5th HEPATITIS C TECHNICAL ADVISORY GROUP

TAG Meeting

IMPROVE HCV LABORATORY DIAGNOSTICS TAG 2018 RECOMMENDATIONS, STATUS OF LABORATORY AND DIAGNOSTICS EFFORTS

Maia Alkhazashvili

National Center for Disease Control and Public Health

The diagnostic landscape for hepatitis C infection: Screening

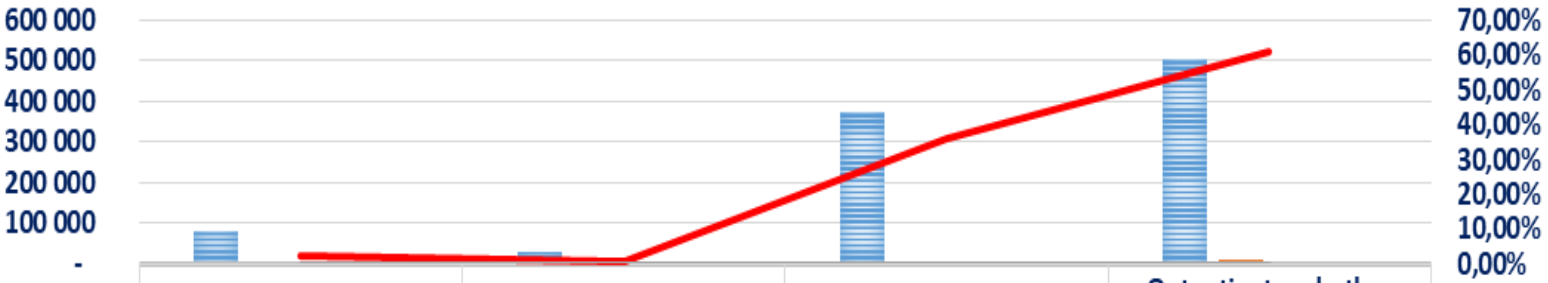
- Screening

Screening Methods	Facility / Population
Rapid tests purchased trough the centralized procurement by the government	**Outpatient clinics, NCDC lab network / General Population, Pregnant women HRS /Risk Groups**
Rapid tests from different vendors	**Inpatient clinics/ Hospitalized patients**
Laboratory based serology methods (ELISA, CLIA, CMIA and etc)	**Blood Banks/ Donors**

- In 2019 – 600,000 rapid tests were purchased in frame of HCV elimination programs (400,000 tests from Healgen and 200,000 tests from Acro Biotech Inc.)
- Lugar Center performed local validation of two different manufacturers rapid test kits, purchased by the government
- Both tests showed 100% sensitivity and specificity

The diagnostic landscape for hepatitis C infection: Screening

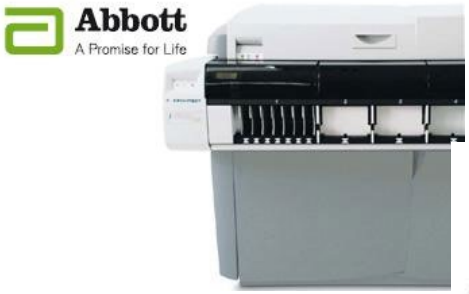
- Since January 2019 year screening rate in outpatient clinics reached more than 50% of the total number of screening conducted in all sites

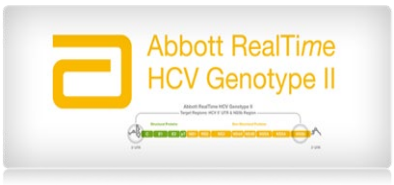


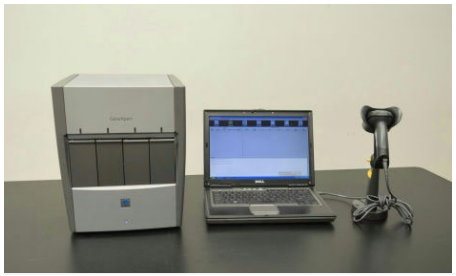
	Blood donors	Pregnant	Hospitalized patients	Outpatient and other groups
Screening	79 686	28 857	374 671	504 051
anti-HCV+	404	167	6 793	11 429
%pos	0,51%	0,58%	1,81%	2,27%
% of HCV tests	8,07%	2,92%	37,95%	51,06%
% of positive HCV tests	2,15%	0,89%	36,15%	60,82%

