

Cost Analysis of Hepatitis C Diagnostic Testing in Georgia

Partnership for Research and Action for Health

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PRAH has been providing guidance to Public Health Research Forum – a strategic partnership of PRAH and International School of Public Health, Tbilisi State Medical University, Georgia. This is very important initiative playing a critical role in improving public health research, public health education, and public health policy and practice in Georgia. Public Health Research Forum provides a flexible and effective mechanism to build partnerships, establish international cooperation, mobilize human and material resources, all of which are so needed for a successful proposal development, fund raising, and implementing various projects and consultancy assignments.

The other member of Public Health Research Forum – International School of Public Health, Tbilisi State Medical University, is a national leading institution for public health training, health research, and health policy development. The school faculty members include national leading experts in public health, epidemiology, biostatistics, environmental health, health care financing, health economics, health policy and planning, etc. Most of the experts that are affiliated with the school are simultaneously holding key positions at the national institutions as well as international organizations and programs active in the field of public health in Georgia. The school faculty includes 20 members, who can be deployed for implementation of various projects and consultancy assignments.

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Disclaimer

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Conflict of Interest Disclosure of Report Authors

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Abbreviation and Acronyms

AASLD - American Association for the Study of Liver Diseases

Ab – Antibody

Ag – Antigen

AIDS Center- National Center of Infectious Diseases, HIV/AIDS and Clinical Immunology

ALP - Alkaline Phosphatase

ALT - Alanine Aminotransferase

AST - Aspartate Aminotransferase

bDNA – Branched DNA [test]

BSS – Behavioral Surveillance Survey

CBC - Complete Blood Count

DNA – Deoxyribonucleic Acid

DETRA – Defence Threat Reduction Agency

GEL – Georgian Lari

GF - Global Fund

GoG – Government of Georgia

MAP – Medical Assistance Programme

MoLHSA – Ministry of Labour, Health and Social Affairs of Georgia

EASL - European Association for the Study of the Liver

EIA - Enzyme-Linked Immunoassays

GT – Gamma-Glytamyl Transpeptidase

GEL – Georgian Lari [currency]

HBsAg – Hepatitis B Virus Superficial Antigen

HBV – Hepatitis B Virus

HCV - Hepatitis C Virus

HIV – Human Immunodeficiency Virus

IDUs – Intravenous Drug Users

IgG – Immune Globulin type G

IgM – Immune Globulin type M

INR - International Normalized Ratio

NGO – Non-governmental Organization

NCDC – National Center of Disease Control of Georgia

PCR – Polymerase Chain Reaction

PTT - Partial Thromboplastin Time

RNA – Ribonucleic Acid

S/R – Simple Rapid [Tests]

STD – Sexually Transmitted Diseases

SVR - Sustained Virologic Response

VCT – Voluntary Counseling and Testing

TMA - Transcription-mediated amplification

WHO – World Health Organization

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Executive Summary

This OSI-supported study on main cost-drivers for Hepatitis C diagnostic testing in Georgia presents summary results of key informant interviews, document reviews and interviews with patients, health care facility managers, insurance companies, importers of HCV diagnostic tests and etc. Based on the study results, the report discusses the options to contain costs related to HCV diagnostic tests and testing services in Georgia and provides actionable, evidence-based recommendations in line with country's development objectives and Health Sector Reform Strategy.

Problem statement: Hepatitis C is one of the public health threats worldwide. About 130–170 million people are chronically infected with hepatitis C virus, and more than 350 000 people die from hepatitis C-related liver diseases each year. Because it is often left untreated, chronic hepatitis is a major cause of liver cirrhosis and primary liver cancer. Hepatitis C is responsible for about 86 000 deaths per year in the Europe Region [WHO, 2012].

The prevalence of Hepatitis C, as well as in many other countries, is not well documented in Georgia. According to official statistics, growing epidemics reached About 46.4 new cases per 100,000 population in 2010 in the country. In addition to the unfavorable health outcomes, Hepatitis C has significant economic impact on the patients and their families, especially for vulnerable and high risk population (injection drug users, blood donors and etc), _ Most Hepatitis C diagnostic and treatment services are not covered by publicly funded programmes and/or private insurance schemes and create insuperable financial barrier to many households to get needed services. Furthermore, recent cross-country assessment shows that some Hepatitis C diagnostic tests in Georgia are significantly more expensive than in selected Eastern European countries, including CIS countries and EU member states [Ocheret D. at al].

In order to support Government of Georgia (GoG) effort to increase the financial access to Hepatitis C diagnostic and treatment services in Georgia, the study aimed to: 1) identify the key cost-drivers for HCV diagnostics both from supply and demand side, 2) obtain the information on these drivers from different data sources and 3) present/analyze the results and 4) develop evidence-based cost-containment recommendations.

Methodology

At the first step, key possible elements that impact the final cost and price of the HCV diagnostic tests and testing services in Georgia have been conceptualized (see Figure 1 below). After identification of the supply- and demand-side cost drivers, data sources for each cost-driver have been identified.

Based on the **conceptual framework, primary data collection** have been conducted through standard set of semi-structured interviews with policy makers, representatives of pharmaceutical industries, health insurance companies, health care facility managers/financial administrators, patients and etc. (Total 58 stakeholders have been interviewed).

In addition to the primary data collection, **desk-review** of the global and national literature has been conducted to identify the evidence-based diagnostic practices in Georgia that will be focus of the study.

The rationale of **sampling methodology** was to include all the layers of data sources (with triangulation of results) from the conceptual framework and not to obtain quantitative data to get representative results.

Hepatitis C financing and pricing policy of HCV diagnostic tests in Georgia

HCV diagnostic and treatment services (except rapid screening tests for specific target population) are not covered by the **publicly funded programmes**. Complete HCV diagnostic services and treatment is covered only for HIV/HCV co-infected patients through the HIV component of the **Global Fund (GF) program**. Currently this program covers HCV diagnostic and treatment services for maximum 100 co-infected patients per year. In addition, state program fully covers symptomatic treatment of acute and chronic hepatitis cases in hospitals for beneficiaries below the poverty line. Specific anti-HCV treatment (interferon/ribavirin) and HCV diagnostic services are not covered under the program.

Private insurance companies cover only small portion of diagnostics needs of HCV patients in the country. HCV screening by simple rapid or ELISA methods is reimbursed only for patients at pre-delivery or pre-operative stages. No other direct and/or additional diagnostic services related to HCV infection (as well as for HBV infection) are covered by insurance companies. Insurance schemes also do not cover any HCV treatment. HCV diagnostic (except HCV screening) and treatment services are not covered also under the **individual private health insurance packages in Georgia**. According to the representatives of private insurance companies, insurance premium for most private health insurance benefit packages is so small that it does not allow covering HCV diagnostic and treatment services.

Regulation of diagnostic tests, as well as medicines in Georgia is market-oriented. To improve the access to diagnostic tests and medicines to the population and improve their quality, GoG introduced several regulatory initiatives aiming decrease of entry barriers in the local market, simplifying drug regulation rules and procedures. Recent changes in the Ministerial Decree #344/N of MoLHSA, 2011 allowing to register the diagnostic tests under the Recognition Regimen create significant opportunities to improve competition among importers of HCV diagnostic tests in the local market and decrease their price. Nevertheless, importers of diagnostic tests identify a few regulatory barriers that prevent them to register HCV diagnostic tests under the recognition regimen.

Market is **self-regulated with regard to wholesale and retail price of HCV diagnostic tests and testing services in health care facilities**; as government does not regulate the price of the HCV diagnostic tests, any importer, wholesale and/or retail distributors can set the price solely based on the company's market strategy. The same applies to prices of medical and diagnostic services; – government does not regulate the price of medical services (including diagnostics). Although Government sets limits to reimburse medical (including diagnostic) services for detection and treatment of specific diseases/conditions under some government-funded health programmes. Other attempts to contain prices of medical/diagnostic services are global budget, capitation and other reimbursement schemes under the government-funded programmes.

To support free competition in the local market and low prices, Tax Legislation of Georgia is also maximally supporting in terms of import and distribution of registered medicines and diagnostic tests in the country (VAT exempt, no customs tax). This allows importers and distributors of HCV

diagnostic tests to avoid access overhead costs on the test-systems. They only pay profit tax (15% of their profit).

Medical services (including diagnostic services) in Georgia are provided mostly by private health facilities and are also exempt from VAT. Medical facilities, despite their organizational and legal status, also do not pay profit tax from the part of the profit from the medical services that will be used to reinvest in medical infrastructure (30). Lab is mostly commercialized. Although the set of CDC laboratories at district, regional and national level are publicly owned and provide lab services on low cost or free of charge (under government and/or donor funded programme).

Despite market-oriented regulatory environment, limited entry barriers and supporting tax policy, the price of RNA testing and genotyping are more expensive in Georgia than in many other countries of the region (including some EU countries).

Summary of HCV diagnostic methods and tests used in Georgia

The national guidelines for the management of Hepatitis C are adapted from the international evidence-based best practices and adopted by the Ministry of labor, Health, and Social Affairs (MoLHSA). The guideline and protocol of management of hepatitis C include a full spectrum of diagnostic methods available globally. All key Hepatitis C diagnostic methods recommended by evidence-based best practices are currently used in Georgia.

According to the National Guideline and international best practices, for the diagnostics of hepatitis C both two main laboratory methods are used, these are serologic (“**antibody testing**”) and nucleic acid-based molecular assays (Scott 2007). Serologic tests are sufficient when chronic hepatitis C is expected, with a sensitivity of more than 99% in the 3rd generation assays. Positive serologic results require **HCV RNA testing** in order to discriminate between chronic hepatitis C and resolved HCV infection from the past. HCV RNA is detectable within a few days of infection and thus, RNA testing is mandatory in diagnosing acute hepatitis C. HCV RNA measurement is also essential in the determination of treatment indication, duration and the outcome (Terrault 2005). It is performed during treatment to decide whether the therapy should be continued or not. It should be repeated 24 weeks after treatment completion to assess whether a sustained virologic response (SVR) has been achieved.

When HCV infection diagnosis is confirmed, the next step in diagnostics is the identification of HCV genotype as a rule by nucleic acid-based techniques. Because the currently recommended treatment durations and ribavirin doses depend on the HCV genotype, **HCV genotyping** is mandatory in every patient who is considered for antiviral therapy (Bowden 2006).

Current best practices only support screening of individuals who are at the increased risk (36). Routine screening of general population is not cost-effective and not supported by A level evidence. According to the National Protocol, only injecting drug users, HIV infected individuals, patients with hemophilia, dialysis and other high risk groups should be screened for HCV (10).

Cost and key cost-drivers of HCV diagnostic tests in Georgia

All HCV diagnostic tests are imported in Georgia. There is no single manufacturer in the country producing HCV diagnostic tests. According to the local manufacturers, there is no incentive to

produce HCV diagnostic tests, local market is small and would not allow covering significant investments associated with production of the tests.

Imported HCV tests in Georgia are produced by 10-15 different manufacturers throughout the world.

The price of **antibody detection rapid and ELISA tests** is not high in Georgia: average wholesale price of these tests varies from 1.5 to 6 GEL. Because of relatively large market of Hepatitis C antibody detection screening tests (these tests are routinely performed during planned surgeries, in high risk individuals and covered by many public, private insurance and donor-funded programmes) competition is tight among importers of these tests. Use of competitive purchasing procedures (tenders) by different Georgian institutions, allowed to further decrease the price of the antibody detection screening tests.

The average wholesale **price of RNA tests** is significantly higher than antibody detection tests and varies from 40 GEL to 180 GEL. Despite the availability of 2-3 times cheaper RNA tests manufactured by “Sacace Biotechnologies” (Italy) that recently entered to the Georgian market, Roshe qualitative and quantitative tests constitutes about 90% of RNA tests’ market in Georgia and is solely imported/distributed by LTD Mirco. Small market and almost exclusive supplier of HCV RNA tests in Georgia leaves the possibility to the importer/distributor company to set the high price of the product. Because of the commercial secret, we were not able to obtain detailed information on the key cost structure and overhead of RNA tests from any private and/or government organization (Georgia Revenue Service, MoHLSA) in Georgia. Because of the same reason, we were not able to document any interdependence of players among importers/distributors and/or providers of HCV diagnostic services that allow “price setting privilege” in the market. But the fact that the price of RNA tests are higher in Georgia than in other European Countries (including EU member states) under supporting tax and drug regulatory policy demonstrates the opportunity to significantly reduce the cost of HCV RNA tests in the country.

There were no known prior attempts to reduce the cost of RNA tests in Georgia except recent appearance of cheaper RNA tests (manufactured by “Sacace Biotechnologies”, Italy) in the market by LTD Irise. Because of the small time period since then, it is difficult to analyze the impact of this intervention to the price of RNA tests in Georgia.

The price of HCV genotype tests in Georgia is also high (on average, 250 GEL). HCV genotyping in Georgia is conducted by reverse hybridization assay Versant HCV Genotype 2.0 System, Manufactured by Siemens Medical Solutions Diagnostics and is exclusively imported/distributed by GPC Ltd. As in case of RNA tests, small market and exclusive supplier of HCV genotype tests (under supportive tax policy of Georgian government), most likely is the reason of high price of HCV genotype tests in Georgia; Under no price regulation and competitive environment, exclusive/monopolistic provider has the freedom to set the high price of HCV genotype tests in the Country. The fact that HCV genotyping is more expensive in Georgia than in other post-soviet countries of the region with similar size markets might serve as a proof of above-mentioned statement.

HCV diagnostic services and their costs in medical facilities: Simple rapid HCV tests are available at large number of medical facilities. HCV screening tests using **ELISA** is less readily available at medical facilities, but still are common screening options at the facilities which own ELISA machines

(ELISA readers). Average price of simple rapid tests varies from 12.5 to 16 Georgian Lari (GEL)¹ and for ELISA tests, from 22.3 to 35 GEL. Relatively big market and many competitors more likely contributed to the fact that both, importers of HCV antibody tests and facilities providing HCV screening services tend to offer competitive prices for HCV screening tests and services. Because of the small price and the fact that antibody detection tests are covered by many public, private insurance or donor-funded programmes, according to the interviewed patients, HCV antibody testing is financially accessible to them. Thus, **the study will not focus on the price-containment strategy of antibody detection HCV tests.**

Prices of HCV Diagnostic Services in Medical Facilities: HCV RNA tests are provided by small number of clinics in Tbilisi (5 facilities) and regions (4 facilities) and HCV genotyping is provided only by 3 facilities in Tbilisi (no regional coverage). Prices of both types of diagnostic tests are very high and range from 305 to 506 GEL. HCV genotyping which is sent for diagnostics outside of Georgia (e.g. in Germany, through Mrcheveli laboratory network) costs over 600 GEL.

Interviews with providers of HCV diagnostic tests show that they usually do not use competitive tenders to purchase HCV RNA and genotype tests. Also, none of the facilities collaborate with other facilities for the purpose of **group purchasing**.

It is important to emphasize that the prices of HCV diagnostic service in health care facilities are less variable than the prices of diagnostic tests. For example, the wholesale price of HCV RNA qualitative and quantitative tests varies from 40-80 GEL and 60-180 GEL respectively, while the price of HCV RNA qualitative and quantitative testing service does not vary much throughout the facilities (192-203 GEL in case of RNA qualitative test, and 304-340 GEL in case of quantitative test). The difference between cost of tests and testing service is understandable for antibody detection tests where the cost of the screening test is not the key driver in the price of HCV antibody testing service (due to facility's other fixed and variable costs, associated with HCV testing). This should not be a case for HCV RNA qualitative/quantitative tests and genotyping. The study results clearly indicate that the prices of HCV RNA qualitative/quantitative tests in the facilities are not based on the real costs of the service/product, and the limited number of facilities (3-8) offering HCV RNA testing and genotyping services benefit from the **price-setting "privilege"** in the market. Such practice is also supported with the fact that RNA testing and genotyping services are solely covered by patients through out-of-pocket payments (in contrast, when the facility implements government and/or private insurance programmes, because of economy of scale or other consideration, facility usually has to "take" the lower price offer from the government/insurance company and set the higher price ("shift the price") for the services covered out-of-pocket and/or initiate other strategies to reduce the cost of diagnostic and medical services).

