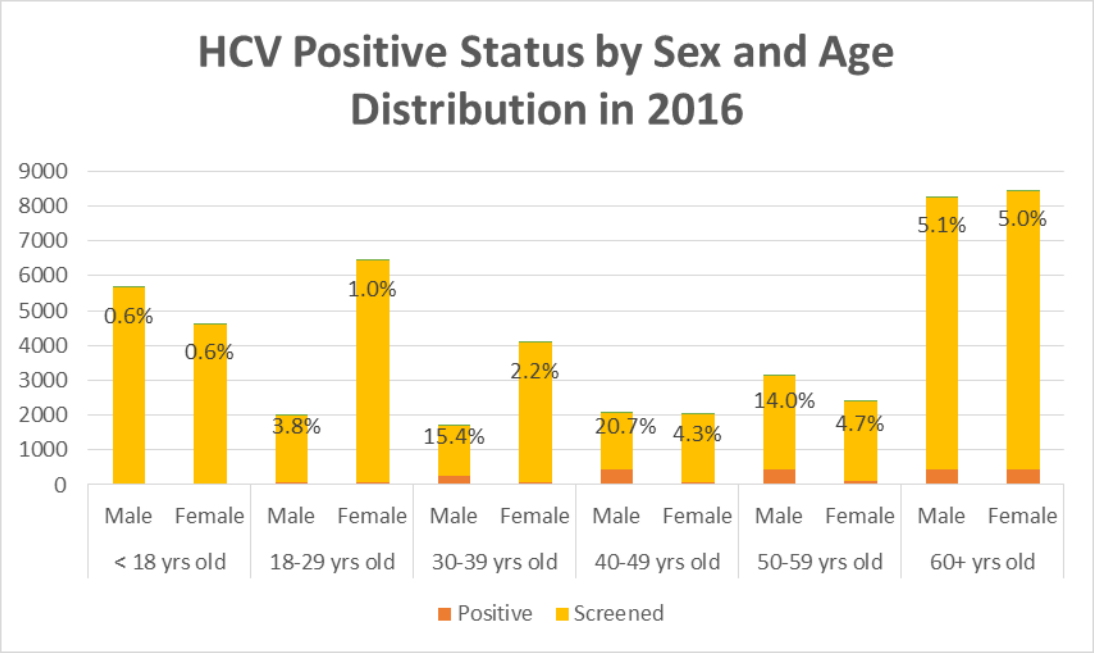


Figure 3.2 Number of HCV-antibody-positive patients hospitalized from November 2016 through December 2016 in Georgia



Challenges

- Since May 26, 2017, most (92%) screening data have been transmitted in a unified electronic module. However, almost 20% of historical data are subject to limitations and require validation, presenting challenges for analysis and interpretation of results. Through December 2016, no single, unified information system existed to determine the proportion of persons testing positive for anti-HCV that receive confirmatory testing, and of those with chronic infection confirmed, linked to care and treatment.
- Analysis of hospital-based screening data revealed low numbers and rates of HCV testing among persons in age groups with the highest burden of disease (e.g., males aged 30–50 years of age).
- Analysis of the quality and utility of HCV screening data from hospitalized patients highlights the need for specific adjustments to the data collection tool, which will be required to ensure both availability of testing dates and eligibility for HCV screening among hospitalized patients.

TAG 2016 Recommendations[§]

3. Identify Persons Infected with HCV

3.1 Provide HCV testing to all males aged ≥30 years (or all persons aged ≥30 years); this strategy can identify >70% of persons living with HCV in Georgia, treating a minimum of 30,000 patients per year as identified through population-based testing.

3.2 Older patients are more likely to have advanced liver disease and will benefit from treatment.

3.3 Demographic-based recommendations will help reduce stigma related to HCV testing.

3.4 Older persons (those aged >60 years) are more likely to use health-care services, and as such are easier to reach.

3.5 Engage a bioethicist to better address stigma-related issues among specific at-risk populations (e.g., health-care workers and young men).

3.6 Expand access to HCV testing for populations with high HCV prevalence and with highest risk of HCV infection, particularly former or current PWID, persons undergoing hemodialysis, and persons being admitted to and released from jails and prisons.

[§]The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring and Evaluation: Screening, 2015–2016

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
3.1 Increase the number of people diagnosed with HCV infection through expanded screening and testing	1. A national screening guideline/protocol established, approved by national authorities, and published		Published guidelines	2	Scale indicators are as follow: 0 = not started; 1 = under development; 2 = draft complete; 3 = published.
	2. Number and percentage of screening sites where a national screening guideline/ protocol is easily accessible	**Numerator** Number of screening sites with on-site access to national guidelines, either electronically through MoLHSA's website or in hard copy	Site survey: Guideline is observed in service area		Data not available Site survey planned in 2018
		Denominator Number of existing sites where screening program is implemented	Site survey		
	3. Number of providers attending the education program for HCV screening		Training records from NCDC	572	Outpatient service providers (clinics or individual family doctors) enrolled in the screening were given instructions on who should receive screening and how to conduct this activity.

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
3.2 Expand HCV testing to better reach high-risk populations	4. Number of adults screened for hepatitis C		Programmatic data from different screening programs	472,890	Number of performed tests during 2015-2016.
	5. Number and percentage of PWID screened for hepatitis C	**Numerator** Number of PWID screened for hepatitis C	Harm reduction program reports **(2015: N=17,103)** **(2016: N=23,969)**	**2015:** 34.4% **2016:** 48.2%	
		Denominator Estimated number of PWID	PWID population size estimation study report **(2015: N=49,700)** **(2016: N=49,700)**		
	6. Number and percentage of prisoners screened for hepatitis C	**Numerator** Number of prisoners screened for hepatitis C	Screening database		Data not available
		Denominator Total number of incarcerated people who were offered screening	Ministry of corrections data		
	7. Number and percentage of pregnant women screened for hepatitis C	**Numerator** Number of pregnant women screened for hepatitis C during the reporting period antenatal clinic sites	Maternal & Child State program (NCDC) **(N=53,852)**	98%	**Excludes**: a) women who miscarry between booking and testing and b) women who

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
		Denominator Total number of pregnant women booked for antenatal care during the reporting period	NCDC Department of Statistics **(N=54,874)**		opt for pregnancy termination between booking and testing
	8. Number and percentage of people living with HIV/AIDS screened for hepatitis C	**Numerator** Number of people living with HIV/AIDS screened for anti-HCV antibodies	National AIDS Center **(2011–2016: N=3,130)** **(2015–2016: N=1,790)**	**2011–2016:** 26.1% **2015–2016:** 14.9%	
		Denominator Estimated number of people living with HIV/AIDS	National AIDS Center **(2011–2016: N=12,000)** **(2015–2016: N=12,000)**		
	9. Number and percentage of TB patients screened for hepatitis C	**Numerator** Number of TB patients screened for hepatitis C	Screening database		Data not available

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
		Denominator 1. Estimated number of people with TB 2. Number of patients diagnosed with TB	1. WHO Global TB Report 2. National TB Program data		
	10. Number and percentage of patients on hemodialysis screened for hepatitis C	**Numerator** Number of patients on hemodialysis screened for hepatitis C during the reporting period	Screening database		Data not available
		Denominator Total number of patients on hemodialysis during the reporting period			
	11. Number and percentage of children born to HCV-positive women screened for hepatitis C	**Numerator** Number of children born to HCV-infected mothers and screened for hepatitis C			Data not available
		Denominator Total number of children born to HCV-positive women during the reporting period			

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
	12. Number and percentage of HCWs (with a risk of percutaneous exposure) screened for hepatitis C	**Numerator** Number of HCWs screened for hepatitis C	Screening database		Data not available
		Denominator Total number of HCWs	MoLHSA		
	13. Number and percentage of hospitalized patients screened for hepatitis C	**Numerator** Number of hospitalized patients who were offered and screened for hepatitis C **(N=48,506)**	1. E-Health Form 066 2. Screening database	**64.9%**	Screening of hospitalized patients was initiated in November, 2016; numerator and denominator are based on the months of November and December, 2016.
		Denominator Total number of hospitalized patients offered anti-HCV screening **(N=74,691)**	E-Health Form 066		

STRATEGY 4:

IMPROVE HCV LABORATORY DIAGNOSTICS

Introduction

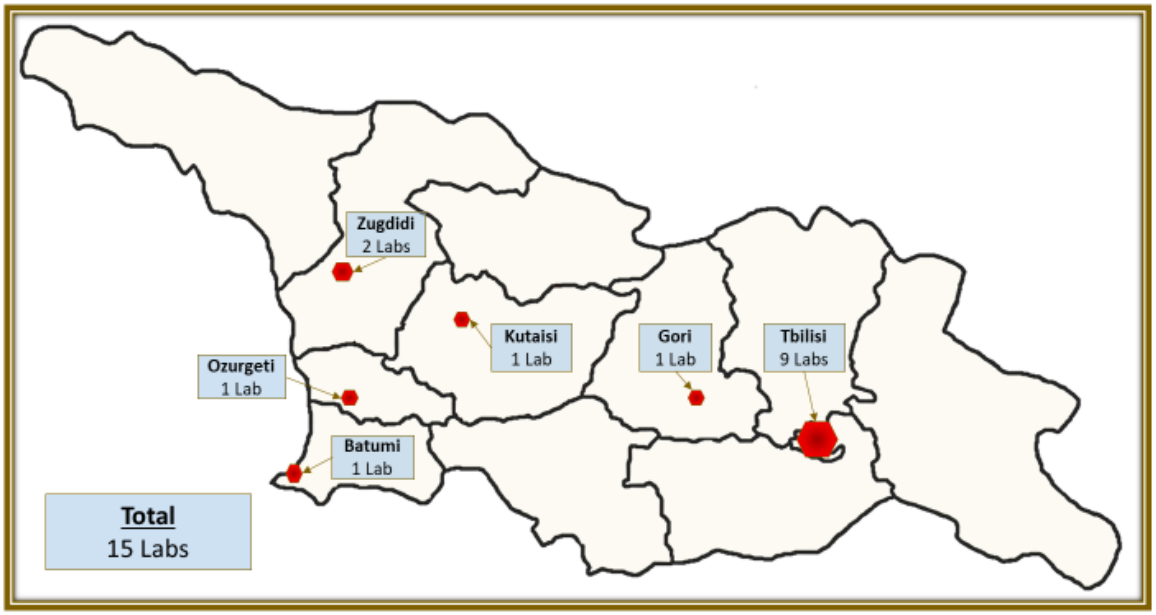
Access to quality diagnostic services is crucial for surveillance, accurate and timely detection of hepatitis C infection, ensuring appropriate follow-up care for those infected with HCV, and documenting cure of infection. As the public health agency responsible for HCV screening and surveillance in Georgia, NCDC uses its laboratory network to improve access to HCV screening for Georgians and to provide external quality assurance for laboratories (both public and private) licensed to perform HCV diagnostic and monitoring tests. The NCDC Public Health Laboratory Network is comprised of two zonal diagnostic laboratories (located in Kutaisi and Batumi), seven laboratory support stations (LSS), and the Richard Lugar Center for Public Health Research (Lugar Center), which serves as the National Reference Laboratory for the country (Figure 4.1).

Figure 4.1 Public Health Network in Georgia

Georgia uses a mixed public-private model for the provision of HCV diagnostic and monitoring tests in accordance with the National Testing Algorithm. Currently, voluntary HCV screening in Georgia occurs in more than 1,000 diverse venues (see Strategy 3. Identify Persons Infected with HCV), including nine

NCDC public health laboratories. Confirmatory testing by viral load is performed in 15 private laboratories (Figure 4.2); of these, 13 undertake HCV genotyping. The Lugar Center performs both HCV RNA and genotyping, and provides National External Quality Assurance (EQA) program.
No standard diagnostic devices are used (i.e., individual laboratories procure NAT instrumentation and reagents independently based on quality and cost). In addition to Abbott's RealTime molecular diagnostic platform for HCV (the reference kit used for EQA), the following five diagnostic tests are available for use in Georgia: Cobas TaqMan HCV quantitative test V2.0 (Roche); Bosphore HCV Quantitation Kit (Anatolia Geneworks); HCV Real TM Quant Dx V1 (Sacace Biotechnologies); HCV Real-Time PCR Kit (Human Diagnostic); and RT-GEPATOGEN-C Quant PCR Amplification Kit (DNA Technology).

Figure 4.2 Distribution of HCV Real-Time PCR -based assays in Georgia



In June 2017, MoLHSA approved use of HCV core-antigen testing to confirm active HCV infection for Elimination Program purposes as an alternative PCR. One Abbott Architect i2000 immunodiagnostic platform has been installed in the Lugar Center Reference Laboratory, which has the potential to support centralized confirmation of active HCV infection, using HCV Core Antigen qualitative and quantitative testing, in anti-HCV -positive persons identified by the screening Program.
A collaborative study involving the Georgia NCDC, Foundation for Innovative New Diagnostics (FIND) and CDC was piloted in 2017 to address key HCV Elimination Program challenges concerning access, quality, and cost of diagnostic tests, with a particular focus on PWID. A primary aim of the study was to determine the impact of on-site confirmatory testing on client retention in the HCV treatment program. Four GeneXpert machines were placed in four harm reduction centers providing HCV screening services and compared to standard of care (rapid test and referral if positive) and rapid test with on-site specimen for confirmation with HCV core-Ag testing at the Lugar center. Results from this study are not yet available, but will be published in future Elimination Program Annual Reports. In addition, 38 GeneXpert machines exist in-country for diagnosis of tuberculosis, and 19 machines are planned to be available in the future and can be used for HCV NAT testing in addition to TB and HIV. Point-of-contact

devices are placed in both NCDC public health laboratories and in clinics of the EVEX Medical Corporation. GeneXpert machines, as noted, can be used for HCV diagnostics.

Progress and Program Outcomes

Georgians receive diagnostic HCV testing through the Hepatitis C Elimination Program. The cost to the patient for diagnostic services varies, as payment is subsidized at different levels based on specific patient criteria (e.g., patient's residence and socioeconomic status). While antibody screening is free of charge for all, confirmatory (virologic, NAT, RNA) diagnosis is free of charge for economically disadvantaged patients; other patients may be responsible for up to 70% of the cost. Co-payments for confirmatory diagnostics remain a deterrent: up to 50% of patients who tested positive after their initial test failed to obtain confirmatory testing and may have been deterred by cost of testing.
In 2015, a standard WHO-adapted tool was used to assess capacity at four clinical laboratories (affiliated with four initial pilot sites for the HCV program in Tbilisi) and eight public health laboratories.

- In March 2015, when assessed for quality, all four clinical laboratories involved in the program at that time met the minimum requirements for HCV testing. However, scores for "total quality" indicator at participating laboratories ranged from 36%-100% (acceptable 75%-100%)
- In November 2015, the TAG recommended improving diagnostic system nationwide through introduction of minimum quality management requirements for the licensing of laboratories participating in the hepatitis C elimination program, were recommended (Box 1).

Box 1. Laboratory Requirements Associated with HCV Elimination Program in Georgia

Minimum quality management requirements for participating laboratory providers

- Availability of an internal quality control system
- Availability of approved standard operating procedures for each laboratory test
- Availability of technical resources for conducting necessary laboratory tests
- Availability of personnel certified according to the rules established by current legislation
- Ability to provide the tests results within 5 working days of sample collection
- Ability to maintain patient records with test results for at least 2 years
- Capacity and experience to conduct all tests determined by the Program

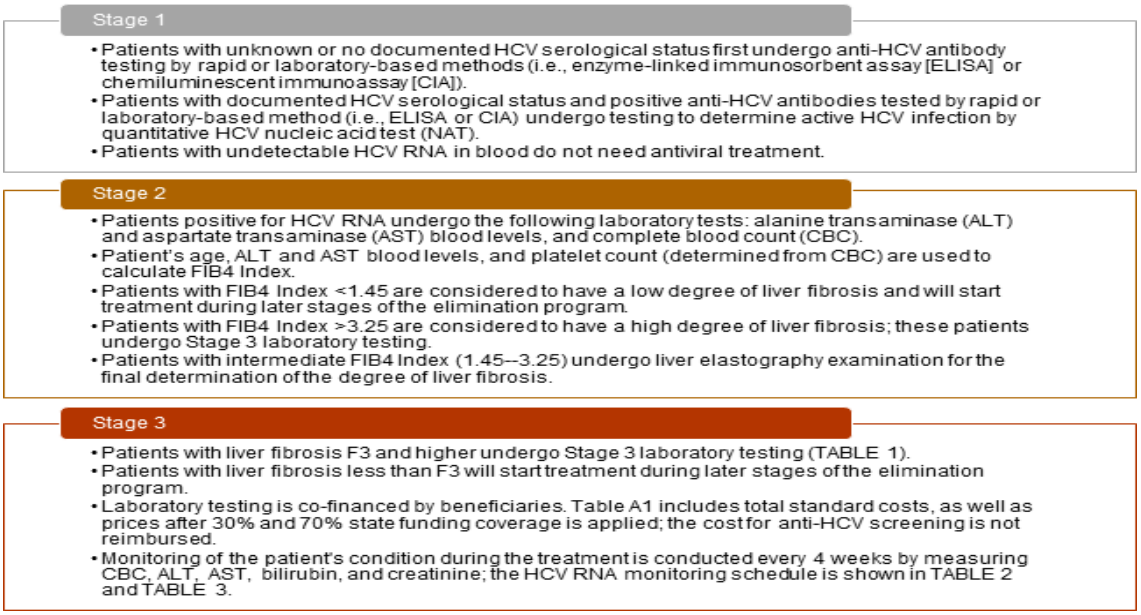
Mandatory laboratory tests

- Anti-HCV detected by Rapid Point of Care Test (RT) or laboratory-based test (i.e., ELISA or CIA; Quantitative HCV NAT)
- HCV Genotyping by line hybridization assay and/or real-time PCR
- Hematological, biochemical, and serological tests as specified in the Table 1

- In July 2016, MoLHSA's Laboratory Working Group developed a regulatory document (Decree #320) for licensing of laboratory service providers, to be implemented January 1, 2017. The licensing requirements focus primarily on infrastructure requirement and require implementation of SOPs for all laboratory tests covered under the license. The next phase of laboratory regulation, laboratory certification, will focus on quality assurance and will require laboratories to demonstrate effective implementation of quality management systems, including successful participation in EQA programs.

- In September 2016, Lugar Center for the first time enrolled in an international EQA program with the College of American Pathologists. To facilitate enrolment of all the participating labs across the country in the EQA programs, a sustainable and affordable local EQA program was necessary.
- In March 2017, with technical assistance from the U.S. CDC, and by using locally sourced and characterized materials, the Lugar Center established the first National EQA program for HCV viral load and genotyping.
- By December 2017, all 15 laboratories performing HCV viral load testing, and all 13 laboratories performing HCV genotyping within the framework of the Elimination Program, were enrolled in EQA program. To date, the Program has dispatched three proficiency testing panels (May, September and December 2017) and provided result reports and recommendations for improvement (if needed).
- In 2016-2017, the Lugar Center conducted a study to evaluate the concordance between Abbott HCV core antigen and viral load testing for confirming active HCV infection in the screening program in general population, and for the monitoring of treatment efficacy at 4 weeks of treatment, end of treatment (EOT), and 12 weeks after completion of treatment (SVR). Overall, concordance between both methods for confirming active infection was 97%, with discordance occurring in those specimens with very low HCV viral load by RNA (<30 IU/ml) and negative HCV core-antigen (HCVcAg) results. For treatment monitoring, agreement between methods was 96.5% (334/346) at the 4-week monitoring point; 98.9% (186/188) at EOT; and 100% (21/21) at SVR. The study demonstrated that HCV core-antigen can be used as an alternative to HCV RNA for confirming active HCV infection and monitoring DAA treatment.
- Currently, HCV provider clinics expanded laboratory services by screening patients for HCV and HIV antibodies, which began as a pilot in November 2016. The laboratory diagnostics algorithm developed for the Elimination Program (Box 2) is being optimized to reduce costs by introduction of alternative HCVcAg testing for confirmation of active HCV infection, and reducing the number of tests necessary for monitoring antiviral treatment and assessing outcomes.

Box 2. Laboratory Diagnostics Algorithm used for Georgia's HCV Elimination Program



Challenges

Several improvements must be made in laboratory diagnostics to support the achievement of reaching the elimination goals for Georgia. Remaining challenges include:

- Lack of a National System to license laboratory professionals;
- Lack of a National Laboratory Certification Program to ensure that laboratories meet quality and biosafety standards;
- Use of non-validated test kits for HCV diagnostics;
- Lack of uniform national SOPs for all the laboratories in the country; and
- Lack of uniform comprehensive training program for laboratory personnel on quality and biosafety standards and practices.

TAG 2016 Recommendations*

4 Improve HCV Laboratory Diagnostics

4.1 Ensure that assays for testing, diagnosis, and treatment monitoring are approved by an international regulatory authority (e.g., WHO, U.S. Food and Drug Administration [FDA], or CE-marked in Europe) or validated by an evaluation protocol, with results reviewed and approved by appropriate experts in the field.

4.2 To detect current HCV infection, test all specimens positive on anti-HCV screening either by HCV-RNA or HCV-core-antigen (when feasible and cost-effective).

4.3 Present to TAG in 2017 all data from monitoring evaluation indicators, particularly results of quality evaluations of laboratories.

*The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring and Evaluation: Laboratory Diagnostics, 2015–2016

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
4.1 Improve laboratory detection of HCV infection	1. Number of laboratories providing HCV laboratory services registered in the National Laboratory Registry		MoLHSA	None	
	2. The Lugar center is functioning as an external quality assurance (EQA) provider for hepatitis C laboratory services		NCDC	Not done yet	Assessment of lab proficiency three times per year.
	3. Proportion of labs providing HCV lab services enrolled in the national hepatitis C EQA program	**Numerator:** Number of laboratories performing HCV laboratory services that are enrolled in national hepatitis C EQA program **Denominator:** Total number of laboratories performing hepatitis C laboratory services	NCDC	None	
	4. Quality Management System standards for certification are defined, approved, and published		Published QMS standards	Not done yet	

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
	5. Proportion of labs providing HCV lab services certified according to national laboratory quality management system (QMS) standards	**Numerator:** Number of laboratories performing hepatitis C laboratory services that are certified according to national QMS standards **Denominator:** Total number of laboratories performing hepatitis C laboratory services	MoLHSA	None	

STRATEGY 5:

PROVIDE COMPREHENSIVE HCV CARE AND TREATMENT

Introduction

The Elimination Program aims to provide universal access to hepatitis C treatment and achieve high cure rates for all persons with HCV infection in Georgia. Reaching this goal is essential to achieving hepatitis C elimination in Georgia. Provision of treatment services coupled with implementation of effective prevention interventions will minimize the infection reservoir and reduce the number of incident cases.

Launched in April 2015, the initial phase of the HCV elimination program prioritized antiviral therapy for HCV- the population at highest risk for HCV-associated morbidity and mortality: infected persons with advanced liver disease, defined as F3 or F4 by METAVIR fibrosis score and/or FIB-4 score > 3.25-. In June 2016, eligibility criteria expanded, allowing all HCV-infected patients to enroll in the program regardless of liver-disease severity. Curative antiviral therapy was provided free of charge through a partnership with Gilead Sciences.

At the start of the program, all participants received sofosbuvir (SOF)-based antiviral treatment regimens, in combination with ribavirin alone or pegylated interferon and ribavirin. Beginning in March 2016, the majority of patients began receiving sofosbuvir/ledipasvir (SOF/LED)-based regimens.

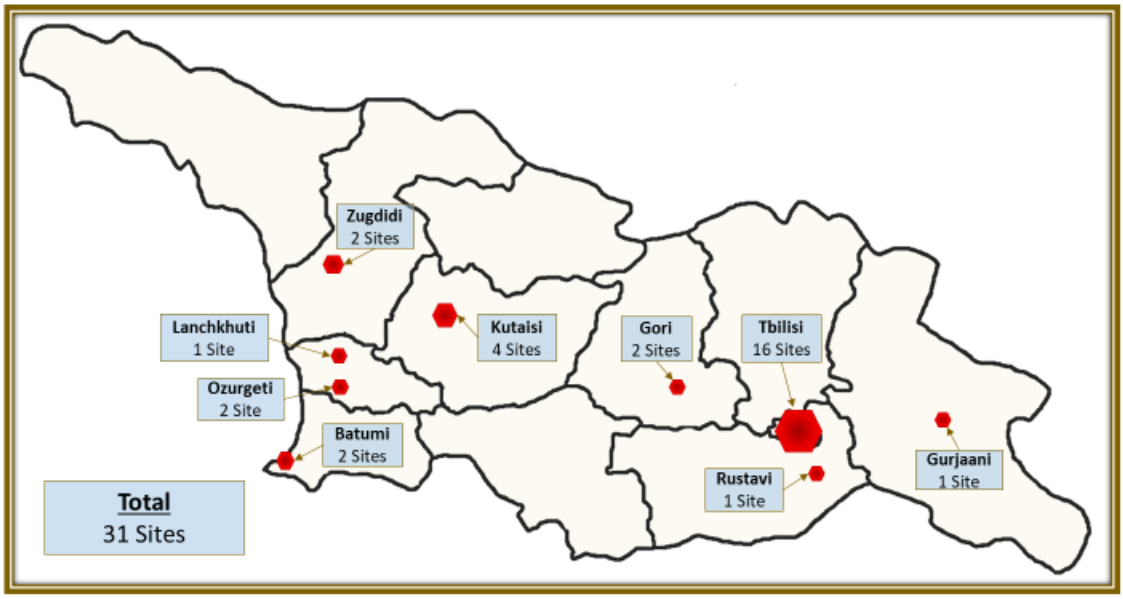
The correct identification of HCV genotype serves as a marker of treatment responsiveness and facilitates clinical decision-making, particularly in countries with a high prevalence of HCV infection [16]. Georgia has HCV genotype 1, 2 and 3 predominantly, however, it has been found that HCV recombinant strain 2k/1b is common among ethnic Georgian HCV patients previously assumed to be infected with HCV genotype 2 [17].

Progress and Program Outcomes

Provision of comprehensive HCV services, patient access, and geographical availability of care have a direct effect on HCV treatment outcomes, and therefore on the burden of disease. Georgia has developed sufficient infrastructure and provider capacity to provide care and treatment to all Georgians living with HCV infection.

At the time of the Elimination Program's launch in April 2015, only four treatment centers located in Georgia's capital of Tbilisi were providing HCV care and treatment services. By October 31, 2017, HCV treatment coverage had expanded to include 31 health facilities throughout the country and 139 physician providers; 16 of the sites are located in the capital city of Tbilisi; four sites in Kutaisi; two sites each in Gori, Batumi, and Zugdidi; and one site each in Rustavi, Gurjaani, Ozurgeti, and Lanchkhuti (Figure 5.1). Diagnostic capacity for the program includes 15 laboratories with polymerase chain reaction (PCR) capacity (nine located in Tbilisi) and 12 sites that measure liver fibrosis with elastography, in addition to routine chemistry and hematologic diagnostics.

Figure 5.1 Geographic coverage of Georgia's HCV Elimination Program



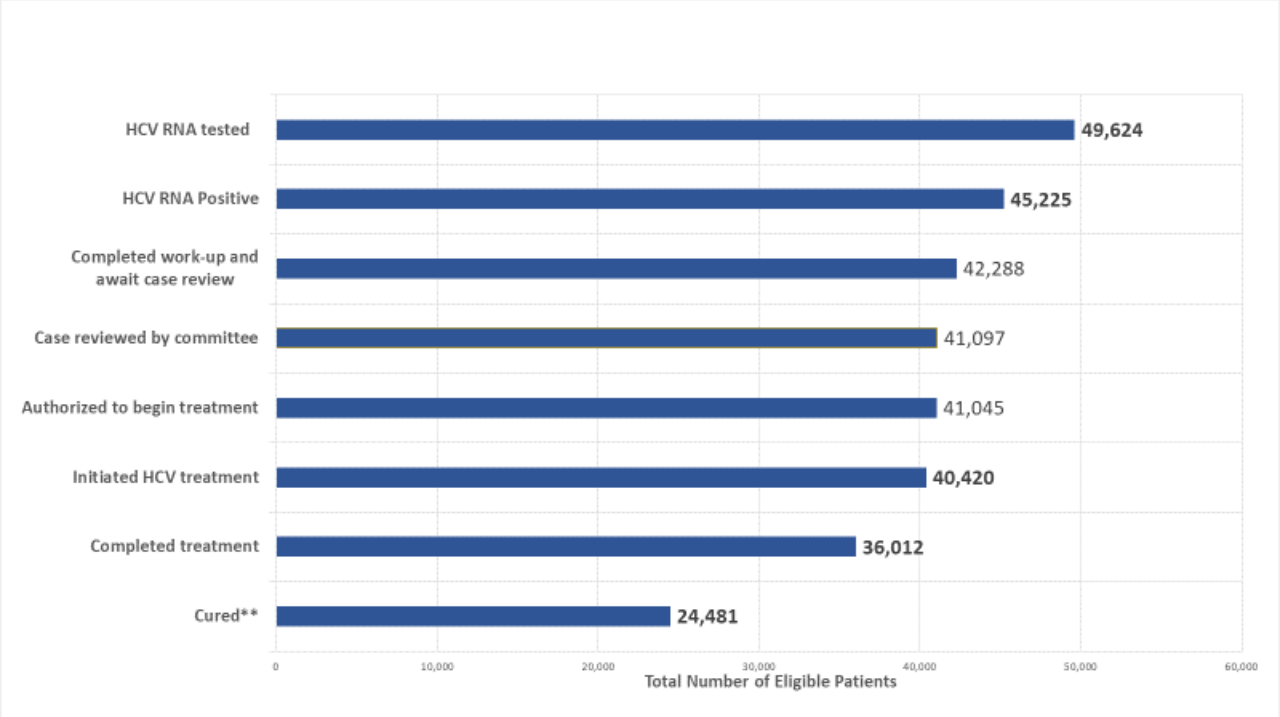
While treatment is provided free of charge, a sliding-scale approach is used for diagnostics and clinical monitoring services, with patients charged based on their ability to pay. Either the government of Georgia (MoLHSA) or the local government pays the remaining balance.

Of 562 infectious-disease physicians and 135 gastroenterologists practicing medicine in Georgia, 139 (as of October 2017) are providing HCV care and treatment services and have been providing services through the HCV Elimination Program. Nevertheless, due to the scope of elimination efforts and limited experience of Georgia's HCV clinical providers with new HCV medications, DAAs, the program partnered with Project ECHO (Extension for Community Healthcare Outcomes) at the University of New Mexico Health Sciences Center (UNMNSC) and the Liver Institute for Education and Research (LIFER) to provide education and clinical consultation. Project ECHO uses telecommunication technology for capacity building, training, and clinical case management support to improve and maintain the quality of HCV treatment services and support appropriate clinical decision-making. Beginning in February 2016, physicians from the four original HCV provider clinics began participating in monthly interactive TeleECHO clinics, where they present complex cases and receive mentoring from the project ECHO team and other experts in the treatment of viral hepatitis infection. Project ECHO has now been expanded to the other HCV providers, with the original four clinics serving as ECHO "hubs" that provide mentoring to 10 newly recruited clinics functioning as "spoke" facilities across the country. From June 2016 through December 2016, 14 bi-weekly telementoring clinic sessions were conducted through the four Tbilisi hubs.

HCV treatment guidelines in Georgia are standardized through the elimination program based on available medications (Appendix 2). The unified treatment protocols and diagnostic and monitoring algorithms implemented in Georgia were based on guidelines from the Infectious Diseases Society of America (IDSA), American Association for the Study of Liver Diseases (AASLD) and European Association for the Study of the Liver (EASL) whenever possible.
Within the framework of the HCV elimination program, a clinical group was established under government order in April 2016 to ensure clinical monitoring of the program, guideline development, and physician training. Since February 2016, more than 100 HCV specialists have attended six on-site training sessions conducted by this clinical group.

The cornerstone of treatment monitoring and evaluation is patient continuum-of-care, or linkage of persons identified as HCV infected to curative care and treatment. From April 28, 2015 through October 31, 2017, a total of 45,225 people were diagnosed with chronic HCV infection (i.e., HCV-positive through RNA testing) in Georgia; of these, 42,288 HCV-infected persons enrolled in the treatment program (i.e., completed the diagnostic workup) (Figure 5.2).

Figure 5.2 Georgia HCV Elimination Program cascade of care, April 28, 2015 through October 31, 2017*



** Of 32,835 patients eligible for SVR assessment, 24,930 were tested, 24,481 (98.2%) achieved SVR, and 7,905 (24%) had missing data.

Summary of Key Findings†:

- Five times more men than women enrolled and started HCV treatment (23,062 vs. 4,533).
- The proportion of enrolled people who initiated antiviral therapy did not differ by gender: 91.6% (23,062 of 25,171) of males and 91.8% (4,533 of 4,936) of females began treatment.
- Over half (58.2%) of all persons treated for hepatitis C infection were aged 30–49 years.
- Over 40% of patients receiving sofosbuvir-based treatment were infected with HCV genotype 3 (Table 3).
- During the initial phase of the program (April 2015 through May 2016), when treatment was prioritized for persons with more severe liver disease, most patients initiating treatment (9,088 of 9,259; 98.2%) had advanced liver disease (≥F3 METAVIR fibrosis score and/or FIB-4 score >3.25). After the expansion of treatment criteria to allow treatment for all persons with HCV infection (beginning June 1 through December 31, 2016), most persons initiating treatment (14,368 of 18,336; 78.4%) had less severe liver disease (<F3 METAVIR fibrosis score and/or FIB-4 score <1.45)

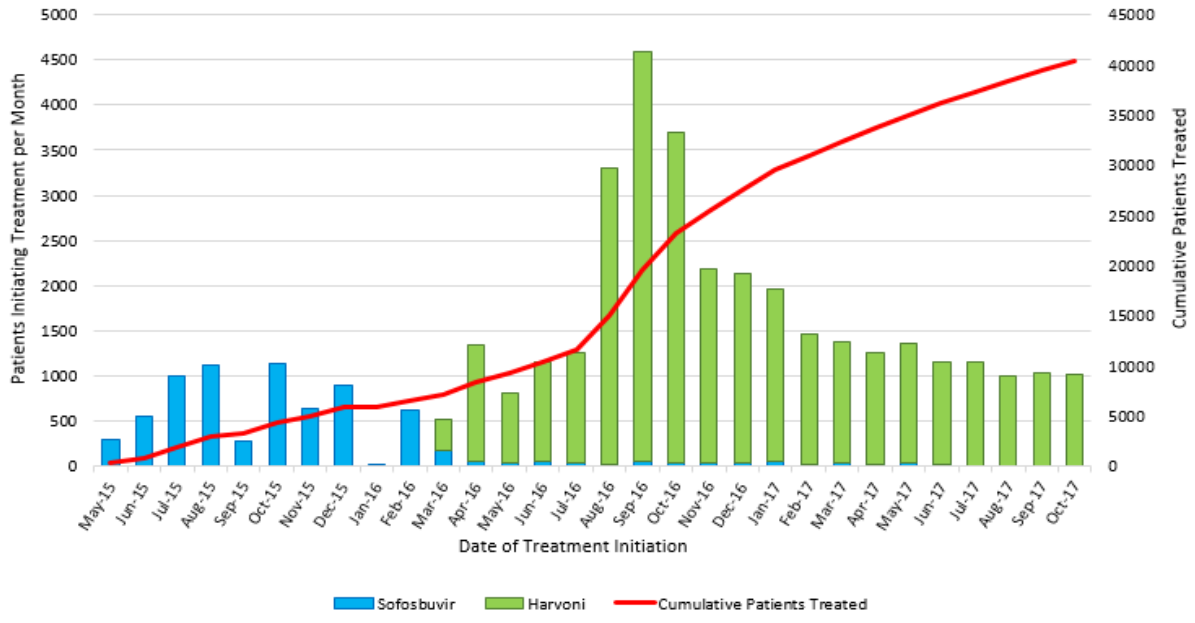
* Provisional data
† Data presented as of December 31,2016

Table 3. Laboratory-confirmed cases of chronic hepatitis by genotype among persons engaged in their first round of HCV treatment, April 28, 2015 through December 31, 2016

HCV Genotype	Number of patients receiving sofosbuvir-based regimen n (%)	Number of patient receiving ledipasvir/sofosbuvir-based regimen n (%)
1	2,455 (34.1)	8,352 (40.9)
2	1,574 (21.9)	5,228 (25.6)
3	3,130 (43.5)	6,147 (30.1)
4	34 (0.01)	662 (3.2)
Missing	-	13 (0.1)
Total	7,193 (100)	20,402 (100)

Treatment rates increased steadily during the first months following program implementation, with treatment uptake reaching 40,420 persons by October 2017. After eligibility criteria expanded, more than five times the number of patients initiated treatment with SOF/LED-based treatment regimens (N=33,078) during March through October 2017 than those treated with the SOF-based treatment regimens (N=6,585) offered from May 2015 through February 2016 (Figure 5.3).