The diagnostic landscape for hepatitis C infection: Confirmation of HCV active infection

Methods	Facility
Quantitative HCV RNA • All platforms • GeneXpert® **HCV VL** • GeneXpert® **FS HCV VL**	HCV treatment provider sites HRS, NCDC HRS, NCDC
Qualitative HCV RNA	HCV treatment provider sites
HCV cAg	Lugar Center for Public Health Research, NCDC







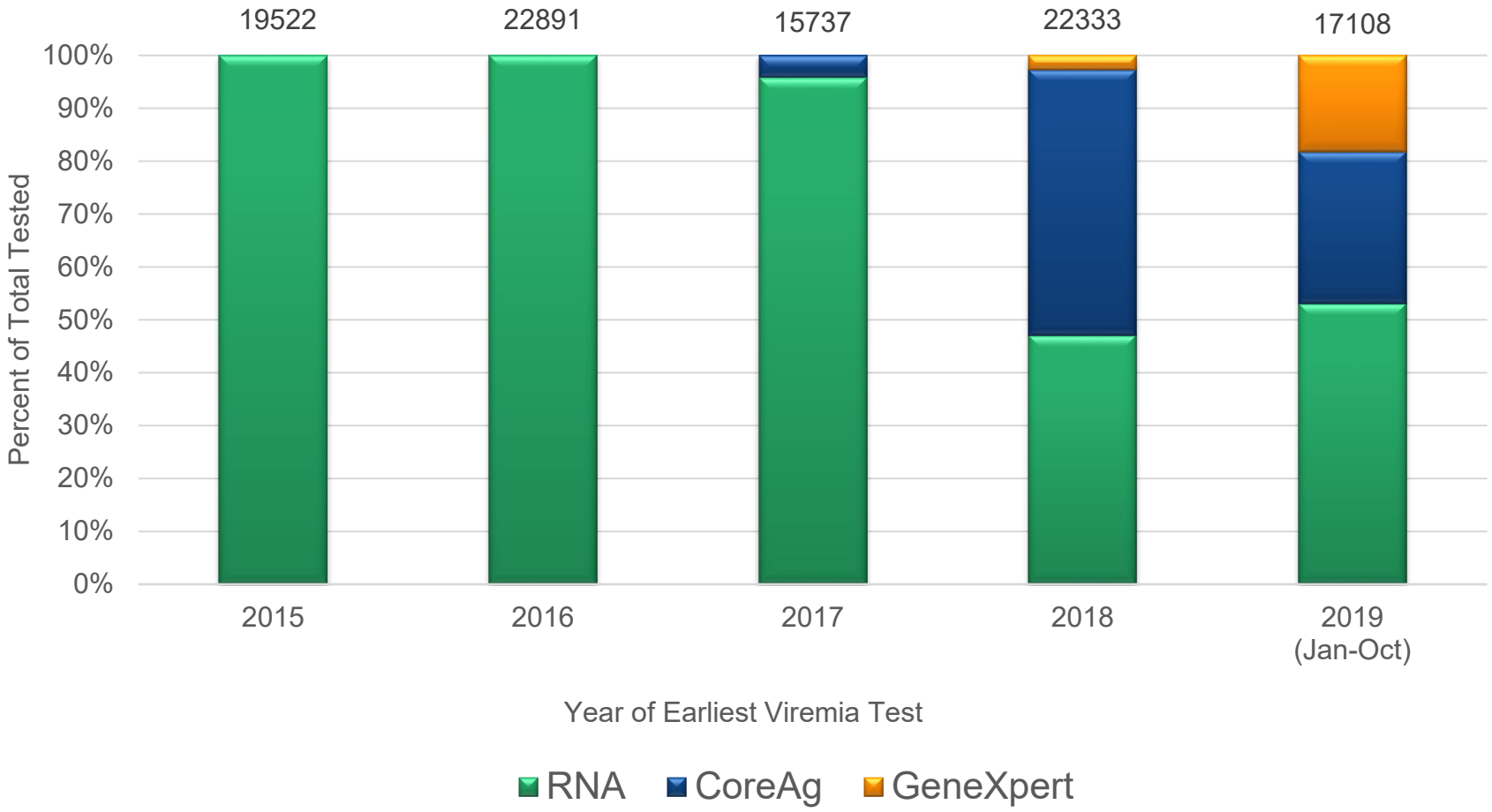
Methods, test-kits and equipment

PCR Equipment	HCV RNA VL kits	HCV Qualitative kits	Genotyping kits
Abbott m2000rt	Abbott RealTime HCV kit	HCV Real Time TmQual (Sacache) ref# TVI-100 FRT	**Abbott** RealTime HCV genotype II kit
COBAS Taqman 48 ROCHE	Cobas TaqMan HCV Quantitative Test V2.0, Roche	Bosphore HCV Detection kit V1, Anatolia Geneworks	**Siemens** Versant HCV Genotype 2.0 LIPA
Applied-Biosystems Quant Studio Dx	RoboGene® HCV RNA Quantification Kit 3.0 Germany	HCV RT. Qual. Sacace Biotechnologies	**Sacace Biotechnologies** RTA HCV Genotyping qRCR kit
COBAS 6800 ROCHE	HCV Real TM Quant Dx V1, Sacace Biotechnologies	RT-GEPATOGEN-C Quant PCR Amplif Kit, DNA Technology	**DNA Technology** RT-GEPATOGEN-C Genotype RNA Ampli Kit
Applied-Biosystems Quant Studio 5 RT PCR	Bosphore HCV Quantitation Kit, Anatolia Geneworks	RTA HCV Qualitative Real Time PCR Kit	**Roche** Cobas, HCV Genotyping
Applied-Biosystems 7500 RT PCR	HCV Real TM Quant Dx V1, Sacace Biotechnologies		**Bosphore,** HCV Genotyping kit v1
Thermo fisher Scientific Quant Studio 5 Real-Time PCR System	HCV Real-Time PCR Kit, Human Diagnostic		**NLM, ITALY** HCV Gen-C 2.0
RotorGene 6000 Qiagen	RT-GEPATOGEN-C Quant PCR Amplification Kit, DNA Technology		
DTlite DNA-Technology	Gene Prof Hepatitic ,,C" virus		
Applied Biosystems 7500 FastDx	Robogene HCV RNA Quantification kit 3.0 (Analytikjena)		