Indeed, all relevant interviewed patients diagnosed with Hepatitis C reported that HCV RNA testing and genotyping were paid by themselves out-of-pocket. Despite the fact that 20% of patients had private insurance packages, they were "**underinsured**" in terms of HCV diagnosis and treatment and paid for these services out-of-pocket. Only 10% of patients reported initial payment of the cheap HCV antibody detection tests through corporate health insurance.

¹ | USD = 1.65 GEL

According to interviewed patients, price of antibody detection HCV tests is not high and they can afford this type of tests. The price of all other tests, especially RNA testing and Genotyping, are expensive and create significant financial burden for them. Cost of quantitative HCV RNA and HCV genotyping tests for poor households is approximately two times higher than their monthly household income.

If we consider: a) households' expenditure related to substance use (monthly expenditure on food and other substance expenses); b) the fact that neither public health programs nor private insurance schemes cover HCV RNA and HCV Genotyping diagnostic services; and c) the lower income quintiles (poor, low-middle and middle) usually do not have savings, it becomes clear that any HCV RNA testing and Genotyping could result in catastrophic health expenditures for these patients and their families. The same applies to the HCV treatment. The mean 24-week treatment price, reported by patients, is 15167 GEL and mean 48-week treatment price is 25500 GEL. About 50% of patients were unable to afford HCV treatment at all as the average price on monthly HCV treatment several times exceeded self-reported household monthly income of poor, low-middle and middle quintiles.

Conclusions and recommendations:

Study results demonstrate that the price of antibody detection HCV tests is not high, mostly covered by public, private insurance and donor-funded programmes and thus, the financial access to HCV antibody testing is not an issue in Georgia. In contrast, the price of RNA and Genotype testing is high and create significant financial burden especially for poor households. Because of the fact that neither publicly funded nor private insurance programmes cover HCV RNA testing and genotyping, there is a greatest need for price reduction of these types of tests especially for poor and vulnerable population. Indeed, 30% of interviewed patients reported difficulties to afford RNA and HCV genotyping as the price of these tests are approximately two times higher than the monthly income of poor households.

In addition to the greater need, there is also more opportunity to decrease the price of HCV RNA testing and genotyping in Georgia; These tests and diagnostic services are exclusively provided by very few (or solo) distributors and service provider facilities. Within enabling regulatory and tax policy of diagnostic tests and laboratory services in Georgia, there is the possibility to increase the competition on HCV RNA and genotyping tests and diagnostic services through increased demand.

In order to reach price reduction on HCV RNA and genotype testing in Georgia, Government's role is crucial to eradicate a few (but important) entry barriers to the HCV diagnostic test market and increase financial access to HCV (RNA testing, genotyping) diagnostic and antiviral treatment services. Because of the cost consideration, poor and vulnerable population often avoid needed in-depth diagnosis and treatment of Hepatitis C. If we consider that not-treated HCV cases have substantial economic and human impact on families/communities due to increased health care costs, lost productivity and are the major cause of premature death while in approximately 40-80% of HCV patients, the infection will clear with timely diagnosis and treatment (45, 46), Government has strong justification to allocate public resources for timely confirmatory HCV diagnostic and treatment services in Georgia.

Based on the analysis of health sector reform context and study results, specific short- and long-term actions are provided in the table below to improve access to the HCV RNA testing and Genotyping in Georgia (the recommendations are expanded in the relevant part of the report):

What: Objectives and activities	Who	When	
		Short term	Long term
to improve access to HCV RNA testing and Genotyping in Georgia			
1. Support price competition of HCV RNA and Genotype Diagnostic tests in the local market		X	
1.1. Negotiations with potential importers of low-cost HCV RNA and Genotyping tests in Georgia	Local Distributor Companies	X	
1.2. Ensuring availability of impartial price information on HCV RNA and HCV Genotyping Diagnosing Tests, available choices and their comparative effectiveness to influence doctors' prescribing decision depending on patient's ability to pay	MoLHSA regulatory agency, managers of medical/laboratory facilities, care providers	X	
2. Eliminate regulatory barriers (including in the Law on Drugs and Pharmaceutical Activity in Georgia)			
2.1. Clearly define the specialty of personnel responsible for distribution of diagnostic tests (Medical Technician or Pharmacologist);	MoLHSA and its regulatory agency, Parliament of Georgia	X	
2.2. For minor (allowable) changes in pharmaceutical products and diagnostic tests systems (such as changes in catalogue number for example) do not require completely new registration procedure under the recognition regimen and allow consequent changes in registration by informing and paying a fee (as it is under National Registration Regimen).	MoLHSA and its regulatory agency, Parliament of Georgia	X	
2.3. In case of Recognition Regimen of registration, do not require provision of very expensive samples of diagnostic tests to Regulatory Agency.	MoLHSA and its regulatory agency, Parliament of Georgia	X	
3. Promote competitive procurement and group purchasing			
3.1. Strengthen capacity of NCDC laboratory network to conduct/offer HCV RNA and Genotyping diagnostic services (including supporting them to use competitive procurement to purchase HCV RNA and Genotype tests	MoLHSA, NCDC, DETRA, Regional Laboratories of NCDC	X	
3.2. Use competitive tendering and group purchasing by medical facilities for purchasing HCV RNA and Genotype tests	Managers of medical corporations or stand alone health care facilities		X
4. Support rational use of specific type of RNA quantitative tests according to the Hepatitis C Management Protocol			
4.1. Provide focused training to prescribe less costly RNA qualitative tests for 1) early detection, 2) determination of disease stage (active, latent), 3) confirmation of virologic response during, at the end of, and after antiviral therapy, and 4) screening blood and organ donations for presence of HCV, and use more costly quantitative HCV RNA tests only in case of need to monitor/predict effectiveness of anti-HCV treatment).	Managers of medical facilities, professional associations, donor agencies	X	
5. Improve affordability of HCV RNA and Genotype Diagnostic and Treatment Services for poor and vulnerable population			
5.1. Development sustainable financing mechanisms for HCV diagnostic (RNA, Genotype) and treatment	MoLHSA, Donor Agencies/implementing partners	X	

5.2. Expand coverage of poor and vulnerable population with HCV diagnostic (RNA and genotype testing) and antiviral treatment services	MoLHSA, Pharmaceutical companies		X
5.3. Use effective strategies (co-financing, service contracting and etc) and public-private partnership (with importers/distributors of HCV diagnostic tests and antiviral drugs) to decrease/contain costs on diagnostic services under the publicly-funded programme covering HCV diagnostic and treatment services	MoLHSA, Pharmaceutical companies, medical/laboratory facilities		X
6. Protect population from the catastrophic expenses, associated with HCV RNA testing, genotyping and treatment services through considering these services in pre-payment schemes			
6.1. Establishing minimum benefit package, a standard set of benefits to be offered by private insurance schemes (both employer- and individual private insurance) that covers HCV diagnostic and treatment for insured population	MoLHSA, private insurance companies, Insurance Mediation Service	X	
6.2. Incorporating HCV RNA/Genotyping in private insurance schemes	Health insurance companies	X	
6.3. Establishment of compulsory medical savings account in Georgia	MoLHSA, MoF, Parliament of Georgia		X
7. Increase demand on HCV diagnostic services through better outreach of target population			
7.1. Scale up the efforts to reach IDUs through VCT services and community-level activities	Government entities, Donors (GF HIV Project, USAID HIV Prevention Project) , NGOs	X	

Because of the commercial interest, we were not able to get detailed information about the cost structure and overhead from suppliers of diagnostic tests and providers of HCV diagnostic services. It hindered the possibility to estimate accurate impact on cost-reduction under the proposed strategy. Given the information that we are able to collect under the study, including price of HCV RNA tests and testing services in the post-soviet countries, with proposed strategy, it is possible to decrease the cost of HCV RNA testing by about 30-40% and decrease of HCV genotyping by at least 30%.

1. Introduction

Epidemics of viral hepatitis C (HCV) is an important public health threat in Georgia. Although HCV treatment needs are not well documented, financial access to HCV diagnostic and treatment in different population groups is far from being satisfactory².

This OSI-supported study analyzes the main cost-drivers for Hepatitis C diagnostic testing in Georgia and presents summary results of key informant interviews, document reviews and interviews with patients, health care facility managers, insurance companies, importers of HCV diagnostic tests and etc. Based on the study results, the report discusses the options to contain costs related to HCV diagnostic tests and testing services and provides actionable, evidence-based recommendations in line with country's development objectives and Health Sector Reform Strategy.

² EHRN, Call for Action: Reduce Prices for Hepatitis C Treatment (2011), available at http://www.harm-reduction.org/images/stories/documents/hcv_call_for_action.pdf

2. Background Information

2.1. Peculiarities of HCV infection epidemic

Hepatitis C virus (HCV) infection remains one of the most important blood-borne diseases worldwide with more than 200 million individuals infected globally [WHO, 2010].

The prevalence of Hepatitis C is not well-documented in many countries. Based on the statistics that are available, it is estimated that 3% of the world population is infected with hepatitis C virus. Most populations in the America, Europe and South-East Asia the prevalence of HCV is under 2.5% (Sharvadze et al). An estimated 9 million are infected with hepatitis C, but most are unaware that they are infected. Because it is often left untreated, chronic hepatitis is a major cause of liver cirrhosis and primary liver cancer. Hepatitis C is responsible for about 86 000 deaths per year in the Europe Region [WHO, 2012].

People who inject drugs are particularly vulnerable to hepatitis and, in some settings; almost all are infected with hepatitis C. As they are also more vulnerable to HIV infection, co-infection with both HIV and hepatitis is particularly common among those who inject drugs in the Region. Between 70-90% of injecting drug users living with HIV also have hepatitis C infection. With increasing availability of effective treatment for HIV, chronic, untreated viral hepatitis is increasingly a major cause of death among people living with HIV in the Region.

As a person with hepatitis may have no symptoms for a long time, the epidemic is largely hidden and was until recently not fully recognized as a public health problem in the Region. As a result:

- Hepatitis surveillance is weak – the number of persons living with different forms of chronic hepatitis are not known accurately;
- The cost of diagnosis and treatment of hepatitis remains very high; and
- Access to prevention and treatment services is limited in many countries of the Region, particularly in eastern European and central Asian countries.

Highlight high HCV prevalence among adult population (above 6% according to the attached article by Sharvadze et al). This might be important, particularly given the limitations of official statistics due to the factors that you well describe - inaccessibility of antibody testing and lack of early diagnostics of the virus and disease.

HCV is endemic in most areas of the world. Infection with HCV becomes chronic in approximately 80% of cases. Chronic infections of hepatitis C can, and often do, lead to end-stage liver diseases such as cirrhosis and hepatocellular carcinoma.

Hepatitis C virus was identified by Choo et al. in 1989. HCV isolates from around the world can be separated into at least 6 major genotypes, each with a number of subtypes. Complete genome sequences are now available for all six HCV types and for several different subtypes of type 1 (a, b and c), 2 (a, b and c) and 3 (a, b and “10a”). Very similar sequence relationships are obtained by analysis of subgenomic fragments, such as individual genes encoding structural and nonstructural

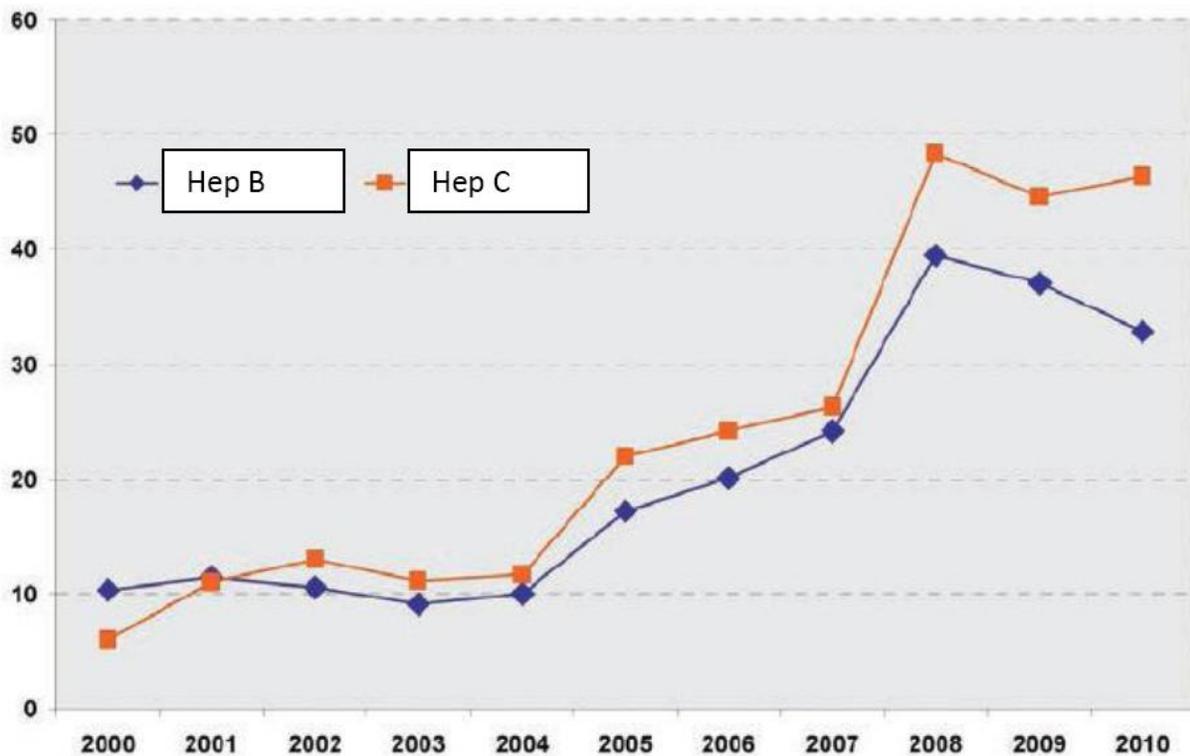
proteins or a short region of NS5B. On this basis it is possible to differentiate consistently among six major genotypes and an increased number of subtypes [Frank et al, 2000, Simmonds et al, 2001, Lauer and Walker, 2001].

HCV is primarily transmitted parenterally in adulthood by injecting drug use, blood transfusion, or other medically-related parenteral exposures. In developing countries, nosocomial exposures, traditional healing practices using non-sterile instruments, and the use of non-sterile needles may contribute to the high prevalence of HCV infection in the general population (Akhtar et al, 2002, Reshetnikov et al, 2001).

2.2. HCV infection in Georgia

As in many other countries, the prevalence of HCV is not well documented in Georgia. According to official statistics, the incidence of Hepatitis C has been increased by 4% [28] and reached 2,067 new cases (46.4 per 100,000 population per year) in 2010 (see Figure 1 below).

Figure 1. Incidence of Hepatitis B and Hepatitis C in Georgia per 100,000 population per year



Source: NCDC, Statistical Year-book, 2010, Georgia

The highest incidence rate was detected in Imereti and Samegrelo Region (101.9 and 73.4 incidence rate per 100,000 accordingly). Tbilisi has the third largest incidence in 2010 (53.4 per 100,000). Among newly detected cases of Hepatitis C only 3% were diagnosed in acute phase.