Figure 5.3 Number of patients initiated HCV treatment during May 2015–October 2017



From April 2015 through October 2017, among patients tested for sustained viral response (SVR), 24,481/24,930 (98.2%) had no detectable virus after their first course of treatment, indicating cure of their infection.
The overall percentage of people achieving SVR with the sofosbuvir-based regimen remained stable from April 2016 (82.6%; N=1,980/2,398) [2] through October 2017 (81.9%; N=4,106/5,012). The introduction of SOF/LED-based regimens has resulted in higher cure rates among patients tested for SVR after treatment completion (98.5%; N=19,928/20,227).

Overall, 1,029 patients received a second round of treatment, most of whom had experienced previous treatment failure (79%; N=811); 893 of these patients (87%) completed a second round of treatment by the end of October 2017. Among 494 patients completing treatment who were eligible for and received post-treatment testing by HCV PCR, 463 (93.7%) had no detectable virus.

Challenges

- The 31 HCV sites established across Georgia through the HCV Elimination Program serve the majority of regions identified in the 2015 seroprevalence survey as having a high burden of HCV. However, a few of these geographic areas (e.g., 4.76% in Samtskhe-Javakheti) are currently unserved by providers specializing in HCV care, requiring residents to travel long distances to access an HCV care facility. The role of geographic accessibility requires further attention.
- The number of persons initiating treatment in 2016 declined steadily from October (N=3,691) through December (N=2,138) despite increases in screening and testing. These findings suggest the need to address gaps in screening and linkage to care, as treatment capacity in the country appears adequate to address the demand. Linking infected persons to care is a challenge, especially for persons who remain unaware of their infection. In addition, optimal treatment options for persons infected with HCV genotype 2k/1b, to include duration of therapy, should be determined and offered as part of the elimination effort.
- To monitor the treatment component of the HCV Elimination Program, MoLHSA developed a national treatment database consisting of two separate data-collection information systems: STOP-C and Elimination C. STOP-C was developed by modifying an existing drug dispensing electronic database and was launched at the start of the Elimination Program, when interferon was used extensively. Because this system proved insufficient for collecting data on HCV screening, linkage to care, and outcomes, MoLHSA launched the second system, Elimination C, in June 2016. The reporting capability of this second-generation system also has limitations, primarily that exported data must be extensively cleaned to enable analysis. Further, joint/merged reports from both treatment databases do not generate automatically because they are “stand alone” systems lacking standard reporting capability. Elimination Program information systems require further refinement, including development of an additional analytical layer that will serve the reporting needs of the key stakeholders and the research needs of the Scientific Committee.

TAG 2016 Recommendations[§]

5 Provide HCV Care and Treatment

- **5.1** Train primary-care clinicians to diagnose and treat HCV infection to reach persons where they are accustomed to receiving medical care.
- **5.2** Offer HCV testing and treatment services at the same location (e.g., harm-reduction centers and primary-care facilities).
- **5.3** By October 2017, launch demonstration projects to identify the best strategies for co-locating HCV testing, diagnosis, and treatment with addiction treatment at OST centers and an NSP site.
- **5.4** Ensure the completion of HCV screening, care, and treatment for incarcerated persons prior to release.

[§]The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring & Evaluation: Care and Treatment, 2015–2016

Objective	Indicator name	Measurement	Data Source	Value/Result
5.1. Promote universal access to HCV care and treatment	1. Proportion of anti-HCV positive persons tested for HCV RNA	**Numerator** Number of persons tested for hepatitis C during the reporting period using HCV RNA testing: **38,113**	Elimination C database	**65.5%**
		Denominator Number of people with a presence of anti-HCV antibodies: **58,223**	Screening database	
	2. Proportion of persons diagnosed with chronic HCV infection	**Numerator** Number of persons diagnosed with chronic HCV infection based on virologic biomarker testing (HCV RNA or HCV core antigen assays[¶]): **36,322**	Elimination C and STOP-C databases	**95.3%**
		Denominator Number of persons tested for hepatitis C during the reporting period using HCV RNA testing: **38,113**	Elimination C and STOP-C databases	

[¶] When HCV core antigen testing for diagnosis of Hepatitis C is approved as the Standard of Care

Objective	Indicator name	Measurement	Data Source	Value/Result
	3. Proportion of persons living with HCV diagnosed	**Numerator** Number of persons diagnosed with chronic HCV infection based on virologic biomarker testing (HCV RNA or HCV core antigen assays): **36,322**	Screening database (MoLHSA)	**24.2%**
		Denominator Estimated number of persons with chronic HCV infection: **150,300**	National sero-prevalence survey conducted in **2015**	
	4. Proportion of persons living with HCV infection who have completed HCV pre-treatment evaluation	**Numerator** Number of persons with chronic HCV infection assessed for genotype and liver disease fibrosis: **30,320**	Elimination C and STOP-C databases	**20.2%**
		Denominator Estimated number of persons with chronic HCV infection: **150,300**	Seroprevalence survey	
	5. Proportion of persons diagnosed with HCV infection who have completed HCV pre-treatment evaluation	**Numerator** Number of persons with chronic HCV infection assessed for genotype and liver disease fibrosis: **30,320**	Elimination C and STOP-C databases	**83.5%**

Objective	Indicator name	Measurement	Data Source	Value/Result
		Denominator Number of persons diagnosed with chronic HCV infection (linked to care and tested positive for HCV RNA): **36,322**	Elimination C and STOP-C databases	
	6. Proportion of persons with HCV infection engaged in antiviral therapy	**Numerator** Number of persons diagnosed with HCV infection who initiated antiviral therapy during the specified timeframe: **27,595**	Elimination C and STOP-C databases	**76.0%**
		Denominator Number of persons diagnosed with chronic HCV infection: **36,322**	Elimination C and STOP-C databases	
	7. Proportion of patients engaged in antiviral therapy who have completed treatment	**Numerator** Number of patients with chronic HCV infection who have completed treatment: **19,778**	Elimination C and STOP-C databases	**71.7%**
		Denominator Number of patients diagnosed with HCV infection who initiated treatment during a specified timeframe: **27,595**	Elimination C and STOP-C databases	

Objective	Indicator name	Measurement	Data Source	Value/Result
	8. Proportion of patients achieving SVR to HCV therapy (whether previously treated or treatment naïve).	**Numerator** Number of patients who completed treatment and achieved SVR (undetectable viral load 12-24 weeks after the end of treatment): **5,356**	Elimination C and STOP-C databases	**84.1%**
		Denominator Number of patients who completed antiviral therapy and were assessed for SVR 12-24 weeks post treatment: **6,366**	Elimination C and STOP-C databases	
	9. Number of physicians providing HCV services OR provider/resident ratio	**Numerator** Number of physicians providing HCV services: **139**	Elimination C and STOP-C databases	**4.6 per 100,000 residents**
		Denominator Estimated resident population: **3,010,200**	Elimination C and STOP-C databases	
	Assessment of patient engagement in HCV care, treatment outcomes and associated factors (including issues related to delays and barriers in accessing care, adherence, loss to follow-up, and other outcomes)		Special research studies	N/A

STRATEGY 6:

IMPROVE HCV SURVEILLANCE

Introduction

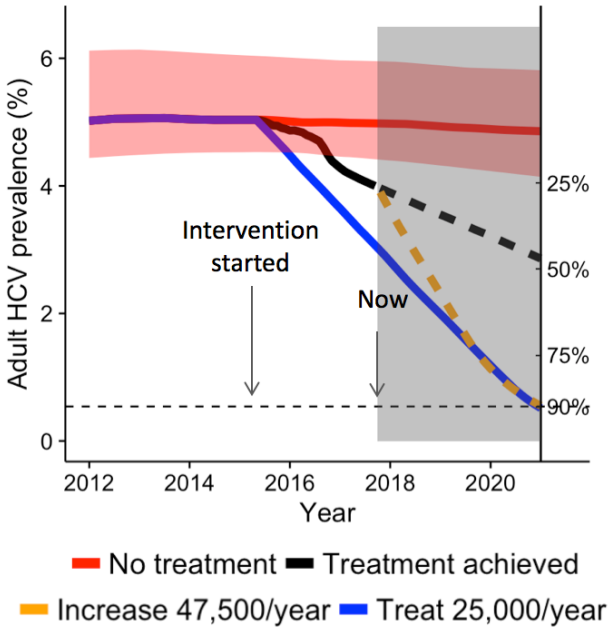
Monitoring progress toward HCV elimination requires a well-functioning surveillance system. HCV surveillance can help direct public health programs through the collection of information on acute and chronic forms of the disease and detection of outbreaks. In Georgia, prior to the launch of the HCV Elimination Program in 2015, an aggregated laboratory data system was used to report acute and chronic[¶] HCV cases on a monthly basis that included 62 Primary Health Centers (PHC) located in each municipality across the country. This system was limited: it did not include data on risk factors for transmission or HCV-associated complications, nor did it collect data on disease distribution in the general population. Before 2015, only one population-based survey on hepatitis C infection had been conducted and was limited to the city of Tbilisi [19]. To elucidate the true burden of hepatitis C in Georgia, a nationwide survey of HCV and HBV prevalence was conducted in 2015 by NCDC in collaboration with the U.S. CDC, paving the way for planning the prevention, screening and treatment interventions (MoLHSA, unpublished data, 2016). Currently, data on patients diagnosed HCV infection are reported to the HCV Elimination Program treatment database (see Strategy 5: Provide Comprehensive HCV Care and Treatment). Due to the challenges associated with and resources needed to establish a robust acute hepatitis surveillance system, this has not been a focus of the program to date.

Progress and Program Outcomes

- In 2015, a national seroprevalence survey was conducted that provided valuable data, including HCV burden and risk factors for transmission (nationally and by region).
- Modeling was used to evaluate the impact of HCV elimination program interventions and to assess the feasibility of achieving 90-95-95 targets by 2020 (University of Bristol, UK). A dynamic transmission model was developed based on current/historical HCV prevalence data by population (e.g., PWID) and numbers of persons treated through the elimination program (unpublished data).

[¶]https://www.path.org/publications/files/CP_phrplus_surv_gdlns_2005_2.pdf

Figure 6.1 Modeling the impact of HCV Elimination Program on HCV prevalence



- During the reporting period, case definitions for acute and chronic hepatitis C[€] were revised based on WHO and CDC guidance [20]. A manual containing the revised case classifications of notifiable diseases, including hepatitis C, was prepared and distributed to PHCs across the country in August 2016.
- Beginning in 2015, three rounds of training courses covering diverse topics (i.e., HCV epidemiology, transmission routes, screening, diagnostic methods and treatment availability, and overview of the HCV elimination program) were conducted at PHCs by specialists from NCDC and invited expert-clinicians. Training sessions were attended by both administrative staff (39%) and epidemiologists (61%); of 128 epidemiologists working at PHCs, 51.6% received training. Regional distribution for course attendance is as follows: 43 staff members (39%) were trained in east Georgia, 37 (34%) in west Georgia (34%), and 29 (27%) in Tbilisi.
- Pre- and post-test questionnaires were prepared and administered to PHC staff to evaluate the effectiveness of the educational interventions. Comparison of pre- and post-test results demonstrated the following.
    - ✓ An 80% increase was observed in the number of participants who were aware of the HCV burden in Georgia (45/103 [44%] at pre-test and 80/102 [78%] at post-test, respectively).

[€] **Unspecified acute hepatitis:** discrete onset of an acute illness with signs/symptoms of an infectious illness (e.g. fever, malaise, fatigue) and liver damage (e.g. anorexia, nausea, jaundice, dark urine, right upper quadrant tenderness, or levels of alanine aminotransferase [ALT] raised more than ten times the upper limit of normal of the laboratory).
Confirmed acute hepatitis C: seroconversion to hepatitis C virus antibodies (anti-HCV); presence of HCV RNA in the absence of anti-HCV; positivity for anti-HCV and negativity for anti-HAV IgM, anti-HBc IgM and anti-HEV IgM;
Chronic HCV infection is defined by the absence of acute hepatitis and the presence of HCV RNA or HCV core antigen AND Anti-HCV positivity.

- ✓ Indicators for stigmatization and discriminatory attitudes towards PWID decreased after completion of training sessions. The proportion of participants who presumed that PWIDs would not adhere to treatment (and therefore that their status was a valid reason to refuse treatment) declined from 33% to 10%.

- Initially, two sentinel medical facilities (Neolab in Tbilisi and Imereti Medicine Development Center in Kutaisi) were selected to collect HCV-related risk-factor data as part of CDC's cooperative agreement project (*Strengthening Surveillance to Assess Real Burden of Viral Hepatitis in Georgia*). However, since June 2016, all HCV care-provider sites participating in the HCV Elimination Program have been routinely collecting and reporting these epidemiologic data through the newly developed "Elimination C" database. Preliminary analysis of data through September 2016 from Tbilisi's Neolab revealed that of the 1,989 patients enrolled in HCV treatment, 87.5% reported alcohol use; among these, 552 (31.7%) reported heavy use, placing them at increased risk for liver disease; 667 (38.3%) reported moderate use[∞].
- The HCV-related morbidity and mortality assessment study is underway. The study protocol was developed, a pilot was conducted in two different clinics in Tbilisi and Gori, and study documents were presented to an ethics committee for review. The target population currently is being determined.
- Beginning in June 2016, HCV reinfection surveillance data have been collected among PWIDs in Tbilisi through a joint effort between Medecins du Monde (France) and the local NGO Health Research Union (HRU). Surveillance objectives include assessing to what degree peer-support interventions delivered to PWID during treatment reduce the risk of reinfection after successful treatment. A sample of 150 successfully treated PWID were followed for one year after achieving SVR12, with 19 anti-HCV negative PWID serving as controls. Data were collected through behavioral questionnaires and HCV RNA testing at 6 and 12 months after the patient reached SVR12. As of May 2017, available data indicate two new HCV infections among PWID achieving SVR (1.4% PY) during 138.9 person-years of follow-up. Similar hepatitis C incidence was observed in the control group (12.9% PY) during 15.5 person-years of follow-up.
- In 2017, NCDC undertook measures to establish a strong collaboration with the Dialysis, Nephrology, and Kidney Transplantation Union of Georgia (DNT Union of Georgia) to strengthen serologic surveillance for hepatitis C infection among hemodialysis patients, create an effective reporting system, and enhance the linkage of HCV-infected hemodialysis patients to HCV care and treatment.

Challenges

- The current hepatitis C surveillance system lacks the capacity to monitor/assess the burden and risk factors for HCV infection in Georgia. Further, it is not possible to determine hepatitis C incidence in the general population or risk subpopulations (e.g., PWID, dialysis patients, and

[∞] https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking

patients undergoing invasive medical procedures). These data are challenging to collect, and very few countries collect such data routinely.

- Availability and quality of data regarding HCV-related morbidity and mortality also must be improved to enable accurate measurement of program and cost effectiveness. Currently, cause of death data is infrequently collected or remains unspecified on vital records. Efforts are needed to assess the burden of end-stage liver disease (ESLD), hepatocellular carcinoma (HCC), and death attributable to HCV. Analyses of data from GeoStat (vital statistics) , the Georgia Cancer Registry , hospital discharge diagnoses (E-Health) and gastroenterology/hepatology and oncology clinics can help to provide useful estimates. Efforts are underway to assess this burden.

TAG 2016 Recommendations§

6 Improve HCV Surveillance

6.1 Target high-risk persons (including PWID and dialysis patients) for case surveillance and/or serologic surveys to identify trends in disease burden, new infections, and response to treatment.

6.2 Create a uniform electronic database to include all HCV surveillance data.

6.3 Repeat the national seroprevalence study in 2021.

6.4 Evaluate the quality of reporting for HCV-associated deaths in national registries to determine whether the data can be used for a baseline mortality assessment and for periodic monitoring to assess the impact of the Elimination Program on HCV mortality trends. If deficits in quality are found and correction is feasible, develop a plan to improve data quality or develop an analysis plan that takes into account limitations of the data.

6.5 Consider collecting data on the association between liver disease (e.g., HCC and cirrhosis) and HCV infection.

§The TAG recommendations in this document have been slightly modified from those in a previous version to maintain grammatical consistency.

Monitoring and Evaluation: Surveillance, 2015–2016

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
6.1 Estimate the national burden of chronic viral hepatitis C	1. Number of HCWs trained in acute HCV case identification and new HCV reporting requirements	Number of designated clinical staff members who complete a short course in HCV case identification, investigation, and reporting	NCDC or other agency involved in training	109	
	2. Average rate of change in HCW knowledge of acute HCV case identification and reporting requirements	Average scores on post training and pre-training assessments		Data not Available	Identify deficiencies to inform any further training and supplement these analyses with qualitative site assessments
	3. Rating of quality and completion of prescribed activities based on national HCV surveillance guidelines/protocols		Evaluation Reports	Data not Available	Evaluate performance levels (i.e., how well case reporting and investigation are being implemented) against those outlined in protocols/guidelines
	4. Number and percentage of patients with a) HCC and b) cirrhosis who are	**Numerator:** Persons screened for HCV infection	Clinic and hospital databases for HCC and cirrhosis	Data not Available	Requires active surveillance to

Objective	Indicator name	Measurement	Data source	Value/Result	Remarks
	screened for hepatitis C				identify cases (at least initially). Case Definitions must be generated
		Denominator: a) Persons diagnosed with HCC b) Persons diagnosed with cirrhosis	Cancer Registry		Patients are those currently in care.
	5. HCV incidence in selected key populations	**Numerator:** Total number of new infections with HCV defined as anti-HCV positive per year	2*	1.4 per year	*PWID subpopulation (N=150) 138.9 person-years of follow-up
		Denominator: Total population minus number of people living with hepatitis C			

PROGRAM-RELATED SCIENTIFIC ACTIVITIES, EVENTS, AND MEETINGS

Scientific Activities

In August 2016, the Scientific Committee (SC) was established to provide a forum for transparency and coordination of the research activities conducted within Georgia's Hepatitis C Elimination Program. Co-chaired by NCDC and CDC representatives, the SC is comprised of the following members:

- MoLHSA
- NCDC
- U.S. CDC
- Infectious Diseases, AIDS, and Clinical Immunology Research Center
- Hepa clinic
- Neolab clinic
- Mrcheveli clinic

The SC convenes once every month to discuss the submitted proposed projects. Data analysis and Institutional Review Board (IRB) submission assistance are provided by U.S. CDC. By the end of October 2017, the SC reviewed 35 research proposals, of which 27 were approved. Research priorities for the HCV Elimination Program were initially focused on analyzing treatment data to assess the effectiveness of treatment regimens available in Georgia and the impact of HCV treatment on morbidity and mortality. More recently, the research focus has expanded to include epidemiologic and other areas of interest, such as evaluation of the limit of detection necessary for a point-of-care HCV test using treatment program data; evaluation of the Xpert HCV VL Assay in resource-limited settings using operators with minimal laboratory experience; and evaluation of the sensitivity, specificity, and quantitation of the Xpert® Fingerstick HCV VL assay for the detection of HCV in capillary and venous whole blood.

Program Events

April 21, 2015

With the signing of an historic Memorandum of Understanding (MoU) between the Government of Georgia and U.S. pharmaceutical company Gilead Sciences on April 21, 2015 and with the help of U.S CDC, efforts to eliminate hepatitis C in Georgia have begun.

Organized by MoLHSA and NCDC with the support of the Division of Viral Hepatitis (DVH) at U.S. CDC and the CDC South Caucasus Office, national HCV workshops are held annually during the spring (usually March or April) in Tbilisi and are attended by representatives of NCDC, CDC, MoLHSA, civil society organizations, clinicians, and international partners.

1st National HCV Workshop
March 12–14, 2014

In March 2014, the First National Workshop on Hepatitis C was organized by U.S. CDC, MoLHSA, NCDC IDACIRC, Bristol University, and Emory University, where the first concept of hepatitis C elimination in Georgia was developed and the feasibility of the program was discussed. The concept was endorsed by the Government of Georgia, and the intention of eliminating HCV infection in the country was declared. As a follow-up step, in April 2014 the concept was discussed at the WHO-supported Hepatitis Summit in Geneva; CDC later assisted in organizing a satellite meeting dedicated to HCV elimination in Georgia at the 49th annual EASL conference in London.

2nd National HCV Workshop, March 26–27, 2015

The objective of the 2015 workshop was to discuss the immediate measures needed to launch the HCV elimination program (referred to as "Phase I" of the elimination program). During the 2-day workshop, work groups discussed and finalized the different aspects of the Phase I program, such as drug logistics, information systems for program management, diagnostic and treatment procedures, and laboratory quality assurance. The workshop helped lay the foundation for the successful launch of the Georgian HCV Elimination Program.

World Hepatitis Day 2015, July 28, 2015

World Hepatitis Day (WHD) was commemorated with various HCV-related activities throughout Georgia. On the day proceeding WHD 2015, MoLHSA and NCDC announced a 2-week HCV screening campaign that would allow every citizen of Georgia to receive free HCV testing at NCDC or one of its conference was held at NCDC, where Minister of Health Davit Sergeenko, along with local and foreign partners, informed

Georgians about the initial phase of the HCV elimination program and provided them with key messages for HCV prevention, vaccination, screening, and treatment. WHD-related activities continued on July 29, when a 1-day workshop (organized by NCDC with support from WHO) was held to facilitate development of a long-term, 2016–2020 HCV elimination strategy. Members of the elimination strategy working group and other stakeholders attended the workshop (e.g., representatives from MoLHSA, NCDC, medical facilities providing services within elimination program, and non-governmental organizations).

First World Hepatitis Summit, September 2–4, 2015, Glasgow, Scotland

WHO, in partnership with the Scottish Government and the World Hepatitis Alliance (WHA), co-organized the first World Hepatitis Summit (WHS) in Glasgow, Scotland on September 2–4, 2015. This Summit brought together top global leaders, national policymakers, and public health experts to garner political and financial commitments required to tackle viral hepatitis epidemics. Dr. David Sergeenko, Minister of Labour, Health, and Social Affairs, represented Georgia as one of the first countries to embark on a national elimination program. The Minister shared the first steps taken by the Georgian government (e.g., development of a national action plan) to demonstrate the feasibility of viral hepatitis elimination, even for middle-income countries with limited health systems.

3rd National HCV Workshop, April 6–8, 2016

With support from CDC, WHO, pharmaceutical company Gilead Sciences Inc., and the Eurasian Harm Reduction Network, MoLHSA and NCDC conducted the 3rd National HCV Elimination Workshop on April 6–8, 2016 in Tbilisi. National and international experts discussed results of the national seroprevalence survey and progress made during the first phase of the elimination program, with particular emphasis on monitoring and evaluation indicators. Workshop participants expressed interest in using data obtained from the seroprevalence survey to refine

components of the elimination program. During the workshop, representatives from WHO headquarters and Georgia's country-based CDC office, along with NCDC's Director General, launched WHO's *Monitoring and Evaluation for Viral Hepatitis B and C: Recommended Indicators and Framework* to guide monitoring of the response both nationally and globally.

World Hepatitis Day, July 28, 2016

On WHD 2016, a press conference was held at NCDC where Davit Sergeenko (Minister of Labor, Health, and Social Affairs) and Amiran Gamkrelidze (Director of NCDC) provided up-to-date information on the progress of the elimination program. These public health leaders highlighted the importance of screening in achieving the elimination goal and encouraged the public to actively seek HCV testing. It was also announced that the government had purchased an additional 150,000 HCV tests that would be used by NCDC to continue providing free testing to all eligible persons wanting to know their HCV status. Dr. Gamkrelidze also presented and officially launched the Georgian version of *Sanford's Guide to Hepatitis Therapy*, which was prepared through a collaboration between Sanford Antimicrobial Therapy Inc. and NCDC. The Guide includes information on epidemiology, diagnosis, treatment, prevention, and other important aspects of viral hepatitis, including sections on HCV epidemiology in Georgia and Georgian HCV treatment protocols. For mobile devices operating on Android OS, the application can be downloaded from the web-page ka.sanfordguide.com or from the Amazon App Store. For iOS users, the web-page is available in a mobile-friendly format.

Technical Advisory Group Meetings

Technical Advisory Group Meeting, November 3-4, 2015

On November 3–4, 2015, MoLHSA, along with experts from the U.S. CDC's DVH, WHO, and other international partners, convened Georgia's first external Hepatitis Technical Advisory Group (TAG) meeting. A total of 11 experts in the field of viral hepatitis prevention and control served as TAG members. The 2-day meeting began with presentations from MoLHSA representatives and elimination strategy workgroup members. TAG members were provided with background information about the burden of viral hepatitis and

elimination program activities in Georgia. Topics covered included the burden of HCV in Georgia, existing care-delivery systems, screening efforts and linkage to care and treatment, models of HCV elimination, proposed 2020 elimination targets, surveillance, preventing transmission, and existing mechanisms for resource mobilization. Best practices from the WHO European Region were also shared.

Following these presentations, breakout groups comprised of TAG members and representatives from the Georgia HCV Elimination Strategy Work Group met to discuss aspects of the draft elimination plan in the context of proposed goals for HCV elimination in the country of Georgia. Taken together, the presentations and work-group discussions informed TAG recommendations.

At the meeting, TAG applauded the Georgian government for recognizing the nation's burden of HCV disease and committing to improve hepatitis C prevention, care, and treatment. TAG recognized the ambitious targets for HCV elimination outlined in the country's HCV Elimination Plan. Based on the presentations, breakout group discussions, and continued discussion with the larger group, TAG provided a set of recommendations to serve as guidance for finalizing the Georgia HCV Elimination Strategy for 2016–2020 (Appendix 2).

2nd Technical Advisory Group Meeting, October 24–25, 2016

Georgia's second external Hepatitis TAG meeting was convened on October 24–25, 2016. A total of nine experts in the field of viral hepatitis prevention and control served as TAG members. The 2-day meeting began with opening remarks from the Health Minister, followed by presentations from Georgia's MoLHSA and NCDC representatives, who provided TAG members with information about the progress of the HCV Elimination Program in Georgia since its launch in April 2015. The presentations covered proposed HCV elimination targets to be reached by 2020 and health economic models of HCV elimination. Also presented was a draft of the national HCV Elimination Plan to reach the 2020 goals, which included strategies to improve a) advocacy/education, b) access to HCV screening, care, and treatment, c) laboratory diagnostics, d) public health surveillance for HCV, and e) prevention of blood-borne HCV transmission. Following the presentations, a TAG member facilitated discussion on ways to improve the draft plan. Taken together, the presentations and discussions informed TAG recommendations, which were later finalized by the TAG chair and submitted to the MoLHSA for consideration in future activities.

Symposium on HCV Elimination Program for Georgia June 2016

On June 18, 2016, MoLHSA collaborated with the Liver institute and Foundation for Education and Research (LIFER) and Project ECHO (Extension for Community Healthcare Outcomes) to hold the National Guidance and Education Advisory Program symposium. Co-chaired by Drs. Nezam Afdhal and Stefan Zeuzem, the Symposium provided a platform for HCV Elimination Program stakeholders to present the progress of the program and discuss the opportunity for incorporating the improved HCV screening and diagnostic testing algorithm, along with new antiviral therapies, into clinical practice in Georgia. The symposium also demonstrated to participants how the Project ECHO model for expanding specialty-care knowledge to community clinicians can help improve treatment coverage among HCV patients in Georgia.

International Liver Congress Meetings

The International Liver Congress April 13–17, 2016, Barcelona, Spain

In 2016, the annual congress organized by EASL provided a forum for over 10,000 liver experts from around the world to meet and share best practices. Representatives from Georgia included MoLHSA and NCDC staff, along with clinicians from HCV provider sites. Georgia's HCV Elimination Program was a key topic presented at several sessions. During the EASL and World Hepatitis Alliance (WHA) joint session, NCDC General Director Dr. Amiran Gamkrelidze shared with the broad audience the progress of the program, results of the 2015 HCV seroprevalence study, and the HCV elimination strategic plan for 2020*.

* The International Liver Congress (ILC) 2016
https://www.youtube.com/watch?v=izIQrOK5f40&list=PLZaQd8Jp9ihy_VHMz7QzHT_2EytK-Vp7C

Major challenges and lessons learned from the initial phase of the HCV elimination program were discussed and were met with keen interest during a special side meeting dedicated to Georgia's HCV elimination initiative and organized by U.S. CDC. The meeting culminated in a signing of the historic 10-year MOU between the Government of Georgia and Gilead Science, Inc., ensuring the continued donation and availability of new DAA medicine through the HCV Elimination Program.

The International Liver Congress, April 19–23, 2017, Amsterdam, Netherlands

For the first time in the history of the International Liver Congress (ILC), in 2017 a special session of the Congress focused solely on Georgia's HCV Elimination Program. During the session, which was organized through joint efforts by EASL and U.S. CDC, international liver experts highly praised Georgian stakeholders for their commitment to the national HCV program and remarkable achievements while engaging in discussions about potential strategies for overcoming major challenges and future directions for the program.

Partnerships

Abbot Diagnostics

Becton Dickinson (BD)

Blood System Research Institute

CDC Foundation

U.S. CDC:

- Division of Viral Hepatitis (DVH)
- South Caucus Office (DGHP)
- Division of Healthcare Quality Promotion (DHQP)
- Division of Cancer Prevention & Control (DCPC)
- Division of Global HIV & TB (DGHT)
- Division of Health Informatics and Surveillance (DHIS)

Emory University

Extension for Community Healthcare Outcomes, University of New Mexico (ECHO)

FIND -Foundation for Innovative New Diagnostics

Georgian Harm Reduction Network

Georgia State University

Gilead Sciences

Government of Georgia (Ministry of Labour, Health, and Social Affairs, the National Center for Disease Control and Public Health)

Global Fund for AIDS, TB, and Malaria

HCV provider clinics

Johns Hopkins University

Liver institute and foundation for education and research (LIFER)

Médecins du Monde (MdM)

Open Society Foundation Georgia

Technical Advisory Group (TAG)

Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET)

University of Bristol

World Health Organization (WHO) headquarters and the WHO Regional Office for Europe (WHO/EUROPE)

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Appendix 1.

Strategies for the Elimination of HCV in Georgia*: Progress and Findings through December 31, 2016†

Strategy 1: Promote Advocacy, Awareness and Education, and Partnerships for HCV-Associated Resource Mobilization

- Two rounds of informational and educational social media campaigns led by the Health Promotion National Program were initiated during 2015–2016.
- Data were collected through a qualitative survey among the general population, from people registered in the HCV treatment program, and from a subgroup of persons who inject drugs.
    - 100% (N=34) of respondents were aware how people contract hepatitis C and how to prevent transmission.

Strategy 2. Prevent HCV Transmission

Persons Who Inject Drugs (PWID)

- A Bio-Behavioural Surveillance Survey (BBSS) was conducted in 2014 to obtain data regarding the approximately 50,000 PWID living in Georgia. HCV prevalence was high (66%) among PWID.

- HCV screening efforts were initiated at needle and syringe program (NSP) sites.
    - 23,969 PWID became aware of their HCV status in 2016 compared with 13,736 in 2014.
    - In 2016, 43.7% (10,469) of PWID tested positive for anti-HCV.
- A qualitative study was conducted by GHRN in 2016, identifying social stigma and financial barriers as major impediments to access to HCV care and treatment among PWID.

Blood Safety

- Data from the national seroprevalence survey identified receipt of blood products as a risk factor for HCV in Georgia. Given the importance of high-quality screening of donated blood in the reduction of transfusion-transmissible infections (TTI), including HCV, since 2011 blood banks involved in the State Safe Blood Program have been required to undergo routine external quality control testing, for which randomly selected aliquots from 5% of all donations are rechecked for TTI by NCDC's Richard Lugar Center for Public Health Research (Lugar Center). No external quality control

mechanisms are established for blood banks that do not participate in the State Program.

- Of 20 existing blood centers, 18 reported collecting a total of 86,608 blood units during 2016 through a national blood registry, of which 92.8% (80,370) donations were made at 12 blood banks enrolled in the National Safe Blood Program.
    - For 2016, a total of 26,379 (37.7%) blood units were collected from voluntary, unpaid blood donors compared with 43,560 (62.3%) from paid donors.
    - Among all blood donors, rates of HCV infection have continued to fall, from 3.9 % (336 of 8,625) in 2006 to 1.8% (912 of 51,731) in 2016.

Infection Control

- An update of national infection prevention and control (IPC) guidelines is underway and is expected to be finalized in 2017.
- A series of trainings in IPC have been conducted using an IPC curriculum accredited by Tbilisi State Medical University.
    - About 3,000 dentists (organized by the Georgian Stomatologists Association) and 50 employees of non-medical facilities (e.g., beauty salons and tattoo parlors) have participated in IPC training.
- An IPC assessment was conducted by Georgia's Ministry of Labour, Health, and Social Affairs (MoLHSA) in 10 major multi-profile hospitals and nine cardiologic clinics located in Tbilisi. According to preliminary findings,
    - 100% of surveyed facilities (N=19) had an appointed IPC focal point, but only 14 (74%) had active IPC committees;
    - 50% of facilities had an IPC training program in place; and
    - 40% of medical facilities met criteria for proper medical waste management.

Strategy 3: Identify Persons Infected with HCV

- Antibody testing was initiated in Georgia free-of-charge through several programs at different sites across the country. Most HCV screening was performed using a rapid test, with the exception of testing conducted through Georgia's Safe Blood Program, where most blood banks employ the enzyme-linked immunosorbent assay (ELISA).
    - As of September 2017, over 1,200,000 HCV screening tests were performed across the country; screening data on 712,534 unique individuals were incorporated into the national screening registry. Among registered persons, more than 8% (N=58,339) had positive anti-HCV results.

- Since November 2016, a total of 542 outpatient service providers received free tests from NCDC and performed 18,900 HCV screenings, for a 7.43% positivity rate.

- A governmental decree was issued on September 16, 2016 mandating all inpatient medical facilities to ensure provision and reporting of anti-HCV antibody testing for all eligible hospitalized patients.
    - As of December 31, 2016, a total of 2,330 (4.9%) of 48,025 hospitalized patients tested were anti-HCV positive; most (67%) were male.
- Data are lacking on the effectiveness of screening and linkage to care, and numbers of persons entering the treatment program decreased during the last 3 months of 2016.

Strategy 4. Improve HCV Laboratory Diagnostics

- In 2015, a standard World Health Organization (WHO)-adapted tool (Box 1) was used to assess capacity at four clinical laboratories (affiliated with four initial pilot sites for the HCV program in Tbilisi) and eight public health laboratories.
    - All laboratories met acceptable laboratory quality standards; however, laboratories scored 36%–100% in "total quality" due to lack of specific external quality control (EQC) programs for viral hepatitis testing.
    - All 4 assessed laboratories were performing molecular tests for quantitative HCV RNA (viral load) and HCV Genotyping.
- The MoLHSA Laboratory Working Group developed a regulatory document (decree #320 dated July 11, 2016) for licensing laboratory service providers, to be implemented January 1, 2017.
- With technical assistance from the U.S. CDC, the Lugar Center has established a National EQA program for HCV viral load and genotyping.
- Projects to assess the benefits and effectiveness of HCV core antigen and point-of-care RNA testing were conducted in 2016-2017.
- In June 2017, MoLHSA approved use of HCV core-antigen testing to confirm active HCV infection for hepatitis C elimination program purposes.

Strategy 5. Provide Comprehensive HCV Care and Treatment

- Prior to program launch, eight clinical sites and two prisons with experience providing interferon-based treatment were assessed and scored based on six domains (leadership/governance, quality of clinical care services, health information systems/management, human resource capacity, access to necessary lab tests, and drug procurement procedures). Critical gaps were identified and recommendations were

developed for staffing, comprehensive on-site HCV trainings, improving patient counseling, and other care- and treatment-related topics.