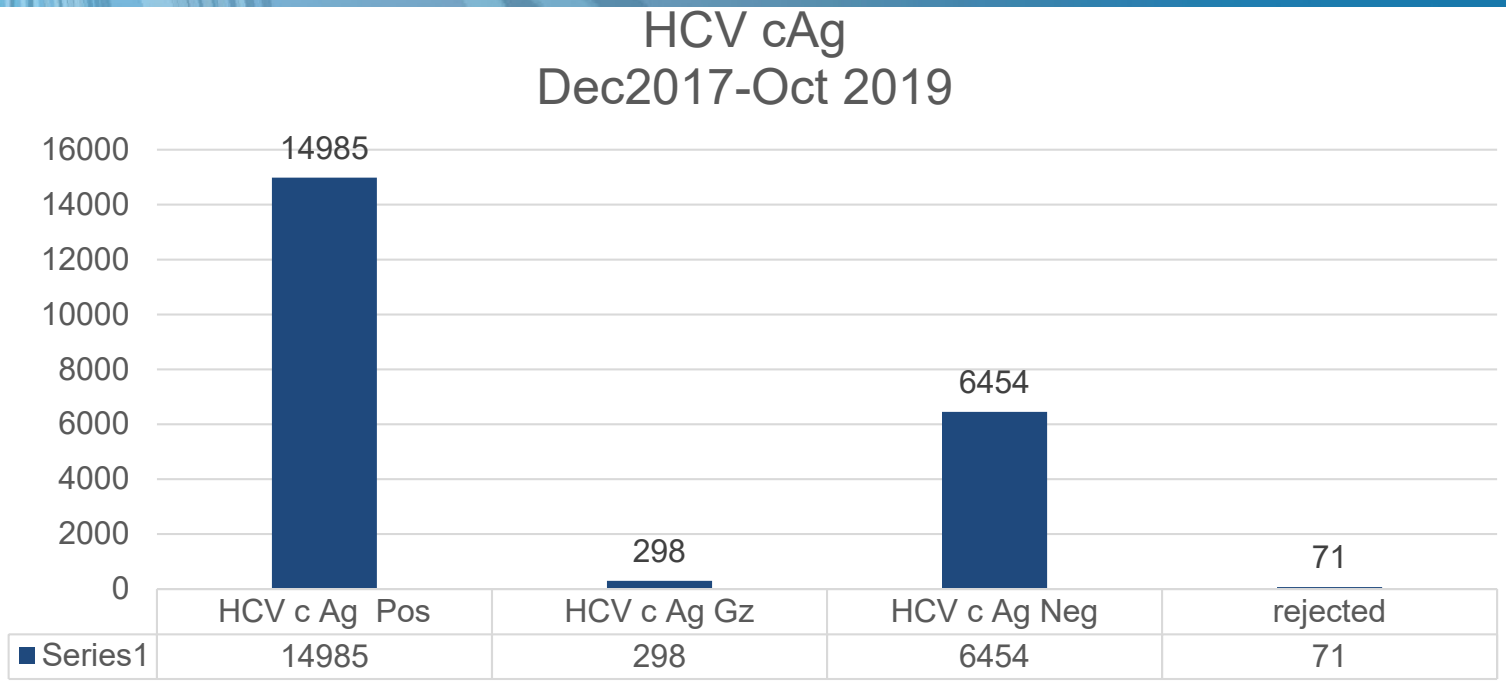
Decentralization of confirmatory testing

- From November 2018, confirmation testing of anti HCV positive hospitalized individuals became decentralized
- According the amendment in the Governmental Decree #169 (N438; 24.08.2018) all service providers are allowed to perform first confirmatory testing using different methods
- Since 2018, optimal and cost-effective confirmatory testing strategies have been implemented
  - GeneXpert HCV VL tests have been introduced in four harm reduction sites (HRS), supported by FIND
  - Since 2019, NCDC Laboratory network started confirmatory diagnostic using GeneXpert HCV VL tests
  - Since October 2019, supported by FIND new diagnostic method - GeneXpert FS HCV VL - was implemented in all sites equipped with Cepheid platforms

Confirmatory tests by year 2015 – 2019 (Oct)