The largest number of Hepatitis C cases was detected in 30-59 age groups (6% according to Sharvadze et al).

The prevalence rates are much higher in high-risk groups; the study of blood donors in Georgia found very high prevalence of HCV (6.9%) and HBV (3.4%) [Butsashvili et al 2001]. In a study of injection drug users, 70.4 % were positive for HCV [Stvilia et al 2006]. Similarly, recent Behavioral Surveillance Surveys (BSS) in Georgia found 57.8% to 76.4% prevalence among surveyed injection drug users (57.8% in Kutaisi in 2007; 64.6% in Tbilisi in 2006 and 76.4% in Batumi, in 2006) [39], [40], [41].

Because of the fact that Hepatitis C frequently progresses without any symptoms and the Hepatitis C risk groups are hard to reach population (for example injection drug users), the prevalence of the disease might be significantly high in Georgia.

2.3. Current State of Art in HCV diagnosis

2.3.1. Approach to the Diagnostics of HCV Infection

Clinical symptoms of hepatitis C are in most cases non-specific and can include fatigue, muscle pain, nausea. They are usually mild in many cases not present. As a result hepatitis C is often diagnosed accidentally, in most cases remains under-diagnosed, which increases the risk of the spread of this virus in the population. Untreated hepatitis C advances to a chronic state in up to 80% of people, which leads to liver cirrhosis in 20-40% with an accompanying risk of hepatic decompensation, hepatocellular carcinoma and death (McHutchison 2004). That's why early diagnostics of HCV infection is very important for the prevention of the spread of HCV as well as for the improvement of the outcome of this infection.

For the diagnostics of hepatitis C both two main laboratory methods are used, these are serologic (so called antibody testing) and nucleic acid-based molecular assays (Scott 2007). Serologic tests are sufficient when chronic hepatitis C is expected, with a sensitivity of more than 99% in the 3rd generation assays. Positive serologic results require HCV RNA measurement in order to discriminate between chronic hepatitis C and resolved HCV infection from the past. When acute hepatitis C is considered, serologic screening alone is insufficient because anti-HCV antibodies may develop late after transmission of the virus. In contrast, HCV RNA is detectable within a few days of infection, making nucleic acid-based tests mandatory in diagnosing acute hepatitis C. HCV RNA measurement is also essential in the determination of treatment indication, duration and the outcome (Terrault 2005). It is performed during treatment to decide whether the therapy should be continued or not. It should be repeated 24 weeks after treatment completion to assess whether a sustained virologic response (SVR) has been achieved.

When HCV infection diagnosis is confirmed, the next step in diagnostics is the identification of HCV genotype as a rule by nucleic acid-based techniques. It should be done in every patient considered for HCV therapy, because the recommended of interferon treatment duration and ribavirin doses differ among the genotypes.

There are also several other methods, like immunohistochemistry, in situ-hybridization or PCR from liver specimens, which play only an accessory role in the diagnosis of hepatitis C because of their low sensitivity, poor specificity and low efficacy compared to serologic and nucleic acid-based approaches.

2.3.2. Serology Methods for HCV Diagnostics

Antibody detection screening tests (Antibody tests): In current clinical practice, antibodies against multiple HCV epitopes are detected by commercially available 2nd, 3rd and 4th generation **enzyme-linked immunoassays** (EIAs). In these tests, HCV-specific antibodies from serum samples are captured by recombinant HCV proteins and are then detected by secondary antibodies against IgG or IgM. These secondary antibodies are labeled with enzymes that catalyze the production of colored, measurable compounds.

The first generation EIAs for the detection of HCV-specific antibodies had a sensitivity of 70–80% and a poor specificity (Scott 2007). The corresponding antibodies occur approximately 16 weeks after viral transmission. Second generation EIAs additionally detect antibodies against epitopes derived from the core region (C-22), NS3 region (C-33) and NS4 region (C-100), which leads to an increased sensitivity of approximately 95% and to a lower rate of false-positive results. With these assays HCV-specific antibodies can be detected approximately 10 weeks after HCV infection (Pawlotsky 2003). To narrow the diagnostic window from viral transmission to positive serological results, a 3rd generation EIA has been completed by an antigen from the NS5 region and the substitution of a highly immunogenic NS3 epitope. This innovation allows the detection of anti-HCV antibodies approximately four to six weeks after infection with a sensitivity of more than 99% (Colin 2001). The clinical specificity, however, is slightly decreased compared to the 2nd generation assays. Anti-HCV IgM measurement can narrow the diagnostic window in only a minority of patients. Anti-HCV IgM detection is also not sufficient to discriminate between acute and chronic hepatitis C because some chronically infected patients produce anti-HCV IgM intermittently and not all patients respond to acute HCV infection by producing anti-HCV IgM. In the case of the 4th generation assays, more antigens are used for the development of the assay which derived from the different HCV genotypes (1a, 1b, 2, and 3) that further increases sensitivity of the test.

False-positive results are more frequent in patients with rheumatic diseases and in populations with a low hepatitis C prevalence, for example in blood and organ donors.

There are several **immunoblotting** methods for the confirmation of positive HCV EIA results. These tests are losing their clinical importance since the development of highly sensitive methods for HCV RNA detection. Immunoblots are used mainly for the identification of serologically false-positive-tested individuals. The sensitivity of immunoblotting is lower compared to EIAs introducing false-negatively cases.

False-negative HCV antibody testing may occur in patients on hemodialysis or in severely immunosuppressed patients like in HIV infection or in hematological malignancies.

EIAs are the most widely used anti-HCV screening tests as they are the most appropriate for screening large numbers of specimens on a daily basis. However, in resource limited countries and small facilities only limited numbers of specimens are usually processed. In such cases individual tests, so-

called “*simple rapid tests*” are more appropriate. Several simple, instrument-free screening tests have been developed including agglutination, immunofiltration (flow through) and immunochromatographic (lateral flow) membrane tests. A positive result is indicated by the appearance of a colored dot or line, or the presence of an agglutination pattern. While most of these tests can be performed in less than 10 minutes, other simple tests are less rapid and their performance requires 30 minutes to 2 hours. The results are read visually. In general, these simple/rapid (S/R) tests are most suitable for use in laboratories that have limited facilities and/or process low numbers of specimens daily (WHO Report 2001).

There is also another type of the serology method which is very *promising alternative to the nucleic acid testing and which has a potential to decrease the cost for HCV diagnosis and management*. This is the HCV core antigen detection assay. However, the introduction of HCV core antigen assay was complicated by difficulties related with the development of specific monoclonal antibodies recognizing all different HCV subtypes and the need for accumulation and dissociation of HCV particles from immune complexes to increase sensitivity. The first HCV core antigen detection system (trak-C, Ortho Clinical Diagnostics) became commercially available in the US and Europe several years ago. The HCV core antigen assay proved highly specific (99.5%), genotype independent, and had a low inter and intra-assay variability (coefficient of variation 5–9%) (Veillon 2003). HCV core antigen is measurable 1–2 days after HCV RNA becomes detectable. The limit of detection was 1.5 pg/ml, which corresponds to an HCV RNA level of approximately 10,000–50,000 IU/ml. In a study of anti-HCV antibody and HCV RNA positive patients presenting in an outpatient clinic, 6/139 people (4%) were HCV core antigen negative. In these patients, HCV RNA concentrations were 1300–58,000 IU/ml highlighting the limitations of the HCV core antigen assay as confirmation of ongoing hepatitis C in anti-HCV-positive patients. As a consequence, this first HCV core antigen assay was mostly withdrawn from the market. Most recently, another quantitative HCV core antigen assay (Architect HCV Ag, Abbott Diagnostics), a further development of the previous assay, was approved by the European Union. This assay comprises 5 different antibodies to detect HCV core antigen, is highly specific (99.8%) and shows equivalent sensitivity for determination of chronic hepatitis C as HCV RNA measurement (Morota 2009). The detection limit corresponds to HCV RNA levels of 600–1000 IU/ml. Further studies are ongoing to show the utility of this more sensitive HCV core antigen assay for diagnosis and management of patients with HCV infection (Mauss et al 2010).

2.3.3. Nucleic Acid Testing for HCV Diagnostics

There are two types of HCV RNA detection assays. Qualitative tests are highly sensitive and are used for diagnosing hepatitis C for the first time, for the screening of blood and organ donations and for confirming Sustained Virologic Response (SVR) after treatment completion. Quantitative HCV RNA detection assays offer the possibility of measuring the viral load exactly over a wide range of copies and are essential in treatment monitoring. For both qualitative and quantitative HCV RNA assays there is a current trend towards switching to the real-time PCR-based assays that can detect HCV RNA over a very wide range, from low levels of approximately 10 IU/ml up to 10 million IU/ml.

Until 1997, HCV quantitative results derived from different HCV RNA test were not standardized. Due to the importance of an exact HCV RNA load determination for management of patients, WHO established the HCV RNA international standard based on international units (IU) which currently is

used in all HCV RNA tests used for clinical diagnosis. Other limitations of earlier HCV RNA detection assays were false-negative results due to polymerase inhibition, false-positive results due to sample contaminations because the reaction tubes had to be opened frequently, or due to under- and over-quantification of samples of certain HCV genotypes (Pawlotsky 2003; Morishima 2004).

Until recently **qualitative assays for HCV RNA** had substantially lower limits of detection in comparison with quantitative HCV RNA assays. The costs of a qualitative assay are also lower compared to a quantitative assay. Therefore, qualitative HCV RNA tests are used for the first diagnosis of acute hepatitis C, in which HCV RNA concentrations are fluctuating and may be very low, as well as for confirmation of chronic hepatitis C infection in patients with positive HCV antibodies. In addition, they are used for the confirmation of virologic response during, at the end of, and after antiviral therapy, as well as in screening blood and organ donations for presence of HCV. The qualitative HCV RNA can be performed by two different approaches:

- Reverse transcriptase-PCR (RT-PCR) based assays
- Transcription-mediated amplification (TMA) of HCV RNA

HCV RNA quantification can be achieved either by target amplification techniques (competitive and real-time PCR) or by signal amplification techniques (branched DNA (bDNA) assay).

Currently there is a trend towards switching from conventional PCR application to the real-time PCR methods. Real-time PCR technology provides optimal features for both HCV RNA detection and quantification because of its very low detection limit and broad dynamic range of linear amplification (Sarrazin 2006). Distinctive for real-time PCR technology is the ability of simultaneous amplification and detection of the target nucleic acid allowing direct monitoring of the PCR process (Higuchi 1992).

Highly effective and almost completely automated real-time PCR-based systems for HCV RNA measurement have been introduced by Roche Molecular Systems (US) and Abbott Laboratories (US). For replacement of the qualitative TMA and the quantitative bDNA-based assays, Siemens Diagnostics has also developed a real-time based PCR.

Although the real-time applications have several advantages over the conventional PCR assays, they need real-time PCR machines, which are quite expensive and this contributes to the high cost of the HCV PCR testing.

In Georgia both qualitative and quantitative HCV RNA PCR tests are in most cases done by Roche systems. Recently new players manufacturing real-time PCR systems (qualitative and quantitative) also were introduced into the Georgian laboratory space. The following test-systems are already registered in Georgia: HCV Real-TM Quant and HCV-TM Qual, manufactured by “Sacace Biotechnologies” (Italy), distributed by “Irise” Ltd.

HCV Genotyping: Six genotypes (1-6), multiple subtypes (a, b, c...) and most recently a seventh HCV genotype have been characterized. These genotypes vary in approximately 30% of their RNA sequence. HCV subtypes are defined by differences in their RNA sequence of approximately 10%. Within one subtype, numerous quasispecies exist and may emerge during treatment with specific antivirals. These quasispecies are defined by a sequence variability of less than 10% (Simmonds 2005). Because the currently recommended treatment durations and ribavirin doses depend on the

HCV genotype, HCV genotyping is mandatory in every patient who is considered for antiviral therapy (Bowden 2006).

Both direct sequence analysis and reverse hybridization technology allows HCV genotyping. Initial assays were designed to analyze exclusively the 5' untranslated region (5'UTR), which had a problem with the high rate of misclassifications especially on the subtype level. Current assays were improved by additionally analyzing the coding regions, in particular the genes encoding the non-structural protein NS5B and core protein, both of which provide non-overlapping sequence differences between the genotypes and subtypes (Bowden 2006).

The following technologies are mostly used in general for the HCV genotyping:

- Genotyping by **reverse hybridizing assay** (Versant™ HCV Genotype 2.0 System (LiPA), Siemens Medical Solutions Diagnostics. It is suitable for indentifying genotypes 1-6 and more than 15 different subtypes and is currently the preferentially used assay for HCV genotyping. By simultaneous analyses of the 5'UTR and core region, a high specificity is achieved especially to differentiate the genotype 1 subtypes (Bouchardeau 2007).
- Genotyping by **direct sequence analysis** (TRUGENE™ HCV 5'NC Genotyping Kit, Siemens). The TruGene assay determines the HCV genotype and subtype by direct analysis of the nucleotide sequence of the 5'UTR region. The accuracy of subtyping is poor because of the exclusive analyses of the 5'UTR (Pawlotsky 2003).
- Genotyping by **real-time PCR technology** (Abbott Real-Time™ HCV Genotype II assay)

It is less time consuming than direct sequencing. Nevertheless, single genotype 2, 3, 4, and 6 isolates were misclassified at the genotype level, indicating a need for assay optimization (Vaghefi 2009).

2.3.4. Application of HCV laboratory methods for the evaluation of different clinical cases of HCV infection

For the identification of **acute hepatitis C**, presence of both anti-HCV antibodies and HCV RNA should be tested. For HCV RNA detection, sensitive qualitative techniques with a lower detection limit of 50 IU/ml or less are required, for example TMA, qualitative RT-PCR or the newly developed real-time PCR systems. Testing for anti-HCV alone is insufficient for the diagnosis of acute hepatitis C because HCV specific antibodies appear only weeks after viral transmission. In contrast, measurable HCV RNA serum concentrations emerge within the first days after infection. However, HCV RNA may fluctuate during acute hepatitis C, making a second HCV RNA test necessary several weeks later in all negatively tested patients with a suspicion of acute hepatitis C. When HCV RNA is detected in seronegative patients, acute hepatitis C is very likely (Mauss et al 2010).