- The findings from a national HCV seroprevalence survey were used as a roadmap for enhancing geographical accessibility to treatment.
    - HCV treatment coverage increased: four treatment centers had received high scores upon assessment of capacity in April 2015, whereas 31 health facilities had received high scores by the end of October 2017.
    - Overall, 40,420 persons initiated treatment; 7,342 began sofosbuvir-based regimens and 33,078 began treatment with a combination of ledipasvir/sofosbuvir.
- Sustained viral response (SVR, a marker for virologic cure) for the patients treated with the sofosbuvir-based regimen (without ledipasvir) reached 81.9% (4,106 of 5,012 patients achieved SVR); the cure rate for those receiving sofosbuvir/ledipasvir combination regimens was 98.5% (19,928 of 20,227 achieved SVR). Project ECHO (Extension for Community Healthcare Outcomes) at the University of New Mexico Health Sciences Center (UNMNSC) and the Liver Institute for Education and Research (LIFER) provided training for capacity building and support for clinical case-management to physicians in Georgia. Georgia is now home to four ECHO hubs.

Strategy 6. Improve HCV Surveillance

- Data modeling was used to evaluate the impact of HCV Elimination Program interventions and assess the feasibility of achieving elimination goals by 2020. The Georgia HCV Elimination Program has accomplished an impressive scale-up of treatment, which has already had an impact on prevalence and incidence and has averted HCV-associated deaths. However, treatment initiation has fallen short of the target, and extensive scale-up will be needed to achieve a 90% reduction by 2020.
- Three rounds of hepatitis C training courses were conducted for 109 primary health-care staff on topics such as epidemiology, transmission routes, diagnostic methods, treatment availability, and elimination-program overview.
- Two sentinel medical facilities (Neolab [Tbilisi] and Imereti Development Center [Kutaisi]) were initially selected to collect HCV-related risk-factor data. Since June 2016, all HCV care-provider sites have been routinely collecting and reporting these epidemiologic data through the newly developed “Elimination C” database. Preliminary analysis of data from one of the sentinel sites (Neolab Clinic) showed that
    - 87.5% patients enrolled in HCV treatment reported alcohol use. Among these, 31.7% reported heavy use, placing them at increased risk for liver disease; 38.3% reported moderate use (https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking).

[*] HCV Elimination Strategies, along with more specific activities towards achieving elimination goals, are published in the English language version of the Elimination Plan (http://moh.gov.ge/uploads/files/2017/akordeoni/failebi/Georgia_HCV_Elimination_Strategy_2016-2020.pdf).

[†] Some strategic directions include data for 2017.

Appendix 2.

Treatment Component (Module) of the Hepatitis C Elimination Program in Georgia

Treatment of Patients Infected with HCV Genotype 1

Interferon-based regimen

Treatment duration: 12 weeks (Recommendation A1)

- Patients infected with HCV genotype 1 can be treated with a combination of weekly peginterferon alfa-2a 180 mcg. or peg-interferon alfa-2b 1.5 mcg/kg, daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively).

Interferon-free regimen

Treatment duration – 24 weeks (Recommendation B1)

- Patients infected with HCV genotype 1 who are interferon-intolerant or IFN-ineligible can be treated with daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively). This combination is used only in those cases when other interferon-free regimens are not available.

NOTE: Both above-mentioned treatment regimens for HCV genotype 1 patients have been excluded from the most recent AASLD guideline. However, because Ledipasvir/Sofosbuvir and other direct acting antiviral drugs (e.g., Simeprevir and Viekira Pak) are not available in Georgia yet, these regimens will continue to be used based on recommendations from a previous EASL guideline.

Treatment of Patients Infected with HCV Genotype 2

Interferon-based regimen

Treatment duration – 12 weeks (Recommendation B1)

- Cirrhotic and/or treatment-experienced patients can be treated with weekly peginterferon alfa-2a 180 mcg. or peg-interferon alfa-2b 1.5 mcg/kg, daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively).

NOTE: About 70% of HCV genotype 2 patients in Georgia are infected with the recombinant form (RF 2k/1b) of the virus. There is no optimal treatment regimen for these patients defined in guidelines, because large-scale clinical trials have not yet been performed. However studies* have demonstrated that patients with 2k/1b recombinant virus treated with treatment regimens recommended for patients with genotype 1 have had similar response.

*Hedskog C, Doehle B, Chodavarapu K, et al. Characterization of Hepatitis C Virus Inter-Genotypic Recombinant Strains and Associated Virologic Response to Sofosbuvir/Ribavirin. Hepatology. doi: 10.1002/hep.27361

Interferon-free regimen

Treatment duration – 12 weeks (Recommendation A1)

- Patients infected with HCV genotype 2 must be treated with daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively).

NOTE: Therapy should be prolonged to 16 or 20 weeks in patients with cirrhosis, especially if they are treatment experienced (Recommendation B1).

Treatment of Patients Infected with HCV Genotype 3

Interferon-based regimen

Treatment duration – 12 weeks (Recommendation A2)

- Patients infected with HCV genotype 3 can be treated with a combination of weekly peginterferon alfa-2a 180 mcg or peg-interferon alfa-2b 1.5 mcg/kg, daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively).

NOTE: This combination is also recommended for treatment-experienced patients.

Interferon-free regimen

Treatment duration – 24 weeks (Recommendation B1)

- Patients infected with HCV genotype 3 who are interferon-intolerant or IFN-ineligible can be treated with daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively). This combination is used only in those cases when other interferon-free regimens are not available.

Treatment of Patients Infected with HCV Genotype 4

Interferon-based regimen

Treatment duration – 12 weeks (Recommendation A2)

- Patients infected with HCV genotype 4 can be treated with a combination of weekly peginterferon alfa-2a 180 mcg or peg-interferon alfa-2b 1.5 mcg/kg, daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively).

NOTE: This therapy is suboptimal in treatment-experienced cirrhotic patients.

Interferon-free regimens

Treatment duration – 24 weeks (Recommendation C2)

- Patients infected with HCV genotype 4 who are IFN-intolerant or IFN-ineligible can be treated with daily sofosbuvir (400 mg) and daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively)

Treatment of Patients with Decompensated Liver Cirrhosis

Interferon-free regimens

Treatment duration – 48 weeks (Recommendation B2)

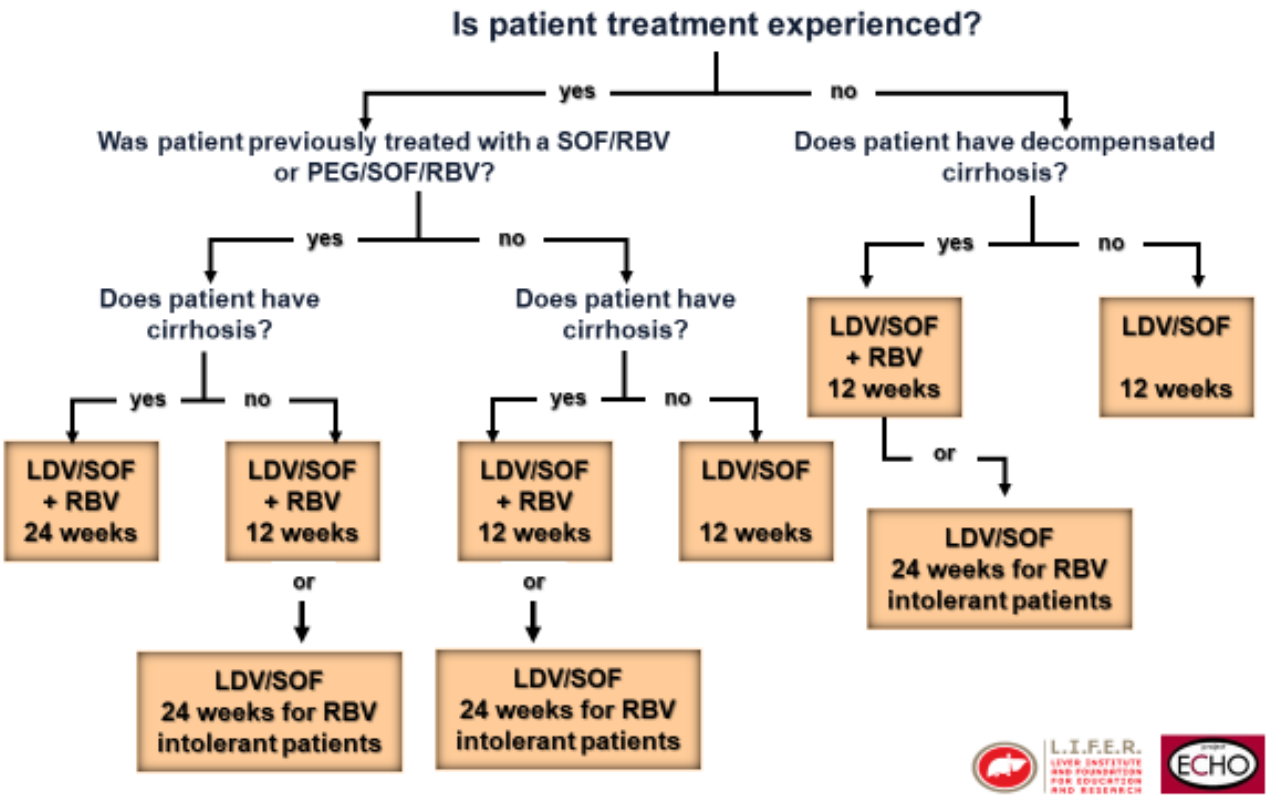
- Daily sofosbuvir (400 mg) and weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively).

NOTE: This regimen is recommended for HCV patients regardless of genotype, who have decompensated cirrhosis (moderate or severe hepatic impairment; Child-Pugh class B or C) who may or may not be candidates for liver transplantation, and for cirrhotic patients (Child-Pugh class A) with hepatocellular carcinoma requiring liver transplantation. This regimen should be used only by highly experienced HCV practitioners at specialized clinics, with consideration of the patient's creatinine clearance rate and hemoglobin level.

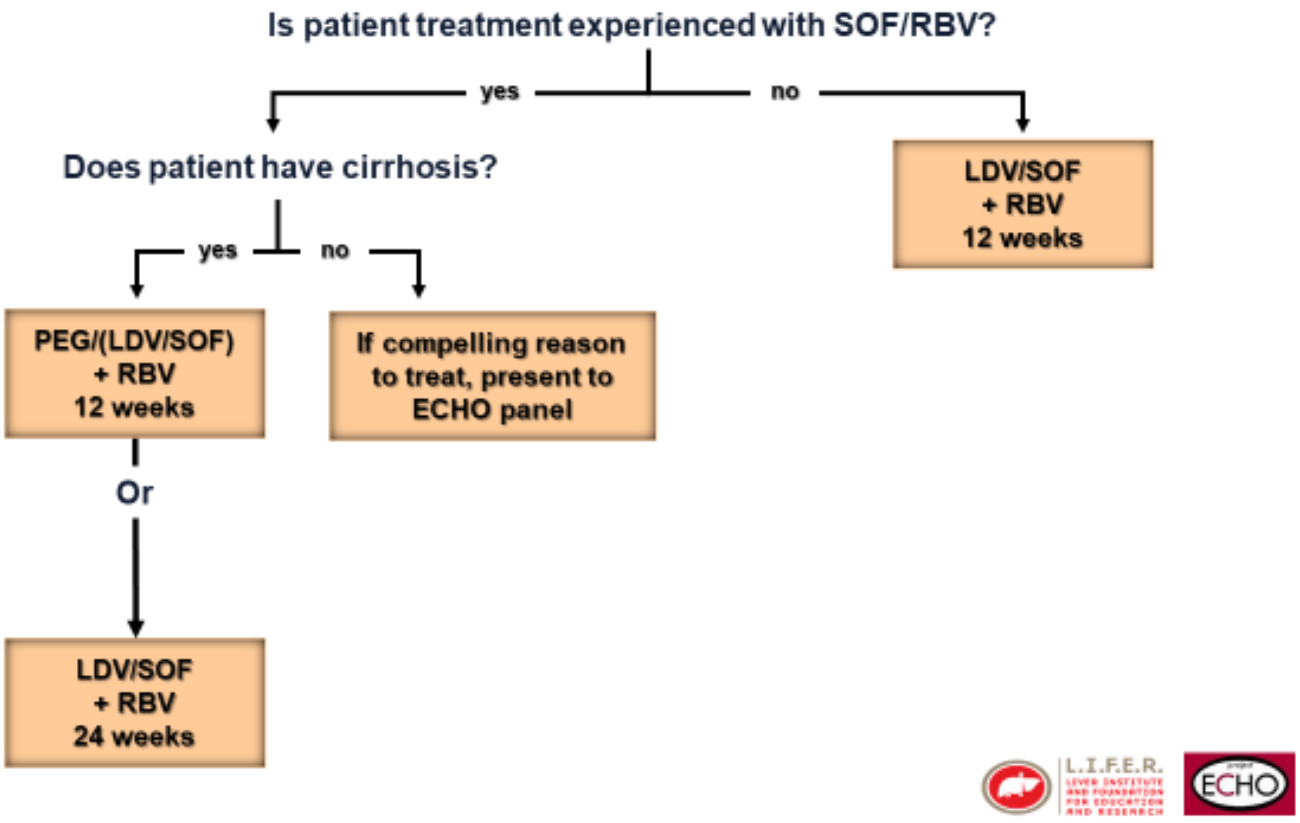
Appendix 3.

HCV Treatment Decision Trees

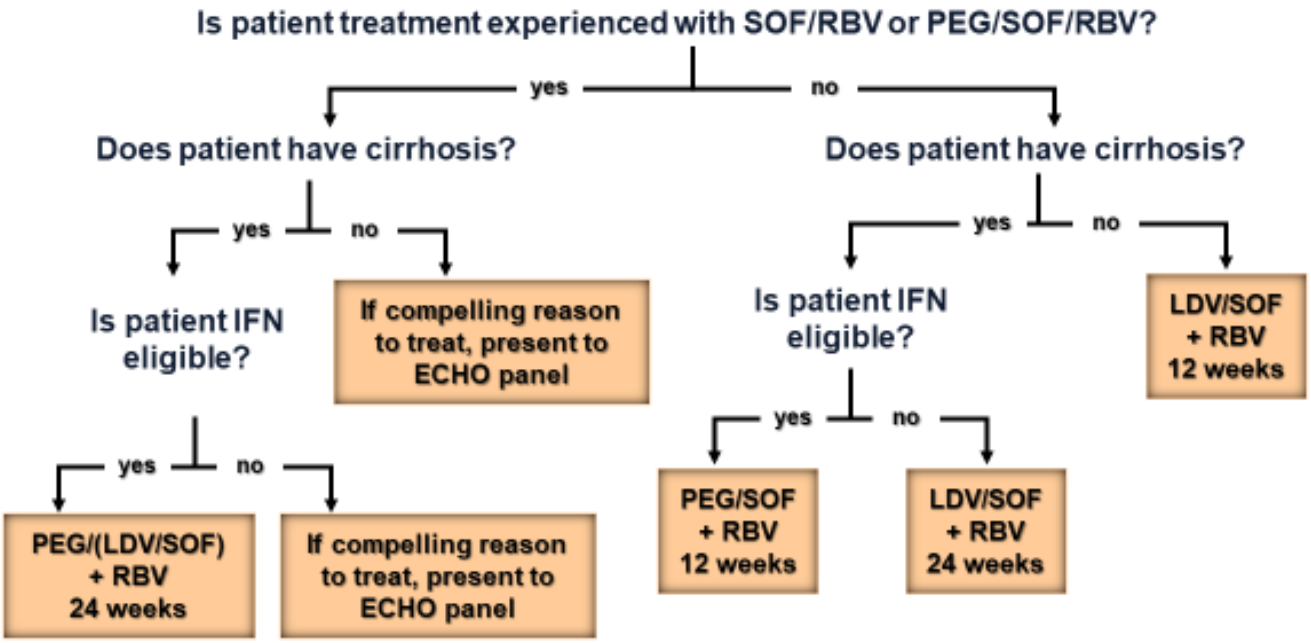
Decision Tree for Patients Infected with HCV Genotype 1



Decision Tree for Patients Infected with HCV Genotype 2



Decision Tree for Patients Infected with HCV Genotype 3



Appendix 4

Scientific Meeting Presentations of the HCV Elimination Program

Abstracts

1. **Prevalence and risk factors for hepatitis B infection in the adult population of Georgia: a nationwide survey**

Abstract Presented at EASL, 2017; Amsterdam, Netherlands.

Authors:
Ana Kasradze*[1], Giorgi Kuchukhidze[1], Davit Baliashvili[1], Stephanie Salyer[2], Amiran Gamkrelidze[1], Maia Tsereteli[1], Nazibrola Chitadze[1], Maia Alkhazashvili[1], Khatuna Zakhashvili[1], Jan Drobeniuc[3], Curtis Blanton[2], Stephen Russell[2], Paata Imnadze[1], Juliette Morgan[4], Francisco Averhoff[3], Liesl Hagan[3]
1 National Center for Disease Control and Public Health, Tbilisi, Georgia; 2 Division of Global Health Protection; 3 Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, United States; 4 Global Disease Detection – South Caucasus Regional Center, Centers for Disease Control and Prevention, Tbilisi, Georgia

Background and Aims:
This abstract presents the prevalence and risk factors of hepatitis B virus (HBV) infection based on a nationally representative survey of hepatitis B and C, conducted in 2015.

Methods:
A cross-sectional, nationwide survey among general population aged ≥18 years (n = 7,000) was conducted using a stratified, multi-stage cluster design with random sampling. Trained data collection teams collected demographic data, medical and behavioral history, risk factors and knowledge about HBV and obtained a blood samples, which were tested for anti-HBc antibodies, and anti-HBc+ samples were screened on HBsAg. Both tests were performed by ELISA. Prevalence of anti-HBc and HBsAg, and bivariate associations between anti-HBc and potential exposures were calculated.

Results:
Prevalence of hepatitis B surface antigen (HBsAg) was 2.9%: 3.4% (95% CI = 2.48-4.34) in males and 2.5% (95% CI = 1.92-3.15) in females. There was no statistically significant difference between urban vs. rural residence (3.1% vs. 2.8%). HBsAg prevalence in Tbilisi (capital) was lower (2.3%) compared to three other major cities (5.1% in Batumi, 5.3% in Kutaisi, 5.2% in Rustavi). Prevalence of anti-HBc was 25.5% nationally. Bivariate analyses revealed significant associations between anti-HBc+ status and history of blood transfusion (OR = 1.9, 95% CI = 1.48-2.37), dialysis (OR = 4.0, 95% CI = 1.08-14.53), injection drug use (IDU) (OR = 2.8, 95% CI = 1.91-4.09), at least one invasive medical procedure (OR = 1.2, 95% CI = 1.05-1.47) and incarceration (OR = 1.9, 95% CI = 1.32-2.86).

Conclusions:
Prevalence of chronic hepatitis B is almost similar to the prevalence in Middle East and the Indian subcontinent (2-5%). The high prevalence of anti-HBc among persons with a history of blood transfusion, dialysis, IDU, invasive medical procedures, and incarceration could indicate that transmission occurs through these exposures, and provides guidance for groups where further efforts to improve education, prevention, and safe injection and blood programs could be concentrated. High prevalence in other major cities compared to the capital indicates the need to strengthen regulations and infection control in these areas. Hepatitis B vaccine has been included in the national immunization schedule since 2002, and coverage among children reached 93.7%. High anti-HBc prevalence among

adults indicates that vaccination should be expanded to adults as part of Georgia's HBV prevention efforts.

2. **Effectiveness of DAA-based treatment of HCV in active people who inject drugs living in middle income countries (MIC): the results of a prospective cohort study in Tbilisi, Georgia**

Abstract Presented at EASL, 2017; Amsterdam, Netherlands.

Authors:
Julie Bouscaillou[* 1], Tamar Kikvidze[2], Maïa Butsashvili[3], Konstantine Labartkava[4], Ina Inaridze[2], Aurélie Etienne[1], George Kamkamidze[3], Ani Gamezardashvili[3], Elisabeth Avril[5], Niklas Luhmann[1]
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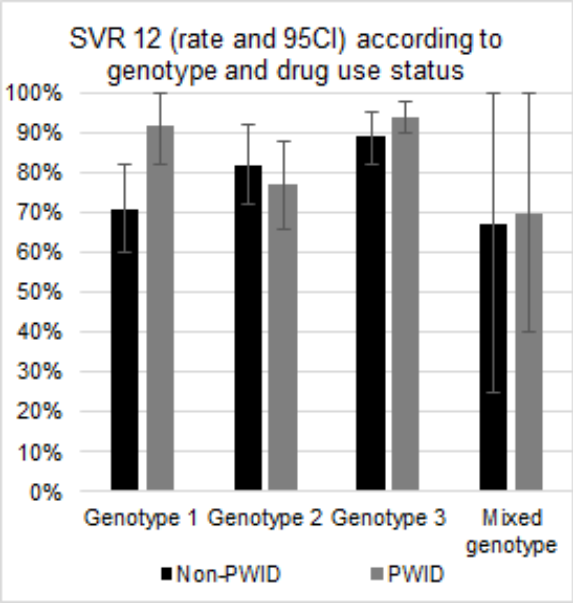
Background and Aims:
Although they carry a high HCV burden globally, active people who inject drugs (PWID) are often excluded from national policies due to concerns about their ability to adhere to care, especially in MIC. Georgia faces high HCV rates (7.1% of antibodies in general population) with 25.6% of the cases being among PWID. An ambitious National HCV elimination Plan was launched in 2015, with initially 7000 treatments dedicated to patients with advanced liver fibrosis (≥F3). We assessed the treatment outcomes in PWID treated in the framework of the National Plan.

Methods:
We followed a prospective cohort of PWID clients of a needle and syringe exchange program and supported by peer workers during treatment. PWID were treated with sofosbuvir and ribavirin +/- pegInterferon according to the genotype, treatment experience and level of fibrosis. We collected data concerning bio-medical parameters, adherence to care, demographics, and behaviors before and during treatment. After a descriptive analysis, we studied the factors associated with adherence to care and sustained virologic response at 12 weeks post-treatment (SVR12) using adjusted logistic regressions. We additionally compared the SVR12 rate to those of patients not reporting any history of injecting drug use (non-PWID), treated at the same clinic, during the same period - adjusting for age, sex, genotype, level of fibrosis, and treatment regimen.

Results:
We included 244 PWID in the 2nd semester of 2015. Mean age was 46.3 years, 0.8% were women, 54.5% had cirrhosis (liver stiffness ≥14 kPa or Fib 4>3.25). Genotypes were distributed as follows: 18.9%, 25.4%, 51.6%, and 4.1% for genotype 1, 2, 3 and mixed genotypes, respectively. 2% (n = 5) had to prematurely stop the treatment, due to serious adverse events. Amongst the others, 88.7% never missed any of the bimonthly medical appointments, 79.1% never missed a dose of medication, and 88.2% reached SVR12. Only cirrhosis (adjusted odd ratio (aOR) 0.28; 95% confidence interval (95CI) 0.10-0.83) was significantly associated with SVR12. Ongoing drug use during treatment was associated with delaying medical appointments, but not with observance nor SVR12. SVR12 rate (80.7%) was not significantly different in the 223 non-PWID (aOR 0.94; 95CI 0.50-1.75 compared to PWID) treated at the same time.

Conclusions:
In this real life experience, PWID were adherent to care and had SVR12 rates similar to those observed in non-PWID. Concerns about PWID ability to engage in care should not be a reason of exclusion from HCV treatment in Georgia.

Figure:



3. High sustained viral response among hepatitis C virus genotype 3 patients with advanced liver fibrosis - real-world data of HCV elimination program in Georgia

Abstract Presented at EASL, 2017; Amsterdam, Netherlands.

Authors:
Maia Butsashvili[*1], Lia Gvinjilia[2], George Kamkamidze[1], David Metreveli[3], Shorena Dvali[4], Tamar Rukhadze[5], Amiran Gamkrelidze[6], Muazzam Nasrullah[7], Juliette Morgan[8], Francisco Averhoff[7]
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Background and Aims:
Georgia has a high burden of hepatitis C virus (HCV) infection with an estimated 5.4% of adults currently infected. On April 28, 2015, in collaboration with CDC and other partners, Georgia launched a comprehensive, national HCV elimination program that included free of charge treatment for all HCV infected persons; in the first phase of the program, patients with moderate and sever liver disease were prioritized to receive treatment. HCV infected patients with genotype 3 are considered difficult to treat with direct acting antivirals (DAAs) compared to genotypes 1 and 2. We aimed to study the real world data of treatment outcome among HCV-infected patients with genotype 3 with advanced liver fibrosis stage.

Methods:
Data from April 28, 2015 through September 30, 2016 from Georgia's national electronic treatment database, developed for the HCV elimination program, were analyzed. Briefly, participating clinics and treatment sites collect and enter sociodemographic, clinical, elastography, and laboratory data, treatment regimens, and outcomes of treatment into the national database. Characteristics and

outcomes of patients with genotype 3 were analyzed. Treatment outcomes were analyzed by degree of liver fibrosis with patients defined as having advanced liver fibrosis (>=F3 by liver elastography or >3.25 by FIB4 score) and treatment regimen, comparing patients receiving sofosbuvir/ribavirin (SOF/RBV) with and without pegylated interferon (INF), depending on interferon eligibility.

Results:

During the study period, 6648 patients with genotype 3 were enrolled in elimination program (34% of all genotypes). The majority, 93.3% were male, and > 52.47% aged 45-60 years. Sustained Virologic Response (SVR) data for patients with advanced liver fibrosis was available among 1536 individuals who completed treatment. The SVR rate among those treated with SOF/RBV/INF for 12 weeks was higher (928/963; 96.4%) that among those treated with SOF/RBV (426/528; 80.7%) for 24 weeks ($p<0.0001$). Fewer patients with cirrhosis (F4) (763/890; 85.7%) achieved SVR compared to those without cirrhosis (defined as F3 or F3/F4) (615/639; 96.2%) ($p<0.0001$)

Conclusions:

The real world data of HCV treatment with SOF/RBV and SOF/RBV/INF from Georgia demonstrated high SVR rates achieved among genotype 3 patients with advanced liver fibrosis.

4. Treatment outcomes of patients with chronic hepatitis C receiving sofosbuvir-based combination therapy within national hepatitis C elimination program in the country of Georgia

Abstract Presented at EASL, 2017; Amsterdam, Netherlands.

Authors:

Tengiz Tsertsvadze[* 1, 2], Amiran Gamkrelidze[3], Muazzam Nasrullah[4], Lali Sharvadze[2, 5], JulietteMorgan[6], Lia Gvinjilia[7], George Kamkamidze[8], David Metreveli[9], Vakhtang Kerashvili[1], MaiaButsashvili[8], Jaba Zarkua[9], Nikoloz Chkhartishvili[1], Akaki Abutidze[1], David Baliashvili[3], Valeri Kvaratskhelia[10], Francisco Averhoff[4]

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Background and Aims:

Georgia has one of the highest HCV prevalence rates in the world. In partnership with the US CDC, and commitment from Gilead Sciences to donate direct acting antivirals (DAAs) , initially sofosbuvir (SOF), the country embarked on the world's first hepatitis C elimination program in April, 2015. A key strategy of this program is to eliminate HCV in the country through identifying and treating all HCV infected persons. We report on the results of the first 18 months of the program.

Methods:

A national treatment database was established, which collected data for each patient enrolled in the program. Treatment-naive and experienced patients with cirrhosis and advanced liver fibrosis were prioritized for enrollment in the treatment program beginning 28 April 2015. Initial treatment consisted of SOF plus ribavirin (RBV) with or without pegylated interferon (INF). Sustained virologic response (SVR) was defined as undetectable HCV RNA at least 12 weeks after the end of treatment. Results for patients who completed treatment and tested for SVR through 30 September 2016 were analyzed.

Results:

Of the 7072 patients who initiated treatment with SOF-based regimens during the study period, 3966 (56%) patients were tested for SVR. HCV RNA was undetectable in 3147 (79%) cases. The lowest response rate was observed among genotype 1 patients (1070/1566; 68%), intermediate response rate was achieved in genotype 2 patients (695/865; 80%), while the highest response rate was among genotype 3 patients (1379/1531; 90%). There were only 4 patients with genotype 4 of which 3 were cured. Among cirrhotic patients, 75% (2154/2857) achieved SVR vs. 90% (993/1109) of patients without cirrhosis. Overall, SOF/RBV regimens achieved lower response rates (68%) than SOF/RBV/INF regimens (90%). Among patients who began treatment, 5% (364/7072) did not complete the treatment course; death (241/364; 66%) was the most common cause for not completing therapy, and most patients who died, 228/241 (95%) had cirrhosis.

Conclusions:

The program achieved high overall response rates although most patients had cirrhosis/advanced liver disease. Lower efficacy of treatment in genotype 2 patients may have been associated with a reported high prevalence of HCV recombinant form 2k/1b, which requires additional treatment regimens to achieve higher cure rate in these patients. With the introduction of additional DAAs, improved response rates are expected, paving the way for Georgia to achieve the goal of HCV elimination.

5. **Projected impact and pathways to success of the hepatitis C virus elimination program in Georgia, 2015-2020**

Abstract Presented at EASL, 2017; Amsterdam, Netherlands.

Authors:

Josephine G. Walker* [1], Liesl Hagan[2], Hannah Fraser[1], Natasha K. Martin[1, 3], Juliette Morgan[4], Muazzam Nasrullah[2], Francisco Averhoff[2], David Otiashvili[5], Ivdity Chikovani[6], Malvina Aladashvili[7], Mark H. Kuniholm[8], Irma Kirtadze[5], Lia Gvinjilia[9], Alexander Asatiani[10], Davit Baliashvili[10], Irma Khonelidze[10], Ketevan Stvilia[10], Maia Butsashvili[11], Tengiz Tsertsvadze[7], Amiran Gamkrelidze[10], Valeri Kvaratskhelia[12], Peter Vickerman[1]

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Background and Aims:

Georgia has one of the highest hepatitis C virus (HCV) prevalences in the world, with 5% of the population ~150,000 people) chronically infected. In April 2015 Georgia and partners launched a national program to eliminate HCV (defined as 90% reduction in HCV chronic prevalence by 2020 compared to 2015 levels) through prevention, diagnostics and curative treatment. As of September 2016, 19,338 patients had initiated and 9,688 had completed treatment, with 80% cured (sustained virologic response). We project the impact of the program in terms of infections and HCV-related deaths averted and assess the feasibility of achieving the elimination goal.

Methods:

We developed a model of HCV transmission incorporating changing demographics of people who inject drugs (PWID) and the general population in Georgia. The model was calibrated to HCV prevalence by age, gender and PWID status with data from a 2015 national serosurvey and PWID surveys from 1997-2015. We estimated infections and deaths averted by 2030 due to the 19,338 initiated treatments (98%

of the first ~9000 treatments were to patients with METAVIR scores of F3-F4). We projected whether the elimination goal will be reached if treatment continues at the current rate of 2100/month or 80% of prevalent infections annually when prevalence is low, including scenarios combining treatment with increased coverage of harm-reduction measures for PWID (opiate substitution therapy (OST) and needle and syringe programs (NSP)) or prioritizing treatments for PWID.

Results:

Without HCV treatment, HCV-related mortality is projected to increase from 534 to 750 deaths/year for 2015-30 while HCV incidence decreases from 6320 to 5548 infections/year for 2015-30 due to changes in injecting drug use patterns since the 1990s. The initiated treatments will avert approximately 2500 HCV-related deaths and 5200 new infections by 2030. We project the elimination goal will be achieved with a 90% reduction in prevalence and 84%reduct ion in incidence by 2020, with increased impact (91-93% reduction in prevalence and 90-94% reduction in incidence) if OST and NSP are scaled up to 75% coverage, treatment is prioritised to PWID at twice the rate of non-PWID, or both.

Conclusions:

Georgia is on the path to achieving the HCV elimination target by 2020 if current rates of HCV treatment continue, especially if treatments for PWID and harm-reduction measures are prioritized. However, to maintain the necessary treatment rate, current rates of case-finding need to be scaled up.

6. Pathways to success for the hepatitis C virus elimination program in Georgia, 2015-2020

Abstract Presented at World Hepatitis Summit, 2017; Sao Paulo, Brazil.

Authors:

Josephine Walker[1], Lia Gvinjilia[2], Muazzam Nasrullah[3], Amiran Gamkrelidze[4], Juliette Morgan[5]
Peter Vickerman[1]

Affiliations: 1 School of Social and Community Medicine, University of Bristol; 2 CDC Foundation, Tbilisi, Georgia; 3 Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention, CDC; 4 National Center for Disease Control and Public Health of Georgia, Tbilisi, Georgia; 5 Global Disease Detection, Division of Global Health Protection, South Caucasus CDC Office, Tbilisi, Georgia

Background:

Georgia has one of the highest hepatitis C virus (HCV) prevalence rates in the world, with >5% of the adult population (~150,000 people) chronically infected. In April 2015, the Georgian government and international partners launched a national program to eliminate HCV through scaling up HCV prevention and treatment interventions, with the aim of achieving a 90% reduction in prevalence by 2020. We project the impact of the HCV treatment program and assess the feasibility of achieving the elimination goal by 2020 under different treatment scenarios.

Methods:

We developed a model of HCV transmission incorporating the changing demographics of people who inject drugs (PWID) and general population in Georgia. Using the 2015 national sero-survey and PWID surveys from 1997-2015, the model was calibrated to data on HCV prevalence by age, gender and PWID status, and the age distribution of PWID. We included data from the treatment program registry in our analysis. We projected whether the elimination goals will be reached if treatment initiations continue at the current rate of 2100/month (25,200 per year).

Results:

Without the national program, the model projects the incidence and prevalence of HCV are already decreasing in Georgia, due to a decrease in injecting drug use and injecting risks since the 1990s, while HCV-related mortality is increasing (Figure 1). From 2015-2030, HCV related mortality will increase from

668 (95% credibility interval 319-1185) to 764 (387-1288) deaths/year, while incident infections will decrease from 5467 (2701-11960) to 3898 (1667-9958) per year, or a 12% (3-19%) reduction in each model run, and prevalence will decrease by 12% (4-18%). With the program, from April 2015 to end of 2016, 27,595 patients had initiated and 19,778 had completed treatment, with 84% cured (sustained virologic response). If treatment continues at its current rate (2100/month) then chronic HCV prevalence will decrease by 87% (73 - 93%) by the end of 2020 and incidence will decrease by the same amount. In contrast, HCV-related mortality is unlikely to reach the WHO elimination goal by 2020, with a 34% (18-48%) reduction being achieved with current treatment rates, increasing to 45% (31-54%) if patients with cirrhosis are preferentially targeted at 80% per year. At current treatment rates, the mortality target will be reached by 2025.

Conclusions:
With current treatment rates, Georgia is on the path to achieving the HCV elimination target for prevalence and incidence shortly after 2020, and the mortality target by 2025.

7. **Real-world effectiveness of sofosbuvir and ledipasvir/sofosbuvir based regimens in hepatitis C virus genotype 3 infection within national hepatitis C elimination program in the country of Georgia**

Abstract Presented at AASLD, 2017; Washington, DC, USA.

Authors:
Tengiz Tsertsvadze[1,2]; Nikoloz Chkhartishvili[1]; Akaki Abutidze[1]; Lali Sharvadze[2,3]; Vakhtang Kerashvili[1]; George Kamkamidze[4]; Mamuka Zakalashvili[5]; Lia Gvinjilia[6]; Muazzam Nasrullah[7]; Amiran Gamkrelidze[8]; Valeri Kvaratskhelia[9]; Stefan Zeuzem[10]; Sanjeev Arora[11]; Karla Thornton[11]; Nezam Afdhal[12]; Francisco Averhoff[7].
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University of New Mexico, Albuquerque, NM, USA; 12 Harvard Medical School, Boston, MA, USA.

Background:
The country of Georgia has a high prevalence of HCV with an estimated 5.4% of adult population living with chronic HCV infection. In partnership with U.S. CDC and commitment from Gilead Sciences to donate direct acting antivirals (DAAs), the country embarked on the world's first hepatitis C elimination program. Genotype 3, which is considered as the most difficult to treat, accounts for 34% of all HCV infections in Georgia. We evaluated the real-world effectiveness of sofosbuvir (SOF) and ledipasvir/sofosbuvir (LDV/SOF) plus ribavirin (RBV) in HCV genotype 3 patients treated within the Georgian elimination program.

Methods:
Data were obtained from the Georgia's hepatitis C elimination program treatment database. The database is secure web-based information system, which collects case-based information on each person enrolled in the program. From April 2015 to March 2016 SOF was the only DAA available and it was prescribed either in combination with pegylated interferon (IFN) and ribavirin (RBV), or only with

RBV. Since March 2016 LDV/SOF plus weight based ribavirin (RBV) became the recommended regimen for HCV Genotype 3 in Georgia. Analysis included 2,200 HCV genotype 3 patients who completed treatment and were assessed for sustained virologic response (SVR) by December 3, 2016.

