Globally, there are an estimated 71 million people living with hepatitis C virus (HCV) infection and 411,000 HCV-attributable deaths annually [1]. HCV is bloodborne and transmitted most often through unsterile medical equipment, infected blood and tissue used for medical procedures, and shared drug injection equipment. HCV infection often progresses asymptomatically for 20–30 years, and most HCV-related deaths result from liver cirrhosis or hepatocellular carcinoma decades after the incident HCV infection [2–6]. HCV accounts for an estimated 27% of cirrhosis and 25% of hepatocellular carcinoma cases worldwide [7].

Georgia is an Eastern European, middle-income country with 3.7 million residents [8]. A 2002 survey in the capital city of Tbilisi found that 6.7% of the general population and 70.4% of persons who inject drugs had antibodies to HCV (anti-HCV, evidence of past or current HCV infection) [9], suggesting that HCV prevalence in Georgia could be among the highest globally. In 2015, Georgia launched the world's first HCV elimination program, aiming to provide universal access to curative, direct-acting antiviral (DAA) treatment at no cost to patients, and to implement nationwide prevention measures to curb transmission [10]. Existing prevalence data have been instrumental in engaging the government's strong support to combat the country's HCV burden, but are outdated and not nationally representative. Data documenting updated nationwide HCV prevalence and risk factors for infection are necessary to effectively plan treatment and prevention services supporting Georgia's HCV elimination goals, and to establish a baseline to track progress toward elimination over time.

This paper presents the results of the first nationally representative HCV seroprevalence survey in Georgia, conducted in 2015 by Georgia's National Center for Disease Control and Public Health (NCDC) in collaboration with the United States Centers for Disease Control and Prevention (CDC). The Georgian government is using these results to plan and implement HCV surveillance, education, prevention, screening, care, and treatment efforts. A follow-up survey is planned to assess the impact of interventions designed to achieve HCV elimination. In addition, planning and conducting this national serosurvey provided an important opportunity to strengthen the public health capacity in Georgia and thereby enhance global health security.

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A cross-sectional, nationally representative seroprevalence survey was conducted in Georgia from May–August 2015 among adults aged ≥18 years using a stratified, multi-stage cluster design. A sample size of 7000 was calculated based on estimated 6.7% anti-HCV seroprevalence [9], a design effect of 2, and an anticipated 70% response rate. The sample was designed to yield a nationwide HCV prevalence estimate, independent prevalence estimates in six pre-selected major cities, and

school education. Field and laboratory procedures, questionnaires, and informed consent forms were piloted in rural and urban areas.

Nurse-phlebotomists collected 10 mL blood specimens from consenting participants. Specimens were centrifuged in the field, transported to public health laboratories for processing and testing, and stored at the Georgian National Reference Laboratory in Tbilisi. Each participant's specimen and questionnaire data were linked using a unique barcode. Personal identifying information was obtained strictly to report laboratory test results to participants, and was removed before epidemiologic analysis.

L b e

Anti-HCV and HCV RNA testing were performed in Georgian public health laboratories. CDC laboratory staff monitored protocols and processes for quality assurance/quality control. All specimens were tested for anti-HCV by enzyme-immunoassay (HCV Ab v4.0 EIA *IVD*, Dia.Pro. Diagnostic Bioprobes Srl, Italy). Anti-HCV-positive specimens were tested for HCV RNA (Sacace™ HCV Real-TM Qual, Sacace Biotechnologies Srl, Italy). Anti-HCV-positive/RNA-negative specimens underwent confirmatory anti-HCV testing using a third generation line immunoassay (INNO--LIA™ HCV Score, *IVD*, Innogenetics N.V., Belgium); specimens that tested positive or indeterminate for anti-HCV in confirmatory testing were re-tested for HCV RNA in the CDC Division of Viral Hepatitis Assay Development and Diagnostic Reference Labora-

Demographic characteristics and reported exposures among survey participants, Georgia HCV serosurvey, 2015