Chronic hepatitis C should be considered in every patient presenting with clinical, morphological or biological signs of chronic liver disease. When chronic hepatitis C is suspected, screening for HCV antibodies by 2nd, 3rd or 4th generation EIAs is adequate because their sensitivity is > 99%. False-negative results may occur rarely in immunosuppressed patients (i.e., HIV) and in patients on dialysis. When anti-HCV antibodies are detected, the presence of HCV RNA has to be determined in order to

discriminate between chronic hepatitis C and resolved HCV infection. Many years after disease resolution, anti-HCV antibodies may become undetectable via commercial assays in some patients

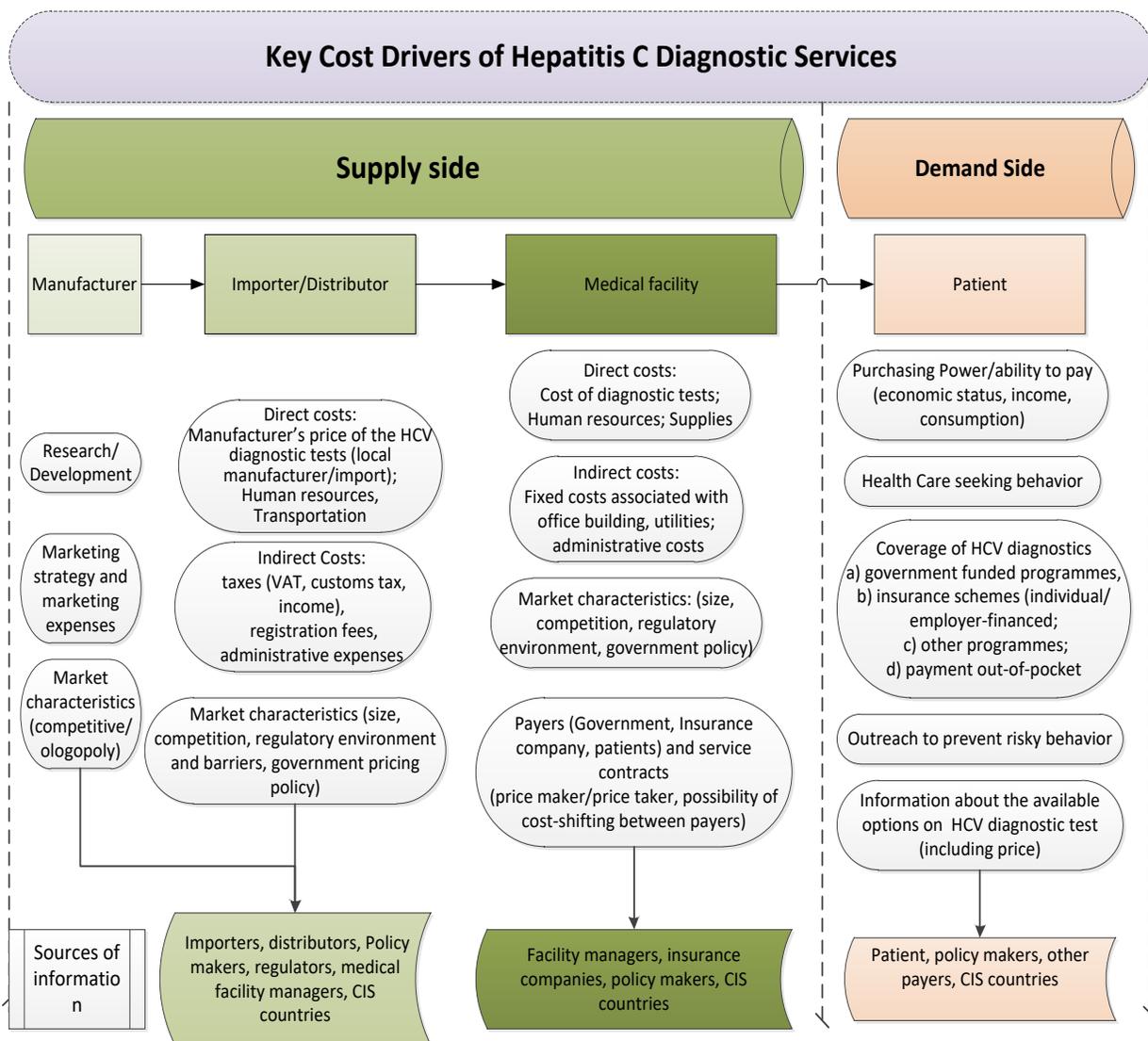
The current **treatment recommendations** for acute and chronic hepatitis C are based on HCV genotyping and on HCV RNA load determination before, during and after antiviral therapy. When HCV RNA has been detected, exact genotyping and HCV RNA load determination is necessary in every patient considered for antiviral therapy. Genotyping is mandatory before treatment initiation, as the dose of ribavirin and optimal treatment duration is determined specifically on the underlying HCV genotype (McHutchison 2004; Terrault 2005). Independent of the HCV genotype, proof of HCV RNA load decrease is necessary to identify patients with little chance of achieving SVR. HCV RNA needs to be quantified before and 12 weeks after treatment initiation and antiviral therapy should be discontinued if a decrease of less than 2log HCV RNA levels is observed. In a second step, HCV RNA should be tested with highly sensitive assays after 24 weeks of treatment because patients with detectable HCV RNA at this time point only have a 1-2% chance of achieving SVR. SVR, defined as the absence of detectable HCV RNA 24 weeks after treatment completion, should be assessed by an HCV RNA detection assay with a lower limit of 50 IU/ml or less to evaluate long-lasting treatment success (Layden-Almer 2006; Manns 2006).

3. Methodology

3.2. Measurement and Data Collection

In order to develop price containment strategy of Hepatitis C diagnostic testing in Georgia, the study aimed to: 1) identify the key cost-drivers for HCV diagnostics both from supply and demand side, 2) obtain the information on these drivers from different data sources and 3) present/analyze the results and 4) develop evidence-based cost-containment recommendations. At the first step, key possible elements that impact the final cost and price of the HCV diagnostic tests and testing services in Georgia have been conceptualized (see Figure 2 below). After identification of the supply- and demand-side cost drivers, data sources for each cost-driver have been identified. To get complete and accurate picture, different data sources have been used for each cost driver. The figure below summarizes possible cost-drivers and primary data sources for gaining the information about them.

Figure2. Key Cost Drivers of Hepatitis C Diagnostic Services



Based on the **conceptual framework**, described in the figure above, **primary data collection** through semi-structured interviews has been conducted from identified data sources. Both qualitative and quantitative data have been collected by trained surveyors (MPH program graduates) by using a standard set of semi-structured questionnaires among following key informants:

- Policy makers
- Representatives of pharmaceutical industries,
- Health insurance companies,
- Health care facility managers/financial administrators
- Patients.

All interviews were also audio taped (using voice recording devices) and entered into the electronic format.

Two senior research team members supervised the data collection conducted by surveyors.

Specific data collection methods included:

National level: semi-structured interviews with key informants. Key informant interviews included a review of country policy, national regulation (or lack there-of) and other internal/external factors affecting the cost of Hepatitis C diagnostic testing.

Key informant interviews were used to understand the major systemic and local factors affecting the cost of the Hepatitis C Diagnostics and their implications to the financial access to HCV diagnostic services to different population groups. In order to accurately understand different perspectives on the key study components, data collection tools were constructed so that it allows to get information from different data sources on each study question.

Key informants included representatives of: Ministry of Labour, Health and Social Affairs of Georgia (MoLHSA), National Center of Disease Control (NCDC), State Regulatory Agency of Medical Activities (National Drug Regulatory Agency), Implementing Agency of Global Fund Programs in Georgia, pharmaceutical industry, health insurance industry, National Screening Center, key informants from Post-soviet countries in the region (see Table 1).

Facility Level:

At facility level, semi-structured questionnaires have been conducted with facility managers and/or financial managers. Surveyors also interviewed patients through combination of semi-structured questions and quantitative multiple-choice questionnaire to assess client knowledge, access to C-hepatitis diagnostic services and all related barriers.

In addition to the primary data collection, desk-review of the global and national literature has been conducted to summarize the most recent evidence on diagnosis of Hepatitis C to identify the best practices of Diagnosis C globally, assess the compliance of national guidelines on diagnosis and management of Hepatitis C with the best international standards, and identify the evidence-based diagnostic practices in Georgia that will be focus of the study.

3.1.1. Sampling Methodology

As indicated above, the study aimed to get complete picture from different players of supply and demand side contributing to the price of HCV diagnostic services. Thus, the rationale of sampling methodology was to include all the layers of data sources (with triangulation of results) from the conceptual framework (see Figure1 above), and not to obtain quantitative data to get representative results. Based on the rationale, sampling criteria for selection of facilities included:

- Minimum 6 facilities (4 urban facilities, and 2 district/regional facilities) for comprehensive interview of managers/financial administrators,
- Minimum 26 facilities for information on C hepatitis diagnostic prices (50% ambulatory clinics/polyclinics and 50% hospitals)

Client Questionnaires: 10 clients were selected for interviews during visits to hospital and outpatient clinics (while waiting to be seen by provider, to receive laboratory service, or upon exiting from provider visit); full notification and consent using standard forms was assured by data collectors.

3.1.2. Ethics Considerations and Procedures

Potential Risks and Measures to Minimize Risks

This study poses minimal risk given that the formative components are non-invasive, consisting of anonymous written questionnaires by patients. The risk to assessment participants is anticipated to be minimal given that the questions and topics discussed are within the realm of day-to-day health service delivery and utilization parameters.

To minimize these risks, all study participants were assured that no individual identifying information (e.g. name) will be used on any of the questionnaires or assessment tools. As part of the informed consent process, all participants assured of their right to decline participation at any time during the interview, including refraining from answering any questions. Prior to an interview and/or group discussion, all study participants were informed that their names will not be linked with any opinions and practices shared, although the study may use quotes in a published document to describe patients perceptions and attitudes.

Safety and Dignity

This study protects the safety and dignity of participants to the greatest extent possible by ensuring voluntary participation, confidentiality, and minimal risk as outlined in adjacent sections of this document.

Informed Consent

All potential subjects were fully consent to study participation prior to enrollment, before any survey or interview questions are administered. Information that will be explained includes: purpose of the study, procedures involved in the study and how long the study will last, foreseeable risks and discomforts, benefits that may arise from the study, efforts to ensure confidentiality, voluntariness of the study, and persons to contact if the subject has questions about the study. The expected duration of the interview were also noted, and the process was explain that every effort will be made to minimize any risks associated with the study, including ensuring an opportunity among individuals to ask questions regarding the study by the person obtaining consent. The person obtaining consent then asked if the potential participant has understood the above statements and if he/she would like to join the study. Once an individual consents to participate in the study, the interviewer signed and dated the consent form to acknowledge that he/she has read the disclosure information, the inform consent process has been administered, and that the individual has orally consented to participate.

Voluntary Participation

As part of the informed consent process, study participants were informed that the decision to be in this study is completely up to them. Study interviewers made sure to emphasize that the potential participant does not have to be in this study if they do not want to. Potential participants were also

informed that if they decide to be in the study initially, but change their mind later, they can discontinue his/her participation in the study at that time. They were also informed of their right to skip any questions or repeated data collection phases at their own discretion.

Disclosure of Complete Information

This assessment disclosed complete information about the assessment to participants. It also used a participatory approach in its formative and evaluative processes to document and analyze barriers, opportunities on improved financial access to C-hepatitis diagnostics.

Incentives to Study Participants

The study did not offer incentives to study participants. As part of the informed consent and information process, study participants were informed that the proposed assessment has several possible benefits for which they might be inclined to support: Information from the study was used to develop recommendations on cost-containments/decrease of C-Hepatitis Diagnostic tests.

Confidentiality and Data Security

All data collected as part of the study are kept confidential and are securely stored at the School of Public Health’s office. Electronic data were stored on a password-protected computer. Hard-copy data (e.g., questionnaires, interview guides, observation checklists, notes, etc.) were locked in an office room. No data collection instruments (including notes), except key informant interviews are include the names of study participants to further protect privacy and confidentiality.

Data collection:

Data collection took place from December 28th 2011 to February 17th, 2012. Interviewers collected information from following data sources (see Table#1 below):

Table 1. Data Collection tools/key informants and number of interviews

Tool #	Tool Name/ Key informant	Number of interviews
1	Questionnaire to officials of the Ministry of Labour, Health and Social Affairs of Georgia (Health Department)	1
3	Questionnaire to officials of the National Center of Disease Control	1
5	Questionnaire to officials of the Global Fund Grant Implementing Agency	1
6	Questionnaire to officials of the Regulatory Agency of Medical Activities	1
7	Questionnaire to the representatives of the pharmaceutical business	4

8	Questionnaire to officials of the State Revenue Service and its Customs Department	Officials refused the interview due to confidentiality reason
9	Questionnaire to representatives of the private health insurance companies	6
10	Questionnaire to the representatives/managers of the medical facilities	Total 32
11	Questionnaire to the representatives of Post-soviet countries in the region	2
12	Patient Questionnaires	10

Note: questionnaires and consent forms have been developed in Georgian language and are available upon request

4. Study Results

4.1. Hepatitis C Management Guideline(s) in Georgia

There is National guideline and the protocol for the Management of Hepatitis C approved by the Ministry of Labor, Health and Social Affairs of Georgia [10]. Besides its main objective – to provide doctors and patients with guidance in making clinical decisions, diagnostic and treatment protocol serves as a tool for external assessment of compliance with evidence-based best practices. Overall these documents correspond to the guidelines developed by the leading professional association in US and Europe, namely AASLD - American Association for the Study of Liver Diseases (Chany et al 2009) and EASL - European Association for the Study of the Liver (EASL, 2011). Adopted National Guidelines and Protocol for Management of Hepatitis C are based on the contemporary scientific evidence, described above to prevent, diagnose and treat the HCV infection.

Current international evidence (as well as national guidelines) does not support screening of individuals who are not at increased risk; there is an Alevel evidence that general population should not be screened for HCV infection [36]. According to **National Protocol of Hepatitis C Management** [10], following groups should be screened for HCV:

- Injecting Drug Users;
- HIV Infected Individuals;
- Patients with Hemophilia,
- Patients on Dialysis;
- Children of HCV positive mothers;
- Medical Personnel with contact of HCV Blood;
- Individuals with unexplained increase of liver enzymes in the blood
- Recipients of organs, tissues, blood or blood products
- Sexual partners of people with hepatitis C

4.2. Hepatitis C Tests available in Georgia

National Guidelines for the Management of Hepatitis C indicate full spectrum of diagnostic methods available globally. All key Hepatitis C diagnostic methods recommended by best international practices are currently used in Georgia. Table 2 below shows the HCV diagnostic tests (by type of tests) registered and distributed in the territory of Georgia.

Table 2. Hepatitis C Diagnostic tests distributed in Georgia in 2011

Type of the test	Name of the Test	Manufacturer	Importer/Distributor
Antibody Detection, simple rapid tests	Hexagon HCV rapid tests	“Human Diagnostics Worldwide GmbH” (Germany)	“Human Diagnostic Georgia Ltd”
	SD Bioline HCV	“Standardia Diagnostics Inc.” (Korea)	“Center for New Biomedical Technologies Ltd”
	Bio Tracer HCV	“Bio Focus Co. Ltd”, (Korea)	“Interlab Ltd.”
	HCV rapid test	“InTec” (China)	“ExpressDiagnostics Ltd”
	HIV, HCV, HBsAg, syphilis Combo	“InTec” (China)	“ExpressDiagnostics Ltd”
	HCV rapid test	“Biotec” (Great Britain) (overall specificity 97-99%)	“Bioland Ltd.”
Antibody Detection, ELISA tests	Immunolisa HCV Ab	“Orgenics Ltd.” (Israel)	“Irise Ltd”
	Ortho HCV ELISA	“Ortho Clinical Diagnostics” (Great Britain)	“GMS Ltd.”
	Ortho HCV Enhanced SAve ELISA	“Ortho Clinical Diagnostics” (USA)	“GMS Ltd.”
	AXM HCV ELISA	“Abbott” (Ireland)	“Spectri Ltd”
	HCV ELISA	South Korea	-
Antibody Detection, Confirmatory test	HCV Blot	“Genelabs Diagnostics” (Singapore)	“Immuna Ltd.”
	HCV AB recombinant	Biotech (Great Britain)	“Bioland Ltd”
	Inno-LIA HCV Score	“Innogenetics” (Belgium)	“GPC Ltd
HCV RNA Qualitative	Amplicor HCV 2.0, (PCR)	Roche Molecular Systems	“Mirco, Ltd”
	HCV-TM Qual	“Sacace Biotechnologies” (Italy)	“Irise Ltd”
HCV RNA Quantitative	Amplicor HCV Monitor 2.0, (PCR)/ Cobas Ampliprep / Cobas TaqMan	Roche Molecular Systems (Germany) (Real-time PCR)	“Mirco Ltd”
	HCV Real-TM Quant	“Sacace Biotechnologies” (Italy)	“Irise Ltd”
HCV Genotyping	Versant™ HCV Genotype 2.0 System (LiPA)	Siemens Medical Solutions Diagnostics	“GPC Ltd”

Source: Questionnaires with Representatives of Pharmaceutical Industry and Medical Facilities

4.3. Prices of the HCV diagnostic tests in Georgia

All HCV diagnostic tests are imported in Georgia. There is no single manufacturer in the country producing HCV Diagnostic tests. According to the local manufacturers, there is no incentive to produce HCV diagnostic tests, local market is small and would not allow recovering significant investments associated with production of the tests (including needed equipment, licenses, GMP Certificate, etc.).