Results:

Of 2,200 patients included, 1,191 (54.1%) had cirrhosis, 1,143 (52.0%) received IFN/SOF/RBV for 12 weeks, 807 (36.7%) received SOF/RBV for 24 weeks and 250 (11.4%) received LDV/SOF/RBV for either 12 or 24 weeks. The IFN/SOF/RBV arm had an overall SVR rate of 96.1% (1,099/1,143) and this regimen was more effective in non-cirrhotic patients versus cirrhotic (97.4% vs. 95.0%, p=0.04). SOF/RBV achieved SVR in 80.3% (648/807) of patients, with higher rates again observed in patients without cirrhosis (88.5% vs. 77.0%, p<0.0001). Among patients on LDV/SOF/RBV, 97.6% (244/250) achieved SVR with no difference between patients with and without cirrhosis. IFN and LDV/SOF based regimens were more effective than SOF/RBV in both cirrhotic and non-cirrhotic patients (p<0.001 in all comparisons).

Conclusions:

Overall SVR in HCV genotype 3 patients was > 95% in IFN based regimens and superior to longer duration SOF/RBV (80% SVR) regimens. However, the addition of LDV to SOF/RBV resulted in excellent 97.6% SVR rates. Therefore LDV/SOF and RBV can be considered as effective treatment option for genotype 3 infection even in difficult to treat patients with compensated cirrhosis.

8. **Predictive factors of treatment outcome among patients included in hepatitis C elimination program in Georgia**

Abstract Presented at AASLD, 2017; Washington, DC, USA.

Authors:

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Background:

In April 2015, in collaboration with CDC and other partners, Georgia launched a comprehensive, national HCV elimination program that included free of charge treatment for all HCV infected persons. The purpose of this study was to evaluate predictive factors for sustained viral response (SVR) among patients treated with direct acting antivirals (DAA) within HCV elimination program in Georgia.

Methods:

Data were extracted from the HCV treatment program database of clinic Neolab, one of the major clinical sites providing HCV care and treatment as part of the HCV elimination program. For all patients included in the program, pretreatment sociodemographic and clinical data, treatment regimen, adherence and monitoring data are collected. Treatment is provided by sofosbuvir/ribavirin (SOF/RBV) with or without interferon (IFN) and sofosbuvir/ledipasvir (LDV) with or without RBV. Treatment outcomes were analyzed by demographic and clinical data, including the degree of liver fibrosis with patients defined as having advanced liver fibrosis (>=F3 by liver elastography or >3.25 by FIB4 score) and treatment regimen. Multivariate analysis using logistic regression was conducted.

Results:

During April 28, 2015–April 30, 2016, a total of 3372 individuals with positive HCV RNA test were included in the treatment program. SVR result was available for 1629 patients by the time of data analysis. Overall, SVR was obtained among 93.2% of patients. By bivariate analysis, variables significantly associated with SVR were treatment regimen (92% cure rate for SOF/RBV/IFN, 77.1% - for SOF/RBV 24-week and 99.4% for SOF/LDV or SOF/LDV/ RBV regimen), genotype (with genotype 3 having highest cure

rate of 95.4% compared to 91.8% and 91.7% for genotype 1 and 2, respectively), liver fibrosis stage (99.9% SVR among patients with low fibrosis level compared to 87.8% among patients with advanced fibrosis), age (99.2% for age=100000 and 21.2% for <100000), ALT, AST and weight. After adjustment, significant association of SVR was observed with genotype, fibrosis stage (aOR=7.12, 95% CI:2.14-17.26), treatment regimen (aOR=1.08, 95% CI: 1.04-1.13) and platelet count (aOR=1.007, 95% CI: 1.003-1.012).

Conclusion:

The presented study showed that by multivariate analysis age, gender, weight and liver enzymes were not associated with SVR, while genotype, fibrosis stage, treatment regimen and platelet count were independent predictors of treatment outcome.

Posters

EMERGENCE OF HEPATITIS C VIRUS GENOTYPE RECOMBINANT FORMS 2k/1b IN GEORGIA

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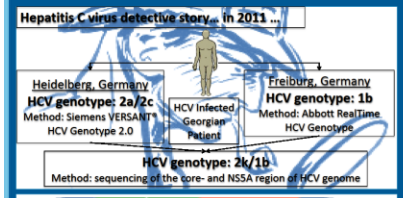
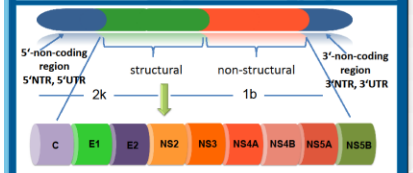
BACKGROUND





The HCV strain belongs to two different genotypes: 5' UTR to within the NS2 region 2k and downstream NS2 type 1b.

Hepatitis C virus (HCV) today is classified into 11 genotypes and many closely related subtypes.
In the early 1990s, Kalinina et al. identified HCV strains with genetic divergence, which was not due to mutations but to fusions of parts of different HCV genomes. The authors suggested the extension of the current classification with the term "recombinant form" (RF).
In 2001, 2k/1b HCV RF was found in St. Petersburg, Russia. Few cases have been identified worldwide. Patients were mainly from Eastern Europe.

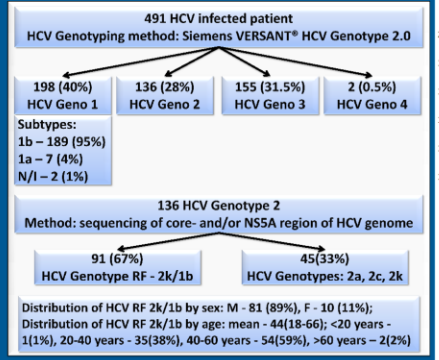
OBJECTIVES

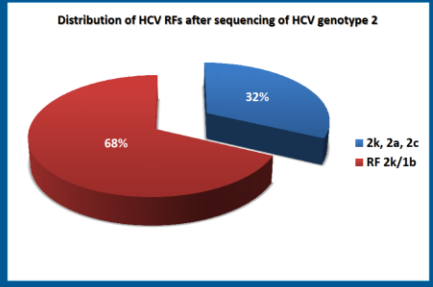
The aim of the study was to evaluate the distribution of HCV recombinant forms in Georgia.

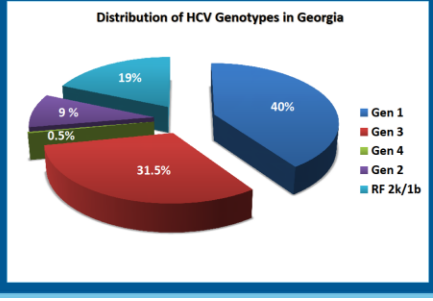
MATERIALS & METHODS

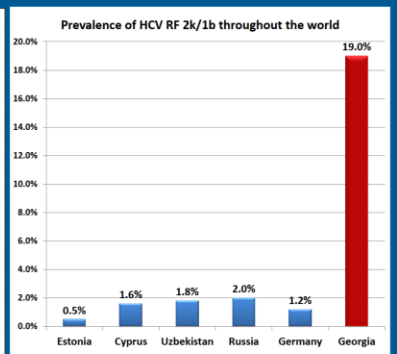
We retrospectively analyzed data of HCV genotypes from Medical Center Mrcheveli, Tbilisi, Georgia 2012-2014 (24 month), in 491 patients with chronic HCV. All samples were sent to Limbach Laboratory, Heidelberg, Germany.
Initially all studies were performed with the VERSANT® HCV Genotype 2.0, a second generation line probe assay, containing probes targeting the 5' non coding region(NCR) and for higher resolution of genotype 1 the core regions of the viral genome. All HCV genotypes 2a/2c were further specified by partially gene sequencing the core- and/or NS5A region.

RESULTS









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SUMMARY

68% of HCV genotype 2 (based on standard HCV genotyping methodology) in Georgia belong to HCV RF- 2k/1b.
Based on the present literature, the prevalence of recombinant forms in different countries do not exceed 2% among of all HCV genotypes.
According to our results, every 5th chronic HCV patient is infected with HCV genotype RF 2k/1b in Georgia!

CONCLUSIONS

We can conclude that the HCV genotype 2k/1b - recombinant form is common in Georgia.
About 19% of all genotypes and 68% of genotype 2 belong to two different genotypes: 5' UTR to within the NS2 region 2k and downstream NS2 type 1b.
Since HCV genotypes still remain the predictors of the outcome of antiviral therapy , the widespread of these genotypes may change the HCV treatment options.
New generation of Direct Antiviral Agents (DAAs) may not depend on HCV genotype in future. Thus, identification of resistance to anti HCV drugs is a diagnostic challenge.

QUESTIONS

1. Why is the HCV RF 2k/1b so frequent in Georgia?
2. Are these HCV recombinant forms really so rare in rest of the world (even in the Former Soviet Union countries)?
3. How effective is the new generation of DAAs going to be on these variants of hepatitis C virus?
4. Are there any risk of drug resistance to HCV RF 2k/1b?

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Hepatitis C Prevalence and Risk Factors in Georgia, 2015: Setting a Baseline for Elimination

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BACKGROUND

- Globally, 130-150 million people live with hepatitis C virus (HCV) infection.[1]
- Georgia is a middle-income Eastern European country with 3.7 million residents. It has high estimated HCV prevalence but lacks current, nationally representative data confirming the HCV burden.
- Georgia launched the world's first HCV Elimination Program in 2015, providing direct-acting antiviral therapy at no cost.[2]
- By 2020, Georgia aims to screen and diagnose 90% of those with chronic HCV, treat 95% of them, and reduce national HCV prevalence by 90%.[3]

OBJECTIVES

The Georgian Ministry of Health and CDC conducted a national HCV seroprevalence survey to:

- Determine baseline HCV prevalence to measure progress toward elimination over time
- Identify risk factors for HCV infection to inform elimination strategies

METHODS

- Stratified, multi-stage cluster design
- Sample size = 7,000 adults ≥18 years
- Collected demographic and risk factor data and blood specimens
- Tested blood specimens for anti-HCV and HCV RNA
- Examined associations between HCV risk factors and anti-HCV status using logistic regression

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RESULTS

HCV Prevalence & Awareness of Infection

- National prevalence
  - anti-HCV: 7.7% (95% CI=6.7-8.9)
  - HCV RNA: 5.4% (95% CI=4.6-6.4)
- Anti-HCV prevalence is higher in:
  - Males (12.1%) vs. females (3.8%) (p<0.0001)
  - Urban (9.5%) vs. rural (5.4%) areas (p<0.0001)
- Descriptively, sub-groups with highest anti-HCV prevalence include males, 40-49 year-olds, persons with history of injection drug use (IDU), and persons with history of blood transfusion (Table 1)
- 64% of anti-HCV+ participants were unaware of their HCV status prior to this survey

Figure 1: Anti-HCV prevalence in major cities and regions of Georgia

*Regional prevalence not calculated due to insufficient sample size
**Occupied territories not included in the survey

Table 1: Sub-groups with highest anti-HCV prevalence

Characteristic	% anti-HCV+ (95% CI)
Males	12.1% (10.2-14.3)
40-49 year-olds	14.0% (11.1-17.6)
Persons with history of injection drug use (IDU)	66.5% (56.0-75.6)
Persons with history of incarceration	42.0% (32.8-51.7)
Persons with history of blood transfusion	
Before blood safety program began in 1997	25.3% (16.2-37.3)
After blood safety program began in 1997	17.4% (10.7-27.1)

Risk Factors for HCV Infection

- Independent risk factors for HCV infection (controlling for sex, age, urban vs. rural residence, and history of incarceration):
  - Ever injected drugs: aOR*=21.4 (95% CI=12.3-37.4)
  - Ever received blood transfusion: aOR*=4.5 (95% CI=2.8-7.2) (no significant difference pre vs. post 1997)
- Peak anti-HCV prevalence among 30-49 year-old males coincides with peak IDU self-reports (Figures 3a-3b)

*aOR = adjusted odds ratio

Figure 2: Percent anti-HCV+ participants reporting risk factors independently associated with HCV infection

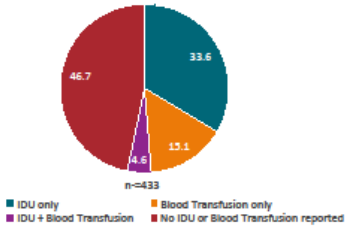


Figure 3a: Anti-HCV prevalence by age and sex

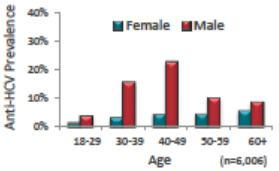
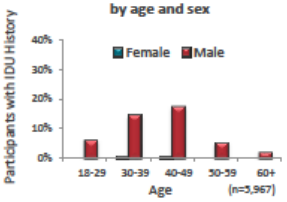


Figure 3b: History of Injection drug use (IDU) by age and sex



CONCLUSIONS

- Georgia has a high burden of HCV infection.
- The majority of persons with HCV in Georgia are unaware of their infection status.
- This survey identified history of IDU and history of blood transfusion as independent risk factors for HCV infection.
- Nearly 50% of anti-HCV+ participants did not report history of IDU or blood transfusion.

RECOMMENDATIONS

To achieve HCV elimination in Georgia:

- Implement comprehensive screening strategies beyond a risk-based approach
- Assess and improve blood safety
- Increase access to harm reduction services and HCV care and treatment among persons who inject drugs

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CONTACT INFORMATION

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Treatment outcomes of hepatitis C virus recombinant form 2k/1b with Sofosbuvir based regimens in Georgia

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MRCHEVELI EUROPEAN LIMBACH DIAGNOSTIC GROUP

INTRODUCTION

Hepatitis C virus (HCV) infection is one of the major causes of liver related morbidity and mortality.
The estimated prevalence of HCV infection in the Republic of Georgia is one of the highest in the world. From April 2015 Gilead Inc. and Georgian Government, with support of Center of Disease Control (CDC) and World Health Organization (WHO), launched National HCV Elimination Project in Republic of Georgia. The goal of the project is to reduce the morbidity, mortality and prevalence, by gradually providing accessibility to prevention, diagnostics and treatment for free with latest DAAs.
During first year of project only Sofosbuvir (SOF) based regimens were available.
It is important to know, that up to 20% of all genotypes belong to the HCV intergenotyping recombinant form RF_2k/1b, which appears to show that Georgia has the highest prevalence of this recombinant virus so far reported worldwide. RF_2k/1b were identified in only GT2 samples and appeared to be up to 70%. According to the limited data about treatment of RF_2k/1b patients with GT2 regimens, sustain virological response (SVR) rates was more similar to GT1 than GT2.

AIM

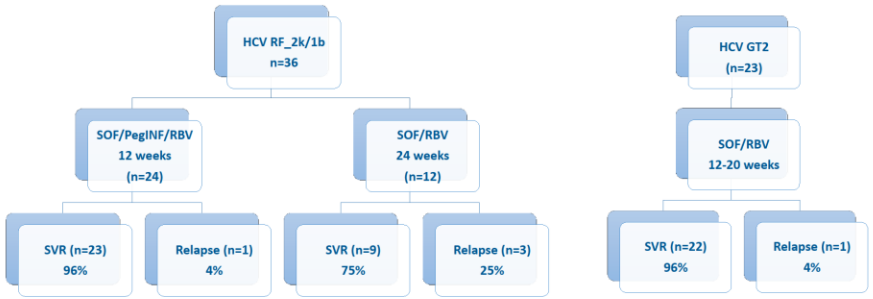
The aim of our study was to define optimal treatment regimen for RF_2k/1b within hepatitis C virus elimination project in Georgia.

METHOD

We retrospectively analyzed the data of GT2 patients identified by INNO-LiPA VERSANT HCV Genotype 2.0 in Medical Center Mrcheveli from May 2015 to May 2016. Partial genome sequencing of core and NS5B regions was performed for identification of RF_2k/1b variants before treatment. All interferon eligible recombinants were treated with Sofosbuvir (SOF) plus Pegilated Interferon (PegINF) plus Ribavirin (RBV) for 12 weeks and interferon ineligible patients with SOF/RBV 24 weeks. We compare SVR12 rates of RF_2k/1b to pure GT2 treated with SOF/RBV-12 or SOF/RBV-20 (depending on presence of cirrhosis). Also we performed regenotyping and partial sequencing of core and NS5B region in randomly selected 20 samples from 95 GT2 (by INNO-LiPA VERSANT) treatment failures from other medical centers treated with SOF/RBV 12 or SOF/RBV 20 weeks.

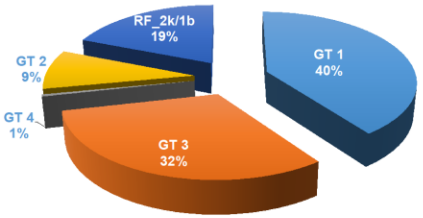
RESULTS

A total number of 67 HCV GT2 samples by INNO-LiPA were analyzed, in which 43 (64%) RF_2k/1b were identified. Antiviral therapy in 23 out of 24 GT2 patients with SOF/RBV for 12 or 20 weeks (depending on presence of cirrhosis) was initiated and SVR12 rates was achieved in 22/23 (96%) patients. 36 out of 43 RF_2k/1b patients were treated with either SOF/PegINF/RBV for 12 weeks (n=24) or with SOF/RBV for 24 weeks (n=12) depending on interferon eligibility criteria. 23/24 (96%) patients achieved SVR 12 rates in interferon-containing group and 9/12 (75%) patients in group without interferon.

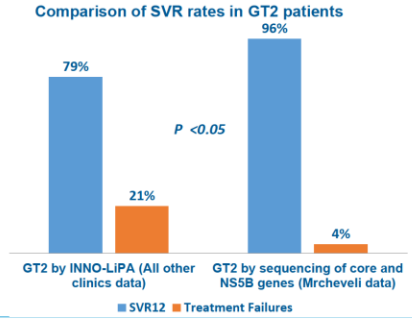


From unspecified genotype 2a/2c patients (n=446) who were treated with SOF/RBV for 12 or 20 weeks depending on presence of cirrhosis, 95/446 (21%) relapsed. Partial genome sequencing of core and NS5B regions of 20 randomly selected samples from 95 treatment failed patients was performed. All samples were consistent to RF_ 2k/1b.

Distribution of HCV Genotypes in Georgia



Comparison of SVR rates in GT2 patients



CONCLUSIONS

Despite the small number of patients our findings suggest that treatment of RF_2k/1b patients with SOF/PegINF/RBV for 12 weeks was more effective than with SOF/RBV for 24 weeks (p = 0.061).

Also we can conclude, that SVR12 rate was significantly higher in GT2 patients, confirmed by sequencing, treated with SOF/RBV 12 or 20 weeks than in unspecified GT2, who were treated with the same regimen (p <0.05).

ACKNOWLEDGEMENTS

The authors wish to express deep gratitude for the support from Ministry of Health, Labor and Social Affaires of Georgia, National Center of Disease Control of Georgia, other medical centers and patients.

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Abbott HCV Core Antigen and HCV RNA comparison study in country of Georgia

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INTRODUCTION

Hepatitis C virus (HCV) infection is endemic in many countries of the world, including Georgia. The government of Georgia launched a HCV elimination program with support from the US Center for Disease Control and Prevention. In 2015 a population-based cross-sectional household sero-survey was undertaken by the Georgian National Center for Disease Control and Public Health (NCDC) to determine the prevalence of hepatitis C (HCV) and B (HBV) virus infection in the country. These data are used to define the burden of HCV/HBV and risk factors for transmission necessary for successfully planning and execution of the HCV elimination program. Assuming an adult population of 2,800,000 with an anti-HCV prevalence of 7.7%, approximately 200,000 anti-HCV+ patients are estimated to require further testing to confirm active infection.

In light of the advances in HCV therapy, simplification of diagnosis confirmation, pre- treatment diagnostic workup and treatment monitoring is required to ensure broad access to interferon-free therapies. HCV core antigen (HCV cAg) testing is rapid, giving results in approximately 60 min, and less expensive than HCV RNA methods

AIM

To evaluate the performance of the ARCHITECT HCV core antigen test to identify patients with an active HCV infection relative to HCV RNA.

METHOD

- A total of 4,235 samples obtained from Blood Banks, Harm Reduction Networks (HRN), Provider Clinics, Screening centers and National Seroprevalence Survey (NSS) with available HCV RNA results were retrospectively tested with the ARCHITECT HCV cAg assay.
- Specimens with HCV cAg concentration <3 fmol/L are considered nonreactive, those with >3 fmol/L – reactive; specimens containing HCV cAg >3 but <10 fmol/L are considered "greyzone" (GZ) and should be re-tested in duplicate.
- A modified HCV testing algorithm that included confirmation of current infection by HCV cAg and reflex testing of HCV cAg negative samples by pooled HCV NAT (Figure 1) was compared to the use of HCV RNA alone.
- The study has the following limitations: many of the samples obtained from the HRN were lipeamic, contained fibrin, or had low volume; due to limited sample volume repeat testing of GZ samples was performed but not in duplicate.

RESULTS

- Overall agreement between HCV cAg and HCV NAT was 97.14% (1258/1294); 2.01% results (26/1294) were discordant and 0.77% (10/1294) were HCV cAg GZ unconfirmed or indeterminate.
- Of the 24 HCV RNA positive / HCV cAg negative samples:
  - From anti-HCV positive samples obtained during the screening activities 16 had viral loads <1,500IU/ml (of these 6 were <30 IU/mL) and 2 had a viral load >4,000 IU/mL, and
  - 6 samples from the HCV seroprevalence study had not quantifiable HCV RNA results, but were qualitatively positive.
- Of the 10 samples with HCV cAg GZ result 3 were HCV RNA negative and 7 were HCV RNA positive (2 had viral load 30,000 IU/mL, 4 were <1,000 IU/mL, and 1 was not quantifiable, but RNA qualitatively positive).
- The two samples which were HCV cAg positive / HCV RNA negative were low reactive <15 fmol/L.
- Estimated cost savings using a reflex algorithm for the confirmation of active infection involving HCV cAg test with sensitivity of 97% and HCV RNA are significant compared to the use of HCV RNA alone.

Abbott ARCHITECT i2000-SR

		HCV RNA		Total
		Positive	Negative	
HCV core Ag	Reactive	938	2*	940
	GZ-reactive	7**	3	10
	Nonreactive	24***	320	344
Total		969	325	1294
Percent Concordance: 97.1%				

* HCVcoreAg Low reactive <15 fmol/L
** 2 samples ~30,000 IU/ML;
4 - <1,000 IU/ML;
1 - qualitative from seroprevalence;
*** 6 samples - <30 IU/ML;
6 - <500 IU/ML;
2 - <1000 IU/ML;
2 - <1,500 IU/ML;
2 - >4,000 IU/ML;
6 - qualitative from seroprevalence;

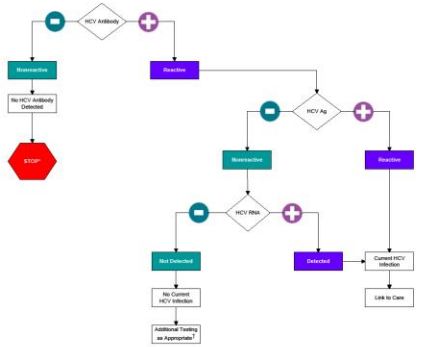

Figure 1: Algorithm for the use of HCV Antigen assay in conjunction with the HCV RNA test for the accurate identification of actively replicating HCV based on the findings of this review and previously published work.[1]

CONCLUSIONS

In this real world study HCV cAg accurately identified >97% of patients with active viremia and 100% accuracy can be achieved by reflexing all anti-HCV positive / HCV cAg negative samples for pooled HCV RNA testing with substantial cost savings. ARCHITECT HCV Core Antigen test can be used as an alternative to HCV RNA testing in a national HCV elimination program.

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  - Clinics "NeoLab", "Mrcheveli", "JO-ANN Medical Clinic" Hematology Institute, Batumi IDH, "Livermed", Imereti MDC
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- NCDC Lugar Center laboratory team- for testing and data analysis
- Abbott Diagnostics - for donating instruments, reagents, supplies and technical support
- US Centers for Disease Control and Prevention (CDC)- for TA in study design and implementation
- Ministry of Labour, Health and Social Affairs of Georgia - for general supervision and support of the study

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Real-World Effectiveness of Sofosbuvir and Ledipasvir/Sofosbuvir Based Regimens in Hepatitis C Virus Genotype 3 Infection Within National Hepatitis C Elimination Program in the Country of Georgia

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INTRODUCTION

- Hepatitis C virus (HCV) has multiple genotypes, of which genotype 3 is the second most common Globally (22% of all HCV infections).[1]
- The prevalence genotype 3 is higher in Georgia, compared to global average, accounting for 34% of all HCV infections in the country.[2]
- HCV genotype 3 has traditionally been difficult to treat, especially among patients with cirrhosis.[3-5]
- In partnership with the US CDC, and commitment from Gilead Sciences to donate direct acting antivirals (DAAs) , Georgia embarked on the world's first hepatitis C elimination program in April, 2015.[6]

AIM

- We evaluated the real-world effectiveness of sofosbuvir (SOF) and ledipasvir/sofosbuvir (LDV/SOF) plus ribavirin (RBV) in HCV genotype 3 patients treated within the Georgian elimination program.

MATERIAL & METHODS

- Study included adult (age ≥18 years) persons with HCV genotype 3 infection treated within the national hepatitis C elimination program.
- From April 2015 through February 2016 Sofosbuvir (SOF) was the only DAA available and it was used in combination with pegylated interferon (IFN) and ribavirin (RBV) for 12 weeks or with RBV only for 24 or 48 weeks.
- From March 2016 Ledipasvir/sofosbuvir (LDV/SOF) was introduced in Georgia and combination of LDV/SOF/RBV for 12 weeks was prescribed to all genotype 3 patients
- Analysis included 2,200 persons, who completed treatment and were assessed for sustained virologic response (SVR) by December 31 2016.
- Data for analysis were extracted from Hepatitis C Elimination Program Treatment Database. Bivariate comparisons were tested using chi-square test. Factors associated with achievement of SVR were assessed in multivariate binomial regression model.

RESULTS

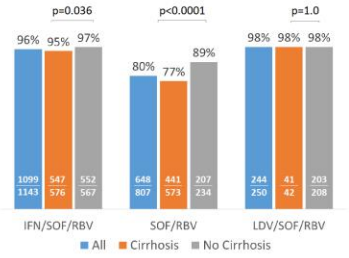
Of 2,200 patients included in the analysis:

- 1,410 (64.1%) were in the age category 45 to 60 years old and 2,096 (95.3) were men
- 1,315 (60.0%) had baseline viral load of <800,000 IU/mL; 121 (5.5%) were co-infected with hepatitis B virus (HBV) and 1,191 (54.1%) had cirrhosis
- 1,143 (52.0%) received IFN/SOF/RBV for 12 weeks, 807 (36.7%) received SOF/RBV for either 24 or 48 weeks and 250 (11.4%) received LDV/SOF/RBV for either 12 or 24 weeks.

Baseline Characteristics

Characteristic	n (%)
Baseline HCV RNA	
<800,000 IU/mL	1315 (60.0)
≥800,000 IU/mL	878 (40.0)
HBV C-infections	
HBsAg-	2079 (94.5)
HBsAg+	121 (5.5)
Cirrhosis	
No (Metavir <F4)	1009 (45.9)
Yes (Metavir F4)	1191 (54.1)
Treatment regimen	
IFN/SOF/RBV	1143 (51.9)
SOF/RBV	807 (36.7)
LDV/SOF/RBV	250 (11.4)

SVR Rates by Treatment Regimen and Cirrhosis



Factors Associated with SVR

	Multivariate analysis		
	RR	95% CI	p value
Baseline HCV RNA			
<800,000 IU/mL	0.98	0.95-1.01	0.2503
≥800,000 IU/mL	Ref		
Cirrhosis			
No (Metavir <F4)	1.06	1.02-1.09	0.0014
Yes (Metavir F4)	Ref		
HBV Co-infection			
HBsAg-	1.17	1.07-1.29	0.0006
HBsAg+	Ref		
Treatment regimen			
SOF/RBV (24 wk)	0.91	0.87-0.95	<0.0001
SOF/RBV (48 wk)	0.85	0.77-0.94	0.0019
SOF/LDV/RBV (12 wk)	1.00	0.95-1.05	0.8890
IFN/SOF/RBV (12 wk)	Ref		

- The IFN/SOF/RBV arm had an overall SVR rate of 96.1% (1,099/1,143) and this regimen was more effective in non-cirrhotic patients versus cirrhotic (97.4% vs. 95.0%, p=0.04)
- SOF/RBV achieved SVR in 80.3% (648/807) of patients, with higher rates again observed in patients without cirrhosis (88.5% vs. 77.0%, p<0.0001)
- Among patients on LDV/SOF/RBV, 97.6% (244/250) achieved SVR with no difference between patients with and without cirrhosis (97.6% vs. 97.6%, p=1.0)
- IFN and LDV/SOF based regimens were more effective than SOF/RBV in both cirrhotic and non-cirrhotic patients (p<0.001 in all comparisons)
- In multivariate analysis persons without cirrhosis and with no HBV co-infection were more likely to achieve SVR. Persons receiving SOF/RBV were less likely to achieve SVR as compared to LDV/SOF/RBV and IFN/SOF/RBV. There was not difference between LDV/SOF and IFN-based regimens

CONCLUSION

- Overall SVR in HCV genotype 3 patients was > 95% in IFN based regimens and superior to longer duration SOF/RBV (80% SVR) regimens.
- The addition of LDV to SOF/RBV resulted in excellent 97.6% SVR rates.
- Therefore LDV/SOF and RBV can be considered as effective treatment option for genotype 3 infection even in difficult to treat patients with compensated cirrhosis

ACKNOWLEDGEMENTS

- Authors acknowledge generous support from Gilead Sciences that donated Sofosbuvir and Ledipasvir/sofosbuvir for National Hepatitis C Elimination Program at no costs
- Authors are grateful to the U.S. Centers for Disease Control and Prevention (CDC) for exceptional technical assistance necessary for initiation and implementation of National Hepatitis C Elimination Program

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AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Prevalence and genotype distribution of hepatitis C virus in Georgia: A 2015 nationwide population-based survey

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EASL The Home of Hepatology — THE INTERNATIONAL LIVER CONGRESS™ 2017, 19-23 APRIL, AMSTERDAM, THE NETHERLANDS

INTRODUCTION

- Georgia is an Eastern European country with estimated high Hepatitis C (HCV) burden. However, country lacked updated, nationally representative data confirming disease burden[1].
- Georgia launched unprecedented HCV elimination program in April 2015, providing new DAAs at no cost to patients[2].
- A nationwide population-based Hepatitis C survey was conducted in 2015 to provide baseline data for the elimination program.

AIM

The survey aimed to:

- Estimate nationwide HCV prevalence
- Determine HCV genotype distribution
- Identify main risk factors for HCV infection in Georgia

METHOD

- The survey used a stratified, multi-stage cluster design (n=7,000) and included adults aged ≥18 years.
- A structured questionnaire collected data on socio-demographics, medical history, lifestyle information and HCV risk factors.
- Serum specimens were obtained and tested for anti-HCV antibody (anti-HCV). Positive samples were tested for HCV RNA and HCV genotype.
- Data were weighted using census data on sex, age, and geography. Descriptive analysis was conducted.

RESULTS

HCV Prevalence and Risk Factors

- National seroprevalence - **7.7%** (95% CI=6.7-8.9)
- Prevalence of chronic HCV infection - **5.4%** (95% CI=4.6-6.4)
- Two risk factors independently associated with anti-HCV+ status: history of injection drug use (IDU) (aOR=21.4, 95% CI=12.3-37.4), reported by 38.2% of anti-HCV positive participants, and ever receiving a blood transfusion (aOR=4.5, 95% CI=2.8-7.2), reported by 19.7% of participants;
- 46.7% of participants did not report either of these two risk factors. Among anti-HCV+ males, 50.9% reported history of IDU, 16.9% reported blood transfusion, and 38.4% reported neither risk factor.
- Among anti-HCV+ females, 2.4% reported IDU, 27.6% reported blood transfusion, and 70.0% reported neither risk factor (Figure 1).

HCV Genotypes

- The most prevalent genotype nationally was GT1b **(40.5%)** followed by GT3 **(34.7%)**, GT2 **(23.6%)** and GT1a **(0.6%)**.
- 0.7% of participants had indeterminate genotype results.
- Genotype distribution varied by sex and reported risk factors, with GT3 most common among males (39.6%) and participants reporting history of IDU (35.3%).
- GT1b was more prevalent among females (62.5%) and participants reporting history of blood transfusion (54.3%) (Figure 2).
- Among participants not reporting either IDU or blood transfusion, GT3 was the most common among males (41.9%), and GT1b was most common among females (64.9%).

Figure 1: HCV Risk Factors Reported among Anti-HCV+ Participants

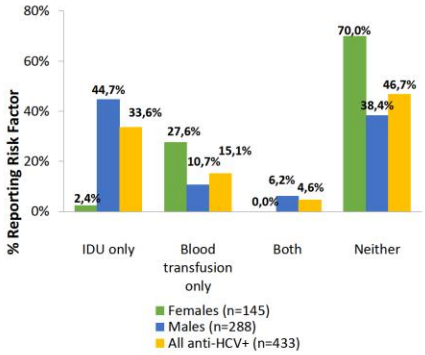
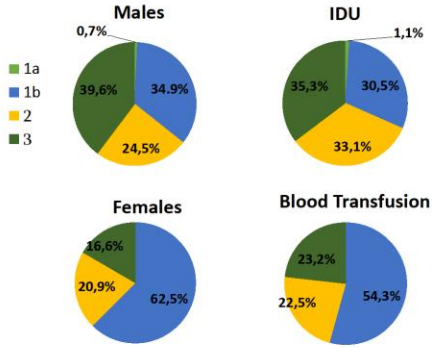


Figure 2: HCV Genotype by Sex and by Risk Factor



CONCLUSIONS

- HCV genotype distribution in Georgia varies by sex and reported risk factors.
- In the general population, genotypes 1 and 3 have similar prevalence
- Introduction of pangenotypic treatment regimens in the Georgian HCV elimination program would be beneficial.

ACKNOWLEDGEMENTS

This survey was conducted in collaboration with the U.S. Centers for Disease Control and Prevention (CDC). The authors thank survey participants, interviewers, phlebotomists, laboratorians and individuals who supported the fieldwork, as well as all respondents who agreed to participate in the survey.

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Regression of liver stiffness (LS) after direct acting anti-viral (DAA) therapy for hepatitis C in the country of Georgia

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INTRODUCTION

Novel DAAs targeting hepatitis C virus (HCV) have revolutionized the treatment of chronic infection by dramatically increasing rates of sustained virological response (SVR). However, patients with severe liver disease remain at risk of life-threatening complications even after achieving an SVR[1]. Several studies have suggested a significant reduction in LS during therapy with pegylated interferon (PEG-IFN) and ribavirin (RBV)[2;3]. To date there are limited data suggesting reversibility of HCV-associated liver fibrosis/cirrhosis after DAA therapy.

AIM

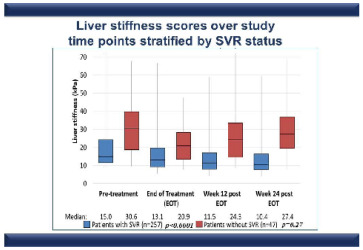
We assessed the impact of DAA therapy on liver fibrosis regression measured by transient elastography in patients with chronic HCV infection..

METHODS

A prospective study was conducted in HCV infected adult patients with advanced liver fibrosis (Metavir F3) or cirrhosis. LS score>14.5 kPa indicated LS-defined cirrhosis. The primary outcome was improvement in liver stiffness measurement (LSM) at week 24 post-treatment measured as 1) decrease in median LS compared to baseline and 2) at least 20% decrease in LSM compared to baseline. Multivariate logistic regression model was utilized to identify factors associated with at least 20% improvement in LSM.