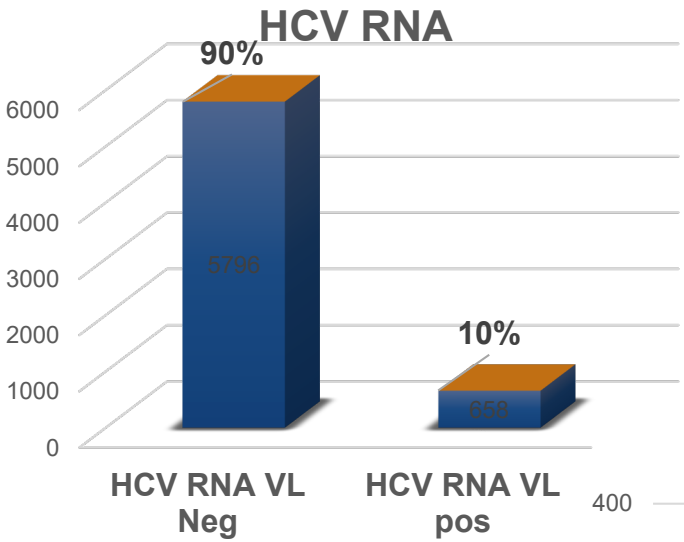


Summary of the HCV core Ag testing: December 2017 - October 2019

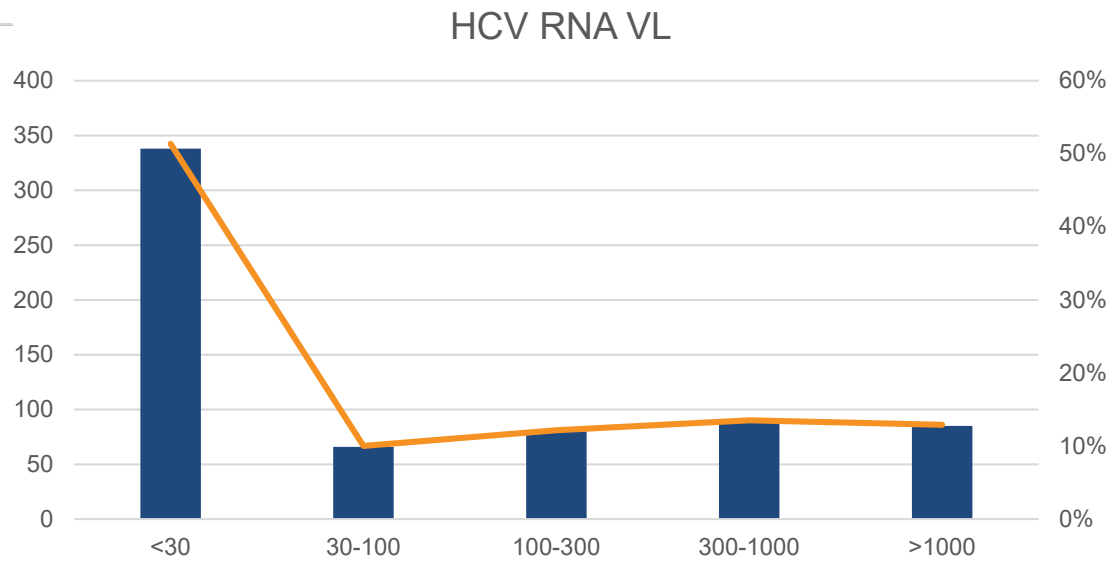


- A total of 21,808 samples were received and, of these:
  - Only 71 (0.3%) were rejected
  - A total of 21,737 samples were tested
  - 14,985 (68.9%) were reactive
  - 6454 (29.6%) were nonreactive

HCV core Ag Negative / HCV RNA VL



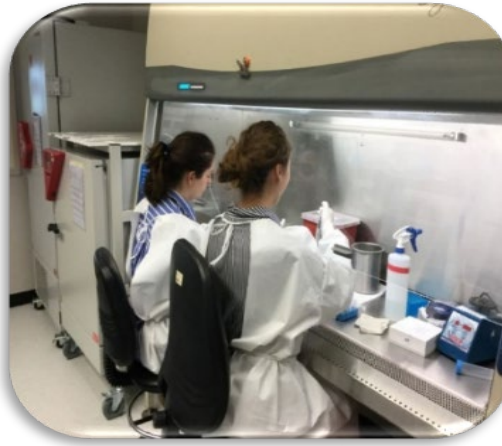
- Of nonreactive, samples 658 (10%) were HCV RNA positive
- 338 (5.2%) had HCV VL <30 IU/mL
- 65 (1%) 40 - 100 IU/mL
- 169 (2.6%) >100 IU/mL
- 85 (1.3%) >1000 IU/mL
- All GZ samples were HCV RNA positive.



Improving quality of HCV testing in Georgia through National External Quality Assurance Program

- Since 2017, the National External Quality Assessment Program (EQAP) for the Detection and Genotyping of Hepatitis C Virus by PCR has been implemented in Georgia with the support of CDC Atlanta