Imported HCV tests in Georgia are produced by 10-15 different manufacturers throughout the world (Germany, Korea, Italy, China, Israel, Great Britain, USA, etc.). As there is significant variation in prices of the different HCV diagnostic tests, we will discuss the local market and prices of the tests by type (antibody tests, HCV RNA testing, Genotyping).

Antibody Detection Screening Tests (Simple Rapid and EIA tests)

According to the information of National Drug Regulatory Agency (Table # 2.1), at least 5-6 importers of the **Simple Rapid Antibody Detection Screening Tests** compete in the Georgia market. Most of these firms are importers and wholesale distributors at the same time. In tenders and competitive bidding organized by different payers, low-price rapid HCV screening tests, produced in China are always the winners. Accordingly, they had the largest share in the local market of rapid HCV tests in 2011 (ExpressDiagnostics Ltd, with its HCV rapid tests, manufactured by “InTec”, China). Distributors of other HCV rapid tests, mostly compete with China tests through: 1) solo contracts with specific health care facilities; 2) *Quality of Services (instant response to any damage, change defective products and etc)*”. According to the importers, wholesale price of rapid HCV tests varies from one to five GEL. Price is differentiated based on the number of tests sold, marketing strategy of the company and other factors. As noted above, due to high competition, the prices of different sellers are very close to each other.

Competition is also tight among importers of **ELISA HCV screening tests**. At least 4-5 importers compete in the local market with average price range 2-6 GEL per ELISA test. Ortho HCV ELISA Test Kits produced in Israel constitute 40% of the market and cost about 3.5 GEL per test. According to the sellers of ELISA tests, they work on the low profit margin to offer competitive price (10-15%). Use of competitive purchasing procedures (tenders) by NCDC allowed to further decrease the price of ELISA tests (about 1.9 GEL per test). Table 2.1 below describes imported simple rapid and ELISA tests and their average price for facilities/purchasers in 2011.

Table 2.1 Antibody Detection Screening Tests Imported In Georgia in 2011

Type of the test	Name of the Test	Manufacturer	Importer/Distributor	Average Wholesale Price for medical facilities:
Antibody Detection,	Hexagon HCV rapid tests	“Human Diagnostics Worldwide GmbH” (Germany)	“Human Diagnostic Georgia Ltd”	

simple rapid tests	SD Bioline HCV	“Standardia Diagnostics Inc.” (Korea)	“Center for New Biomedical Technologies Ltd”	2 GEL (170 GEL/96 kit)
	Bio Tracer HCV	“Bio Focus Co. Ltd”, (Korea)	“Interlab Ltd”	2.5 GEL (75 GEL /30 kit)
	HCV rapid test	“InTec” (China)	“ExpressDiagnostics Ltd”	1.5 GEL (150 GEL/96 Kit)
	HIV, HCV, HBsAg, syphilis Combo	“InTec” (China)	“ExpressDiagnostics Ltd”	
	HCV rapid test	“Biotec” (Great Britain) (overall specificity 97-99%)	“Bioland Ltd”	1.7 GEL (2550 GEL/ 1500 kit)
Antibody Detection, ELISA tests	Immunolisa HCV Ab	“Orgenics Ltd.” (Israel)	“Irise Ltd”	3.4 GEL (290-350 GEL/96 Kit)
	Ortho HCV ELISA	“Ortho Clinical Diagnostics” (Great Britain)	“GMS Ltd.”	-
	Ortho HCV Enhanced SAVA ELISA	“Ortho Clinical Diagnostics” (USA)	“GMS Ltd.”	-
	AXM HCV ELISA	“Abbott” (Ireland)	“Spectri Ltd”	-
	HCV ELISA	South Korea	-	1.9 GEL (180 GEL/96 kit) tender of 2011
	HCV ELISA	“Roche” (Germany)	-	6 GEL (600 GEL/96 kit)

Source: National Regulatory Agency of Medical Activity, interviews with purchaser organizations and/or importers

Antibody Detection Confirmatory Tests

By December 2011, at least 3 antibody detecting confirmatory tests from 3 different manufacturers and importer companies are registered in Georgia (see Table #3). Detailed information on these tests was not provided by importers. According to the providers of HCV confirmatory diagnostic services (medical facilities); these tests were purchased through tenders by AIDS Center, with average price 85 GEL.

Table 3. Antibody Detection Confirmatory Tests registered and imported in Georgia

Type of the test	Name of the Test	Manufacturer	Importer/ Distributor	Average Wholesale Price for medical facilities
Antibody Detection, Confirmatory test	HCV Blot	“Genelabs Diagnostics” (Singapore)	“Immuna Ltd”	85 GEL (Tender)
	HCV AB recombinant	Biotech (Great Britain)	“Bioland Ltd”	-
	Inno-LIA HCV Score	“Innogenetics” (Belgium)	“GPC Ltd”	85 GEL (Tender)

Source: facility Manager Questionnaires

Qualitative and Quantitative HCV RNA Testing

In Georgia both qualitative and quantitative HCV RNA PCR tests are in most cases done by Roche systems. Recently new players manufacturing real-time PCR systems (qualitative and quantitative) also were introduced into the Georgian laboratory space. The following test-systems are already registered in Georgia: HCV Real-TM Quant and HCV-TM Qual, manufactured by “Sacace Biotechnologies” (Italy), distributed by “Irise” Ltd.

According to the key informants, importer firm of the HCV RNA detection assays manufactured by Roche Molecular Systems (Germany) is almost monopoly supplier of the tests with more than 90% of market share. It is important to emphasize that, Roshe RNA assays cost almost 2.5-3 times more than the tests of its competitor, “Sacace Biotechnologies” (Italy) that have recently entered the local market (see Table 4 below). The cheaper RNA tests produced by “Sacace Biotechnologies” are not adequately used by laboratories despite the fact that they do not require additional device to conduct such tests. Real-Time PCR machines are open systems and could be used both for Roche diagnostic test-systems as well as for test-systems manufactured by other companies. Entrance of alternative lower cost HCV RNA tests in the local market has a potential to reduce the costs for HCV molecular diagnostics in the country.

Table 4. Qualitative and Quantitative HCV RNA tests in Georgia and some of their alternatives, available globally

Type of the test	Name of the Test	Manufacturer	Importer/ Distributor	Average Price for facilities
HCV RNA Qualitative	Amplicor HCV 2.0, (PCR)	Roche Molecular Systems	“Mirco Ltd”	90 GEL
	HCV-TM Qual	“Sacace Biotechnologies” (Italy)	“Irise Ltd”	40 GEL
HCV RNA Quantitative	Amplicor HCV Monitor 2.0, (PCR)/ Cobas Ampliprep / Cobas TaqMan, (Real-time PCR)	Roche Molecular Systems (Germany)	“Mirco Ltd”	180 GEL (9,000 GEL/48 kit)
	HCV Real-TM Quant	“Sacace Biotechnologies” (Italy)	“Irise Ltd”	60 GEL (2,850 GEL/ 48 kit)
	HCV SuperQuant (PCR)	National Genetics Institute	Available globally, not available in Georgia	
	Versant HCV RNA 3.0, (bDNA)	Siemens Medical Solutions Diagnostics		
	Abbott RealTime HCV, (Real-time PCR)	Abbott Diagnostics (Ireland)		

Source: Questionnaires with Representatives of Pharmaceutical Industry and Medical Facilities

HCV Genotyping

HCV genotyping in Georgia is generally conducted by using reverse hybridization assay Versant™ HCV Genotype 2.0 System (LiPA), manufactured by Siemens Medical Solutions Diagnostics,

imported by GPC Ltd. Small market with exclusive supplier of HCV genotyping in Georgia leaves the possibility to importer/distributor company to set the high price of the product for the health care facilities (see Table 5).

Table 5. HCV Genotyping assay in Georgia and some of its alternatives, available globally

Name of the Test	Manufacturer	Importer/ Distributor	Average Price for facilities
Versant™ HCV Genotype 2.0 System (LiPA)	Siemens Medical Solutions Diagnostics	“GPC Ltd”	250 GEL (10000 GEL/40 kit)
TRUGENE HCV 5'NC Genotype II Assay	Siemens Medical Solutions Diagnostics	Available globally but not available in Georgia	
Real Time HCV Genotype II Assay	Abbott Diagnostics (Ireland)		

Source: Pharmaceutical Industry and Medical Facilities

Table 6 below briefly describes key importers/distributors of HCV diagnostic tests in Georgia and their average wholesale price for the purchasers (including medical facilities). As the Table 6 shows, the price of antibody detection screening tests in Georgia is not high partly because of many different players in the local market. In contrast, the price of RNA and Genotyping assays are high. One of the key contributors to high prices of these tests is small market with practically no competition. It is highly likely that increased demand on these types of tests and regulatory interventions that would increase the number of importers and types of HCV RNA and Genotyping assays in the local market would decrease the price of the tests in Georgia. Indeed, surveyed importers/distributors expressed the readiness to review their pricing strategy/prices on HCV RNA and genotyping diagnostic tests if other competitors enter the local market.

Table 6. Importer Companies of HCV diagnostic tests and their wholesale/retail price range

Type of test	Importer companies of HCV Diagnostic Tests	Average Wholesale/Retail Price/range per a test in GEL for medical facilities
Antibody Detection tests(rapid tests)	5-6 importer companies	1-5
Antibody Detection , ELISA tests	4-5 importers (Test Kits produced in Israel constitute 40% of the market)	2-6
Antibody Detection, Confirmatory tests	3 importers	85
HCV RNA Qualitative	2 importer companies: Roche tests are leader in the local market In PCR (90%), “Sacace Biotechnologies” products (Italy) cover less than 10%	40-80
HCV RNA Quantitative		60-180
HCV Genotyping	One importer company: GPC Ltd (Versant™ HCV Genotype 2.0 System (LiPA), Siemens Medical Solutions	250

	Diagn). Additionally, Mrcheveli Network provides diagnostic service outside of Georgia (higher cost)	
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Source: Pharmaceutical Industry and Medical Facilities

4.3.1. Key costs drivers reflecting price of the HCV diagnostic tests

Regulation of HCV Diagnostic Tests in Georgia

Regulation of diagnostic tests, as well as medicines in Georgia is quite liberal. To improve the access to diagnostic tests and medicines to the population and improve their quality, Government of Georgia (GoG) introduced several regulatory initiatives aiming decrease of entry barriers in the local market, simplifying drug regulation rules and procedures. As the results of regulatory changes: “300 new medicines were registered through a mutual recognition regimen” (see the section below for more details) [29].

Registration

HCV diagnostic tests are regulated by Law on “Medicines and Pharmaceutical activity” of Georgia [31]. According to the Law, HCV diagnostic tests need to be registered before they can be sold in the country. The HCV diagnostic tests, as well as other tests and medicines are registered by Departmental Registry at the Agency of State Regulation of Medical Activities (Agency) at the Ministry of Labor, Health and Social Affairs of Georgia (MoLHSA).

Recent changes in Law on “Medicines and Pharmaceutical Activity” of Georgia regulating pharmaceutical products imported and sold in Georgia attempt to simplify the registration process for new medicines entering the market. According to the Law, importers or pharmaceutical manufacturers can register their products based on the two types of “recognition”: prior recognition by an accepted international partner (recognition regimen) or national recognition (national regimen).

Table #7 below shows the key advantages of the Recognition Regimen of the Registration to the National Regimen in terms of time, financial resources and documents needed to complete the registration.

Table 7. Comparison of Recognition and National Regimens of Registration (Medicines and Diagnostic tests)

Key components	Recognition Regimen of Registration	National Regimen of Registration
Examination of the product by Agency	Medicines/diagnostic tests be registered in Georgia based on their acceptance by a <i>approved intergovernmental pharmaceutical regulatory body or the regulatory body of foreign country</i> (European Medicines Agency (EMA), regulatory bodies of various European countries, the United States of America, Japan, Australia and New Zealand).	The product undergoes full scientific and technical examination to establish its standardization, quality, safety and clinical effectiveness.

Type of importing party	Law does not limit either the type of importing party or the purpose of the import. For the sake of the recognition procedure, the interested party may be any natural or legal person wishing to register/ admit certain pharmaceutical products into the market, notwithstanding the aim of the import.	Pharmaceutical manufacturers or trade license holders only are allowed to register tests under this regimen
Registration Fee	500 GEL (300 USD)	2,500 GEL (1,500 USD) for a brand name pharmaceutical product and 400 GEL (240 USD) for generic pharmaceutical product
Allowed Languages of Registration Documentation	Allows for homology identification documents in several languages: Georgian, English or Russian, (including electronically)	The administrative documents should be filed in Georgian whereas the scientific and technical documents may be submitted in Georgian, English or Russian (including electronically)
Timeline of registration	7 business days	54-55 days: - 14 days to review the documents; - 2 months to conduct a scientific and technical examination of the product to establish its standardization, quality, safety as well and therapeutic worth; -10 days to issue a document allowing the admission of the pharmaceutical product into the Georgian market
Needed documents	Much less scientific information and technical specification than for National Regimen	Administrative and scientific and technical information

Source: Law on “Medicines and Pharmaceutical Activity” of Georgia [31] and [35]

As the Table 7 indicates, recognition regimen significantly simplifies the procedure not only in terms of time, needed documentation and financial resources, but most importantly, broadens the number of organizations eligible to import the diagnostic test or medicine; Recognition regimen does not limit either the type of importing party or the purpose of the import. Importing party could be any interested person/entity wishing to register/admit certain pharmaceutical products into the market.

Prior to August 2011, HCV diagnostic tests (as all diagnostic tests imported in the country) had to be registered under the National Regimen. Recent changes in the Ministerial Decree #344/N of MoLHSA (Ministerial Decree #01-39/N, MoLHSA, 08/10, 2011) allowed to register the diagnostic tests under the Recognition Regimen. **These changes create significant opportunities to improve competition among importers of HCV diagnostic tests in the local market and decrease their price.**

Nevertheless, importers of diagnostic tests identify a few regulatory barriers that prevent them to register HCV diagnostic tests under the recognition regimen. Specifically, key informants noted that:

- According to the Law on Medicines and Pharmaceutical Activity, if there is any change (including minor changes) in the specification of the product/test system (for example, change in the catalogue number) registered under the recognition regimen, old registration of the

product should be annulated and the test system should be registered again as completely new product, with 500 GEL registration fee. In contrast, such changes do not require new registration under the National Regimen: importer informs the agency and only pays 50 GEL for the changes in the existing registration.

- In case of Recognition Regimen of registration, it is also required to provide a sample of the pharmaceutical product, _"two standard packages or the quantity required for two tests". According to the key informants, these tests are required in spite the fact that there is no laboratory capacity in Georgia to assess the quality of HCV RNA (qualitative/quantitative) and/or genotyping tests (storing these tests create significant problems for the Regulatory agency itself as PCR tests, for example need to be kept at -20°C). Importers consider this requirement as important financial barrier: in many cases, one package (kit) of HCV RNA (qualitative/quantitative) and/or genotyping tests costs more than 3000 GEL (see the section above on the prices of diagnostic tests).