RESULTS

Of total 304 patients, 172 (56.6%) had LS-defined cirrhosis pre-treatment. SVR was achieved in 257 (84.5%) patients treated with either interferon-containing (PEG-IFN/RBV/Sofosbuvir (SOF) - 12 weeks) or interferon-free regimens (SOF/RBV for 12, 20 or 24 weeks, SOF/Ledipasvir (LDV)±RBV-12 or 24 weeks). LSM decreased from baseline median of 16.9 (IQR: 11.8 – 27.7) kPa to post-treatment week 24 score of 11.9 (IQR: 8.2–20.9) kPa ($p<0.0001$). LS significantly reduced during treatment, but improvement continued off treatment only in patients who achieve an SVR. Of total 304 patients, 198 (65.1%) achieved at least 20% reduction in LS. In multivariate analysis SVR was significantly associated with this reduction ($p<0.0001$) regardless of the addition of Interferon to the treatment regimens (SOF/RBV vs. PEG-IFN/SOF/RBV– OR:1.90, 95% CI:0.94-3.82; SOF/LDV±RBV vs. PEG-IFN/SOF/RBV–OR:1.94, 95% CI: 0.96-3.94). Despite decreasing baseline LSM, more than half of cirrhotic patients remained cirrhotic at week 24 post-treatment.



Factors associated with ≥20% improvement in LSM

	Multivariate analysis	
	OR (95% CI)	p value
Age (per year increase)	0.98 (0.95-1.01)	0.23
Gender		
Male	1	
Female	2.66 (1.01-7.01)	0.047
Baseline LSM		
≤14.5 kPa	1	
>14.5 kPa	1.06 (0.61-1.81)	0.85
Treatment regimen		
PEG-IFN/SOF/RBV	1	
SOF/RBV	1.90 (0.94-3.82)	0.07
SOF/LDV±RBV	1.94 (0.96-3.94)	0.06
SVR		
Not achieved	1	
Achieved	14.38 (5.88-35.11)	<0.0001

Baseline characteristics	All (n=304)	SVR (n=257)	No SVR (n=47)	p value
Age, median years (IQR)	49 (43 – 55)	48 (43-54)	52 (46-59)	0.03
Gender, n (%)				
Male	268 (88.2)	227 (84.7)	41 (15.4)	0.83
Female	36 (11.8)	30 (83.3)	6 (16.7)	
Heavy alcohol drinking, n (%)				
No	281 (92.4)	237 (84.3)	44 (15.7)	0.99
Yes	23 (7.6)	20 (87.0)	3 (13.0)	
Body Mass Index, n (%)				
<28	178 (58.6)	153 (86.0)	25 (14.0)	0.42
≥28	126 (41.4)	104 (82.5)	22 (17.5)	
Diabetes mellitus, n (%)				
No	264 (86.8)	227 (86.0)	37 (14.0)	0.07
Yes	40 (13.2)	30 (75.0)	10 (25.0)	
Platelet count, n (%)				
≥150X10⁹/l	179 (58.9)	157 (87.7)	22 (12.3)	0.07
< 150X10⁹/l	125 (41.1)	100 (80.0)	25 (20.0)	
ALT, n (%)				
< 100 IU/mL	178 (58.6)	153 (86.0)	25 (14.0)	0.42
≥ 100 IU/mL	126 (41.4)	104 (82.5)	22 (17.5)	
Alkaline phosphatase, n (%)				
< 150 IU/mL	280 (92.1)	241 (86.1)	39 (13.9)	0.01
≥ 150 IU/mL	24 (7.9)	16 (66.7)	8 (33.3)	
Total bilirubin, n (%)				
≤ 18.8 µmol/l	246 (80.9)	215 (87.4)	31 (12.6)	0.005
> 18.8 µmol/l	58 (19.1)	42 (72.4)	16 (27.6)	
Albumin, n (%)				
≥ 35 g/l	286 (94.1)	245 (85.7)	41 (14.3)	0.03
< 35 g/l	18 (5.9)	12 (66.7)	6 (33.3)	
INR, n (%)				
≤1.5	289 (95.1)	244 (84.4)	45 (15.6)	0.99
>1.5	15 (4.9)	13 (86.7)	2 (13.3)	
HCV genotype, n (%)				
1	142 (46.7)	112 (78.9)	30 (21.1)	0.001
2	50 (16.5)	39 (78.0)	11 (22.0)	
3	112 (36.8)	106 (94.6)	6 (5.4)	
Baseline LSM, n (%)				
≤14.5 kPa	132 (43.4)	122 (92.4)	10 (7.6)	0.009
>14.5 kPa	172 (56.6)	135 (78.5)	37 (21.5)	
Treatment regimen, n (%)				
PEG-IFN/SOF/RBV	153 (50.3)	137 (89.5)	16 (10.5)	<0.0001
SOF/RBV	84 (27.6)	54 (64.3)	30 (35.7)	
SOF/LDV±RBV	67 (22.1)	66 (98.5)	1 (1.5)	

CONCLUSIONS

SVR achieved after DAA treatment is associated with regression in LS. However, regardless of achieving SVR liver damage persists in significant proportion of patients. Thus, early treatment of HCV-infected patients can significantly prevent residual liver damage.

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Effectiveness of ledipasvir/sofosbuvir in hepatitis C virus genotype 1, 2 and 3 infection: real-world data from Georgian hepatitis C elimination program

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INTRODUCTION

- Effectiveness of ledipasvir/sofosbuvir (LDV/SOF) in HCV genotype 1 infection is well established. [1]
- Few studies assessed LDV/SOF in genotype 2 and 3 infection and data on effectiveness are limited. [2]
- In April 2015, the country of Georgia, with the support of the US CDC and Gilead Sciences, launched a national hepatitis C elimination program. [3]
- Since March 2016, LDV/SOF was recommended for all HCV genotypes within Georgia's HCV elimination program.

AIM

- We report on real-world effectiveness of LDV/SOF-based regimens for various genotypes in Georgia.

MATERIAL & METHODS

- Study included treatment naïve and treatment-experienced adult (age ≥18 years) persons with HCV genotype 1,2 and 3 infection treated within the national hepatitis C elimination program.
- Non-cirrhotic genotype 1 patients received LDV/SOF only, while persons with cirrhosis received it in combination with ribavirin (RBV). Genotype 2 and 3 patients received LDV/SOF in combination with RBV.
- Analysis included 1,588 persons, who completed treatment and were assessed for sustained virologic response (SVR) by December 31, 2016.
- Data for analysis were extracted from Hepatitis C Elimination Program Treatment Database. Bivariate comparisons were tested using chi-square test.

RESULTS

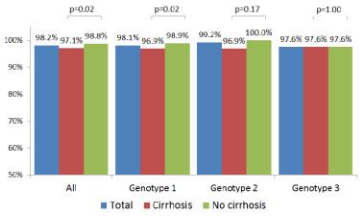
Of 1,588 patients included in the analysis:

- 822 (51.8%) were in the age category 45 to 60 years old and 1,255 (79.0%) were men.
- 821 (51.7%) had baseline viral load of <800,000 IU/mL; 124 (7.8%) were co-infected with hepatitis B virus (HBV) and 597 (37.6%) had cirrhosis.
- 1,080 (68.0%) patients had genotype 1, 258 (16.2%) – genotype 2, and 250 (15.7%) – genotype 3.

Baseline Characteristics

Characteristic	n (%)
Baseline HCV RNA	
<800,000 IU/mL	762 (47.9)
≥800,000 IU/mL	821 (51.7)
HBV Co-infection	
HBsAg-	1464 (92.2)
HBsAg+	124 (7.8)
Cirrhosis	
No (Metavir <F4)	991 (62.4)
Yes (Metavir F4)	597 (37.6)
Treatment regimen	
LDV/SOF (12 wk)	846 (53.3)
LDV/SOF (24 wk)	89 (5.6)
LDV/SOF/RBV (12 wk)	638 (40.2)
LDV/SOF/RBV (24 wk)	15 (0.9)

SVR Rates by Genotypes and Cirrhosis Status



- Overall SVR rate was 98.2% (1559/1588), including 98.1% (1,059/1,080) in genotype 1, 99.2% (256/258) in genotype 2 and 97.6% (244/250) in genotype 3 (p=0.32).
- Overall, 97.1% (580/597) of patients with cirrhosis achieved SVR vs. 98.8% (979/991) of patients without cirrhosis (p=0.02).
- Difference by cirrhosis status was statistically significant only in genotype 1 – 96.9% among cirrhotic patients and 98.9% among non-cirrhotic patients (p=0.02).
- In genotype 2 patients 96.9% of cirrhotic patients achieved SVR compared to 100% among non-cirrhotics (p=0.17).
- The same SVR rate of 97.6% was observed in all subgroups of genotype 3 patients (p=1.00).

CONCLUSION

- LDV/SOF-based treatment was highly effective in this real-world cohort, including in patients with cirrhosis.
- High cure rates were observed in all genotypes.
- Combination of LDV/SOF/RBV appears to be an effective treatment option for genotype 2 and 3 infections.

ACKNOWLEDGEMENTS

- Authors acknowledge generous support from Gilead Sciences that donated Sofosbuvir and Ledipasvir/sofosbuvir for National Hepatitis C Elimination Program at no costs
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AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Ledipasvir / Sofosbuvir plus Ribavirin as highly effective regimen for RF1_2k/1b patients within Georgian national hepatitis C elimination program

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ABSTRACT

Aim. Hepatitis C virus (HCV) recombinant strainRF1_2k/1b is common in ethnic Georgians. This chimera virus contains genomic fragments of genotype 2 and genotype 1 and is misclassified as genotype 2 if only structural region is studied. We aimed to evaluate impact of RF1_2k/1b strain on Direct Acting Anti-viral (DAA) treatment outcomes within Georgian national hepatitis C elimination program.

Methods. Study included 167 patients with HCV genotype 2 as determined by 5 untranslated region/Core (5'UTR/Core) genotyping assay. In addition to standard genotyping non- structural 5B (NS5B) region was sequenced and genotyping results were compared. Study patients were treated within national hepatitis C elimination program with sofosbuvir/ribavirin (SOF/RBV), interferon/sofosbuvir/ribavirin (IFN/SOF/RBV) or ledipasvir/sofosbuvir/ribavirin (LDV/SOF/RBV) regimens respectively.

Results. Of 167 patients evaluated 129 had RF1_ 2k/1b genotype, while remaining 38 were infected with either 2a, 2c or 2k subtypes. Overall, sustained virologic response (SVR) was achieved more in genotype 2 than RF1_2k/1b patients (97.3% vs. 80.6%, p=0.004). LDV/SOF/RBV for 12 weeks was highly effective among both genotype 2 and RF1_ 2k/1b (100.0 % and 97.9%, p=0.99) patients. Among 129 RF1_2k/1b patients SVR rate among LDV/SOF/RBV for 12 weeks was superior (97.9% SVR) to SOF/RBV for 12 (56.4%, p<0.0001) or 20 weeks (79.2%, p=0.01). IFN/SOF/RBV 12 week also demonstrated better response than SOF/RBV 12 weeks (88.9% vs. 56.4%, p=0.02) in these patients.

Conclusions. High prevalence of RF1_2k/1b strain can significantly affect treatment outcomes. In our study, IFN/SOF/RBV and especially LDV/SOF/RBV found to have significantly higher SVR in patients infected with RF1_2k/1b strain as compared to standard HCV genotype 2 treatment with SOF/RBV 12 or 20 weeks. There is need for reassessing existing modalities for the management of HCV genotype 2 infections, especially in areas with high prevalence of RF1_2k/1b strain.

OBJECTIVES

We aimed to evaluate impact of RF 1_2k/1b strain on Direct Acting Anti-viral (DAA) treatment outcomes within Georgian national hepatitis C elimination program.

METHODS

Study included 167 patients with HCV genotype 2 as determined by 5 untranslated region/Core (5'UTR/Core) genotyping assay. In addition to standard genotyping non-structural 5B (NS5B) region was sequenced and genotyping results compared. Study patients were treated within Gerogian national hepatitis C elimination program with sofosbuvir/ribavirin (SOF/RBV), interferon/sofosbuvir/ribavirin (IFN/SOF/RBV) or ledipasvir/sofosbuvir/ribavirin (LDV/SOF/RBV) regimens respectively.

RESULTS

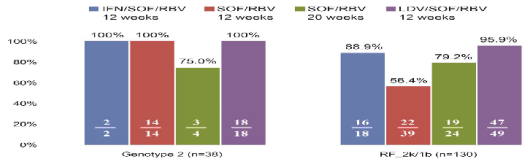
- Of 168 patients evaluated 129 had RF1_ 2k/1b genotype, while remaining 39 were infected with either 2a, 2c or 2k subtypes.
- SVR was achieved in more genotype 2 than RF1_2k/1b patients (94.9 % vs. 80.5%, p=0.04).
- LDV/SOF/RBV for 12 weeks was highly effective among both genotype 2 and RF1_ 2k/1b (94.7% and 97.9%, p=0.49) patients.
- Among 129 RF1_2k/1b patients SVR rate among LDV/SOF/RBV for 12 weeks was superior (97.9% SVR) to SOF/RBV for 12 (56.4%, p<0.0001) or 20 weeks (79.2%, p=0.01).
- IFN/SOF/RBV 12 week also demonstrated better response than SOF/RBV 12 weeks (88.9% vs. 56.4%, p=0.02) in these patients.

Table 2. SVR rates among patients with RF1_2k/1b recombinant

Regimen	All (n=130)	
IFN/SOF/RBV 12 wk	88.9% (16/18)	0.02
SOF/RBV 12 wk	56.4% (22/39)	
IFN/SOF/RBV 12 wk	88.9% (16/18)	0.68
SOF/RBV 20 wk	79.2% (19/24)	
IFN/SOF/RBV 12 wk	88.9% (16/18)	0.29
LDV/SOF/RBV 12 wk	95.9% (47/49)	
SOF/RBV 12 wk	56.4% (22/39)	0.10
SOF/RBV 20 wk	79.2% (19/24)	
SOF/RBV 12 wk	56.4% (22/39)	<0.0001
LDV/SOF/RBV 12 wk	95.9% (47/49)	
SOF/RBV 20 wk	79.2% (19/24)	0.035
LDV/SOF/RBV 12 wk	95.9% (47/49)	

Table 1. SVR rates by treatment regimen and genotype (n=168)

Regimen	All (n=168)	Genotype		
		2 (n=38)	2k/1b (n=130)	p value
IFN/SOF/RBV 12 wk	90.0% (18/20)	100.0% (2/2)	88.9% (16/18)	0.99
SOF/RBV 12 wk	67.9% (36/53)	100.0% (14/14)	56.4% (22/39)	0.002
SOF/RBV 20 wk	78.6% (22/28)	75.0% (3/4)	79.2% (19/24)	0.99
LDV/SOF/RBV 12 wk	97.0% (65/67)	100.0% (18/18)	95.9% (47/49)	0.99
Total	83.9% (141/168)	97.4% (37/38)	73.8% (104/130)	0.01



CONCLUSIONS

- **High prevalence of RF1_2k/1b strain can significantly affect treatment outcomes.**
- **IFN/SOF/RBV and especially LDV/SOF/RBV found to have significantly higher SVR in patients infected with RF1_2k/1b strain as compared to standard HCV genotype 2 treatment with SOF/RBV 12 or 20 weeks.**
- **There is need for reassessing existing modalities for the management of HCV genotype 2 infections, especially in areas with high prevalence of RF1_2k/1b strain.**

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Predictive factors of treatment outcome among patients included in hepatitis C elimination program in Georgia

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INTRODUCTION

Georgia has a high burden of hepatitis C virus (HCV) infection. In 2015, Ministry of health of Georgia with National Center for Disease Control and Public Health (NCDC) and US Centers for Disease Control and Prevention (CDC) conducted the study where a national probability sample of approximately 6000 adults in Georgia was tested for HCV infection, yielding a prevalence estimate of 7% for chronic HCV with an estimated 5.4% of adults currently infected.

On April 28, 2015, in collaboration with CDC, Gilead Sciences and other partners, Georgia launched a comprehensive, national HCV elimination program that included free of charge treatment for all HCV infected persons. If successful, the viral reservoir will be substantially reduced and will dramatically decrease the risk of HCV transmission in the country.

AIM

The aim of this study was to evaluate predictive factors for sustained viral response (SVR) among patients treated with direct acting antivirals (DAA) within HCV elimination program in Georgia.

MATERIAL & METHODS

The Elimination Program requires participating clinics and treatment sites to collect pre-treatment socio-demographic, clinical and laboratory data, prescribed medications, treatment adherence and monitoring data.

These data are collected using standardized protocols, and entered in information management system STOP-C - Georgia's national electronic treatment database, developed for the HCV elimination program.

Data collected includes HCV genotype and viral load, level of liver fibrosis, risk factors for HCV infection and treatment-related laboratory data, including SVR at week 12-24 after completion of treatment.

The Elimination Program requires all patients to have a pre-treatment FIB4 score, which is computed from age, ALT, AST and platelet count. A FIB4 score is interpreted as follows: below 1.45 (low), 1.45-3.25 (equivocal), and greater than 3.25 (advanced fibrosis). For those in the equivocal range, a liver elastography is conducted and results recorded.

Data were extracted from the HCV treatment program database of clinic Neolab, one of the major clinical sites providing HCV care and treatment as part of the HCV elimination program. For all patients included in the program, pretreatment sociodemographic and clinical data, treatment regimen, adherence and monitoring data are collected. Treatment is provided by sofosbuvir/ribavirin (SOF/RBV) with or without interferon (IFN) and sofosbuvir/ledipasvir (LDV) with or without RBV. Treatment outcomes were analyzed by demographic and clinical data, including the degree of liver fibrosis with patients defined as having advanced liver fibrosis (>=F3 by liver elastography or >3.25 by FIB4 score) and treatment regimen. Multivariate analysis using logistic regression was conducted.

RESULTS

- During April 28, 2015–April 30, 2016, a total of 3372 individuals with positive HCV RNA test were included in the treatment program.
- SVR result was available for 1629 patients by the time of data analysis. Overall, SVR was obtained among 93.2% of patients.

By bivariate analysis, variables significantly associated with SVR were:

- Teatment regimen (92% cure rate for SOF/RBV/IFN, 77.1% - for SOF/RBV 24-week and 99.4% for SOF/LDV or SOF/LDV/RBV regimen)
- Genotype (with genotype 3 having highest cure rate of 95.4% compared to 91.8% and 91.7% for genotype 1 and 2, respectively)
- Liver fibrosis stage (99.9% SVR among patients with low fibrosis level compared to 87.8% among patients with advanced fibrosis)
- Age (99.2% for age<35 with 92.7% for older patients), gender (96.6% for females and 92.7% for males)
- Platelet count (6.2% for >=100000 and 21.2% for <100000)
- ALT, AST and weight.

After adjustment, significant association of SVR was observed with:

- Genotype (aOR=2.12, 95% CI: 1.14-7.26)
- Fibrosis stage (aOR=7.12, 95% CI: 2.14-17.26)
- Treatment regimen (aOR=1.08, 95% CI: 1.04-1.13)
- Platelet count (aOR=1.007, 95% CI: 1.003-1.012

CONCLUSION

The presented study showed that by multivariate analysis age, gender, weight and liver enzymes were not associated with SVR, while genotype, fibrosis stage, treatment regimen and platelet count were independent predictors of treatment outcome.

ACKNOWLEDGEMENTS

Georgia HCV elimination program is conducted under the leadership from the Georgia Ministry of Labor, Health, and Social Affairs [MoLHSA] with strong stakeholder support, including partnership and technical assistance from CDC, and commitment from Gilead Sciences to donate direct-acting antiviral HCV medications (DAAs).

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DISCLOSURES

None

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The changing role of injecting drug use in the hepatitis C virus epidemic in Georgia and paths to elimination

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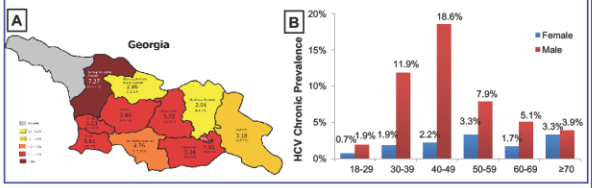
Introduction

Georgia has one of the highest hepatitis C virus (HCV) prevalence rates in the world, with >5% of adults chronically infected (**Figure 1**). In 2015 Georgia and partners launched a national program to eliminate HCV (defined as 90% reduction in HCV chronic prevalence by 2020 compared to 2015 levels) through prevention, diagnostics and curative treatment. As of December 31, 2016, 27,595 patients had initiated treatment, reaching ~2,100 treatments/month[1].

The population has a high historical rate of injecting drug use (>4% of adults and 38% of those with chronic HCV report injecting drugs[2]), which is thought to drive the heterogeneity in levels of infection by sex and age group (**Figure 1B**).

We explored the contribution of PWID to the HCV epidemic and the feasibility of reaching a 90% reduction in prevalence and incidence by 2020.

Figure 1: *Chronic HCV prevalence by region (A) and sex and age group (B) in Georgia, from 2015 Georgia National Serosurvey[2]*

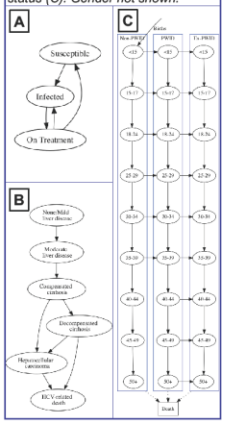


Methods

We developed a dynamic model of HCV transmission incorporating the changing demographics of PWID and the general population in Georgia (**Figure 2**). The model includes 9 age classes with time-varying, age and gender-specific recruitment rates to injecting drug use, and age-specific injection cessation rates (**Figure 2C**), and accounts for liver disease progression and death attributable to HCV (**Figure 2B**).

We used Markov Chain Monte Carlo Approximate Bayesian Computation (MCMC-ABC) in R[3,4] to calibrate the model to data on PWID age distributions and HCV prevalence by age, gender, and PWID status from the 2015 national sero-survey and PWID surveys 1997-2015[5]. Final parameter sets were used to project the impact of treatment strategies to 2020. Model projections included two calibration scenarios that account for uncertainty in the impact of harm reduction interventions (HR). The **high HR impact scenario** assumes HR directly resulted in observed reductions in the prevalence of HCV amongst new PWID over the last 20 years (reduced HCV incidence in PWID by 58% since 2000), whereas the **low HR impact scenario** assumes a lower efficacy for OST and NSP in line with estimates from a recent systematic review[6] (reduced HCV incidence in PWID by 14% since 2000).

Figure 2: *Schematic of model compartments: infection status (A), liver disease (B), age and PWID status (C). Gender not shown.*



Results

HCV epidemic dynamics

Both model calibration scenarios (high and low HR impact) agree with current epidemic patterns amongst PWID and the general population (**Figure 3**). Successive sero-surveys of PWID since 1997 show average age of PWID increasing and recruitment to injecting decreasing; the model suggests this means that the population of active PWID in Georgia is declining from a peak in the late 1990s (**Figure 4**). The HCV population attributable fraction for PWID (**PAF**, the proportion of HCV infections due to injecting drug use) shows PWID were the main driver of the epidemic in the past, but their contribution has declined over time (**Table 1**).

Figure 3: *Modelled estimates of HCV prevalence in 2015 by group and age, compared to sero-survey data[2], for high and low HR impact scenarios.*

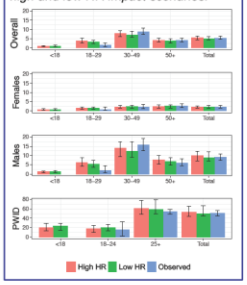


Figure 4: *Projected population size of current, former, and ever (current + former) PWID over time, for high and low HR scenarios. Points show available estimates for adult PWID[2,7].*

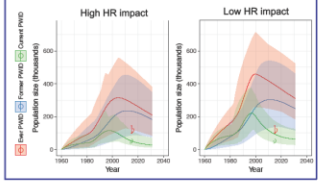


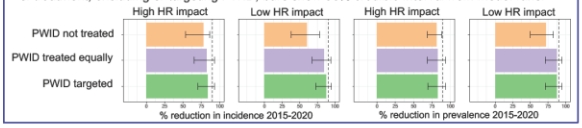
Table 1: *Past and future HCV PAF for PWID*

Time Period	High HR impact	Low HR impact
	PAF (95% Credible Interval)	
1985-2000	0.77 (0.60-0.88)	0.61 (0.39-0.79)
2000-2015	0.32 (0.16-0.56)	0.55 (0.36-0.73)
2015-2030	0.1 (0-0.44)	0.34 (0.11-0.55)

Impact of treatment scale-up

High rates of treatment for PWID are essential for achieving a 90% reduction in incidence and prevalence at current treatment rates in Georgia (2100/month, **Figure 5**). Model projections show that if PWID are not treated, incidence and prevalence reductions never reach 90% by 2020 (**Figure 5, orange bars**). If PWID have equal access to testing and treatment as the rest of the population (such that 21% (6-46%) of treatments go to active PWID in the first year) then 20% of model runs achieve a 90% decrease in prevalence by 2020 (**Figure 5, purple bars**). Further targeting of PWID at double the rate of the general population (**Figure 5, green bars**), or scaling up HR coverage, achieves minimal additional impact because the high rate of treatment rapidly reaches the majority of PWID. To improve the chances (to 85% probability) of achieving a 90% decrease in prevalence by 2020 with PWID having equal access to treatment, initiation rates need to increase by 30% to 2700/month. This treatment rate also achieves a 90% reduction in incidence in 73% of model runs.

Figure 5: *Projected % reduction in HCV prevalence and incidence by 2020 under current rate of treatment, excluding or targeting PWID, bars show 95% credible interval from model runs.*



Conclusions

In Georgia, injecting drug use drove the HCV epidemic in the past, and current and former PWID are infected with HCV at high prevalence. Although the PWID contribution to the HCV epidemic has declined over time, reaching active PWID for HCV treatment is essential to reduce prevalence and incidence to the target by 2020 or shortly afterwards. While the elimination program has included a dramatic increase in PWID access to HCV testing and treatment over the past few years, and a program in Tbilisi has demonstrated the feasibility of reaching high rates of HCV treatment success among PWID[8], barriers to HCV treatment access for PWID include continued stigmatization and criminalization of drug use. The Georgia elimination program must continue to make every effort to reach PWID in order to achieve HCV elimination.

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INHSU 2017, Jersey City, USA

NEXT GENERATION SEQUENCE-BASED CHARACTERIZATION OF HEPATITIS C VIRUS RF1_2k/1b STRAIN IN COUNTRY OF GEORGIA

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INTRODUCTON

Hepatitis C virus (HCV) is a single-stranded positive-sense RNA virus, belonging to the Flaviviridae family, and exhibits substantial global sequence diversity. Globally, around 140 million people live with chronic HCV infection. The HCV particle consists of a core of genetic material (RNA), surrounded by an icosahedral protective shell of protein, and further encased in a lipid (fatty) envelope of cellular origin. Two viral envelope glycoproteins, E1 and E2, are embedded in the lipid envelope (Figure 1). The structural organization of the ORF genome-encoded protein is as follows: NH2–C–E1–E2–p7–NS2–NS3–NS4A–NS4B–NS5A–NS5B–COOH (Figure 2). This polyprotein yields at least ten different parts through the cleaving activity of host and viral proteases. HCV includes three structural proteins (core, E1, and E2), a small protein (p7), and six non-structural proteins (NS2, NS3, NS4A, NS4B, NS5A, and NS5B). The core protein forms the viral capsid through its RNA-binding capacity. The two envelope glycoproteins (E1 and E2) make viral entry possible. This constitutes a crucial step in its viral life cycle. E2 contains highly variable regions (HVRs) with amino acid sequences differing up to 80% between different isolates.

The C-terminal domain of NS3 has helicase/NTPase activity. Its functions include RNA binding and unwinding of regions of the extensive secondary structure, aside from RNA-stimulated NTPase activity. NS4A acts as a cofactor for NS3 protease activity. The NS3/4A protease activity results in cleavage of the viral nonstructural proteins. Recruitment of other viral non-structural proteins, NS4B forms the replication complex. The role of NS5A is not entirely clear. It is also probably important in viral replication. NS5B being an RNA-dependent RNA polymerase (RdRP) ensures the synthesis of new genomic RNA, and is consequently considered a central component of the HCV replication complex. The high genomic heterogeneity of HCV is the result of the lack of proof-reading activity of this RdRP (Figure 2).

HCV strains isolated in different parts of the world were classified into six major genotypes (i.e., genotypes one to six) and numerous subtypes (Table 1 A & B). Until 2001, HCV was thought to evolve in a clonal manner, with diversity generated through the accumulation of mutations. However, several events of inter- and intra-genotypic homologous recombination have been reported to date from various parts of the world. A 2k/1b recombinant was found in St. Petersburg, Russia, thought to have emerged by homologous recombination during minus-strand synthesis via template switching and seems to be circulating among intravenous drug users in Russia. Isolates of this strain, labeled RF1_2k/1b, have also been found in Ireland, Estonia, Uzbekistan, Western Siberia, and France.

Previous studies showed that RF1_2k/1b strain is common among ethnic Georgian patients previously assumed to be infected by genotype 2. More than 70% of HCV genotype 2 patients are infected with RF1_2k/1b strain based on the discordant results from 5'UTR and 3'UTR amplification based genotyping methods. The purpose of the study was to confirm and characterize the presence of suspected HCV RF1_2k/1b strain among Georgian patients using Next Genome Sequence (NGS) technology. HCV recombinant RF1_2k/1b appears to be widespread in Georgia, highlighting the need for further studies investigating recombination events in epidemiological studies.

Structure of HCV

Simplified diagram of the structure of HCV

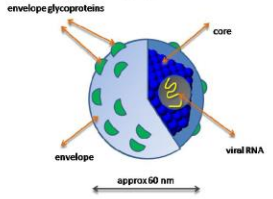

Figure 1. Simplified diagram of structure of HCV particle. The HCV particle consists of a core of genetic material (RNA), surrounded by an icosahedral protective shell of protein, and further encased in a lipid (fatty) envelope of cellular origin. Two viral envelope glycoproteins, E1 and E2, are embedded in the lipid envelope (source Wikimedia Commons)

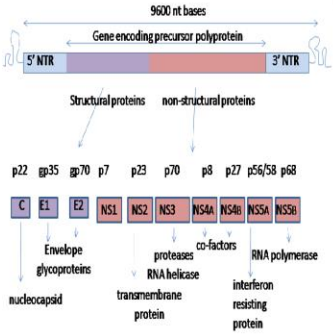

Figure 2. Genome organization of HCV. At the 5' and 3' ends of the RNA are the UTR, that are not translated into proteins, but are important to translation and replication of the viral RNA. The 5' UTR has a ribosome binding site (IRES — Internal ribosome entry site) that starts the translation of a very long protein containing about 3,000 amino acids. The large pre-protein is later cut by cellular and viral proteases into the ten smaller proteins (Wikimedia Commons).

A

HCV Genotype	Subtypes
Genotype 1	1, 1a, 1b. 1c, 1e, 1g, 1h, 1i, 1j, 1k, 1l, 1m, 1n
Genotype 2	2, 2a, 2b. 2c, 2d, 2e, 2f, 2i, 2j, 2k, 2l. 2m, 2q, 2r, 2t, 2u
Genotype 3	3, 3a, 3b, 3d, 3e, 3g, 3h. 3i, 3k
Genotype 4	4, 4a, 4b, 4c, 4d, 4f, 4g, 4k, 4l, 4m, 4r, 4o, 4p, 4q, 4r, 4s, 4t, 4v, 4w
Genotype 5	5a
Genotype 6	5, 5a, 5b, 6c, 6d, 6e, 6f, 6g, 6h, 5i, 6j, 6k, 6l, 6m, 6n, 6o, 6p, 6q, 6r, 6s, 6t, 6u. 5v, 6w, 6xa, 6xb, 6xc, 6xd, 6xe
Genotype 7	7a

B

Genotype or subtype	Location of estimated recombination breakpoint(s) Gene(s)	Nucleotide position(s)[a]	Source
1a/1c	E1, E2	1407, 2050	10
1a/1c	Core, E1, E2, NS2, NS3	801, 1261, 2181, 3041, 3781	4
1b/1a	NS5B	8320	47
1b/1a	Core	387	48
2/5[b]	NS2/NS3	3420–3440	49
2b/1a	NS2/NS3	3405–3416	50
2b/1b	NS2/NS3	3443	51
2b/1b	NS2/NS3	3399	52
2b/1b	NS2	3298–3305	9
2b/6w	NS2/NS3	3429	53
2k/1b	NS2/NS3	3175	6
4d/4a	Between E2 and NS5A	Unknown	54
6a/6o	NS5B	8345	11
6e/6h	NS5B	8356	11
6e/6o	NS5B	8358	11
6n/6o	NS5B	8372	11

Table 1. HCV is classified into seven genotypes numbered 1-7 and subtypes by numbers and letters (e.g. 1b). Genotypes 5 and 7 are represented with one subtype 5a and 7a accordingly. **(A)** HCV intergenotypic recombination tends to occur between the structural and **(B)** nonstructural genome regions.

MATERIALS AND METHODS

RNA isolation, detection, sequencing

In this study HCV genotype 2 clinical samples from chronic HCV patients enrolled in national hepatitis C elimination program at Infectious Diseases, AIDS and Clinical Immunology Research Center of Georgia were analyzed. HCV viral load was done by Cobas Taqman with the detection limit of 25 Iu/ml and initial HCV genotyping by INNO LiPA line probe assay. The NGS of HCV conducted at Genome Center of National Center for Disease Control and Public Health (NCDC)/Lugar Center.

RNA library preparation was conducted using NEBNext Ultra RNA Library Prep Kit for Illumina (New England BioLabs). RNA was reverse transcribed, amplified (12 PCR cycles) using indexed primers, and then purified using appropriate volume Ampure XP beads (Beckman Coulter). Libraries were quantified (Qubit HS DNA assay kit; Invitrogen) and assessed for fragment sizes (Bioanalyzer 2100, High Sensitivity kit; Agilent). Metagenomic (host-pathogen) RNA sequencing libraries were sequenced with 500 cycle sequencing kit on the Illumina MiSeq sequencing system with v3 chemistry.

Low-quality bases were trimmed from demultiplexed sequences using CLC Bio workbench 8.5. Human sequences were excluded by mapping reads to the human reference genomes available at NCBI. HCV-derived paired reads were assembled *de novo* into contiges; reads were mapped back to the assembly using CLC Bio Workbench 8.5. Genotypes 2k, 1b and recombinant RF 2k/1b available at NCBI were used for analysis as references.

RESULTS

Reference based analysis of HCV2 specimen using HCV RF1_2k/1b and subtype 2k references

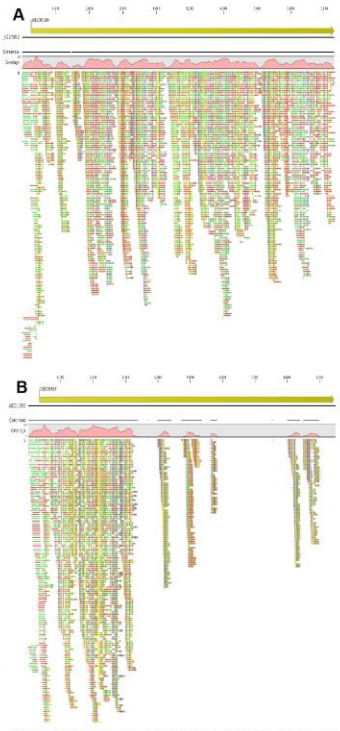

Figure 3. Read mapping analysis of HCV clinical specimen HCV2 for analysis, HCV RF1_2k/1b (accession number JX227952, A), and HCV subtype 2k (accession number AB031663, and B) references were used. With RF1_2k/1b, we got almost 100% coverage, while 2k reference mostly covered the left part of the entire genome, suggesting that we have recombination with 2k subtype.

RESULTS

Read mapping to HCV subtype 1b reference of HCV2 specimen

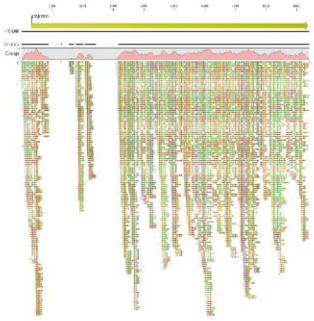

Figure 4. Read mapping analysis of HCV clinical specimen HCV2 for analysis we used 1b (accession number M58335) reference. With 1b reference, most of the reads were aligned with the left part of the genome, suggesting the we have recombination with 1b subtype.

Reference based analysis of HCV3 specimen using HCV RF1_2k/1b and subtypes 2k and 1b references

Figure 5. Read mapping analysis of HCV clinical specimen HCV3 for analysis, HCV RF1_2k/1b (accession number JX227952), subtype 2k (accession number AB031663), and subtype 1b (accession number M58335) references were used. With RF1_2k/1b, we got almost 100% coverage.