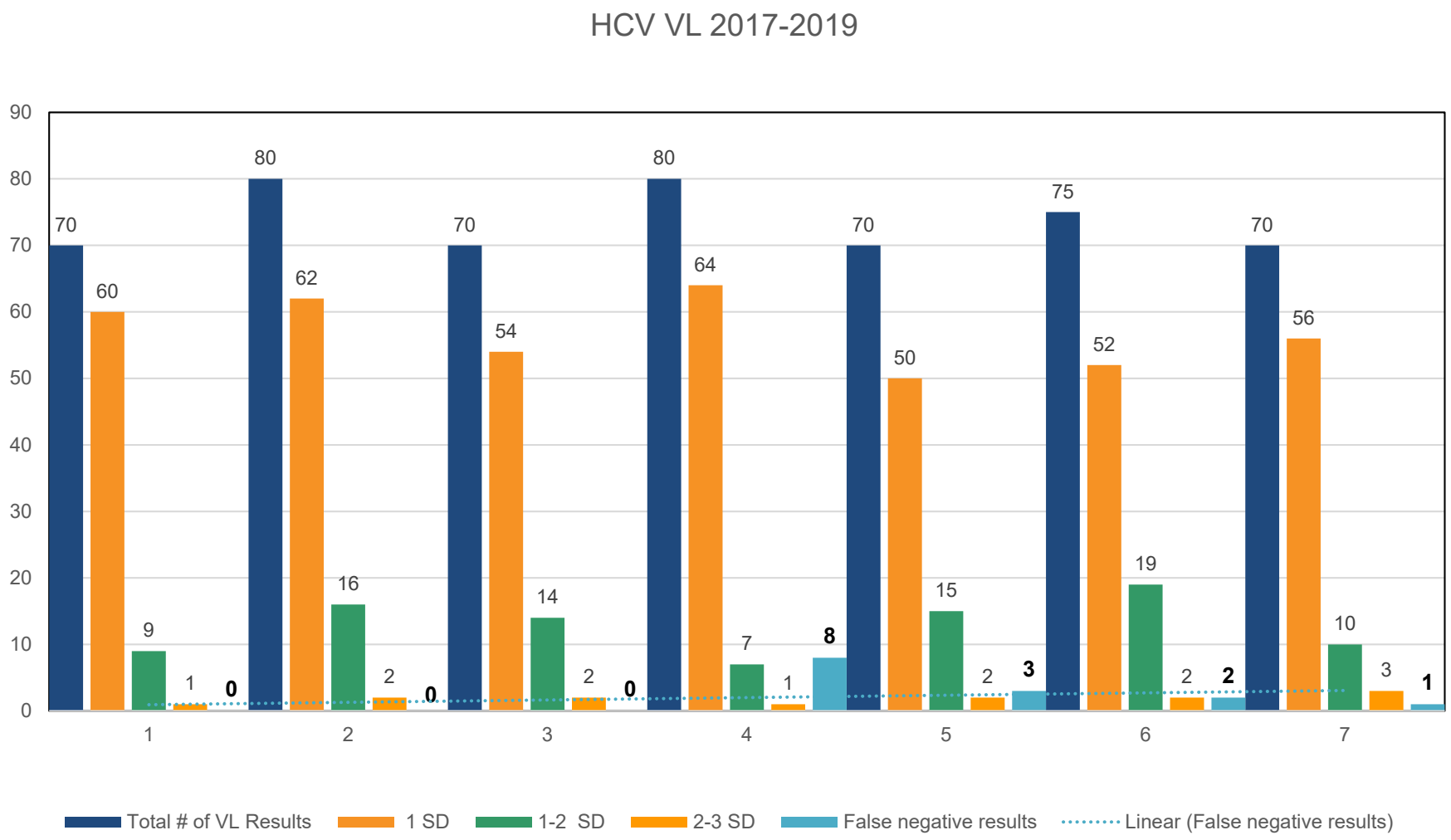
- The NCDC/Lugar Center is producing the National HCV Proficiency Testing (PT) panels for HCV testing based on CAP model.



- The aim of EQAP is to help monitoring and to improve quality of the clinical and public health laboratory by assessing their ability to use molecular diagnostic technologies within the routine clinical setting.