Considering abovementioned requirements of the Law in terms of renewing registration for minor reasons, which is often associated with additional paperwork and resources, importers *prefer to register HCV test systems under the National Regimen and avoid applying for registration under the Recognition regimen. Thus, in case of HCV diagnostic tests, Recognition Regimen does not allow importers to decrease the entry barriers in the local market.*

Despite these difficulties, almost all importers of HCV diagnostic tests agree that there are no significant barriers in the legislation that prevent free competition in the local pharmaceutical market. In contrast, they recommend more strict regulation to avoid entrance of many players in the market with low quality HCV diagnostic tests.

Import, distribution and realization of HCV tests

No permit is needed to import the HCV diagnostic tests in Georgia. Wholesale distribution of HCV diagnostic tests is provided by: 1) authorized pharmacy and 2) pharmaceutical warehouses. Distributors can also be retail sellers of the products.

Legislation is also liberal in terms of wholesale and retail price regulation of HCV diagnostic tests; any importer, wholesale and/or retail distributors can set the price solely based on the company's market strategy.

Taxes

To support free competition in the local market and low prices, Tax Lagislation of Georgia is also maximally liberal in terms of import and distribution of registered medicines and diagnostic tests in the country. Specifically, new Tax Code of Georgia (Article 168. Subarticle 1. Paragraph L) exempts import, temporary import and delivery of test-systems that are registered by the Ministry of Labour, Health and Social Affairs of Georgia from **Value Added Tax** (18% of the product price). In addition to the VAT, imported diagnostic test-systems are **also free from import (customs) tax** (Tax Code of Georgia, Article 199, Subarticle 1, Paragraph E), [30].

This allows importers and distributors of HCV diagnostic tests to avoid access overhead costs on the test-systems. They only pay **Profit Tax** (15% of their profit).

Other costs

Among other costs of wholesale/retail sellers of HCV diagnostic tests are costs associated with hiring/training human resources distributing HCV diagnostic products. Sellers identify inconsistencies in legislative framework of diagnostic tests that increase their costs. Specifically, Law on “Medicines and Pharmaceutical activity” of Georgia [31] does not clearly define the class to which HCV diagnostic tests belong. This is important to identify the specialist responsible for distribution of the HCV diagnostic tests; if the tests belong to the pharmaceutical products, then they should be distributed by pharmacists. If diagnostic tests are considered as medical devices, they have to be distributed by person with medical technician with experience in medical devices.

According to the key informants (distributors), in many countries (including Europe), HCV diagnostic tests belong to medical devices; they are “in vitro” products and their application do not need pharmacists trained in safe and effective medication use. On the other hand, the use of HCV RNA and Genotyping tests require extensive experience in diagnostic equipment/medical devices that pharmacists usually do not have in Georgia, as pharmaceutical education in the country does not consider acquiring relevant knowledge and skills. Usually, medical technicians receive formal education in use of diagnostic equipment and medical devices. Because of unclear legislation, distributors either have to train pharmacists in use of highly sensitive diagnostic equipment and/or hire both, pharmacists and medical technicians to distribute HCV diagnostic tests. Obviously, this factor increases the costs of HCV diagnostic tests and consequently, the price of them in the local market.

4.4. HCV diagnostic services and their costs in medical facilities

Simple Rapid HCV tests are available at large number of medical facilities both in Tbilisi and regions, including out-patient clinics, clinical laboratories, women’s consultation centers, blood banks, Voluntary Counseling and Testing (VCT) centers, diagnostic centers and hospitals.

HCV diagnostics using **ELISA** is less readily available at medical facilities, but still are common diagnostic options at the facilities which own ELISA machines (ELISA readers).

Other types of HCV diagnostic tests are available only in limited number of facilities (see Table 8 below for detailed information) in big cities of Georgia (Tbilisi, Kutaisi, Batumi, Telavi, Zugdidi).

Table 8. Information about the type/list of facilities providing HCV diagnostic services and Geographic coverage with the services

Type of test	Geographic coverage
Antibody Detection simple rapid tests	Accessible throughout the country (Hospitals, Ambulatories, Blood Banks, VCT centers, Clinical Laboratories)

Antibody Detection ELISA Tests	Accessible throughout the country (Hospitals, Ambulatories, Blood Banks, Diagnostic Laboratories, Including NCDC network)
Confirmatory tests	Five big cities (Tbilisi, Batumi, Kutaisi, Telavi, Zugdidi)
RNA Qualitative	Limited # of facilities: Tbilisi: Infectious Diseases, AIDS and Clinical Immunology Research Center, “Hepa” Ltd., “NeoLab” Ltd., “Mrcheveli” Ltd., “Aversi” Clinic and “New Hospital”; Regions: central laboratories in Batumi, Kutaisi, Telavi and Zugdidi.
RNA Quantitative	
Genotyping	Only Tbilisi, Outside of Georgia: through “Mrcheveli” Network

Source: Questionnaires with key Informants, provider facilities and pharmaceutical industry

The study looked at the price of HCV diagnostic services in different types of health care facilities and geographic locations.

The results of the interviews with managers/representatives of health care facilities and patients demonstrates interesting trend: average price of HCV screening tests are almost the same in ambulatories and hospitals, while the price of all other HCV diagnostic tests in Ambulatories/ stand alone laboratories are higher than in hospitals (see Table 9 below). Usually, ambulatories have lower fixed costs than hospitals (building, equipment, labor cost of administrative unit and etc.). This fact allows ambulatories/polyclinics to propose lower price on HCV diagnostic services than hospitals. The fact that price of the RNA/Genotyping tests are higher in ambulatories allows us to conclude that the price-setting strategies of interviewed health care facilities are not fully based on the analysis of the costs associated with provision of HCV diagnostic the services.

It is also important to mention that, because of the larger number of diagnostic tests needed, hospitals may use tenders or competitive purchases to contain costs (economies of scale). Among interviewed hospitals, almost none of them (except one) use tenders or group purchasing to lower the cost of HCV diagnostic services.

Analysis of antibody detection screening tests (rapid and ELISA) show that there is almost no difference in the price between different types of medical facilities and between geographic locations. Average price of simple rapid tests varies from 12.5 to 16 GEL, and from 22.3 to 35 GEL for ELISA tests. This fact clearly shows that because of the many competitors in the market, both, importers of HCV screening tests and facilities providing HCV screening services tend to offer competitive prices for HCV diagnostic tests and screening services (see the Table 9 below).

HCV confirmatory diagnostic services in Georgia usually purchase confirmatory tests through competitive tenders (usual price 85 GEL per test) and do not add any overhead to the price as far as confirmatory tests are not usually used for commercial purposes.

HCV RNA tests are provided by small number of clinics in Tbilisi (5 facilities) and Regions (4 facilities) while Genotyping is provided only by 3 facilities in Tbilisi (no regional coverage). Prices of both types of diagnostic tests are very high and range from 305 to 506 GEL. HCV genotyping which is sent for diagnostics outside of Georgia (e.g. in Germany, through Mrcheveli network) costs over 600 GEL ((see table # 9 below).

Table 9. Prices of diagnostic tests and HCV diagnostic services in different types of facilities and geographic location

Type of test	Retail/distribution price range, GEL	Average Price testing in health care facilities in GEL	Price range of HCV testing in Tbilisi in GEL		Price range of HCV testing in Regions, GEL	Price range reported by patients, GEL
			Ambulatories	Hospitals		
Rapid Antibody detection tests	1-5	15	15-16	16	10-15	15-20
Antibody detection ELISA tests	2-6	28	22-50	30-40	12-30	17-25
Antibody Detection Confirmatory test	85	85-90	85-90	85-90	No information	No information
RNA Qualitative	40-80	203	192-225	192	None	237.5
RNA Quantitative	60-180	322	304-340	304	304	700
Genotyping	250	500	300-616	506	None	700

Source: Questionnaires with Key Informants, Representatives of Medical Facilities and Pharmaceutical Industry

Additional diagnostic investigations for HCV infection and their cost in Georgia

Along with the main diagnostic investigations described above there are several additional methods used for the further characterization of the clinical severity of the HCV infection and overall status of the patient. These methods include:

- Complete Blood Count (CBC) (The cost range in Georgia is 6-20 GEL);
- Blood Biochemistry (ALT, AST, G_GT, ALP, Billirubine, Albumin, PPT, INR, etc.)(The cost for each biochemical component ranges from 5 to 15 GEL);
- Liver Ultrasound investigation with Doppler (Cost ranges in Georgia is 30-50 GEL).

In addition, following diagnostic tools are only available in the limited number of specialized centers:

- Liver elastography (Fibro Scan), cost range 90-110 GEL
- Combined serological markers of the Fibrosis (e.g. Fibro Test), cost range 290-400 GEL
- Liver biopsy – over 750 GEL.

The average total price for the investigations needed for the definition of the HCV specific treatment strategy and for the management of the patient during the therapy course approximately equals to 1,600 GEL.

Although these tests are important contributors in the total price of HCV diagnostic services, the study focused on the cost-analysis of only direct HCV diagnostic tests in Georgia.

4.4.1. Key Cost Drivers Reflecting the Price of HCV Testing in Medical Facilities

Interviews with providers of HCV diagnostic tests show that they usually do not use competitive tenders to purchase HCV diagnostic tests (especially RNA and genotyping tests). Also, none of the facilities collaborate with other facilities for the purpose of **group purchasing**. The price of the test includes transportation to the facility.

Representatives of financial departments of medical facilities indicated that the variable costs (price of the tests, associated supplies, salary of personnel directly involved in testing, etc) contribute to the 60-70 % of the HCV testing price, fixed costs 10% and the profit 10-20% of the price of the HCV tests (10% rapid tests, 20% RNA and/or genotyping). Fixed costs differ for different types of HCB tests, PCR of Genotyping have higher fixed costs associated with amortization of expensive HCV diagnostic equipment while HCV rapid tests do not need special equipment at all. On the other hand, not all ELISA screening tests are used from a test kit (96 tests in a kit for example) at the same time and the cost of lost (non-used) tests increases the price of the HCV screening tests. For example: only about 60-80 ELISA tests are utilized out of a screening test kit containing 96 tests. To balance the loss, financial department increases the price of HCV testing by 40-60%.

Table 10 demonstrates that average testing price in health care facilities is significantly higher than the cost of the HCV diagnostic tests. It is important to emphasize that the prices of HCV diagnostic service in health care facilities are less variable than the prices of diagnostic tests. For example, the wholesale price of HCV RNA qualitative and quantitative tests varies from 40-80 and 60-180 consequently while the price of HCV RNA qualitative and quantitative testing service does not vary much throughout the facilities (192-203 GEL in case of RNA qualitative and 304-340 GEL in case of quantitative). The difference between cost of tests and testing service is understandable for rapid tests where the cost of the screening test is not the key driver in the price of HCV rapid screening service (due to facility's other fixed and variable costs, associated with HCV testing). But this should not be a case for HCV RNA qualitative/quantitative tests. If we consider that other costs of facilities associated with RNA qualitative testing are the same in case of using test systems of different manufacturers, the price of HCV RNA testing should be much less when using RNA qualitative tests produced by Sacace Biotechnologies' products, Italy (that cost about 40 GEL) than RNA qualitative tests produced by Roshe (cost about 80 GEL). The same applies to the quantitative tests: the difference in price among **two key importers** of HCV quantitative tests is even higher (60-180 Gel) while the price of HCV quantitative diagnostic service ranges only from 304 to 340 GEL (see Table 10 below).

Table 10. Prices (and their variance) of HCV diagnostic services as the % of price of diagnostic tests

Type of test	Competition in the market		Retail/distribution price range, GEL	Average Price testing in health care facilities in GEL	Average Price of testing in facilities as the % of tests' price	Price range on HCV testing between facilities
	Importers of HCV diag. Tests	Medical Facilities providing testing				

Antibody detection Rapid tests	5-6 importer companies;	Multiple facilities throughout Georgia	1-5	15	300-1000%	10-16
Antibody detection ELISA tests	4-5 importers	Multiple facilities throughout Georgia	2-6	28	460-1400%	12-50
Antibody Detection Confirmatory test	Three importers	Limited facilities 5-8	85	87	100-105%	No information
RNA Qualitative	Only 2 importer companies	Maximum facilities 5-8	40-80	203	253-500%	192-225
RNA Quantitative	Roshe and "Sacace Biotech" tests		60-180	322	179-536%	304-340
Genotyping	Only one importer	Only 3 lab. Tbilisi; outside of Georgia	250	500	200%	300-616

Source: Questionnaires with Key Informants, Representatives of Medical Facilities and Pharmaceutical Industry

Abovementioned analysis clearly shows that the price of HCV RNA qualitative/quantitative tests in the facilities are not based on the real costs of the service/product, and the limited number of facilities (3-8) offering HCV RNA testing benefit from the **price-setting “privilege”** in the market.

Interviews with health care facilities providing HCV diagnostic service reported that they use **price shifting strategy** for the rapid tests: because the fact that almost all public/private insurance schemes cover HCV screening through rapid or ELISA methods for patients at pre-delivery or pre-operative stages, medical facilities provide HCV testing under public/private insurance schemes on lower price than for patients paying out-of-pocket (“shifting” costs from patients having private/public insurance coverage to patients, paying for the services out-of-pocket).

Incorporating other HCV diagnostic services (RNA/Genotyping) in insurance schemes have potential to further decrease the price and improve the access to these services in Georgia; facilities will be encouraged to consider cost of HCV RNA/Genotype testing during negotiations with Insurance companies (through switching from “price-making” to “price taking” strategy). Under increased demand and stimulating competitive environment, facilities will also be encouraged to find other cost-containment strategies to decrease the price of HCV diagnostic tests (such as use of competitive tenders and/or group purchasing for costly RNA and genotyping tests, look at low-cost analogues of the tests and etc.).

4.5. Prices of HCV diagnostic tests in Georgia and other post-soviet countries in the region

The prices of HCV diagnostic tests and treatment differ significantly in Georgia and other post-soviet countries in the region. According to the EHRN Report on HCV Treatment Access [32]: “None of the countries (besides Lithuania), where assessment has been conducted, have satisfactory access to HCV treatment. Lithuania is the only country where treatment is covered by social security. Governments

either request **funding from international donors** (currently Georgia from the Global Fund³ and previously Ukraine from the World Bank⁴) to cover very limited treatment need – specifically people living with HIV/HCV co-infection, or allocate insufficient funding to purchase HCV treatment by **non-transparent schemes** like Russia where still the majority of people in need are not enrolled into treatment⁵. In Kyrgyzstan HCV treatment is available only for those patients who can cover all expenses **from their own pockets** with most of people in need not willing to cover the high price. The cost of pegylated interferon in combination of ribavirin is the most significant yet not the single expense associated with HCV treatment”.

A cost of diagnostic procedures is also a barrier for treatment enrollments in many of post-soviet countries of the region. Even in Lithuania, where the access to HCV diagnostic and treatment services are satisfactory; laboratory staff of Vilnius University Hospital Santariskiu Klinikos reported that: “there is obvious lack for HCV-RNA tests reagents, and very often patients need to pay themselves when tests are conducted repeatedly. The price for such a test is ~57 USD dollars”; Also, per Lithuanian expert (Erika Matuizaite), HCV diagnostic and treatment services create important financial barriers for those who are not covered by mandatory health insurance scheme: “Even comparatively low price of Anti-HCV test price is barrier for members of vulnerable groups (injecting drug users, sex workers and others) who can’t afford to pay for it”... Cost for other HCV diagnostic tests (if to do them from your own money) is much higher and that is definitely barrier for members of vulnerable groups. On the other hand, there is no point to pay for HCV diagnostic tests if treatment is not accessible, affordable”.

Table 11 below, from EHRN Report on HCV Treatment Access [32] describes cost sharing between governments, donor-funded programmes and patients in Georgia and other post-soviet countries in the region.