SUMMARY

The recombinant strain designated as RF1_2k/1b was first time reported in Russia. Other groups have also described this genotype among patients in Ireland, Estonia, Uzbekistan, Cyprus, France, Germany, and Israel. This strain was later fully sequenced showing recombination breakpoint positions in NS2-NS3 region of HCV genome. National population-based seroprevalence survey conducted in 2015 reported that HCV genotype 2 is the third most common genotype accounting for 24.5% from all HCV infection in the country. These whole genome sequence-based study shows the occurrence of RF1_2k/1b recombinant strain in ethnic Georgian population suggesting that this strain may be circulating in Georgia.

ACKNOWLEDGMENTS

The work was made possible by the support provided by the CDC (Center for Disease Control and Prevention, Atlanta, GA, USA).

15th European Meeting on HIV & Hepatitis - Treatment Strategies & Antiviral Drug Resistance 7 - 9 June 2017 Rome, Italy

HCV GENOTYPE DIVERSITY AMONG PATIENTS TREATED WITH ANTIVIRAL MEDICATIONS IN GEORGIA

N 45

George Kamkamidze, Maia Kajaia, Tinatin Abzianidze, Ana Gamezardashvili, Lasha Gulbiani, Maia Butsashvili

Clinic NeoLab & Health Research Union, Tbilisi, Georgia

INTRODUCTION

Georgia has a high burden of hepatitis C virus (HCV) infection. In 2015, Ministry of health of Georgia with National Center for Disease Control and Public Health (NCDC) and US Centers for Disease Control and Prevention (CDC) conducted the study where a national probability sample of approximately 6000 adults in Georgia was tested for HCV infection, yielding a prevalence estimate of 7% for chronic HCV with an estimated 5.4% of adults currently infected.

On April 28, 2015, in collaboration with CDC, Gilead Sciences and other partners, Georgia launched a comprehensive, national HCV elimination program that included free of charge treatment for all HCV infected persons. If successful, the viral reservoir will be substantially reduced and will dramatically decrease the risk of HCV transmission in the country.

Different studies suggest that antiviral treatment outcome is associated with genotype, treatment regimen and liver fibrosis stage.

Identification of HCV genotypes is important for outbreak investigations as well as for determination of antiviral treatment duration and prognosis of its outcome.

METHODS

The Elimination Program requires participating clinics and treatment sites to collect pre-treatment socio-demographic, clinical and laboratory data, prescribed medications, treatment adherence and monitoring data.

These data are collected using standardized protocols, and entered in information management system STOP-C - Georgia's national electronic treatment database, developed for the HCV elimination program.

Data collected includes HCV genotype and viral load, level of liver fibrosis, risk factors for HCV infection and treatment-related laboratory data, including SVR at week 12-24 after completion of treatment.

The Elimination Program requires all patients to have a pre-treatment FIB4 score, which is computed from age, ALT, AST and platelet count. A FIB4 score is interpreted as follows: below 1.45 (low), 1.45-3.25 (equivocal), and greater than 3.25 (advanced fibrosis). For those in the equivocal range, a liver elastography is conducted and results recorded.

Consecutive patients with HCV infection treated during 2013-2016 in outpatient clinic NeoLab, which represents one of the main sites in Georgia responsible for HCV diagnostics and treatment, have been studied. 5 ml blood from each subject has been collected in EDTA containing tubes. HCV antibodies were defined by ELISA. Samples from antibody-positive subjects were investigated by HCV RNA real-time PCR (Sacace, Italy). Among subjects positive by HCV RNA PCR the HCV genotypes have been determined by HCV genotype real-time PCR assay (Sacace, Italy) or alternatively by Versant HCV Genotype v2 (Siemens, Ghent, Belgium).

RESULTS

3310 participants were involved in study. Among them 431 (13%) were females and 2862 (87%) were males. The mean age was 44.6.

Out of 3310 patients enrolled 859 (30.1%) had genotype 1, 745 (26.1%) had genotype 2 and 1189 (41.6%) had genotype 3. Genotypes 4, 5 and 6 have not been detected in any of our patients.

Significant difference has been observed in the distribution of genotypes between the patients with and without history of intravenous drug use (IDUs).

Among 1101 patients ever using injection drugs the genotype distribution was as follows: genotype 1 – 286 (26.5%), 2 – 299 (27.7%) and 3 – 477 (44.1%), while among 764 non-IDUs the genotype distribution was as follows: genotype 1 – 277 (37.2%), 2 – 203 (27.2%) and 3 – 251 (33.7%), The difference between these two subgroups was statistically significant ($p<0.0001$).

The prevalence of mixed genotypes was significantly higher ($p<0.01$) among IDUs vs. non-IDUs.

CONCLUSIONS

Our study has shown the higher proportion of HCV genotype 3 and presence of mixture of two genotypes among IDUs in comparison with patients with no history of intravenous drug use.

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3. Bouscaillou J, et al. Hepatitis C among people who inject drugs in Tbilisi: an urgent need for prevention and treatment. Int J Drug Policy. 2014; 25(5): 871-878.

ACKNOWLEDGEMENTS

Georgia HCV elimination program is conducted under the leadership from the Georgia Ministry of Labor, Health, and Social Affairs [MoLHSA] with strong stakeholder support, including partnership and technical assistance from CDC, and commitment from Gilead Sciences to donate direct-acting antiviral HCV medications (DAAs).

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15th European Meeting on HIV & Hepatitis – Treatment Strategies & Antiviral Drug Resistance 7 - 9 June 2017 Rome, Italy

HCV TREATMENT OUTCOME AMONG HCV/HBV CO-INFECTED PATIENTS IN GEORGIA

N 87

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INTRODUCTION

Georgia has a high burden of hepatitis C virus (HCV) infection. In 2015, Ministry of health of Georgia with National Center for Disease Control and Public Health (NCDC) and US Centers for Disease Control and Prevention (CDC) conducted the study where a national probability sample of approximately 6000 adults in Georgia was tested for HCV infection, yielding a prevalence estimate of 7% for chronic HCV with an estimated 5.4% of adults currently infected.

On April 28, 2015, in collaboration with CDC, Gilead Sciences and other partners, Georgia launched a comprehensive, national HCV elimination program that included free of charge treatment for all HCV infected persons. If successful, the viral reservoir will be substantially reduced and will dramatically decrease the risk of HCV transmission in the country.

AIM

The aim of this study was to evaluate HCV treatment outcome among patients co-infected with hepatitis B virus (HBV) – HBsAg positive individuals.

METHODS

The Elimination Program requires participating clinics and treatment sites to collect pre-treatment socio-demographic, clinical and laboratory data, prescribed medications, treatment adherence and monitoring data.

These data are collected using standardized protocols, and entered in information management system STOP-C - Georgia's national electronic treatment database, developed for the HCV elimination program.

The Elimination Program requires all patients to have a pre-treatment FIB4 score, which is computed from age, ALT, AST and platelet count. A FIB4 score is interpreted as follows: below 1.45 (low), 1.45-3.25 (equivocal), and greater than 3.25 (advanced fibrosis). For those in the equivocal range, a liver elastography is conducted and results recorded.

Data from one of the major clinical sites in Tbilisi, capital of Georgia, providing HCV treatment within elimination program were analyzed. The database contains sociodemographic, clinical and laboratory data, treatment regimens, and outcomes of treatment.

Different treatment regimens were used: sofosbuvir and ribavirin with or without pegilated interferon and sofosbuvir/ledipasvir combination with or without ribavirin depending on genotype and disease severity.

Treatment outcome was estimated by sustained viral response (SVR) at 12-24 weeks after treatment.

Chi-square test was used to determine the association between SVR and presence of HBsAg at baseline.

RESULTS

The total number of patients during the study period was 1128.

The majority (90.3%) was male and about half of patients were at the age group of 45-60 years.

HBsAg prevalence was higher among males compared to females (2.2% vs 0.5%).

The SVR rate was not significantly different among patients co-infected with active HBV from those having HCV mono-infection (93.1% and 90.7%, respectively, p=0.48).

The prevalence of anti-HBs was 27.9% with only 9 patients (<1%) being vaccinated against HBV infection.

The SVR rate was similar among anti-HBs positive and negative patients (90.4% vs 91.7%, respectively, p=0.31).

CONCLUSIONS

The treatment outcome was similar among patients co-infected with HCV/HBV and mono-infected with HCV treated with DAAs within HCV elimination program in Georgia.

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2. Mitruka K, et al. Launch of a nationwide hepatitis C elimination program – Georgia, April 2015. MMWR Morb Mortal Wkly Rep. 2015; 64(28): 753-757.
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Increased HIV Case Detection through Integration of HIV Testing in Georgian Hepatitis C Elimination Program Screening Activities

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National Center for Disease Control and Public Health of Georgia

Objective

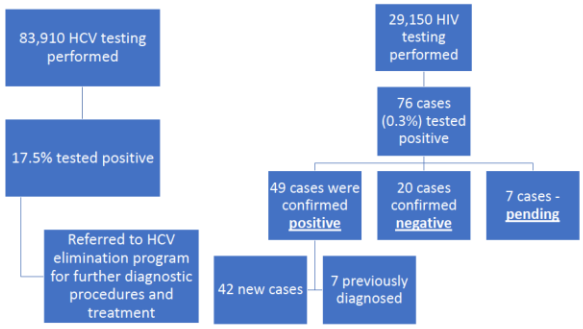
The objective of this programmatic approach was to increase HCV and HIV case detection in general population by combined testing strategies.

Methods

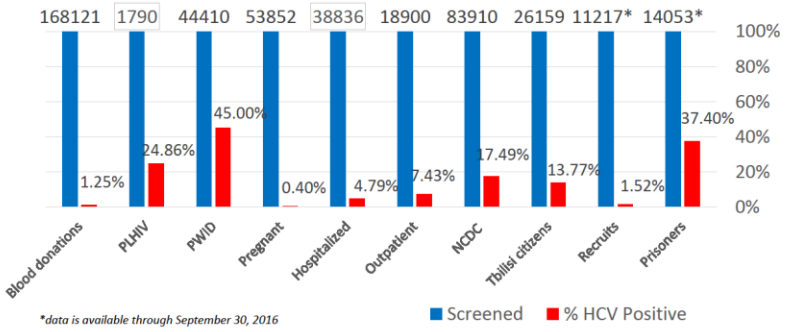
In 2015, Georgia launched unprecedented National Hepatitis C Elimination Program, aimed to dramatically decrease HCV prevalence in the country by 2020 (currently seroprevalence of HCV in Georgia is 7.7% and prevalence of chronic disease is 5.4%) Starting from November, 2015, any citizen of Georgia can obtain free HCV testing at the National Center for Disease Control and Public Health (NCDC) and its regional branches. In addition, every person willing to be tested for HCV was offered free HIV test. Both HIV and HCV testing are performed by rapid immunochromatographic tests. Positive HIV cases were referred to national AIDS center for confirmation.

Results

Through December, 2016, 83,910 voluntary HCV testing and 29,150 voluntary HIV testing were performed at NCDC and its regional network. Rate of positive HCV test result was 17.5%. All positive cases were referred to HCV treatment component of National Elimination Program. Rate of positive HIV test result was 0.26% (76 out of 29,150). Out of 76 persons who tested positive, further diagnostic procedures confirmed HIV in 42 new cases who were then enrolled in the HIV treatment program.



HCV Screening in different programs 2015-2016



**data is available through September 30, 2016*

Conclusions

Free of charge HIV testing was offered only for high-risk groups until 2015. Preliminary results from combined testing indicates that HIV prevalence in general population remains low.

Considering the low prevalence of HIV in Georgia, extra cases found by the combined screening approach was significant contributing factor for early detection of HIV cases. Nationwide HCV elimination program appears to be an effective mechanism that can be used to increase case detection of HIV in Georgia and Integration of HIV testing within HCV screening should be maintained and further expanded.

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HCV Treatment Outcome Among Patients Attending Opioid Substitution Therapy Clinics

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Background

Georgia is the country with high prevalence of HCV (estimated 7% of the adult population has antibodies to HCV). One of the main routes of infection transmission is injection drug use. Different studies show up to 92% seroprevalence among Georgian PWIDs. In 2015 Georgian Government started HCV elimination program with support of international partners. The aim of the study was to evaluate treatment outcome among patients receiving opioid substitution therapy (OST).

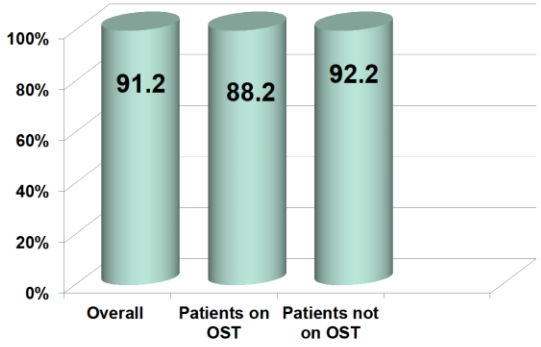
Methods

Patients with history of injection drug use and treated within HCV elimination program with direct acting antiviral agents with or without pegilated interferon were included in the study. Consecutive patients reporting ever using injection drugs treated in outpatient clinic NeoLab, which represents one of the main HCV treatment sites in Georgia responsible for HCV diagnostics and treatment, have been studied. The analysis was conducted for the patients who completed the treatment course and have their sustained viral response (SVR) data available at 12-24 weeks after the treatment.

Results

Overall, 465 patients with above described criteria were enrolled in the study. Out of these, majority were males (99.1%) with age range of 22-79 years (mean age was 45.3 years). 102 Patients reported being on OST. Overall SVR rate was 91.2%. By bivariate analysis there was no significant difference between SVR rates among patients being on OST and never receiving OST services (88.2% and 92%, respectively, P=0.16).

SVR rate among PWIDs treated within HCV elimination program



Conclusions

The study has shown that treatment outcome is similar among patients attending OST clinics with other patients with history of drug use.

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Hepatitis C elimination program in Georgia

David Sergeenko[1], Valeri Kvaratskhelia[1], Amiran Gamkrelidze[2], Irina Tskhomelidze[1], Davit Baliashvili[2], Maia Tsereteli[2], Tengiz Tsertsvadze[3], Lia Gvinjilia[4], Juliette Morgan[5], Muazzam Nasrullah[6], Maia Butsashvili[7], Lali Sharvadze[8], David Metreveli[9], Francisco Averhoff[6]

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Background

Georgia, a country in the Caucasus region of Eurasia, considering serosurvey data (performed with technical support of US CDC) has a high prevalence of hepatitis C virus (HCV) infection.

Characteristic	n	%	Estimated # nationwide ≥18 years
Anti-HCV+	425	7.7%	208,800
HCV RNA+	311	5.4%	150,300

In April 2015, Georgia government announced HCV as a priority and committed to eliminate the disease by 2020 and launched the unprecedented Hepatitis C Elimination Program, initially focused on treating HCV-infected persons with severe liver disease using curative regimens based on new direct-acting antivirals (DAAs). Starting in June, 2016, inclusion criteria were removed, expanding enrollment eligibility to include patients regardless of disease stage.

Why Georgia?

Features that made Georgia an ideal setting for eliminating HCV:

- High prevalence
- Small population
- Political will
- Diagnostic and human capacity
- Close partnership with US CDC and other organizations

Substantial progress has been made to eliminate HCV infection in Georgia, and the country has demonstrated the ability for rapidly scale up of care and treatment services. To achieve elimination, there still some challenges remain, including increasing access to care and treatment services and implementing a comprehensive approach to prevention and control of HCV infection.
Georgia's HCV elimination program could provide lessons for future programs to control HCV infection worldwide, particularly as treatment becomes more affordable and more countries seek to provide care and treatment services.

History and Overview of the HCV Elimination Program 2014-2016

2014
Negotiations with US CDC, Gilead Sciences Inc. and other partners

1st National Workshop on Hepatitis C and Establishment of National Committee for HCV

Treatment with "Sofosbuvir" based regimens

2015 (April)
Approval of HCV elimination action plan and Launch of state program

2015 (July)

2015 (Nov)
1st TAG

2015 4th (Quarter)
Assessment of electronic database "Stop C"

2016 (1 Quarter)
Grant for development of new electronic program

First stock of Ledipasvir/Sofobusbuvir

2016 (April)
Side session for Georgia at "EASL"
Long term agreement between Company Gilead Sciences, In.

2016 (June)
New "Elimination C" program was launched

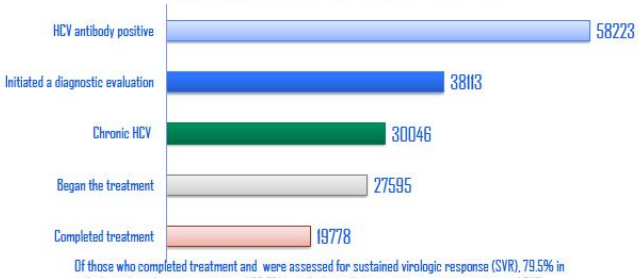
Eligibility criteria were removed

2016 (October)
2nd TAG
Establishment of Georgia HCV Elimination Scientific Committee

2016
4th National Hepatitis C Elimination Workshop

"EASL" Special session

Care cascade April 2015-December 2016



Of those who completed treatment and were assessed for sustained virologic response (SVR), 79.5% in sofosbuvir-based regimen group and 98.2% in sofosbuvir/ledipasvir treatment group attained SVR

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[2] National Center for Disease Control and Public Health of Georgia
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[4] CDC Foundation
[5] Global Disease Detection, Division of Global Health Protection, South Caucasus CDC Office, Tbilisi, Georgia
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Conflicts of Interests

No conflicts of interest to report.

POSTER REFERENCE NUMBER: 161

Hepatitis C Screening and Linkage to Care as Part of a Nationwide Elimination Program in the Country of Georgia

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BACKGROUND

Georgia has an estimated 150,000 individuals (5.4% of the adult population) infected with hepatitis C virus (HCV).[1] In 2015, in collaboration with CDC and other partners, the government of Georgia embarked on an ambitious national program to eliminate HCV by 2020.[2] The program initially focused on providing HCV treatment to infected persons with advanced liver disease, but included treatment for all beginning in July 2016. Achieving the 2020 elimination target of 90% reduction in prevalence will require high quality HCV screening and linkage to care services.[2,3]

We aimed to characterize screening activities, including timing and location of screening, the process for linkage to the national treatment program, and how data are collected for monitoring screening activities.

METHODS

We interviewed key stakeholders, including public health officials and program administrators to identify ongoing screening activities during 2015-2016. We conducted site visits at each of the screening programs and discussed screening and linkage to care reporting practices. Additionally, we explored each program's data collection and management process and obtained data on the number and results of rapid HCV antibody tests by screening program.

RESULTS

During January 2015–December 2016, 472,890 HCV screening tests were performed, of which 11% were positive. Results of the screening tests by program are shown in Figure 1. Of note, the highest percentage of positive individuals were identified through screening at the Georgian Harm Reduction Network (GHRN), which serves primarily individuals who inject drugs. Screening in inpatient and outpatient facilities did not begin until November 2016, so data included in Figure 1 for these settings represents only two months of data.

Number of screening sites in the program in each included: blood banks (N=17), National Center for Disease Control and Public Health (NCDC) headquarters and NCDC regional centers (N=9), antenatal clinics (N=296), the GHRN (N=14 stationary and six mobile vans), screening centers operated by the City of Tbilisi (N=2), prisons (N=4), military accession centers (N=1), the government HCV management center in Tbilisi (N=1), and the national HIV/AIDS treatment center (N=1), inpatient facilities (N=273), and outpatient service providers (N=542).

We identified ideal steps for patient and data from for HCV screening, shown in Figure 2. With the exception of the HCV Management Center, the other screening programs did not have the capacity to directly link HCV-positive individuals with care, or enter their information in the national treatment database to allow follow-up. As an example, Figure 3 shows the actual flow of patients and data through the GHRN screening program.

CONCLUSIONS

There are several programs conducting screening for HCV in Georgia, resulting in a large number of tests with a high aggregate proportion of positive results. With the exception of one program, the HCV Management Center, during 2015 and 2016 there was no system in place to monitor the effectiveness of these programs and ensure linkage to care for those testing positive. The development of such a system, which is ongoing, is critical to reach the HCV elimination targets set by the country.

RESULTS

Figure 1. Unique Anti-HCV Screening Tests and Positive Results, by Screening Program — January 2015-December 2016

* Inpatient and outpatient data from November and December 2016 only.

Figure 2. Ideal flow of patients and data through the HCV screening in Georgia.

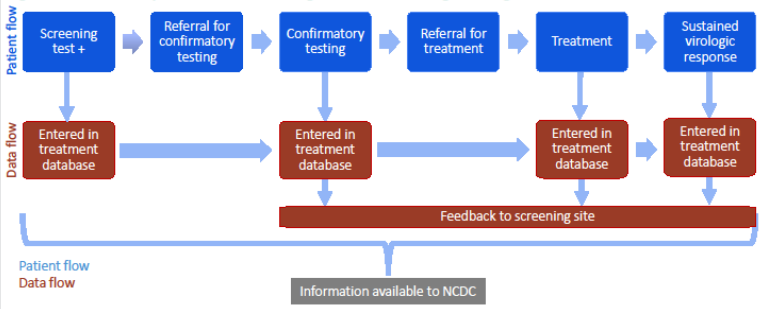
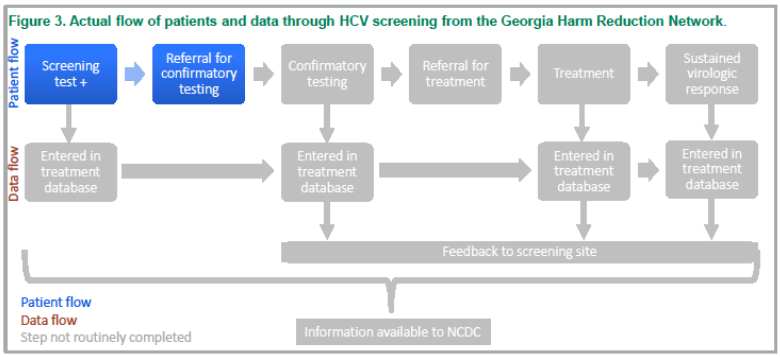


Figure 3. Actual flow of patients and data through HCV screening from the Georgia Harm Reduction Network.



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CONFLICTS OF INTEREST

No conflicts of interest to report.

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Feasibility of Measuring Hepatitis C Virus (HCV) Core Antigen to Monitor Success of Direct Acting Antiviral (DAA) Treatment of Hepatitis C

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BACKGROUND

- In light of recent advances in HCV therapy, simplification of diagnosis confirmation, pre- treatment diagnostic workup and treatment monitoring is required to ensure broad access to interferon-free therapies.
- HCV core antigen (HCVcAg) is a serologic marker of HCV infection highly concordant with HCV RNA testing, the current standard of care.
- The aim of this study was to determine percent agreement between HCVcAg test and HCV RNA in the monitoring of patients on DAA therapy in an ongoing HCV elimination program in the country of Georgia.

METHODS

- A total of 976 samples were collected at Baseline, Week 4, End of Treatment (EOT), and 12 weeks post treatment by three provider clinics in Georgia.
- HCV RNA and genotype testing was conducted at the clinics.
- Specimens were tested with the ARCHITECT HCVcAg assay at National Center for Disease Control and Public Prevention.
- Percent agreement between HCVcAg and HCV RNA results was calculated based on qualitative results.

RESULTS

- The agreement between HCVcAg and HCV RNA in the Pre-Treatment specimens was 98.3% (414/421) (Figure 1).
- The agreement between specimens from the 4 week monitoring point was 96.5% (334/346) (Figure 2).
- At EOT and 12 weeks post treatment, the agreement between HCVcAg and HCV RNA was 98.9% (186/188) (Figure 3) and 100% (21/21), respectively, (Figure 4).

Figure 1.

HCV core Ag and HCV RNA Agreement in Pre-treatment Samples

		HCV RNA		Total
		Positive	Negative	
HCV core Ag	Positive	414	0	414
	Negative	7	0	7
Total		421	0	421

Percent Agreement: 98.3%

Figure 2.

HCV core Ag and HCV RNA Agreement in Week 4 Treatment Samples

		HCV RNA		Total
		Positive	Negative	
HCV core Ag	Positive	1	13	14
	Negative	1	331	332
Total		2	344	346

Percent Agreement: 95.9%

Figure 3

HCV core Ag and HCV RNA Agreement in EOT Samples

		HCV RNA		Total
		Positive	Negative	
HCV core Ag	Positive	1	1	2
	Negative	1	185	186
Total		2	186	188

Percent Agreement: 98.9%

Figure 4

HCV core Ag and HCV RNA Agreement in SVR Samples

		HCV RNA		Total
		Positive	Negative	
HCV core Ag	Positive	2	0	2
	Negative	0	19	9
Total		2	19	21

Percent Agreement: 100%

CONCLUSIONS

- This study indicates high agreement (≥98%) between HCVcAg and HCV RNA in the Pre-Treatment, EOT and 12 week post treatment specimens among patients treated with DAA.
- The observed pre-treatment agreement in this study is similar to those we reported previously.
- These data suggest that the HCVcAg can be used as an alternative to HCV RNA for monitoring the DAA treatment of hepatitis C with the potential to reduce the overall cost of diagnostics.

REFERENCES

- Cloherty G. et al., **Role of Serologic and Molecular Diagnostic Assays in Identification and Management of Hepatitis C Virus Infection.** J Clin Microbiol 54:000–000. doi:10.1128/JCM.02407-15

CONFLICTS OF INTEREST

- In relation to this presentation, I declare that there are no conflicts of interest, except G. Cloherty: Assc. Research Fellow, Volwiler Society; Head Infectious Disease Research. ABBOTT Diagnostics

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Disparate Genotyping Results Obtained Between A Commercially Available Assay And Sanger Sequencing Of Different Genomic Regions Of Hepatitis C Virus

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ABSTRACT

Background: The government of Georgia has engaged in a national elimination program for hepatitis C virus (HCV). High rates of the HCV recombinant genotype 2k/1b, which has suboptimal response rates to genotype 2 treatment regimens, have been reported in Georgia. Reliable and cost-effective diagnostics for HCV genotyping are required to ensure optimal treatment strategies.

Materials & Methods: A cross-sectional, nationally representative serosurvey of 7,000 individuals aged ≥18 years was conducted in Georgia in 2015 using a US Centers for Disease Control and Prevention (CDC) testing algorithm. HCV RNA was detected in 311 samples, 300 were genotyped at the National Center for Disease Control (NCDC) in Tbilisi, Georgia, using the commercially available HCV Real-TM Genotype kit (Sacace Biotechnologies, Srl., Como, Italy), henceforth referred to as the Sacace 5'-UTR assay. External quality control of all samples was conducted at US CDC which included HCV RNA quantitation and sequencing of the HCV NS5b region, which remains the gold standard of HCV genotyping.

Results: Concordant results between the genotypes determined by the Sacace 5'-UTR assay and NS5b sequencing were found in 246 samples. The recombinant 2k/1b genotype was identified by NS5b sequencing in 6 (4.6%) samples genotyped as 1b and in 33 (47.8%) samples genotyped as 2 by the Sacace 5'-UTR assay. All 12 (17.4%) samples genotyped as 2 by the Sacace 5'-UTR assay were determined to be genotype 1b by NS5b sequencing and 3 samples unable to be genotyped by the Sacace 5'-UTR assay were resolved by NS5b sequencing as genotype 3a in 1 and 2k/1b in 2 samples.

Conclusions: These data reveal a significant limitation of a commercially available HCV genotyping method which targets the 5'-UTR. Since pan-genotypic treatment regimens are not yet the standard of care, incorrect genotyping may have implications for achieving sustained virologic response in patients treated with genotype-specific regimens.

BACKGROUND

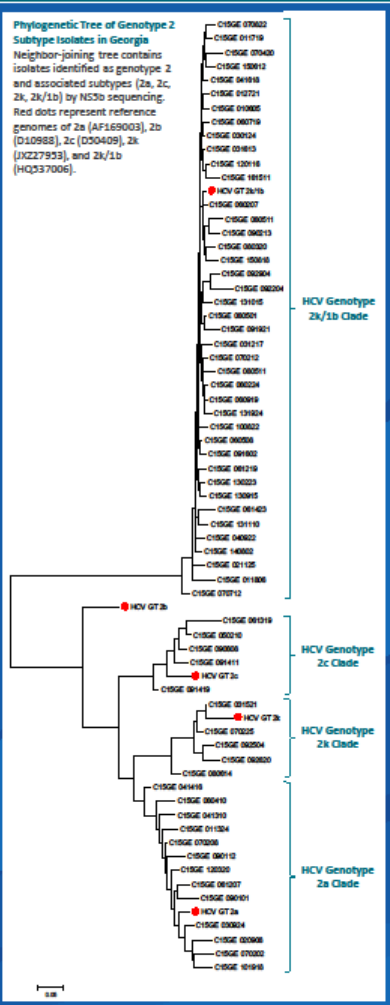
Persons infected with HCV recombinant strain 2k/1b treated as a genotype 2 infection have suboptimal response rates, whereas regimens used for genotype 1 treatment have shown to be more effective. With an HCV prevalence of 7.7%, and a uniquely high rate of recombinant strain 2k/1b prevalence, Georgia has one of the highest burdens of HCV in the world. In response to this epidemic, the government of Georgia plans to reduce infection prevalence of HCV by 90% by 2020 through implementation of their Strategic Plan for the Elimination of Hepatitis C Virus in partnership with CDC, WHO, and other entities. This strategy requires reliable and cost-effective diagnostics including HCV genotyping in order to ensure optimal treatment options for all HCV infected persons.

METHODS

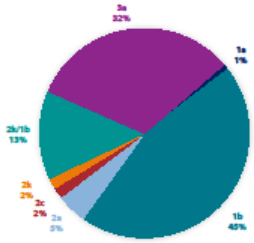
- Methods at NCDC (2015)
  - Cross-sectional, nationally representative serosurvey
    - 7,000 individuals
    - ≥18 years old
    - Stratified, multi-stage cluster design
  - Serum specimens
    - N = 6010
    - 425 anti-HCV positive by ELISA (DiaPro, Milan, Italy);
    - 300 HCV RNA positive (HCV Real-TM Genotype kit, Sacace Biotechnologies, Srl., Como, Italy) targeting 5'-UTR region
- Methods at CDC (2016)
  - HCV RNA quantification
    - qRT-PCR CDC LDT[1]
  - HCV NS5b sequencing[2]
  - Phylogenetic analysis conducted using MEGA software

Phylogenetic Tree of Genotype 2 Subtype Isolates in Georgia

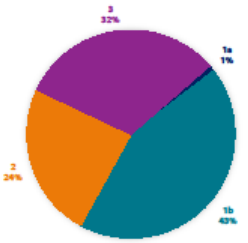
Neighbor-joining tree contains isolates identified as genotype 2 and associated subtypes (2a, 2c, 2k, 2k/1b) by NS5b sequencing. Red dots represent reference genomes of 2a (AF169003), 2b (D10988), 2c (D50409), 2k (JX227953), and 2k/1b (HQ537006).



Genotypic Distribution of Hepatitis C Virus in Georgia by NS5b Sequencing



Genotypic Distribution of Hepatitis C Virus in Georgia by Sacace 5'-UTR Assay



Genotype by Sacace 5'-UTR assay	Genotype by NS5b sequencing								
		1a	1b	2k/1b	2a	2c	2k	3a	Total
	1a	3							3
	1b		124	6					130
	2		12	33	14	5	5		69
	3							95	95
	3/2			1					1
	NG			1				1	2
	Total	3	136	41	14	5	5	96	300

Genotyping Concordance/Discordance Results between 5'-UTR genotyping and NS5b sequencing

Rows represent genotype determination by Sacace 5'-UTR assay. Columns represent genotype determination through NS5b sequencing. NG = not genotyped.

RESULTS

- HCV genotyping concordance between methods in 246 samples:
  - 1a = 3
  - 1b = 124
  - 2a = 14, 2c = 5, 2k = 5
  - 3 = 95
- HCV genotyping discordance between methods in 54 samples:
  - 2k/1b = 41
  - 1b = 12
  - 3a = 1
- Total number of the circulating recombinant form 2k/1b among all HCV RNA positive persons was 41 (13.7%)

CONCLUSIONS

- The sequence data obtained from the 1st nationally representative survey may serve as a reference database for disease surveillance and transmission studies in Georgia.
- 12 HCV genotype 2 isolates identified by the Sacace 5'-UTR assay, later identified as HCV genotype 1b by NS5b sequencing could represent 2k/1b recombinants.
- Data reveal a significant limitation of the Sacace 5'-UTR assay, by incorrectly genotyping patients infected with 2k/1b recombinant strains as genotype 2.
  - Pan-genotypic treatment regimens are not yet standard of care, incorrect genotyping may have implications for achieving sustained virologic response in patients treated with genotype-specific regimens.