COLLEGE of AMERICAN PATHOLOGISTS

EQA Program Results Summary: Quantitative Viral Load



EQA Program Results Summary: Qualitative Assay

PT panel round	# of labs reporting	% with correct result	% False negative result	% False positive result	*Notes
1st-June 2018	12/18	**24** (100%)	- (0%)	- (0%)	*6 labs didn't perform the test
2nd-September 2018	12/18	**24** (100%)	- (0%)	- (0%)	*6 labs didn't perform the test
3th-January 2019	13/18	**21** (79,8%)	**5** (19,2%)	- (0%)	*5 labs didn't perform the test
4th May 2019	13/18	11 (100 %)	- (0%)	- (0%)	*2 labs didn't perform the test

EQA Program Results Summary: HCV Genotyping

PT Round	# of Labs reporting	# of Labs do not perform test	Genotype	% with correct result
1st July 2017	12/14	**2**	**3**	100%
2nd Sept 2017	14/16	**2**	**1b**	100%
3rd Dec 2017	12/16	**4**	**1b**	100%
4th July 2018	13/18	**5**	**1b/2**	36% *absolute correct
5th Sept 2018	12/18	**6**	**3**	100%
6th Jan 2019	14/18	**4**	**1b**	100%
7th May 2019	13/18	**1**	**1b/2**	23.08% *absolute correct

EQA Program Results Overview

- Qualitative interpretation: five laboratories reported false negative results in January 2019.
- False negative result reported by two laboratories in January and one laboratory reported false negative result in May 2019 in quantitative HCV RNA test.
- In the comparative analysis of the EQA Program results, a relatively small number of results were between 2 and 3 SD from the mean results.
- In most cases, problems included improper use of quantitative PCR calibrators, not following manufacturers' recommendations for PCR platform-reagent combinations.

Challenges

- Lack of quality training and monitoring at community-based testing sites
- Lack of continuing educational programs in laboratory medicine
- No NEQA Programs in clinical chemistry and Hematology, and centralized authorization body to collect EQA results, analyze and establish mechanism for corrective action of non-conforming testing sites
- Sustainability of the National EQA programs and archiving samples

Sustainability of archiving samples

- Continue support for archiving of key blood samples for future research and public health applications (e.g. outbreak investigations).
  - Both HCV treatment contract and confirmatory testing informed consent documents includes verbiage on sample archive
    - HCV baseline confirmation using HCVcore Ag
  - Rejected blood samples should be re-defined so they are not assigned to the bio-waste category
    - Blood bank samples are collected including seronegative samples for HCV, HBV and HIV. Blood banks are requested to send plasma bags of rejected blood (Jo Ann and Kvantaliani)
  - Aliquots of samples are collected as part of the FIND funded projects

- Archived samples have been used:
  - Evolution of sensitivity and specificity of HCV rapid test kits, purchased by the government for Hepatitis C screening sites
  - Preparation of EQA panels for the HCV diagnostic/treatment providers and Blood banks

TAG recommendations

TAG recommendations for 2019	Current Status
Ensure that rapid tests used for screening are of high quality, and consistent with WHO Testing Guidelines and Perform local validation of rapid tests supervised at the Lugar Center, NCDC in field conditions	Validation of the rapid tests are implemented and used within the centralized purchasing process
Ensure quality training and monitoring at community-based testing sites so that testing meets WHO Testing Guidelines	Still remains as a challenge
Conduct proficiency testing, including clinical chemistry and blood cell counts, at all levels and establish mechanism for corrective action of non-conforming testing sites	Still remains as a challenge

TAG recommendations

TAG recommendations for 2019	Current Status
Mandate laboratories participating in the elimination program participate in an external quality assurance program to address the trend of labs opting out of participation in the program.	National HCV EQA schemes is implemented and all laboratories participating in HCV program receiving EQA panels
Investigate discordant test results patients to identify and rectify the causes	Ongoing
Continue support for archiving of key blood samples for future research and public health applications (e.g. outbreak investigations)	By supporting Abbott Diagnostic project will be continuing
Utilize optimal and cost-effective confirmatory testing strategies (e.g. conventional RNA/NAT, HCV Core antigen, and GenXpert) that may vary depending on setting.	Different type of confirmatory tests are implemented throughout Georgia

Acknowledgment

- TAG members
- MOLSHA
- NCDC/ Lugar Center
- US CDC
- FIND
- Abbott Diagnostics
- Cepheid
- Clinics providing HCV diagnostic and treatment

Thank you !