Table 11. Costs sharing between governments, patients and international donors (for 2011)

	Georgia	Kazakhstan	Kyrgyzstan	Lithuania	Russia	Ukraine
Antibody testing	Patient; exceptions: (1) IDUs/clients of Global Fund supported needle-exchange programs, (2) for citizens of Tbilisi, tests are provided free-of-	Patient; exceptions: PLHIV, children	Patient; exceptions: IDUs and prison inmates through of Global Fund supported needle-exchange/pri	Patient	Patient or state health insurance depending on the region	Patient; exception: IDUs/clients of Global Fund supported needle-exchange programs

³ AIDSPAN Extract from the Round 9 Georgia HIV Proposal Form Section 4.5.1, available at http://www.aidspan.org/documents/globalfund/trp/round_9/Georgia-HIV-4.5.1.pdf

⁴ Open Society Institute (2010) Ignorance is No Longer an Option: Why and How to Respond to the Hepatitis C Epidemic in Ukraine available at http://www.harm-reduction.org/files/pdf/4-country/43en_Ukraine.pdf

⁵ ИТРС-ру (2011) Россия на пути к всеобщему доступу: между властью и эпидемией (Russia on its way to the universal access: between authority and epidemics), available in Russian at http://itpcru.org/netcat_files/10/196/Alternative_report_2011ru.pdf

	charge by a pharmaceutical company		son programs			
PCR (viral load)	Patient; exceptions: PLHIV, Global Fund Round 8 program	Patient;	Patient	State health insurance (doesn't cover unemployed individuals which is a common case among drug users)	Patient	Patient
PCR (genotyping)	Patient; exceptions: PLHIV, Global Fund Round 8 program	Patient;	Patient	State health insurance (doesn't cover unemployed individuals which is a common case among drug users)	Patient	Patient
Biochemical blood test			Patient	State health insurance (doesn't cover unemployed individuals which is a common case among drug users)	State health insurance	
Hormones test			Patient	Patient	Patient	
Biopsy			Patient	Partly by state health insurance (doesn't cover unemployed drug users) + partly by patient		
Fibroscan			Patient	N/a	Patient	
Hepatitis B vaccination			Patient	Patient	Patient	Patient
Pegylated interferon	Patient; exceptions: PLHIV, Global Fund Round 8 program	Patient; since 2011 Government agrees to pay for drugs, but majority of clients still are charged for treatment	Patient	State health insurance (doesn't cover unemployed drug users)	Patient; exceptions: PLHIV – covered by National Priority Health Program; sporadically – people without HIV.	Patient; around 10 persons with co-infection will be enrolled into treatment in 2012
Ribavirin	Provided by pharmaceutical companies free of charge		Patient	Provided by pharmaceutical companies free of charge	Patient; exceptions: PLHIV – covered by National Priority Health Program; sporadically – people without HIV.	Patient; around 10 persons with co-infection will be enrolled into treatment in 2012
Antidepressants		Patient	Patient	Patient	Patient	Patient

HCV diagnostic services are more expensive in Georgia than in Post-soviet countries in the region (Ukraine, Kazakhstan, Russia, and Latvia), while the treatment is cheaper (there are preferential prices for Georgian population set by pharmaceutical companies on Pegassus (Interferon) and Pegintron, whereas Ribavirin is made available by these companies free of charge for patients). Indeed, Georgia has the highest HCV diagnosing price among other post-soviet countries listed in Table 12 in terms of HCV RNA (both qualitative/quantitative) and HCV genotyping. Specifically, average testing price of HCV RNA quantitative tests is 6-12 times higher, HCV quantitative diagnostic services cost 4-5 times higher, and HCV Genotyping 4-14 times higher than in other countries.

Such significant difference in the HCV RNA and HCV Genotyping service prices in these countries may be caused by big local markets (higher demand) and use of cheaper HCV diagnostic tests by local manufacturers. According to Ukrainian expert (Kyryk Dmytro): *“Ukrainian DNA-laboratory (Kyiv) uses HCV RNA tests produced by two Russian companies: DNA-technology and Central Institute of Epidemiology. The quality of these tests is correlated to EU standards”*.

With regard to prices in Latvia of Lithuania, the prices for HCV diagnostic testing in public and, for some HCV diagnostic tests, even in private sector, is smaller than in Georgia. Thus, the price of RNA and genotyping HCV diagnostic tests are even higher in Georgia than in some EU member states, _ Latvia and Lithuania do not have a major buying volume because of small population and often imported medicines and goods are sold at similar prices like in other EU countries due to European Union’s single market policy.

Table 12. Average HCV testing Price in Georgia and in other post-soviet countries

Type of test	Retail/distribution price range per a test in Georgia	Average Testing Price in Georgia	Average Testing Price in Ukraine	Average Testing Price in Russia	Average Testing Price in Kazakhstan	Average Testing Price in Latvia	Average Testing Price in Lithuania
Antibody detection Rapid Tests	0.6-3\$	9\$	10\$	-	-	-	8\$ in Public 19\$ in Private labs
Antibody detection ELISA tests	1.2-3.6\$	17\$	10\$	-	-	-	
RNA Qualitative	24-48\$	121\$	10\$	14\$	21\$	21\$	57\$ in public
RNA Quantitative	40-107\$	193\$	40\$	35.8 \$	55\$	46\$	
Genotyping	150\$	291\$	20\$	23\$	27\$	64\$	76\$ in public 260 \$ private labs

Source: Georgia: key informants under Hep. C Study; Latvia and Kazakhstan - internet sources; Russia - EHRN Report on HCV Treatment Access [32], Ukraine: Kyryk Dmytro, International Alliance on HIV/AIDS in Ukraine; Lithuania -Erika Matuzaite, Policy and Advocacy Program Officer.

Another important reason why the price of HCV RNA testing and HCV Genotyping is lower than in Georgia is the fact that these countries (i.e. Lithuania with even with smaller local market) heavily use tenders and competitive purchasing of HCV-RNA and HCV Genotype tests as cost-containment tools. For example, National Health Insurance Fund under the Ministry of Health of Lithuania uses tender

procedures to procure (for the lowest suggested price) reagents for HCV-RNA and HCV genotyping tests. In 2011, “Interlux” company provided 6,400 HCV RNA and 1,300 HCV HCV genotyping tests for ~270 000 USD dollars (on average, ~35 USD for each test). As the result, the price of HCV-RNA and HCV genotyping in public laboratories of Lithuania cost 57 USD and 76 USD correspondingly while both tests can reach ~260 USD dollars in private laboratories⁶ (See Table 12 above). Indeed, according to Lithuanian expert: *“Tender and increasing competition among manufacturers is one of the best strategies to reduce prices of HCV diagnostic tests. According to laboratory staff of Vilnius University Hospital Santariskiu Klinikos, tenders reduced price of reagents about 50 % over the past few years”*.

Because of the big competition in the local market, both in terms of test importers and providers of HCV tests, **the price of rapid screening and ELISA tests in Georgia do not differ from other countries** (See Table #12 above). Increased demand on HCV testing in target groups and improved competition among suppliers of HCV tests (including entering other low-cost HCV diagnostic tests in Georgian market) and diagnostic services in the local market would have potential to reduce the cost of the HCV RNA and Genotyping services in Georgia.

4.6. Public, Donor-funded or Other Programs Covering HCV Diagnostic and Treatment Services

Publicly Funded Programmes

Within the state program “Management of Infectious Diseases” (operates since 15 February, 2011) treatment of some clinical conditions related to HCV infection are partially covered by state funds. The overall budget of this program is 3 mln. GEL [33]. Maximum amount of 680 GEL can be reimbursed for the acute viral hepatitis cases, maximum 660 GEL - for the chronic hepatitis cases with the high clinical activity and maximum 1,100 GEL for the chronic hepatitis cases with cirrhosis. Patients under 18 years co-finance 20%, 18-60 year - 50%, and patients over 60 years co-finance 30% of the price of the treatment. For children under 3 years and beneficiaries of Medical Assistance Program for Poor (mostly population below the poverty line), the program fully covers **symptomatic treatment** of acute and the chronic hepatitis cases in hospitals. Specific **anti-HCV treatment (interferon/ribavirin) and HCV diagnostic services** are not covered under the program.

Screening on HCV (along with HIV, HBV and syphilis) antibodies is free of charge for all blood donors in Georgia under the publicly funded Safe Blood Program. According to program design, the screening should be conducted through ELISA method (rapid tests should be used only in exceptional cases). HCV screening is also conducted routinely in HIV infected patients (under publicly funded GF supported HIV programmes).

To support evidence-based interventions in hepatitis C financing, through state funded program on Early Detection and Screening of Diseases, NCDC conducts the study on C-hepatitis sero-prevalence, which considers screening of selected risk groups: 1) patients after hemotransfusion, 2) patients with

⁶ http://www.sorpo.lt/en/pacients_information/genetic_tests

Sexually Transmitted Diseases (STD) and 3) Patients after endoscopic procedures (total 3,500 patients) through rapid HCV tests.

In Tbilisi, a municipal program provides free screening for the breast, cervical, prostatic and rectal cancers. Additional component to this program was introduced during the last year which includes screening of 3,000 subjects (age group 20-55 years) on the presence of HCV antibodies. The screening is performed using rapid tests. Further follow-up towards the definitive diagnostics of HCV infection is not covered by this program.

State also covers screening of HCV under penitentiary system (in symptomatic patients (i.e. prisoners with icterus) and patients with history of injecting drug use) as well as treatment of limited number (10) of incarcerated Hepatitis C patients.

Donor-funded programmes

Complete HCV diagnostic services and treatment is covered only for HIV/HCV co-infected patients through the HIV component of the **Global Fund (GF) program**. Currently this program covers HCV diagnostic and treatment services for maximum 100 co-infected patients per year.

The program also covers HCV screening services for IDUs through rapid tests. Under this programme, screening of HCVs is conducted by harm reduction organizations providing needle exchange and voluntary counseling and testing (VCT) of IDUs.

USAID-funded HIV Prevention Project also covers rapid screening of IDUs and their partners through VCT services (over 1,700 IDUs and their partners tested in 2011).

Other HCV Diagnostic Programmes

There are also several small programmes implemented by NGOs that mainly focus on HCV screening, education and advocacy of high-risk populations (injecting drug user, symptomatic prisoners, etc.). National Center of Infectious Diseases, HIV/AIDS and Clinical Immunology conducts free HCV screening tests twice per year.

To increase demand on confirmatory and HCV RNA diagnostic tests, starting from 2011, local representative of ROSHE finances rapid HCV screening program for 3,000 patients (22-55 years age category) at National Screening Center. Patients with positive results are sent to “Hepa” (providing RNA testing through Roshe HCV RNA tests) for confirmation. Confirmatory antibody and/or HCV RNA/Genotyping tests are not covered by the programme and, in most cases, patient pays for the diagnostic service out-of-pocket.

Private Insurance Schemes

Private insurance companies cover only small portion of diagnostics needs of HCV patients in the country. HCV screening by rapid or ELISA methods is reimbursed only for patients at pre-delivery or pre-operative stages. No other direct and/or additional diagnostic services related to HCV infection (as well as for HBV infection) are covered by any of the insurance companies registered in Georgia, in exception of very rare cases (a few costly corporate insurance contracts). Insurance schemes also do not cover any HCV treatment options (exception is costly VIP corporate insurance package of GPI

Holding, for example, that covers only first month of treatment of HCV patients). HCV diagnostic (except HCV screening) and treatment services are not covered under any **individual private health insurance packages in Georgia**.

According to the representatives of private insurance companies, insurance premium for most benefit packages is so small that it does not allow covering HCV diagnostic and treatment services. Some insurance companies cover symptomatic treatment of HCV complications.

4.7. Financial Access to C Hepatitis Diagnostic and Treatment Services in Georgia

This section summarizes results of the questionnaire administered to 10 HCV positive patients in two facilities. Small sample size does not allow us to generalize the results on entire patient population in Georgia, but study results still show significant trends on financial access to the Hepatitis C diagnostic and treatment services in Georgia.

Client Sample Characteristics

Demographics: Two clients were under age 30. Eight clients reported undergraduate level education or higher. Six clients reported to be unemployed and one - self-employed, other three patients were employed in private sector.

Self-reported Health Status: All 10 interviewed patients had Hepatitis C. Half of them self-reported existence of chronic hepatitis. Three patients with HCV reported co-morbid conditions: two - depression, one - diabetes, disease of thyroid gland, and cancer.

Self-reported economic status: Two patients reported to be poor, three belong to low-middle, four - to middle and one - upper middle income groups. None of the patients reported to be well-off. The poor patients reported that they spend more during a month than earn. Low-middle and middle class patients monthly spend almost the same as earn. Only upper middle class patients are able to save about 14% of their monthly income.

Monthly expenditures in absolute numbers were approximately three times higher in the upper income class, but patients with low-middle and middle economic status did spend two times more on food and other basic expenses as the proportion of monthly income than the upper class patients. Similarly, patients from low middle and middle quintile groups reported spending much larger proportion of their monthly income on health (both on drugs and diagnostic tests) than the upper middle quintile, although in absolute terms, low middle quintile devoted much less on health than upper middle.

The health expenses were paid by patients mostly out-of-pocket. Only one patient was a beneficiary of Medical Assistance Program (MAP) program (Government funded health program for households below the poverty line); two patients have individual and employer-based private insurance packages, and seven patients reported to be uninsured.

Despite the fact that two patients had private insurance, they were **underinsured** for HCV diagnosis and treatment; Hepatitis C positive patients reported that insurance packages do not provide them the

coverage and they paid for the services out-of-pocket. Only one patient reported initial payment of the HCV tests (rapid) through corporate health insurance.

Patient Self-reported Expenses on HCV Diagnostic and Treatment

Among patient sample, three patients reported C-hepatitis diagnostic testing during 12 months period. Seven patients did any kind of HCV test more than one year ago. Mean expenses of patients on HCV diagnostic tests, as well as their range are provided in the Table 13 below, which shows that patient self-reported expenses on HCV diagnostic tests are overall consistent with the HCV test prices reported by facilities, except expenses on HCV genotyping and total costs on HCV diagnostic tests (Antibody, PCR, Genotype) where patient-reported expenses are higher than facility-reported price for the same service.

Table 13. The price of the HCV tests, HCV diagnostic testing and average price on HCV tests, reported by patients

Type of test	Retail/distribution price range per a test reported by key informants, GEL	Price range of testing in health care facilities reported by key facility managers, GEL	Average Price reported by patients in GEL
Antibody rapid tests	Detection, 1-5	15-20	15-20
Antibody ELISA tests	Detection, 2-6	12-50	17-25
RNA Qualitative	40-80	192-225	235-500
RNA Quantitative	60-180	304-340	
Genotyping	250	300-616	300-700
All together (Antibody, PCR, Genotyping)	436 (max)	836	915-1000

Source: Questionnaires with Key Informant and Representatives of Medical Facilities, Pharmaceutical Industry and Patients

According to patients, price of screening tests is not high and they can afford it. The price of all other tests, especially PCR and Genotyping tests, are expensive and create significant financial burden for them. Average amount per case of quantitative HCV RNA testing and HCV genotyping for poor households was approximately 1.5-2 times higher than their monthly household income. Furthermore, total cost on HCV diagnostic tests (ELISA, PCR, Genotyping) create difficulties to all patients - their cost exceeded the monthly household income of poor, low-middle and middle income quintiles.

Thus, if we consider: a) households’ needs to substance expenditure (monthly expenditure on food and other substance expenses); b) the fact that neither public health programs nor private insurance schemes cover HCV RNA RNA and HCV Genotyping diagnostic services; and c) the lower income quintiles (poor, low-middle and middle) practically do not have savings, it becomes clear that any HCV RNA and Genotyping diagnostic tests could be catastrophic for these patients and their households.