CONTACT INFO

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National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

Division of Viral Hepatitis

Oral Presentations

1. HCV Infection in Georgia - Current Status and Future Action Plans, David Metreveli

   Presented at HCV Infection and Disease & Recent Advances in Liver Diseases, 2015; New Delhi, India
2. HCV Elimination in Georgia, Valeri Kvaratskhelia

   Presented at EASL Special Meeting, 2015; Austria, Vienna
3. National-level Elimination of Hepatitis C: The Republic of Georgia Experience, Valeri Kvaratskhelia

   Presented at AASLD, 2015; San Francisco, California, US
4. Progress Towards Hepatitis C Elimination in Georgia, David Sergeenko

   Presented at World Hepatitis Summit, 2015; Glasgow, Scotland
5. Hepatitis C Elimination in Georgia, Amiran Gamkrelidze

   Presented at World Hepatitis Summit, 2015; Glasgow, Scotland
6. Hepatitis C Elimination in Georgia, Maia Tsereteli

   Presented at Viral Hepatitis Prevention Board Meeting, 2015; London, UK
7. Panel Discussion on HCV Treatment in Developing Countries, Maia Butsashvili

   Presented at International Network on Hepatitis among Substance Users Meeting, 2015; Sidney, Australia
8. Ensuring Quality of Laboratory Diagnostic in Georgia, Jan Drobeniuc
   Presented at the 3rd National Hepatitis C Elimination Workshop, 2016, Tbilisi, Georgia
9. Abbott HCV core Ag and HCV RNA Comparison Study, Nazibrola Chitadze
   Presented at the 3rd National Hepatitis C Elimination Workshop, 2016, Tbilisi, Georgia
10. National Hepatitis C Elimination Program of Georgia, Tengiz Tsertsvadze

    Presented at Paris Hepatitis Conference, 2016; Paris, France
11. HCV Elimination Program in Georgia, Maia Butsashvili

    Presented at International Network on Hepatitis among Substance Users Meeting, 2016; Oslo, Norway
12. Care and treatment component of the national hepatitis C elimination program: Outcomes of phase I and future directions, Tengiz Tsertsvadze

    Presented at EASL, 2016; Barcelona, Spain
13. HCV Elimination in Georgia: developing an evidence-based Elimination Plan, Juliette Morgan

    Presented at EASL Georgia Side Meeting, 2016; Barcelona, Spain
14. Burden of HCV and Evolution of Elimination Program in Georgia, Amiran Gamkrelidze

    Presented at EASL Georgia Side Meeting, 2016; Barcelona, Spain
15. HCV Elimination in Georgia: Progress and Challenges, Francisco Averhoff

    Presented at EASL Georgia Side Meeting, 2016; Barcelona, Spain
16. Evaluation of HCV program in Georgian Prisons, Maia Butsashvili

Presented at EASL WHO Session, 2016; Barcelona, Spain

17. HCV Treatment among PWID, Maia Butsashvili

    Presented at EASL Georgia Side Meeting, 2016; Barcelona, Spain
18. Surveillance of Hepatitis C in Georgia, Maia Tsereteli

    Presented at WHO Regional Technical Consultation on Dissemination of the WHO guidelines on HIV and Viral hepatitis for 12 Eastern European and Central Asian Countries, 2016
19. Assuring the Quality of HCV Diagnostics in Georgia though Establishing a National EQA Program, Beth Skaggs
    Presented at the 4th National Hepatitis C Elimination Workshop, 2017, Tbilisi, Georgia
20. Feasibility of HCV core Ag for Monitoring in DAA Treatment, Nazibrola Chitadze.
    Presented at the 4th National Hepatitis C Elimination Workshop, 2017, Tbilisi, Georgia
21. Architect HCV core Ag Assay- The Way Forward, Maia Alkhazashvili
    Presented at the 4th National Hepatitis C Elimination Workshop, 2017, Tbilisi, Georgia
22. Regression of liver fibrosis over a 24-week period after completing direct acting antiviral (DAA) therapy in patients with chronic hepatitis C receiving care within the national hepatitis C elimination program in Georgia, Ekaterine Dolmazashvili
    Presented at 13th International workshop on co-infection -HIV-Hepatitis, 2017; Lisbon, Portugal

23. National Hepatitis C Elimination Program of Georgia, Tengiz Tsertsvadze

    Presented at Paris Hepatology Conference, 2017; Paris, France
24. Hepatitis C Elimination Program in Georgia, Amiran Gamkrelidze

    Presented at EASL FIND Side Meeting, 2017; Amsterdam, Netherlands
25. Burden of HCV and Use of National Seroprevalence Survey Findings for Developing Effective Screening Programs in Georgia

    Presented at EASL, 2017; Amsterdam, Netherlands
26. History and Overview of the HCV Elimination Program, David Sergeenko

    Presented at EASL Georgia Special Session, 2017; Amsterdam, Netherlands
27. The Vital Role Of Laboratory Diagnostic Services the HCV Elimination Program, Jan Drobeniuc

    Presented at EASL Georgia Special Session, 2017; Amsterdam, Netherlands
28. HCV treatment among PWID in Georgia, Maia Butsashvili

    Presented at EASL Georgia Special Session, 2017; Amsterdam, Netherlands
29. The Importance of Prevention, Care and Treatment of HCV Among Injection Drug Users, Maia Butsashvili

    Presented at EASL, 2017; Amsterdam, Netherlands
30. Progress in HCV Care and Treatment: The Cornerstone of the Elimination Program, Tengiz Tsertsvadze Presented at EASL, 2017; Amsterdam, Netherlands

31. History and Overview of the HCV Elimination Program, David Sergeenko

    Presented at Carter Center, 2017; Atlanta, GA, USA
32. HCV Situation in Georgia and Overview of HCV Research Experience, Tengiz Tsertsvadze

Presented at National Institute of Allergy and Infectious Diseases of National Institute of Health, 2017

33. US-Georgia Collaboration in HIV/AIDS and Hepatitis C, Tengiz Tsertsvadze

    Presented at National Institute of Allergy and Infectious Diseases of National Institute of Health, 2017

34. HCV elimination program successes and challenges, Maia Butsashvili

    Presented at Australasian Viral Hepatitis Elimination Conference, 2017; Cairns, Australia

35. Ledipasvir/Sofosbuvir plus Ribavirin as highly effective regimen for RF1_2k/1b patients within Georgian national hepatitis C elimination program, Marika Karchava

    Presented at AASLD, 2017; Washington, DC, USA

36. HCV Elimination Program in Georgia, Amiran Gamkrelidze

    Presented at 7th International Tehran Hepatitis Conference, 2017; Tehran, Iran

37. The Birth of the HCV Elimination in Georgia: the focus on strategic information, Amiran Gamkrelidze Presented at World Hepatitis Summit, 2017; Sao Paulo, Brazil

38. Assessing the burden of disease: the planning, conduct, and use of a National Seroprevalence Survey, Amiran Gamkrelidze

    Presented at World Hepatitis Summit, 2017; Sao Paulo, Brazil

39. Monitoring the care cascade: developing a robust screening and treatment information system, Lia Gvinjilia

    Presented at World Hepatitis Summit, 2017; Sao Paulo, Brazil

40. The critical role of research in HCV elimination, Tatia Kuchuloria

    Presented at World Hepatitis Summit, 2017; Sao Paulo, Brazil

41. Modelling the epidemic to guide interventions, Peter Vickerman

    Presented at World Hepatitis Summit, 2017; Sao Paulo, Brazil

Appendix 5

Publications Related to the HCV Elimination Program

Abstracts

1. **Impact of hepatitis C virus recombinant form RF1_2k/1b on treatment outcomes within the Georgian national hepatitis C elimination program**
   Hepatology Research. 2017 (Epub ahead of print)
   Authors:
   Karchava M[1,2], Chkhartishvili N[1], Sharvadze L[1,2,3], Abutidze A[1,2], Dvali N[1], Gatserelia L[1,2], Dzigua L[1], Bolokadze N[1,3], Dolmazashvili E[1,2,3], Kotorashvili A[4], Imnadze P[4], Gamkrelidze A[4], Tsertsvadze T[1,2,3]
   1 Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia; 2 Hepatology Clinic- Hepa, Tbilisi, Georgia; 3 Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia; 4 National Center for Diseases Control and Public Health, Tbilisi, Georgia.
   Abstract Aim:
   Hepatitis C virus (HCV) recombinant form RF1_2k/1b is common in ethnic Georgians. This chimera virus contains genomic fragments of genotype 2 and genotype 1 and is misclassified as genotype 2 by standard genotyping. We aimed to identify RF1_2k/1b strains among genotype 2 patients and assess its impact on treatment outcomes.
   Methods:
   The study included 148 patients with HCV genotype 2 as determined by 5-untranslated region/core genotyping assay. RF1_2k/1b was identified by sequencing the non-structural protein 5B region. Patients were treated within the national hepatitis C elimination program with sofosbuvir/ribavirin (SOF/RBV), interferon (IFN)/SOF/RBV, or ledipasvir (LDV)/SOF/RBV.
   Results:
   Of 148 patients, 103 (69.5%) had RF1_ 2k/1b. Sustained virologic response (SVR) data was available for 136 patients (RF1_ 2k/1b, n = 103; genotype 2, n = 33). Sustained virologic response was achieved in more genotype 2 patient than in RF1_2k/1b patients (97.0% vs. 76.7%, P = 0.009). Twelve weeks of LDV/SOF/RBV treatment was highly effective (100% SVR) in both genotypes. Among RF1_2k/1b patients, LDV/SOF/RBV for 12 weeks was superior (100% SVR) to SOF/RBV for 12 weeks (56.4%, P < 0.0001) or 20 weeks (79.2%, P = 0.05). Twelve weeks of IFN/SOF/RBV also showed better response than SOF/RBV for 12 weeks (88.9% vs. 56.4%, P = 0.02) in these patients.
   Conclusions:
   High prevalence of the RF1_2k/1b strain can significantly affect treatment outcomes. Treatment with IFN/SOF/RBV and especially LDV/SOF/RBV ensured significantly higher SVR in patients infected with RF1_2k/1b strain compared to standard HCV genotype 2 treatments with SOF/RBV. There is a need to reassess existing methods for the management of HCV genotype 2 infections, especially in areas with high prevalence of the RF1_2k/1b strain.

2. **Comparative Study of Fib-4 Index and Transient Elastography among Patients with Chronic Hepatitis C Virus Infection in the Country of Georgia**

Georgian Medical News. 2017 March;(264):81-86

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Abstract:

Liver biopsy remains the reference standard for fibrosis staging. However, it has several limitations, which have led to the development of non-invasive methods. We evaluated liver fibrosis severity among HCV infected patients by comparing transient elastography (TE) and FIB-4 index. Retrospective study was conducted. Clinical data for 750 patients were obtained. The mean age of the study population was 51 years; 595 (79.3%) were male and 155 (20.7%) were female. TE and tests on biological samples were performed within one-week timeframe. Additional analyses of prothrombin index, albumin concentration, splenomegaly on abdominal ultrasound and esophageal varices on upper gastrointestinal endoscopy were performed among selected patients. Comparable results were observed among 534 patients (71.2%). FIB-4<1.45 had a negative predictive value of 89% to exclude significant fibrosis and FIB-4>3.25 had a positive predictive value of 100 % to confirm the existence of significant fibrosis. Inconclusive FIB-4 score was obtained in 170 (22.7%) patients. Of them 127 (74.7%) had significant fibrosis (F3-F4) by TE. Discordant results (FIB-4 <1.45 and Liver Stiffness Measurement (LSM) >9.5 kpa) were observed in 46 (6.1%) of patients. Low prothrombin index, low albumin concentration, splenomegaly and esophageal varices were significantly (p<0.001) correlated with TE results. Discrepancy showing high FIB-4 score and low LSM was not observed in our cohort. There was a good correlation between TE and FIB-4 score. FIB-4 could rapidly replace expensive methods to assess liver fibrosis severity in some scenarios. However, our study demonstrated superiority of TE. LSM correlated better with indirect markers of significant fibrosis.

3. **Access to hepatitis C treatment for people who inject drugs in low and middle income settings: Evidence from 5 countries in Eastern Europe and Asia**

International Journal of Drug Policy. 2015 November;26(11):1081-7

Authors:

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BACKGROUND:

People who inject drugs (PWID) are disproportionately affected by the hepatitis C (HCV) epidemic. Of the estimated 16 million PWID worldwide, approximately 8 million live with chronic HCV, and around 26% and 23% of the global HCV infections among PWID occur in East/Southeast Asia and Eastern Europe respectively. Globally, few PWID have access to treatment for HCV.

METHODS:

We conducted a systematic literature review and internet survey in 2014 to document the

burden of disease, access to diagnosis and treatment and the existence of national policy and treatment guidelines for HCV. We included Georgia, Russia, Ukraine, Myanmar and Indonesia as countries with injection drug use epidemics.

FINDINGS:

HCV antibody prevalence among the general population ranged from 0.80% in Indonesia to 5% in Georgia, and among PWID from 48.1% in Myanmar to 92% in Georgia. PWID carried a significant burden of disease, ranging from 2.7% in Indonesia to 40.4% in Russia. Yearly treatment uptake was under 1% for the general population and PWID in all countries. Diagnostic tools and disease staging investigations as well as pegylated interferon/ribavirin treatment were available at a range of prices. Despite policy and treatment protocols for HCV in the majority of countries, strategies focusing on PWID were largely absent.

CONCLUSION:

PWID are a priority group for treatment, and access to treatment should be based on sound national policy, accessible public treatment programmes and functional surveillance systems.

4. **Identification of hepatitis C virus 2k/1b intergenotypic Recombinants in Georgia**
Liver International. 2017, August 7 (Epub ahead of print)
Authors:
Zakalashvili M[1], Zarkua J[1], Weizenegger M[2], Bartel J[2], Raabe M[2], Zangurashvili L[1], Kankia N[1], Jashiashvili N[1], Lomidze M[1], Telia T[1], Kerashvili V[1], Zhamutashvili M[1], Abramishvili N[1], Hedskog C[3], Chodavarapu K[3], Brainard DM[3], McHutchison JG[3], Mo H[3], Svarovskaia E[3], Gish RG[4], Rtskhiladze I[1], Metreveli D[1]

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BACKGROUND AND AIMS:

This study aimed to evaluate the prevalence of the hepatitis C virus intergenotype recombinant strain RF1_2k/1b in Georgia, confirm viral recombination by full genome sequencing, and determine a genetic relationship with previously described recombinant hepatitis C viruses.

METHODS:

We retrospectively analysed data from 1421 Georgian patients with chronic hepatitis C. Genotyping was performed with the INNO-LiPA VERSANT HCV Genotype 2.0 Assay.

RESULTS:

Virus isolates were assigned to nonspecific hepatitis C genotypes 2a/2c (n = 387) as performed by sequencing of core and NS5B genes. Subsequently, sequencing results classified the core region as genotype 2k and the NS5B region as genotype 1b for 72% (n = 280) of genotype 2 patients, corresponding to 19.7% of hepatitis C patients in Georgia. Eight samples were randomly selected for full genome sequencing which was successful in 7 of 8 samples. Analysis of the generated consensus sequences confirmed that all 7 viruses were 2k/1b recombinants, with the recombination breakpoint located within 73-77 amino acids before the NS2-NS3 junction, similar to the previously described RF1_2k/1b virus. Phylogenetic analysis revealed clustering of the Georgian 2k/1b viruses and RF1_2k/1b, suggesting that they are genetically related.

CONCLUSIONS:
The 19.7% prevalence of RF1_2k/1b in Georgia patients is far higher than has generally been reported to date worldwide. Identification of recombinants in low income countries with a high prevalence of HCV infection might be reasonable for choosing the most cost-effective treatment regimens.

5. **Regression of liver fibrosis over a 24-week period after completing direct-acting antiviral therapy in patients with chronic hepatitis C receiving care within the national hepatitis C elimination program in Georgia: results of hepatology clinic HEPA experience**
European Journal of Gastroenterology and Hepatology. 2017 November;29(11):1223-1230
Authors:
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1 aHepatology Clinic 'HEPA' bInfectious Diseases, AIDS and Clinical Immunology Research Center cIvane Javakhishvili Tbilisi State University, Tbilisi, Georgia.
OBJECTIVE:
We assessed the impact of direct-acting antiviral (DAA) therapy on liver fibrosis regression measured by transient elastography (TE) in patients with chronic hepatitis C virus (HCV) infection.
PATIENTS AND METHODS:
A prospective cohort study was carried out in HCV monoinfected patients with advanced liver fibrosis or cirrhosis receiving interferon (IFN)-containing or IFN-free DAA therapy. Liver stiffness (LS) score more than 14.5 kPa indicated LS-defined cirrhosis. The primary outcome was improvement in liver stiffness measurement (LSM) at week 24 after treatment measured as (a) decrease in the median LS compared with baseline and (b) at least a 20% decrease in LSM compared with baseline. A multivariate logistic regression model was utilized to identify the factors associated with at least a 20% improvement in LSM.
RESULTS:
Of a total of 304 patients, 172 (56.6%) had LS-defined cirrhosis before treatment. LSM decreased from the baseline median value of 16.9 (interquartile range: 11.8-27.7) kPa to a post-treatment week 24 score of 11.9 (interquartile range: 8.2-20.9) kPa (P<0.0001). Of a total of 304 patients, 198 (65.1%) achieved at least a 20% reduction in LS. In multivariate logistic regression analysis, sustained virological response (SVR) was associated significantly with this reduction (P<0.0001). The addition of IFN to the treatment regimen had no impact on the decrease in LSM. Despite decreasing baseline LSM, more than half of the LS-defined cirrhotic patients remained cirrhotic at week 24 after treatment.
CONCLUSION:
In patients with advanced fibrosis, pretreatment LS significantly reduced during DAA therapy. SVR was the only independent factor associated with the regression in LSM. However, irrespective of achieving SVR, liver damage still persisted in a substantial proportion of patients. Thus, early treatment of HCV-infected patients can significantly prevent residual liver damage , irrespective of achieving SVR, liver damage still persisted in a substantial proportion of patients. Thus, early treatment of HCV-infected patients can significantly prevent residual liver damage.

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World Hepatitis Day — July 28, 2015

July 28, 2015, marks the fifth annual World Hepatitis Day, established in 2010 by the World Health Organization to increase awareness and understanding of viral hepatitis. Millions of acute hepatitis infections occur each year, and approximately 400 million persons are living with chronic hepatitis B or hepatitis C (*1*). An estimated 1.4 million persons die each year from the various forms of viral hepatitis (*1*). The theme of this year's World Hepatitis Day is "Prevent Hepatitis. Act Now." Key messages will focus on risks, safe injection practices, vaccination, and testing and treatment.

This issue of *MMWR* includes a report describing the launch of a nationwide hepatitis C elimination program in Georgia, a country with a high burden of hepatitis C. The initial phase of the program is focused on increasing access to affordable diagnostics, free treatment of persons with severe liver disease who are at highest risk for hepatitis C–related morbidity and mortality with new curative regimens, and building capacity to achieve program goals of prevention of transmission and elimination of disease. Georgia's program might provide information and experience that can inform similar efforts in other parts of the world.

A second report summarizes viral hepatitis surveillance and outbreak data from a national surveillance system in India for epidemic-prone diseases. This report sheds light on the burden and epidemiology of acute viral hepatitis in India, particularly hepatitis A and E, and highlights the important role that routine hepatitis surveillance can play in guiding prevention efforts.

Additional information about World Hepatitis Day is available at http://worldhepatitisday.org. Resources for health professionals are available at http://www.cdc.gov/hepatitis.

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Launch of a Nationwide Hepatitis C Elimination Program — Georgia, April 2015

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Hepatitis C virus (HCV) infects an estimated 130–150 million persons globally and results in an estimated 700,000 deaths annually from hepatocellular carcinoma or cirrhosis (*1*,*2*). Georgia, a middle-income Eurasian country, has one of the highest estimated HCV prevalences in the world (*3*). In 2011, Georgia began offering treatment to a limited number of HCV-infected persons. Beginning in 2013, when new oral medications that can cure >90% of HCV infections were licensed (*4*,*5*), Georgia engaged partners to develop a comprehensive

INSIDE

Continuing Education examination available at http://www.cdc.gov/mmwr/cme/conted_info.html#weekly.

U.S. Department of Health and Human Services
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HCV prevention and control plan, during which the concept of elimination of HCV transmission and disease emerged. To prepare for the launch of an HCV elimination program, Georgia requested CDC's assistance to describe HCV epidemiology, evaluate laboratory and health care capacity, and conduct program monitoring and evaluation. This report describes the activities undertaken to prepare for the program, launched in April 2015, and early results of its initial phase, focused on improving access to affordable diagnostics and free curative treatment for HCV-infected persons with severe liver disease. A national population-based serosurvey began in May 2015, and four clinical sites and their laboratories were selected as initial pilot sites; since June, three additional sites have been added. Through July 3, 2015, a total of 6,491 persons sought treatment, and 6,177 (95.2%) initiated diagnostic work-up. Among these, 1,519 (24.6%) completed work-up, 1,474 (97.0%) of whom initiated treatment. Georgia is scaling up capacity to meet the demand for HCV treatment and is collaborating with CDC and other partners on development of a comprehensive HCV elimination plan that includes specific goals and activities needed to achieve them.

Based on the finding of 6.7% anti-HCV seroprevalence in a survey in Tbilisi, Georgia's capital and largest city, in 2002 (*3*), an estimated 250,000 persons among the country's 3.7 million inhabitants might be infected with HCV. Injection drug use is a major risk factor for HCV infection (*3*), although unsafe injection and blood safety practices also contribute to the infection burden (*6*). The prevalence of HCV infection is high among prisoners (50%) (Georgia's Ministry of Labor, Health, and Social Affairs [MoLHSA], unpublished data, 2015), injection drug users (50%–70%) (*7*), and persons infected with human immunodeficiency virus (HIV) (47%) (*8*).

Anti-HCV serologic testing is widely available in Georgia. However, tests for RNA to identify active infection, genotyping to determine strain, and fibrosis staging to assess severity of liver disease (all necessary for clinical decision-making) are expensive and more difficult to obtain. Georgia's universal health care system requires most persons to pay out-of-pocket for HCV diagnosis and treatment, resulting in treatment of only 100–150 patients annually, before 2011 (MoLHSA, unpublished data, 2015). In 2011, Georgia implemented programs to increase access to HCV treatment with pegylated interferon and ribavirin (PEG/RBV) among HIV-coinfected persons, prisoners, and the general population (Table), which has resulted in approximately 1,685 Georgians receiving treatment to date.

In 2013, the government of Georgia requested technical assistance from CDC to develop a comprehensive HCV prevention and control strategy. CDC, MoLHSA, and other national and international partners met in 2014 and identified a national HCV seroprevalence survey and improved access to new curative HCV treatment as initial priorities. The potential for HCV elimination in Georgia was recognized on the basis of the absence of a nonhuman viral host, available effective diagnostics, prevention, and treatment (*9*,*10*), and the country's small size and population, experience with HIV prevention and control programs, strong political will, and public support.

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TABLE. Key strategies, activities, and outcomes before implementation of a nationwide hepatitis C elimination program — Georgia, 2011–2015

Strategy	Period	Activity	Outcome
Improve treatment access	2011–present	Free PEG/RBV treatment for up to 110 HIV/HCV co-infected persons per year through Global Fund for AIDS, TB, and Malaria	428 persons received treatment*
	2014–present	Free HCV screening, diagnostics for all incarcerated persons Free PEG/RBV treatment for up to 500 incarcerated persons with fibrosis stage ≥F2 (moderate disease) per year	406 persons received treatment*
	2014–present	Reduced price (60%) PEG/RBV treatment for 10,000 persons	851 persons received treatment*
	2015	5,000 free courses of sofosbuvir (Sovaldi), followed by 20,000 free courses of ledipasvir-sofosbuvir (Harvoni) per year through Gilead Science	1,474 persons received treatment†
Secure political commitment	2014	Georgian government prioritizes hepatitis C control	Establishment of national HCV commission
Partnership development	2013–2015	Engagement of international public health, academic, and industry partners to strengthen HCV response, with goal of elimination	CDC technical support Commitment from Gilead to provide free new curative medications
Capacity assessment	2015	Assessment of four clinical and eight public health laboratories	Development of test validation panels Recommendation for QA/QC plan
		Assessment of eight clinical sites and two prisons	Identification of first elimination program sites (i.e., total of seven sites to date, including four initial pilot sites in Tbilisi) Identification of critical gaps
National planning	2015	Definition steps for the initial phase of elimination program (key activities and treatment protocols)	Approval of initial activities and treatment protocols
Monitoring and evaluation	2015	Expanded data system used to track care and treatment during interferon access program	Development of STOP-C data management system to monitor and evaluate HCV continuum of care
Provider education	2015	Training of providers in HCV management	Ongoing
Defining disease burden	2015	National seroprevalence survey	Ongoing
Raising awareness	2015	Public campaign "STOP-C" developed by Georgia's Ministry of Labor, Health, and Social Affairs and partners to raise awareness for diagnosis and treatment of hepatitis C	Ongoing

Abbreviations: PEG/RBV = pegylated interferon and ribavirin; HCV = hepatitis C virus; HIV = human immunodeficiency virus; QA/QC = quality assurance and quality control.
* As of July 2015.
† During April 28–July 3, 2015.

Georgia committed to building its capacity to implement an HCV elimination program. of ledipasvir-sofosbuvir (Harvoni) annually at no cost. The HCV elimination program was to be initially focused on treating HCV-infected persons with severe liver disease and providing discounted HCV diagnostic services. Georgia requested assistance from CDC to 1) conduct a national survey to define epidemiology and disease burden, 2) assess laboratories and health care providers to identify sites with capacity to participate in the initial phase of the elimination program, and 3) monitor and evaluate the program (Table).

A stratified, multistage cluster survey designed to select a nationally representative sample of 7,000 adults, calculated based on current HCV prevalence estimates and an anticipated 70% response rate, was launched in six major cities (including Tbilisi) and 10 rural regions in May 2015. Serum samples for anti-HCV antibody (and, if positive, HCV RNA and genotyping) and data on behavioral risk factors are collected during household visits. The survey will allow calculation of independent HCV prevalence estimates for the six major cities and most rural areas surveyed once analyzed by fall 2015.

Eight clinical sites and two prisons with experience providing interferon-based treatment were assessed and scored based on six domains: leadership and governance, quality of clinical care services, health information systems/management, human resource capacity, access to necessary laboratory tests, and drug-procurement procedures. A standard World Health Organization–adapted tool was used to assess capacity at four clinical laboratories (affiliated with some of the assessed clinical

sites) and eight public health laboratories regarding biosafety, specimen collection and accessioning, equipment and test kit use, staff competency, quality assurance and quality control (QA/QC), and reporting and communication.*

A data management system (STOP-C) was developed to collect demographic, diagnostic, clinical, and pharmacy data on patients registered for treatment, which permits data entry by health care providers as well as the Central Social Service Agency (based at MoLHSA in Tbilisi). CDC provided technical support in identifying key variables for monitoring the HCV continuum of care.

Four of the highest scoring clinical sites in Tbilisi and their corresponding laboratories were selected as initial pilot sites for the elimination program. All four laboratories provide point-of-care and laboratory-based anti-HCV testing, viral load determination, and genotyping. Although one of the laboratories had International Organization for Standardization 15189 medical laboratory certification,† which specifies requirements for quality and competence in medical laboratories, all lacked external QA/QC procedures, and efforts are underway to develop such a program and validate test kits. The health care provider assessment revealed limited experience with the new HCV medications and a need for additional training and case management support. Since June 2015, three additional clinical sites with moderate scores and their laboratories in two other cities have been added to meet demands for HCV diagnosis and treatment; improvement in capacity is ongoing at these sites.

An HCV Elimination Program Treatment Inclusion Committee, consisting of clinicians, patient advocacy representatives, and media, was established to review each (de-identified) patient record to determine treatment eligibility and appropriateness of provider-recommended regimens, and to ensure transparency and equitability of access to treatment. As of July 3, 2015, among 6,491 HCV-positive persons who sought treatment, 6,177 (95.2%) initiated diagnostic work-up, of whom 1,519 (24.6%) had completed evaluation and obtained required documentation for treatment consideration. The committee has evaluated and approved 1,474 (97.0%) of these patients for treatment initiation, and all 1,474 have started treatment.

Discussion

The response to the initial phase of Georgia's HCV control program has been larger than that for earlier PEG/RBV access programs. Increased demand likely is the result of the availability of free, effective, well-tolerated, and curative treatment options, coupled with affordable diagnostics for HCV-infected persons with advanced liver disease, who are at greatest risk for morbidity and mortality. Additional provider training and case management support are remaining challenges. MoLHSA initially limited the number of participating sites, to ensure quality and appropriate clinical decision making; the recent addition of three new sites should reduce program delays and facilitate program expansion, and assessment of additional providers and laboratories is ongoing. Monitoring and evaluation will continue, and efforts are ongoing to develop an external QA/QC system to be used by laboratories to achieve and maintain biologic safety and quality diagnostic standards.

Although HCV is a strong candidate for elimination in Georgia, many challenges exist, including the asymptomatic, chronic nature of disease, which results in diagnostic delays, and ongoing transmission in health care settings and among hard-to-reach populations (e.g., injection drug users) with potential for reinfection. To address these challenges, Georgia is developing a comprehensive elimination plan that addresses advocacy and communication, surveillance (including quality diagnostics), prevention (e.g., infection control, blood safety, and harm reduction), and testing and linkage to care.§ An international technical advisory committee is being formed to help define achievable and measurable elimination goals and indicators, and determine priority activities. Additionally, MoLHSA has

Summary

What is already known on the topic?

Hepatitis C virus (HCV) infection is a serious health problem that affects an estimated 130–170 million persons globally and results in an estimated 700,000 deaths annually. In 2013, new all-oral, well-tolerated regimens were licensed that can cure >90% of HCV infections. The country of Georgia has one of the world's highest estimated HCV prevalences.

What is added by this report?

In April 2015, Georgia launched a hepatitis C elimination program that will initially focus on treating HCV-infected persons who have severe liver disease with new curative regimens, providing discounted HCV diagnostics to all persons, and building capacity to eventually diagnose and treat all Georgians infected with HCV. A national serosurvey was launched in May 2015, and seven clinical sites have opened to diagnose and treat HCV. Georgia is scaling up capacity to meet the high demand for HCV treatment.

What are the implications for public health practice?

Georgia has increased access to HCV testing and treatment as part of preparatory phase of a national HCV control program with goals for the elimination of HCV transmission and disease in the country. Georgia's program can provide information and experience that will assist similar efforts in other parts of the world.

* Additional information available at http://www.who.int/ihr/publications/laboratory_tool.

† Additional information available at http://www.iso.org/iso/catalogue_detail?csnumber = 56115.

§ Additional information available at http://www.who.int/csr/disease/hepatitis/GHP_framework.pdf.

begun to implement broader HCV control activities, including a campaign to raise awareness, provision of free HCV testing to identify HCV-infected persons unaware of their infection status, and improved infection control practices. Georgia's elimination program can provide information and experience that will assist similar efforts in other parts of the world.

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National Progress Toward Hepatitis C Elimination — Georgia, 2015–2016

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The country of Georgia has a high prevalence of hepatitis C virus (HCV) infection, associated with exposures to HCV in health care settings with inadequate infection control and unsafe injections among persons who inject drugs (*1*). In April 2015, in collaboration with CDC and other partners, Georgia embarked on a program to eliminate HCV infection, subsequently defined as achieving a 90% reduction in prevalence by 2020. The initial phase of the program focused on providing HCV treatment to infected persons with advanced liver disease and at highest risk for HCV-associated morbidity and mortality. By April 27, 2016, a total of 27,392 HCV-infected persons registered for the program, 8,448 (30.8%) started treatment, and 5,850 patients (69.2%) completed HCV treatment. Among patients completing treatment who were eligible for posttreatment testing, 2,398 received polymerase chain reaction (PCR) testing for HCV at least 12 weeks after completion of treatment; 1,980 (82.6%) had no detectable virus, indicative of a sustained virologic response* (i.e., cure). Major challenges to achieving elimination remain, including the need to increase access to care and treatment services and implement a comprehensive approach to prevention and control of HCV infection. As a global leader in this effort, the Georgia HCV Elimination Program can help pave the way for other countries experiencing high rates of HCV infection to undertake similar initiatives.

Georgia is a country with a population of 3.7 million (*2*) and borders the Black Sea, Russia, Turkey, Armenia, and Azerbaijan. Results from a serosurvey conducted in 2015 among adults found an estimated HCV infection prevalence (i.e., tested HCV-antibody positive) of 7.7% (5.4% tested positive for active infection by PCR) (Georgia Ministry of Labor, Health, and Social Affairs [MoLHSA], unpublished data, 2016). With strong stakeholder support, including partnership and technical assistance from CDC, and commitment from Gilead Sciences to donate direct-acting antiviral HCV medications (DAAs), Georgia embarked on the world's first HCV elimination program on April 28, 2015 (*1*). Initially, four treatment centers located in Tbilisi (Georgia's capital) provided HCV treatment to program participants. By April 27, 2016, the number of treatment centers had increased to 17 and they were located throughout the country, with staff members that included 95 physicians and infectious disease specialists or gastroenterologists providing HCV treatment services. All patients had access to point-of-care and laboratory-based HCV antibody testing, viral load determination, and genotyping. Noninvasive tests used to determine the degree of hepatic fibrosis included the following: FIB-4 score, which combines age and standard blood tests (platelet count, alanine aminotransferase, aspartate aminotransferase) (*3*), and ultrasound or transient elastography, which measures the decrease in tissue elasticity that accompanies liver fibrosis (*4*,*5*). Genotyping was performed for all patients who tested positive for HCV by PCR. Six major genotypes of HCV are recognized worldwide, and treatment of HCV infection varies by genotype (*6*). Patients with advanced liver disease (F3 or F4 by METAVIR† fibrosis score) were prioritized to receive treatment during the first year of the program.

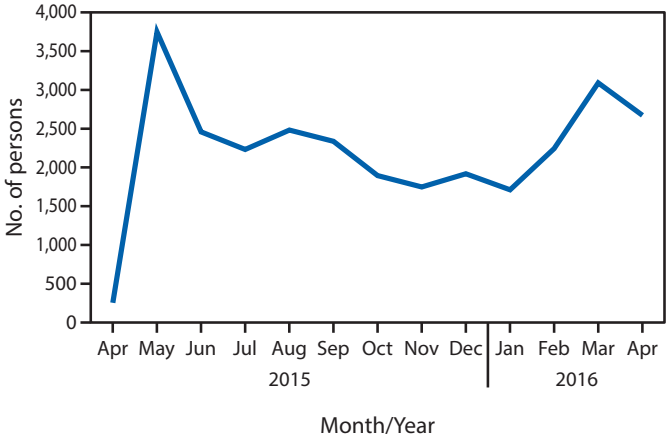
A sliding-scale approach was used for diagnostics and clinical monitoring, with patients charged based on their ability to pay and the local government or MoLHSA paying the balance. All program participants received sofosbuvir-based treatment regimens, provided free-of-charge by Gilead Sciences; the Georgian government purchased additional medications (i.e., pegylated interferon and ribavirin) and provided them at no cost to patients for whom such treatment was indicated.

During April 28, 2015–April 27, 2016, a total of 27,392 patients with evidence of HCV infection (positive HCV antibody test results) had enrolled in the program. The number of enrollees peaked during the first month of the program and generally declined over time (Figure 1). The number of patients initiating HCV treatment in the country increased linearly during the year, to a total of 8,448 (Figure 2). Of those enrolled, 27,155 (99.1%) initiated diagnostic workup, including confirmation of active HCV infection and assessment of hepatic fibrosis to determine eligibility for treatment. Among those enrolled in the program, 9,615 (36.3%) completed diagnostic workup, and 8,448 (87.9%) initiated treatment for HCV (Figure 3). Most patients treated (92.8%) met advanced liver disease criteria. The most common treatment regimens

* Sustained virologic response is defined as undetectable (or below the lower limit of quantification) HCV RNA at 12–24 weeks after cessation of treatment (Wedemeyer H, et al., http://onlinelibrary.wiley.com/doi/10.1002/hep.25888/pdf).

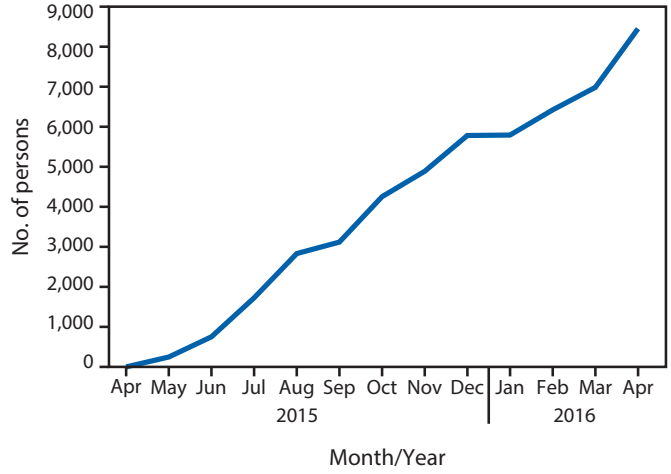
† The METAVIR score is a semiquantitative classification system that consists of an activity score and a fibrosis score, specifically designed and validated for patients with HCV (Bedossa P, et al., http://onlinelibrary.wiley.com/doi/10.1002/hep.510240201/pdf).

FIGURE 1. Number of persons with positive hepatitis C virus (HCV) results enrolling in treatment program, by month — nationwide HCV elimination program, Georgia, April 2015–April 2016*



Source: Georgia Ministry of Labor, Health, and Social Affairs.
* The number of clinical sites increased from four in April 2015 to 17 in April 2016.

FIGURE 2. Cumulative number of persons (N = 8,448) with positive hepatitis C virus (HCV) results who started HCV treatment, by month — nationwide HCV elimination program, Georgia, May 14, 2015–April 27, 2016



Source: Georgia's HCV Elimination Program Treatment Database.

were sofosbuvir in combination with ribavirin (45.4%), and sofosbuvir in combination with ribavirin and pegylated interferon (33.9%).

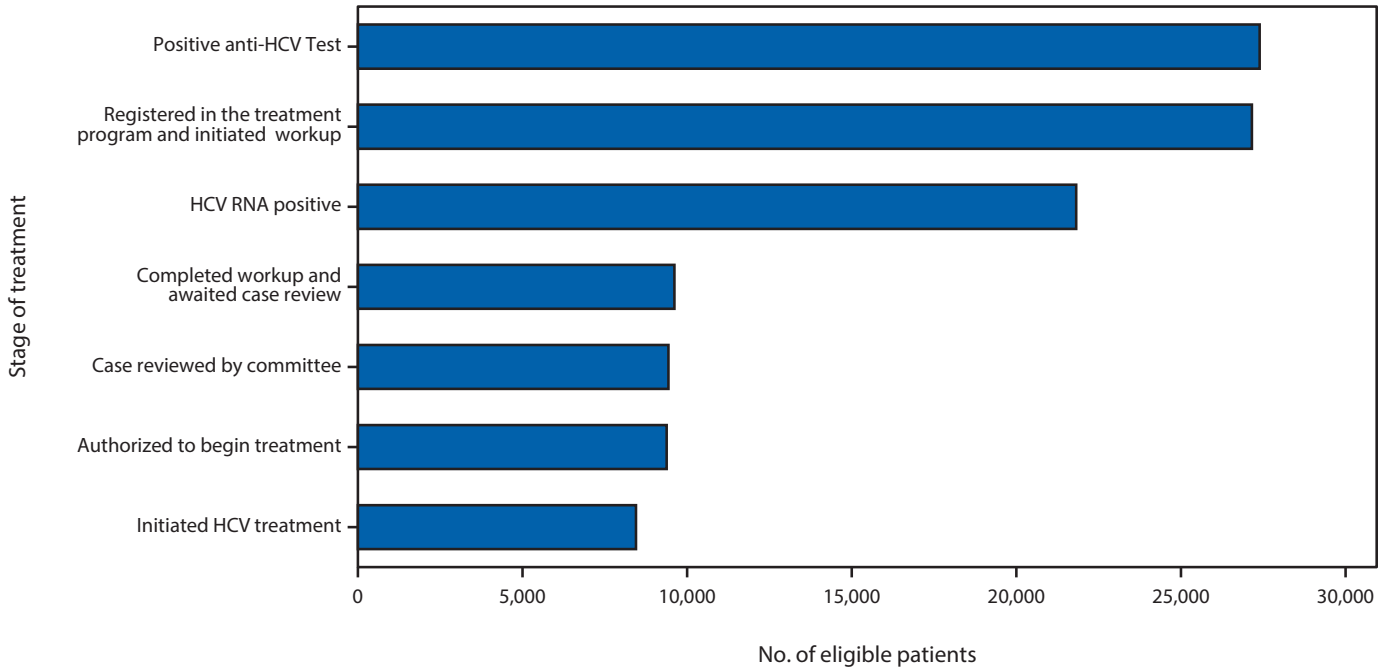
Outcome data for patients treated through April 2016 indicated that among 2,398 persons eligible for a sustained virologic response determination 12 weeks after completion of treatment and who were tested for the presence of HCV RNA, levels of HCV RNA were undetectable in 1,980 (82.6%) of those tested, indicating a virologic cure. Among those completing their course of treatment who were tested, cure rates were lowest among genotype 1 patients (72.6%; 724 of 997 patients), intermediate among those infected with genotype 2 (84.7%; 421 of 497), and highest among those with genotype 3 (92.4%; 834 of 903). Among the 8,448 who initiated treatment, 325 (3.8%), did not complete the treatment course; 173 of the 325 patients died, and 80 discontinued treatment because of an adverse event.

In mid-February 2016, Gilead Sciences began providing (free-of-charge) the newer ledipasvir/sofosbuvir DAA combination drug regimen to the program. Among participants who initiated treatment in the first year, 11.7% (n = 985) received the new regimen. This included 162 persons who restarted treatment with ledipasvir/sofosbuvir after introduction of this combination DAA for various reasons, primarily failure to achieve viral clearance after initial treatment course (n = 155). Treatment outcome data are not available for patients receiving this combination therapy.

Discussion

The Georgia HCV Elimination Program made substantial progress in its first year. Since the launch of the program in April 2015, 27,392 HCV-infected persons were enrolled and 8,448 initiated treatment, which represents a >400% increase in the number treated compared with the total number of HCV-infected persons treated in the country during the previous 4 years (*1*). Persons with advanced liver disease, who are at highest risk for morbidity and mortality, were prioritized for treatment during the first year, and >90% of those treated met this criteria as determined by ultrasound or transient elastography. Rates of virologic cure were >80% among this population. The effect on prevalence of active HCV infection, estimated at 5.4% in 2015, will be reassessed in several years as the HCV elimination program progresses and treatment coverage expands, curing most Georgians currently living with HCV infection. Georgia has taken a collaborative, informed approach to eliminating HCV infection. Together with CDC, the World Health Organization (WHO), and other international partners, Georgia's MoLHSA developed a technical advisory group (TAG), which convened its first meeting in November 2015. To help Georgia reach its proposed elimination goals, TAG recommended that MoLHSA address gaps in advocacy and awareness; surveillance; prevention of transmission, including harm reduction; blood safety; infection control in health and non–health care settings; and evidence-based screening and linkage to care (*7*). Several strategies were proposed at the meeting, including assessing Georgia's prevalence of disease and risk factors for transmission; implementing measures to prevent transmission; identifying all persons living with HCV infection; and providing patients with access to high-quality diagnostics and free treatment with DAA medications. In response to TAG recommendations and collaboration with CDC, Georgia's MoLHSA is developing

FIGURE 3. Cascade of care for hepatitis C virus (HCV)-infected patients — nationwide HCV elimination program, Georgia, April 28, 2015–April 27, 2016*,†



Abbreviation: MOLHSA = Ministry of Labor, Health, and Social Affairs.
* Patients with positive anti-HCV test began treatment at one of 17 provider sites; data from MOLHSA's financial reimbursement system.
† Of the patients who initiated HCV treatment, 162 (1.9%) with different indications have restarted HCV treatment.

a comprehensive HCV elimination plan to address important challenges and outline steps and strategies for enhanced screening and linkage-to-care activities, expansion of HCV treatment to reach populations at high risk for infection, and development of a surveillance system to assess progress toward achieving elimination goals.

Despite notable progress during the last year, major challenges remain. To ensure high-quality screening and monitoring as the program expands, a laboratory quality assurance and quality control system covering all treatment centers is needed. To monitor progress toward elimination goals, surveillance systems capable of capturing data from affected populations and those with acute disease are needed, allowing for monitoring trends and risk factors for infection. Collection of quality and timely treatment data is important to monitor the progress of the care and treatment program. These gaps will be addressed in Georgia's comprehensive HCV elimination plan, which is currently under development. As the HCV treatment program continues to expand and the number of providers and sites that provide HCV care and treatment services grows, the capacity of the information system will need to be increased. Georgia's MoLHSA is anticipating this growth and is working with partners to ensure the system is upgraded to handle additional demands.

In its first year, Georgia's HCV elimination program primarily served patients who already knew their infection status, voluntarily came to participating clinics, and enrolled in the program. However, most persons living with HCV infection are unaware of their HCV infection and consequently are not participating in the program and not receiving care and treatment. Georgia is developing a comprehensive plan that will increase patient testing, ensure that tested patients are informed of their test results, and ensure that those who test positive for HCV antibodies are provided confirmatory testing and if infected, linked to care and treatment services. As more Georgians are tested for HCV, the demand for treatment will increase. Primary care providers and settings serving populations at high risk (e.g., centers providing services such as opioid substitution therapy and needle and syringe provision to people who inject drugs) need to be prepared to provide HCV treatment, as the demand for therapy is anticipated to exceed the current capacity of providers offering treatment (i.e., infectious disease specialists and gastroenterologists).

In the near future, Georgians will likely have access to even newer DAAs associated with high rates of virologic cure regardless of HCV genotype, suggesting that genotype testing might not remain a prerequisite for treatment. Use of these antiviral medications is expected to simplify HCV diagnostics

Summary

What is already known about this topic?

Georgia is among the countries worldwide with the highest prevalence of hepatitis C virus (HCV) infection. The recent availability of highly effective, direct-acting antivirals (DAAs) capable of curing >90% of persons treated has made HCV elimination a possibility. On April 28, 2015, Georgia committed to an elimination plan, embarking on an ambitious program that included HCV screening and provision of curative treatment at no cost to infected persons.

What is added by this report?

During the first year of the HCV elimination program in Georgia, 27,392 persons enrolled in the treatment program, and 8,448 initiated treatment with DAAs. Most persons (92.8%) who began treatment had advanced liver disease. Among 2,398 persons who completed treatment and were tested to determine treatment response, >80% were cured of their HCV infection. Georgia is developing a comprehensive HCV elimination plan that will include prevention and enhanced screening and linkage to care, with the goal of reaching HCV elimination by 2020.

What are the implications for public health practice?

Substantial progress has been made to eliminate HCV infection in Georgia, and the country has demonstrated the ability for rapidly scale up of care and treatment services. To achieve elimination, substantial challenges remain, including increasing access to care and treatment services and implementing a comprehensive approach to prevention and control of HCV infection. Georgia's HCV elimination program could provide lessons for future programs to control HCV infection worldwide, particularly as treatment becomes more affordable and more countries seek to provide care and treatment services.

and patient management and monitoring in Georgia, allowing more patients to receive timely treatment. In many low-to-middle income countries with a high prevalence of HCV infection, access to advanced diagnostics is limited. Specific models of care and treatment that use simplified testing and patient management are needed to demonstrate feasibility of HCV-related care and treatment in resource-limited settings like Georgia.

The World Health Assembly endorsed the WHO strategic framework for hepatitis prevention that includes goals for the elimination of hepatitis C as a public health threat by 2030, with interim measures by 2020 (*8*). Georgia's HCV elimination program model could provide important lessons for future initiatives to control HCV infection worldwide, particularly as testing is simplified, treatment becomes more affordable, and more countries seek to address the growing prevalence of HCV infection.

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The Role of Screening and Treatment in National Progress Toward Hepatitis C Elimination — Georgia, 2015–2016

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Georgia, a country in the Caucasus region of Eurasia, has a high prevalence of hepatitis C virus (HCV) infection. In April 2015, with technical assistance from CDC, Georgia embarked on the world's first program to eliminate hepatitis C, defined as a 90% reduction in HCV prevalence by 2020 (*1*,*2*). The country committed to identifying infected persons and linking them to care and curative antiviral therapy, which was provided free of charge through a partnership with Gilead Sciences (*1*,*2*). From April 2015 through December 2016, a total of 27,595 persons initiated treatment for HCV infection, among whom 19,778 (71.7%) completed treatment. Among 6,366 persons tested for HCV RNA ≥12 weeks after completing treatment, 5,356 (84.1%) had no detectable virus in their blood, indicative of a sustained virologic response (SVR) and cure of HCV infection. The number of persons initiating treatment peaked in September 2016 at 4,595 and declined during October–December. Broader implementation of interventions that increase access to HCV testing, care, and treatment for persons living with HCV are needed for Georgia to reach national targets for the elimination of HCV.

In 2015, an estimated 5.4% of the adult population of Georgia (approximately 150,000 persons) had chronic HCV infection, and of those, nearly two thirds were unaware of their infection (Georgia Ministry of Labour, Health, and Social Affairs [MoLHSA], unpublished data, 2016). Populations with the highest rates of HCV infection include men, persons aged 30–59 years, persons with a history of injection drug use, and persons with a history of receipt of blood products (MoLHSA, unpublished data, 2016). Initially, when the program was launched in April 2015, national guidelines limited treatment to HCV-infected persons with advanced liver disease, defined as one or both of the following: F3 or F4 by METAVIR fibrosis score (a system used to assess the histological extent of hepatic inflammation and fibrosis in patients with hepatitis C infection) on transient elastography or FIB-4 score (a noninvasive test based on a combination of biochemical values and patient age) >3.25 (*3*,*4*). In June 2016, treatment eligibility criteria were expanded to include all HCV-infected persons, regardless of disease severity.

HCV screening programs began in January 2015, before the launch of the program, and screening services continue to be provided at various settings at no cost (Table). During January 2015–December 2016, a total of 472,890 HCV screening tests* were conducted, 50,962 (10.8%) of which were positive for HCV antibody. The highest rate of HCV antibody–positive screening tests (45.0%) was among persons who attended programs providing services for persons who inject drugs; the lowest rate (0.4%) was among women attending antenatal clinics (Table). Persons who screen positive for HCV antibody are referred to the treatment program for confirmation of chronic HCV infection using polymerase chain reaction (PCR) testing for detection of HCV RNA. Once chronic HCV infection is confirmed, the person is invited to enroll in the treatment program.

When the treatment program began on April 28, 2015, four treatment centers operated in Georgia, all located in Tbilisi, the capital and largest city. By December 2016, the number of treatment centers had increased to 27 nationwide. From the start to December 31, 2016, a total of 58,223 persons with positive HCV antibody test results sought confirmation of chronic HCV infection through the treatment program, among whom 38,113 (65.5%) initiated a diagnostic evaluation, including confirmation of HCV infection by

TABLE. Number of screening tests* for hepatitis C virus (N = 472,890) and percentage testing positive, by group screened — Georgia, 2015–2016

Group screened/Location of screening	No. screening tests	% HCV positive
Blood donors	168,121	1.3
NCDC	83,910	17.5
Pregnant women/ANCs	53,852	0.4
Hospitalized patients†	48,025	4.9
Persons who inject drugs	44,410	45.0
Tblisi citizens§	26,159	13.8
Outpatients†	18,900	7.4
Prisoners	14,053	37.4
Military recruits	11,217	1.5
HCV screening or treatment center	2,453	31.4
Persons living with HIV	1,790	24.9
Total	**472,890**	**10.8**

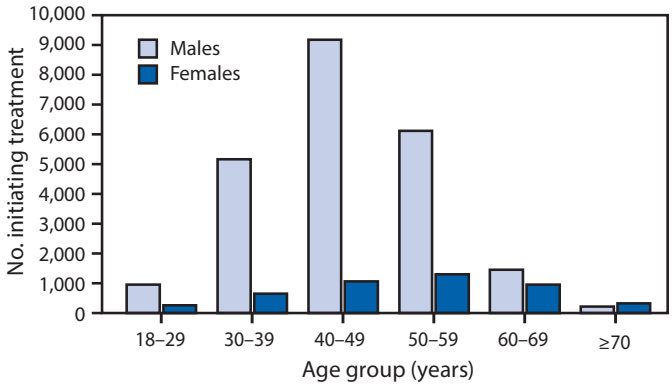
Abbreviations: ANC = antenatal clinic; HCV = hepatitis C virus; HIV = human immunodeficiency virus; NCDC = National Centers for Disease Control and Public Health headquarters and regional centers.
* Number of HCV screening tests (not individual persons) reported to NCDC.
† Data are from November 1–December 30, 2016.
§ Screening centers operated by the city of Tbilisi.

* Hepatitis C virus rapid tests by all screening programs except blood banks that mostly used enzyme immunoassay.

PCR testing; of those who initiated a diagnostic evaluation, 30,046 (78.8%) were confirmed as having chronic HCV infection and completed the diagnostic workup, and 27,595 (91.8%) of whom began treatment. Men accounted for 23,062 (83.6%) of all persons starting treatment, including 9,180 men aged 40–49 years, representing one third of all persons who initiated treatment (Figure 1). The average number of persons starting treatment each month increased nearly 300% from April 2015–May 2016 (661 per month) to June–December, 2016 (2,619 per month), peaking in September 2016 at 4,595. A decline occurred from October through December 2016 (Figure 2). During the initial phase of the program (April, 2015–May, 2016), when treatment was prioritized for persons with more severe liver disease, most patients initiating treatment (9,088 of 9,259; 98.2%) had advanced liver disease (≥F3 METAVIR fibrosis score or FIB-4 score >3.25). After the expansion of treatment criteria to allow treatment for all persons with HCV infection (beginning June 1 through December 31, 2016), most persons initiating treatment (14,368 of 18,336; 78.4%) had less severe liver disease (<F3 METAVIR fibrosis score or FIB-4 score <1.45) (Figure 2).

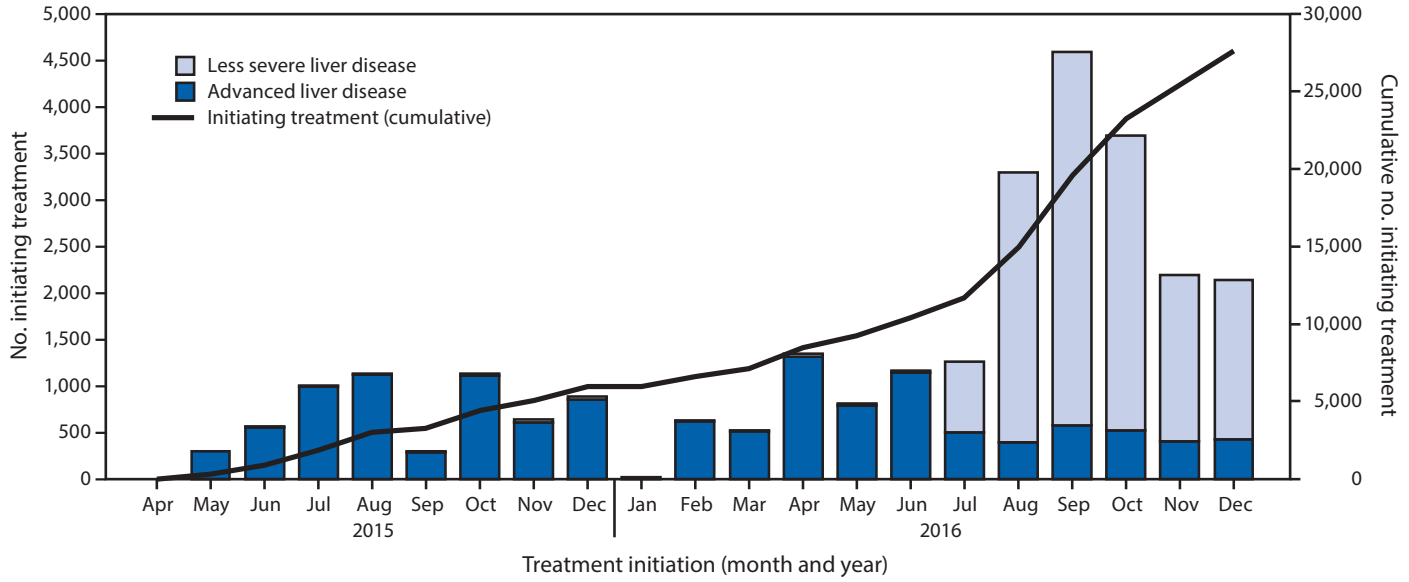
As of December 31, 2016, a total of 19,778 persons completed treatment, and 6,366 (32.2%) eligible patients received testing for SVR (undetectable HCV RNA ≥12 weeks after treatment completion) (*5*). SVR was observed for 5,356 (84.1%) persons tested, indicating that they were cured of their infection. Among the 75.0% (4,774/6,366) who received sofosbuvir (without ledipasvir) treatment regimens, 3,793 (79.5%) achieved SVR, and among the 25.0% (1,592 of 6,366) who received ledipasvir/sofosbuvir-based treatment regimens, 1,563 (98.2%) achieved SVR. Among 537 (1.9%) persons who did not complete treatment, 371 (69.1%) died from their liver disease or another cause during the course of treatment, and the other 166 (30.1%) discontinued treatment for other reasons.

FIGURE 1. Number of persons initiating treatment for hepatitis C virus infection, by sex and age group — Georgia, April 2015–December 2016*



* The age group "18–29 years" includes five female patients aged 13–17 years.

FIGURE 2. Number of persons initiating treatment for hepatitis C virus infection and cumulative number initiating treatment, by severity of liver disease* and month — Georgia, April 2015–December 2016



* Less severe liver disease defined as <F3 METAVIR fibrosis score and/or FIB-4 score <1.45; advanced liver disease defined as ≥F3 METAVIR fibrosis score and/or FIB-4 score >3.25.

Discussion

Since the launch of the Georgia HCV Elimination Program in April 2015, progress has been made in providing treatment to and curing persons infected with HCV, including a 300% increase in the average monthly number of patients initiating treatment during the second half of 2016. These gains are attributed to an increase in the number of treatment sites, expansion of treatment eligibility criteria, and introduction of a newer, highly effective all-oral combination antiviral drug (ledipasvir/sofosbuvir) (*6*). However, enrollment in the treatment program declined considerably during the last 3 months of 2016. This decline is likely because of patients' lack of awareness of their infection status or lack of access to the treatment program for HCV-infected persons who were aware of their infection. The data in this report suggest that a substantial proportion of persons tested and found positive for HCV antibodies are not successfully referred for evaluation of HCV infection. Through December 2016, approximately 20% of the estimated 150,000 Georgians living with HCV infection entered the treatment program. Increased measures to identify infected persons and link them to care and treatment are needed to reach the 2020 elimination goal of 90% reduction in HCV prevalence.

At the launch of the program in 2015, national serologic survey data revealed about one third of HCV-infected Georgians were aware of their infection (MoLHSA, unpublished data, 2016). Data are lacking on how many of the approximately 51,000 persons who screened positive for HCV during 2015 and 2016 accessed the program to receive confirmatory testing (which unlike initial screening, is not free of charge) and entered the treatment program if chronic HCV infection was confirmed. Changes in government policies that target large at-risk populations, offer free HCV confirmatory testing and additional diagnostic evaluation for patients with confirmed HCV infection, increase the number of providers that can provide testing and treatment services, and support campaigns to expand public awareness and demand for HCV services can increase HCV screening and treatment rates.

Although approximately 470,000 HCV screening tests were reported during 2015–2016, many at-risk Georgians remain unscreened. HCV prevalence varied markedly across different screening settings and programs: screening conducted at antenatal clinics yielded a low proportion of persons screening positive, and screening at corrections and harm-reduction facilities yielded high HCV prevalence rates. Targeted provision of testing and linkage to care services might increase the detection of persons with HCV infection, and thereby, the number entering the treatment program.

Summary

What is already known about this topic?

An estimated 150,000 persons in the country of Georgia (5.4% of the adult population) are infected with hepatitis C virus (HCV). In April 2015, in collaboration with CDC and other partners, Georgia launched a program to eliminate HCV by 2020. An important strategy is the identification of HCV-infected persons and provision of curative antiviral therapy.

What is added by this report?

During April 28, 2015–December 31, 2016, a total of 27,595 HCV-infected persons started therapy, 19,778 (71.7%) of whom completed treatment. Among 6,366 (32.2%) who completed treatment and were tested for treatment response, 5,356 (84.1%) were cured of their HCV infection. The average number of persons who initiated treatment each month increased threefold from April 2015–May 2016, when treatment was limited to persons with severe liver disease, to June–December 2016, after expansion of the eligibility criteria to allow treatment of all HCV-infected persons. During the last 3 months of 2016, the number of persons entering the treatment program declined steadily, suggesting that identification and linkage to care of HCV infected persons in the country might be slowing.

What are the implications for public health practice?

The Georgia HCV Elimination Program has made substantial progress since its launch in April 2015; the country has demonstrated the ability to scale up HCV care and treatment services rapidly. Enhancing HCV testing and linkage to care and treatment services are critical to reaching the 2020 HCV elimination goal. Lessons learned from the Georgia elimination program can inform programs in other countries striving to eliminate HCV as a public health threat.

Reaching the 2020 HCV elimination goals will require innovative strategies to increase awareness, expand access to high-quality screening, and remove diagnostic and treatment barriers which may include costs associated with confirmatory testing and diagnostic workup, stigma, and distance to treatment centers. Increased impact can be achieved by providing services at primary care settings and settings serving populations at high risk (e.g., syringe service programs for injection drug users).

Elimination of HCV infection in Georgia hinges not only on strategies that identify, treat, and cure persons of their infection, but also on those that prevent new infections. To ensure a comprehensive approach to HCV elimination, MoLHSA developed a *Strategic Plan for Elimination of Hepatitis C in Georgia* (*7*). In addition to proposing actions to improve HCV screening and linkage to care, the plan identifies strategies for preventing new infections, including improving safety of the blood supply, ensuring infection control in health care settings, and providing persons who inject drugs with harm-reduction services.

The findings in this report are subject to at least three limitations. First, data from the screening and treatment programs could not be independently verified and might be subject to data entry errors. Second, the screening data reported might include persons who received repeat testing; thus it is not known whether each HCV antibody test represents a single person screened. Finally, HCV screening data are not linked to treatment data, and as a result, this analysis could not assess the effectiveness of linkage of screening to the care and treatment program.

Despite notable progress during the first 20 months of the Georgia HCV elimination program, challenges to Georgia achieving the national targets for HCV elimination by 2020 remain. High-quality screening, innovative linkage-to-care strategies, and cost-effective and simplified diagnostic and treatment regimens are needed. Provision of free-of-charge services for HCV screening, diagnosis, care, and treatment in settings serving populations at high risk for HCV infection and in primary care settings can decrease barriers to access of treatment services. MoLHSA is working with CDC and other international partners to address challenges and introduce innovative strategies. Pangenotypic direct-acting antiviral drugs that are effective across the different genotypes of HCV, point-of-care HCV RNA testing, and HCV core antigen testing are likely to be introduced in late 2017 or 2018 and could have a substantial impact on improving access and simplifying diagnosis and treatment. Information systems capable of linking screening and treatment data are being developed to improve efficiencies. With increased access to HCV treatment services and full implementation of the country's strategic plan, Georgia can achieve the goal for HCV elimination in 2020. Lessons learned from this program can inform similar initiatives in other countries and help curb the global epidemic of viral hepatitis (*8*).

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Conflict of Interest

No conflicts of interest were reported.

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ELIMINATING VIRAL HEPATITIS

HCV elimination — lessons learned from a small Eurasian country, Georgia

Muazzam Nasrullah[1], David Sergeenko[2], Amiran Gamkrelidze[3] and Francisco Averhoff[1]

In April 2015, in partnership with the US Centers for Disease Control and Prevention and Gilead Sciences, the country of Georgia launched the world's first national HCV elimination programme, aiming to reduce HCV prevalence by 90% by 2020. After 2 years of progress, how can the Georgia experience inform global approaches to eliminating HCV?

In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy on Viral Hepatitis 2016–2021, which calls for the elimination of viral hepatitis as a public health threat by 2030 (a 90% reduction in new infections caused by HBV and HCV infections and a 65% reduction in deaths from these infections)[1]. An estimated 71 million people have HCV globally, resulting in ~400,000 deaths annually; most mortality is caused by hepatocellular carcinoma and end-stage liver disease[2]. The WHO estimates that 1.75 million new HCV infections occurred worldwide in 2015, with wide variations in incidence; transmission mode also varies by country, but the most common modes globally are associated with unsafe health-care practices, followed by injection drug use[2].

The absence of a known non-human reservoir and latent cellular reservoir, coupled with availability of highly effective, direct-acting antiviral agents (DAAs) capable of curing >90% of HCV infections[3], sets the stage for population-wide HCV elimination. All-oral DAAs are simple to administer (typically requiring single daily dosing regimens of 8–12 weeks), are less costly than they were when first introduced because of availability of generic formulations, have increased tolerability and efficacy over interferon-based therapy, and require less patient monitoring[3,4]. Programmes equipped with improved cost-effective diagnostics required to identify individuals infected with HCV, such as HCV core antigen testing, along with national policies that facilitate testing services in high-risk populations have the potential to enhance the linkage to care and treatment. All-oral DAA regimens require minimal patient monitoring, enabling decentralization of HCV care and treatment services, and are safe and effective[3]. Together, these advancements, coupled with prevention strategies including improved infection control, blood safety and provision of harm reduction services to people who inject drugs, make elimination of HCV possible.

Elimination of HCV is feasible in Georgia for several reasons, including: a highly motivated government and civil society that was demanding action (many people from all social strata had family or friends dying of end-stage liver disease or liver cancer); a highly skilled and inspired core group of clinicians with a passion for treating HCV infection; a large burden of disease in a relatively small country (3.7 million population); and a complex epidemiology, including varying modes of transmission and genotypes. The country engaged the US Centers for Disease Control and Prevention (CDC) in 2013 to provide technical assistance and subsequently secured a commitment from Gilead Sciences to provide DAAs for treatment, free of charge, to all Georgians living in the country with HCV infection. To set the stage for a HCV elimination programme, Georgia conducted a national serological survey to estimate HCV prevalence. The survey found a high prevalence of HCV infection: 5.4% of adults, meaning that ~150,000 people are living with HCV infection. Prevalence was higher among men and those aged 30–59 years (Georgia Ministry of Labour, Health, and Social Affairs (MOLHSA), unpublished data, 2016). The seroprevalence survey identified injection drug use and receipt of blood products as risk factors associated with HCV infection (MOLHSA, unpublished data, 2016). Georgia embarked on the world's first HCV elimination programme in April 2015 and set a very ambitious elimination target: a 90% reduction in HCV prevalence by 2020 (REF. 5).

Following the launch of the programme, Georgia initiated key activities and implemented programmes to achieve the elimination target (FIG. 1). The initial phase of the elimination programme focused on providing HCV treatment to persons who were infected and had advanced liver disease (F3 or F4 by METAVIR fibrosis score and/or FIB-4 score >3.25), because these persons are at highest risk of HCV-associated morbidity and mortality[5]. In June 2016, the country expanded the eligibility criteria to treat all HCV-infected individuals. From programme launch through 31 December 2016, nearly 28,000 people initiated treatment, and of those who completed treatment and received PCR testing for HCV at least 12 weeks after completion of treatment, nearly 5,400 (84%) had achieved cure (that is, had no detectable virus). Through

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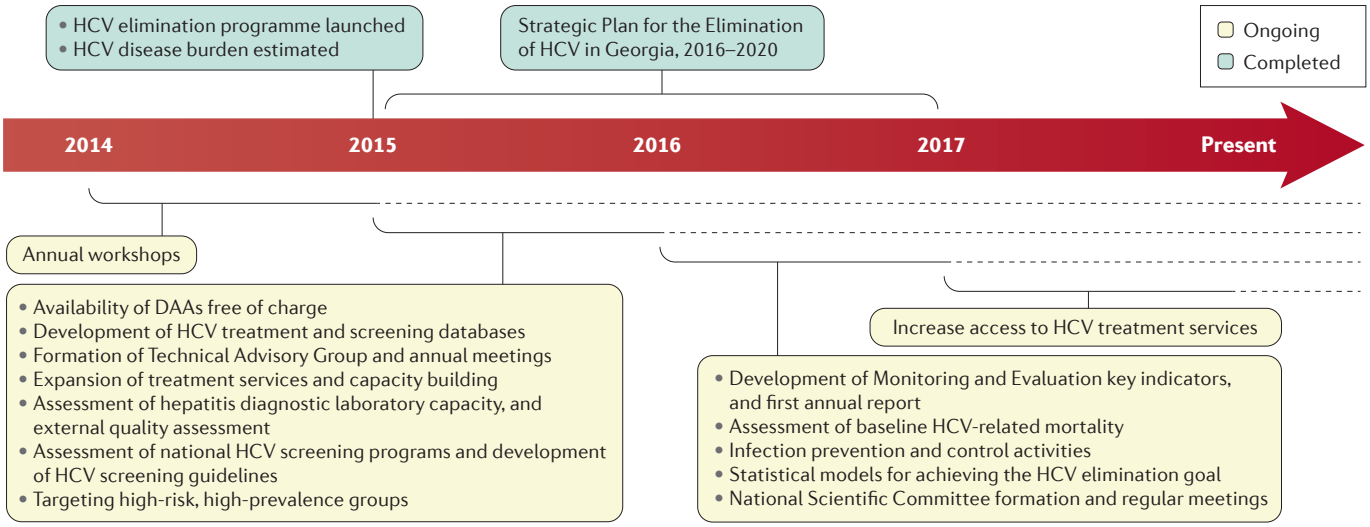

Figure 1 | **Key activities for the nationwide HCV elimination programme in Georgia.** Full details of all activities are described in Supplementary information S1 (table).

December 2016, an estimated 2,500 premature HCV-related deaths and 5,200 new infections were averted[6].

Although the Georgia HCV elimination programme has made substantial progress since initiation, with rapidly scaling-up care and treatment services, after a 20 month project period only ~20% of the Georgian population living with HCV have received treatment. During the last 3 months of 2016, the number of persons entering the treatment programme declined steadily, suggesting that the first-tier, readily achievable programme initiative — providing treatment to those who know they are infected and are motivated to seek treatment — is nearing completion. In response, Georgia is ramping up screening and linkage to care and treatment services. Outreach and provision of services for the most at-risk populations, including people who inject drugs, is also a priority. The next few years are an opportunity for Georgia to demonstrate how to tackle these more complex elimination activities.

Much of Georgia's success can be attributed to the country's openness to working with partners providing technical assistance and support. CDC was the first international partner, with Gilead Sciences coming on board soon thereafter. Since the launch of the programme in April 2015, additional partners (see Acknowledgment section) are now contributing to the HCV elimination efforts in Georgia. Through statistical modelling, countries like Belgium[7] and Greece[8] are gauging whether they, too, can achieve the WHO's HCV elimination goals and are assessing the measures needed to curtail incidence and lower prevalence of HCV. In 2017, the National Academies of Science, Engineering, and Medicine set goals for the elimination of HBV and HCV as public health threats in the USA[9]. DAA costs are decreasing globally and the cost-effectiveness of elimination has been documented[10], developments that promote achievement of HCV elimination goals. Nonetheless, Georgia is the only real-world setting in which a comprehensive HCV elimination programme has been launched.

A key lesson from this experience is that availability of curative treatment alone is not enough to achieve HCV elimination; instead, a comprehensive approach to elimination must be taken, to include screening and linkage to care and treatment policies and programmes, high-quality diagnostics, surveillance, provision of services to high-risk and marginalized populations, and measures to prevent transmission. Although formidable challenges exist, lessons from this model elimination programme can inform similar initiatives in other countries, regardless of income level. The Georgia HCV elimination programme will continue to evolve as innovative screening strategies, diagnostics, and prevention and treatment options are implemented, providing valuable lessons for the world.

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Competing interests statement
The authors declare no competing interests.

SUPPLEMENTARY INFORMATION
See online article: S1 (table)
ALL LINKS ARE ACTIVE IN THE ONLINE PDF

Supplementary Table 1: Key activities for a nationwide HCV elimination program — Georgia

Activities	Time period	Details	Status
Estimating HCV disease burden	2015	National seroprevalence survey	Completed
Information systems	2015-present	Development of STOP-C national treatment database	Completed
		Development of ELIMINATION-C national treatment database launched in June 2016	Completed*
		Development of national HCV screening database	Ongoing
Strategic Plan for the Elimination of HCV in Georgia, 2016–2020	2015-2017	Components of the plan include: (1) Advocacy, awareness and education (2) Preventing HCV transmission through harm reduction** among persons who inject drugs, blood safety, infection control in healthcare and non-traditional healthcare settings (3) Identification of persons through HCV screening (4) Laboratory diagnostics (5) Care and treatment (6) Surveillance	Completed
Monitoring and evaluation	2016	Monitoring and evaluation key indicators relevant to all six components of the strategic plan for the elimination of HCV in Georgia	Completed
	2017	First annual monitoring and evaluation report	Ongoing
Technical Advisory Group (TAG)***	2015-present	First (2015) and second (2016) annual TAG meetings held in Tbilisi	Completed
Screening	2015-present	Assessment of national HCV screening programs	Completed
		Development of national HCV screening guidelines/recommendations	Completed
		National screening implementation plan	Ongoing
Treatment	2015-present	Treatment sites expanded	Ongoing

		from 4 to 27	
		Capacity building through Tele-ECHO (Extension for Community Healthcare Outcomes) clinics, and Liver Institute and Foundation for Education and Research (LIFER) seminars	Ongoing
Baseline HCV-related mortality	2016-present	Assessment of baseline HCV-related mortality using vital statistics, medical chart abstraction, and cancer registry	Ongoing
Infection prevention and control (IPC)	2016-present	Assessment of IPC practices in hospital settings and dental facilities	Completed
		Development of IPC training curriculum	Ongoing
		Training of physicians, dentists, and other allied medical personnel on IPC training	Ongoing
Laboratory diagnostics	2015- present	Hepatitis diagnostic laboratory capacity using modifiedWHO tool[i]	Completed
		Pilot studies for validation of core antigen test sensitivity and specificity as a screening and/or confirmatory test for HCV	Completed
		External quality assessment (EQA) of participating laboratories in the national HCV elimination program	Ongoing
Models of HCV elimination	2016-present	Statistical models to prioritize high-risk, high-prevalence populations for achieving the HCV elimination goal	Ongoing
Targeting high-risk, high-prevalence groups	2015	Treatment effectiveness in prison system	Completed
	2017-present	Provision of HCV treatment at harm-reduction** sites	Ongoing
Increase access to HCV treatment	2017-present	Simplified diagnostics and monitoring of HCV-infected patients	Ongoing
		Primary-care physicians treating uncomplicated cases of HCV	Ongoing

Annual workshops	2014-present	2014: HCV elimination conceived 2015: Preparation for launch 2016: *Strategic Plan for the Elimination of HCV in Georgia*; monitoring and evaluation 2017: Implementing TAG recommendations	Completed
National Scientific Committee	2016-present	Formation of the National Scientific Committee with permanent members from MoLHSA†, NCDC††, four major clinics in Tbilisi, and CDC	Completed
		Analyses of ongoing HCV treatment data, research proposals, pilot studies, abstract and manuscript writing, and dissemination	Ongoing

*Undergoing improvements and merging with STOP-C

**Centers providing services such as opioid substitution therapy and needle and syringe provision to people who inject drugs

***A total of 10-15 experts in the field of viral hepatitis prevention and control from outside the country of Georgia serve as members of TAG

†Ministry of Labour, Health, and Social Affairs, Georgia

†† National Center for Disease Control and Public Health, Georgia

[i] World Health Organization. Laboratory assessment tool. 2012 [cited 2016 May 28]; Available from: http://apps.who.int/iris/bitstream/10665/70874/3/WHO_HSE_GCR_LYO_2012.2_eng.pdf?ua=1&ua=1.