The same applies to the HCV treatment. The mean 24-week treatment price reported by patients is 15,167 GEL and mean 48-week treatment price is 25,500 GEL. According to them, only five and four patients conducted 24-week and 48-week treatment, respectively through out-of-pocket payments and only one patient received therapy under MAP programme. It is important to emphasize that among interviewed patients; **only MAP beneficiary knew** that Government covers some HCV diagnostic and treatment services.

About half of interviewed patients were unable to afford HCV treatment at all. This is obvious if we consider the fact that average price on monthly HCV treatment several times exceeds self-reported household monthly income of middle, low-middle and poor quintiles.

Indeed, all interviewed HCV positive patients experienced problems with financial access to HCV diagnostic and treatment services. Majority of patients reported affordability of prescribed anti-HCV drugs as the single greatest barrier to access the HCV diagnostic and treatment while only one patient reported difficulties to afford HCV diagnostic tests. In addition, two patients reported financial access to both HCV diagnostic and treatment services as a problem. Thus, total 30% of interviewed patients reported difficulties to afford HCV diagnostic tests.

5. Conclusions

Study results demonstrate that the price of antibody detection HCV tests is not high and mostly covered by public, private insurance and donor-funded programmes. Due to relatively large market, there is more competition and better price-self-regulation in the market for antibody testing. As the fact of this, the price of HCV antibody detection screening tests in Georgia is similar to the prices of other post-soviet countries in the region. Because of abovementioned points, financial access to HCV antibody testing is not an issue in Georgia. In contrast, the price of RNA and Genotype testing is high and create significant financial burden especially for poor households.

Because of the fact that neither publicly funded nor private insurance programmes cover HCV RNA testing and genotyping, there is a greatest need for price reduction of these types of tests especially for poor and vulnerable population. Indeed, 30% of interviewed patients reported difficulties to afford RNA and HCV genotyping as the price of these tests are approximately two times higher than the monthly income of poor households.

In addition to the greater need, there is also more opportunity to decrease the price of HCV RNA testing and genotyping in Georgia. In contrast with antibody detection HCV screening tests, HCV RNA and Genotype tests and diagnostic services are exclusively provided by very few (or sole) distributors and service provider facilities. Within enabling regulatory and tax policy of diagnostic tests and services in Georgia, there is the possibility to increase the competition on HCV RNA and genotyping tests and diagnostic services in the country through increased demand on these services.

In order to reach price reduction on HCV RNA and genotype testing in Georgia, Government's role is crucial to eradicate a few (but important) entry barriers to the HCV diagnostic test market and increase financial access to HCV (RNA testing, genotyping) diagnostic and antiviral treatment services. Because of the cost consideration, poor and vulnerable population often avoid needed in-depth diagnosis and treatment of Hepatitis C. If we consider that not treated HCV cases have substantial economic and human impact on families/communities due to increased health care costs, lost

productivity and are the major cause of premature death while in approximately 40-80% of HCV patients, the infection will clear with timely diagnosis and treatment (45, 46), Government has strong justification to support timely confirmatory diagnostic and treatment services of Hepatitis C.

6. Cost-containment strategy and recommendations

Study results clearly show that there is an urgent need to develop actionable recommendations to improve financial access to HCV diagnostic and treatment services.

Within the context of current health sector reform, specific recommendations include:

1) **Support price competition of HCV Diagnostic tests in the local market**

In order to decrease the cost in the local market, generally, one of the key interventions is support local production, but in Georgia case, interventions supporting production of the HCV diagnostic tests are not recommended. First, because that the local market is small: due to high investment costs associated with manufacturing, production of small number of tests would not allow to reduce the unit cost significantly. Thus, the manufacturing price of the test would not be able to compete with imported HCV diagnosing tests produced by manufacturers with large domestic and/or international market. As there is no internationally recognized regulatory agency in Georgia that could provide a credible proof of quality internationally, local companies could not also try to compete in export markets for HCV diagnostic tests in order to increase its size and allow substantial economies of scale in production to have a successful business.

Despite the fact that lack of price control mechanism might be a challenge for getting prices of HCV diagnostic tests down, considering country's macroeconomic policy and development strategy, it is not feasible to regulate the prices of HCV diagnostic tests in the market.

Analysis of local competition among importers of HCV diagnostic tests demonstrated that the competition among importers and distributors of HCV screening tests is high because of many players in the market and cheap rapid tests produced in China. In contrast, the market is not competitive for HCV RNA (only two competitors, with 90% share of one company in the market) and Genotyping tests (only one supplier of genotyping tests). **Improved competition among suppliers of HCV tests**, including negotiations with potential importers of low-cost HCV RNA and Genotyping tests would reduce the cost of the HCV RNA and Genotyping services in Georgia.

One of the key interventions to support competition in the local market both in terms of HCV RNA and HCV Genotyping Diagnosing Tests and testing services **is ensuring availability of impartial price information on HCV RNA and HCV Genotyping Diagnosing Tests and price of diagnostic testing in different health care facilities**. Diagnostic test markets (as entire health market) are imperfect market with significant "information asymmetry" meaning that demand side (consumers, payers) do not have the information to make the best possible choices in the interest of their own health and/or economic welfare. Thus, strengthening demand side with price information on diagnostic tests in light with their effectiveness is necessary to utilize market mechanisms for cost-containment. MoLHSA (with its implementing regulatory agency) and health care facilities can play significant role to make information on choices of HCV diagnostic tests from different manufacturers and their

comparative effectiveness accessible to the public. This information is very important to influence doctors' prescribing decision depending on patients' ability to pay.

2) **Eliminate regulatory barriers**

Elimination of regulatory barriers is also powerful way to improve competition in the local market. Despite recent changes in regulatory environment of diagnostic tests and pharmaceutical products that allowed entering more than 300 new medicines and diagnostic tests in Georgia, there is still a need to eliminate regulatory barriers in the Law on Drugs and Pharmaceutical Activity in Georgia (see the section above). Specifically:

- Clearly define the specialty of personnel responsible for distribution of diagnostic tests (Medical Technician or Pharmacologist);
- For minor (allowable) changes in pharmaceutical products and diagnostic tests systems (such as changes in catalogue number for example) do not require completely new registration procedure under the recognition regimen and allow consequent changes in registration by informing and paying a fee (as it is under National Registration Regimen).
- In case of Recognition Regimen of registration, do not require provision of very expensive samples of diagnostic tests to Regulatory Agency.

These changes in legislation are essential to utilize the benefit of recognition regimen for HCV diagnostic tests (currently, because of abovementioned barriers, most HCV diagnostic tests are registered under National Registration Regimen) and save resources of importers (financial, time). Most importantly, the benefit of Recognition Regimen is that it does not limit either the type of importing party or the purpose of the import: the interested party may be any natural or legal person wishing to register/admit certain diagnostic test the market, while National Regimen only allows registration applications from pharmaceutical manufacturers or trade license holders. Thus, creating enabling environment that supports use of Recognition Regimen of Registration of diagnostic tests will stimulate additional importers of HCV diagnostic tests in the market (with consequent decrease of their price).

3) **Promote competitive procurement and group purchasing**

Competitive procurement and group purchasing are other effective strategies to increase competition and decrease the price of HCV diagnostic tests. This study demonstrates several local and international examples (from post-soviet countries) that, because of the economies of scale, it is possible to buy HCV diagnostic tests on less price through competitive tendering procedure. For example, NCDC purchased South Korean ELISA 96 test kits on 180 GEL through centralized tender among Georgian distributors, while the price of ELISA tests for wholesale or retail buyers in the market is 300-350 GEL. ELISA testing in NCDC laboratories of Georgia (Tbilisi, Kutaisi, Batumi, Ozurgeti, Zugdidi, Ambrolauri, Poti, Akhaltsikhe, Telavi, Gori) will be conducted through service contracts with medical facilities on affordable price (10-15 GEL). NCDC laboratories have the possibility to broaden their diagnostic capacity and offer wide range of diagnostic services (including HCV RNA and genome testing). In addition to service contracts with health care facilities, NCDC laboratory network (with its different levels of laboratories, including referral laboratory) will conduct all diagnostic tests under the Government-funded Public Health Programmes. **Strengthen**

capacity of NCDC laboratory network to conduct/offer HCV RNA and Genotyping diagnostic services in the future will decrease the cost of these services in Georgia and improve financial and geographic access to these services (in contrast with private laboratories, NCDC laboratories do not aim to get profit from diagnostic services).

Recent changes in ownership and organization of health service delivery system in the country with private ownership and establishing the **big medical corporations of ambulatory and hospital facilities under insurance companies create opportunities to introduce effective cost-containment strategies such as competitive tendering and group purchasing** (Managers of health care facilities under the corporation may integrate effort to reduce costs and purchase goods and services together).

Among provider level interventions, **rational use of specific type of RNA quantitative tests** according to the Hepatitis C Management Protocol will more likely contribute to the decreased price of HCV diagnostics. Specifically, use less costly RNA qualitative tests for 1) early detection, 2) determination of disease stage (active, latent), 3) confirmation of virologic response during, at the end of, and after antiviral therapy, and 4) screening blood and organ donations for presence of HCV, and use **more costly quantitative HCV RNA tests only in case of the need to monitor and predict effectiveness of anti-HCV treatment**.

4) **Improve affordability of HCV RNA and Genotype Diagnostic and Treatment Services for poor and vulnerable groups**

Analysis of coverage of different population groups with HCV diagnostic and treatment services and patient questionnaires (see previous for more details) clearly show that neither publicly funded nor insurance programs provide full financial access to HCV diagnostic and treatment services.

State program on “Management of Infectious Diseases” fully covers symptomatic inpatient treatment in case of acute viral hepatitis (maximum 660 GEL), chronic hepatitis (maximum 680 GEL) hepatitis with the high clinical activity (maximum 1100 GEL) for MAP beneficiaries, but **specific anti-HCV treatment (interferon/ribavirin) and HCV diagnostic services are not covered under the program**. HCV diagnostic and treatment services are only covered (fully or partially) for limited number of target patients (100 HIV/Hep C co-infected patients under the GF grant and 10 patients under penitentiary system).

If we consider the fact that 1) total price on HCV diagnostic tests (ELISA, PCR, Genotyping) and monthly treatment price exceeds to mean monthly household income for poor, low-middle and middle income patients 2) households’ needs to substance expenses (monthly expenditure on food and other basic expenses); 3) the fact that neither public health programs nor private insurance schemes cover HCV RNA and HCV Genotyping diagnostic and treatment services; and 4) the lower income quintiles (poor, low-middle) usually do not have savings, it becomes clear that any HCV RNA and HCV Genotyping diagnostic tests and/or HCV treatment expenses could be catastrophic for these patients and their households.

Thus, there is essential need to **improve the coverage of the poor and vulnerable population with HCV diagnostic and treatment services under the publicly-funded programmes, with parallel use of cost-containment strategies** (co-financing, service contracting and etc.).

Aware about the financial difficulties related to HCV diagnostic and treatment services, MoLHSA is trying to address this issue through creation of the special working group under the ministry. Incorporation of RNA diagnostic and treatment services into publicly funded and private insurance schemes would significantly reduce the cost of diagnostic services through effective contracting mechanisms from one hand and supporting competitive environment in the market due to increased demand on HCV RNA and genotype tests and relevant diagnostic services (as it happened in case of antibody detection screening tests described above).

5) **Promote HCV diagnostic and treatment services in pre-payment schemes**

Private insurance companies cover only small portion of diagnostics needs of HCV patients in the country. HCV screening by rapid or ELISA methods is reimbursed only for patients at pre-delivery or pre-operative stages. No other direct diagnostic and/or additional diagnostic services related with HCV infection (as well as for HBV infection) are covered by any of the insurance companies registered in Georgia, in exception of very rare cases. Insurance schemes also do not cover any HCV treatment options (exception is very costly VIP corporate insurance package in a few cases). HCV diagnostic (except HCV screening) and treatment services are not covered also under any **individual private health insurance packages in Georgia**.

By avoiding covering HCV diagnostic and treatment services health insurance companies contradict with the concept of the insurance (protect population from the irregular and unpredictable catastrophic health expenses, associated with illnesses by pooling risks of many people). In contrast, many private benefit packages offer coverage of small and predictable expenses (such as annual check-ups for example).

In order to ensure that people have adequate coverage and financial protection from catastrophic health expenses when they purchase insurance, MoLHSA should establish **minimum benefit package**, a baseline, standard set of benefits to be offered by private insurance schemes (both employer- and individual private insurance) that among other irregular/unpredictable expenses **covers HCV diagnostic and treatment for insured population**. Such interventions are successfully used in many countries, including the US. [34]. To properly manage their own financial risks associated with expanded benefit packages, insurance companies may introduce different risk-reduction and cost-containment strategies (for example: deductibles and co-payments with insured population, contracting mechanisms with medical facilities, reorganizing care practices with gate keeping and strong focus on prevention of diseases and their complications and etc.).

Incorporating HCV diagnostic testing (HCV RNA/Genotyping) in insurance schemes has also potential to decrease the price of RNA and genotype diagnostic service in Georgia. Analysis of cost drivers and the price of HCV RNA qualitative/quantitative diagnostic testing (see section #X for details) demonstrates that the price of these services in the facilities are not based on the real costs of the service/product and the limited number of facilities (3-8 total), providing HCV RNA testing services in Georgia, benefit from the price-making “privilege” in the market. If insurance companies have to pay for HCV diagnostic and treatment services under public (e.g., in case of Medical Insurance for Program for Poor) and/or private insurance packages, facilities will be encouraged to consider the cost of HCV RNA/Genotype testing during negotiations with Insurance companies (as it is now for

HCV screening tests) and will most likely to switch their tactics from “**price-making**” to “**price taking**” strategy. Better financing of HCV RNA and genotyping diagnostic services will increase demand on them and stimulate competitive environment among facilities where facility managers will use different cost-containment tools to decrease the price of HCV diagnostic services (including group purchasing and competitive tenders as noted above).

Among other methods to improve access to health care (including HCV diagnostic and treatment services) is **establishment of compulsory medical savings account in Georgia** that is successfully used in Singapore (the country with the lowest infant mortality rate in the world and the highest life expectancy from birth). This system allows the population to put aside part of their income into a Medisave account to meet future personal or immediate family's healthcare needs.

6) **Increase demand on HCV diagnostic services through better outreach of target population**

Current evidence (A level) does not support screening of persons who are not at increased risk [36]. Among target groups that should be screened for HCV (IDUs, HIV Infected Individuals; Children of HCV positive mothers, patients with Hemophilia, Patients on Dialysis and others), the biggest and the most hard-to reach group is IDUs. Estimated size of IDU population in Georgia is around 40,000 [37]. The 2008 UNAIDS country report estimates that current prevention activities in Georgia are reaching only 20% of IDUs.

Disease prevalence data from BSSs [39], [40], [41] among IDUs in Tbilisi (2006), Batumi (2006) and Kutaisi (2007) show that, around **57.8% to 76.4% of IDUs are infected with the hepatitis C virus.**

Several government, donor (GF HIV Project, USAID HIV Prevention Project) and non-governmental initiatives try to reach IDUs through VCT services and community-level activities. Further scale up of these efforts with improved counseling and testing services of IDUs on Hepatitis C would significantly increase demand on HCV diagnostic services in Georgia. Increased demand will stimulate the competitiveness in the local market and more likely to contribute to the decreased price of HCV diagnostic services.

7) In line with activities directed to improve financial access to HCV diagnostic services, **development of sustainable financing mechanisms of HCV treatment** is essential to respond to the main barrier of the patients with Hepatitis C (financial access to HCV treatment).

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