Characteristic	n	Weighted % (95% CI)
Total Sample	6296	100.0
Sex		
Female	3868	53.8 (52.0, 55.5)
Male	2428	46.2 (44.5, 48.0)
Missing	0	
Age		
18–29	1115	19.4 (18.2, 20.7)
30–39	1177	19.4 (17.9, 20.9)
40–49	1070	18.6 (17.2, 20.0)
50–59	1140	16.5 (15.4, 17.7)
≥ 60	1790	26.1 (24.5, 27.8)
Missing	4	
Geography		
Urban	3350	56.7 (52.7, 60.6)
Rural	2946	43.3 (39.4, 47.3)
Missing	0	
Employment status		
Employed	2120	37.8 (35.6, 39.9)
Student	172	3.6 (2.9, 4.4)
Homemaker	1483	19.1 (17.7, 20.6)
Retired	1405	20.0 (18.7, 21.5)
Unemployed (able to work)	1110	19.5 (18.0, 21.1)
Missing	6	
Highest level of education completed		
Completed less than elementary/primary school	43	0.7 (0.5, 1.1)
Completed elementary/primary school	612	8.5 (7.3, 9.8)
Completed secondary school	2567	40.2 (38.1, 42.3)
Completed professional/technical school	1157	16.6 (15.3, 18.0)
Completed university/college or higher	1912	34.0 (31.6, 36.4)
Missing	5	
Yearly household income		
≤ 6000 GEL/year (≤ 4400 USD)	2867	45.6 (43.0, 48.3)
6001–12,000 GEL/year (4400–6800 USD)	953	18.5 (16.8, 20.3)
12,001–24,000 GEL/year (6800–13,600 USD)	724	12.6 (11.3, 13.9)
> 24,000 GEL/year (> 13,600 USD)	1339	23.3 (21.1, 25.8)
Missing	413	
Ever injected drugs		
Yes	208	4.2 (3.5, 5.2)
No	6042	95.8 (94.8, 96.5)
Missing	46	
Ever incarcerated		
Yes	240	4.6 (3.8, 5.7)
No	6037	95.4 (94.3, 96.2)
Missing	19	

. Anti-HCV prevalence by demographic and exposure subgroup in unadjusted and adjusted models, Georgia HCV serosurvey, 2015

Characteristic		Anti-HCV Prevalence		Unadjusted Models		Final Adjusted Model	
	Total n	n	Weighted % (95% CI)	Crude OR (95% CI)		Adjusted OR (95% CI)	p-value
Demographics							
Sex							
Female	3671	145	3.8 (3.0, 4.9)	1			
Male	2339	288	12.1 (10.2, 14.3)	3.5 (2.5, 4.8)	< 0.0001		
Missing	0						
Age							
18–29	1063	23	2.4 (1.5, 4.0)	1			
30–39	1140	94	8.8 (6.8, 11.3)	3.9 (2.2, 6.8)	< 0.0001		
40–49	1026	128	14.0 (11.1, 17.6)	6.5 (3.9, 11.1)	< 0.0001		
50–59	1096	79	7.0 (5.2, 9.5)	3.0 (1.6, 5.8)	0.0006		
60+	1681	109	6.7 (5.0, 9.0)	2.9 (1.6, 5.4)	0.0007		
Missing	4						
Geography							
Urban	3155	290	9.5 (8.0, 11.4)	1.8 (1.4, 2.5)	< 0.0001		
Rural	2855	143	5.4 (4.4, 6.6)	1			
Missing	0						
Employment Status							
Employed/student/ homemaker/unpaid worker/retired	4939	286	5.9 (5.0, 7.1)	1			
Unemployed*	1065	147	15.0 (12.3, 18.1)	2.8 (2.1, 3.7)	< 0.0001		
Missing	6						
Exposures							
Ever injected drugs							
Yes	205	150	66.5 (56.0, 75.6)	37.6 (23.5, 60.0)	< 0.0001	21.4 (12.3, 37.4)	< 0.0001
No	5762	283	5.0 (4.3, 5.9)	1			
Missing	43						
Ever incarcerated							
Yes	236	98	42.0 (32.8, 51.7)	11.3 (7.5, 17.1)	< 0.0001		
No	5757	335	6.0 (5.1, 7.0)	1			
Missing	17						
Have any tattoos							
Yes	626	104	16.2 (12.2, 21.1)	2.8 (1.9, 4.0)	< 0.0001		
No	5372	329	6.5 (5.5, 7.6)	1			
Missing	12						
Number of medical injections in last 6 months							
0	3656	233	6.7 (5.6, 7.9)	1			
1	541	40	6.6 (4.3, 10.2)	0.99 (0.60, 1.65)	0.98		
> 1	1648	144	9.5 (7.5, 12.1)	1.48 (1.10, 1.99)	0.01		
Missing	165						

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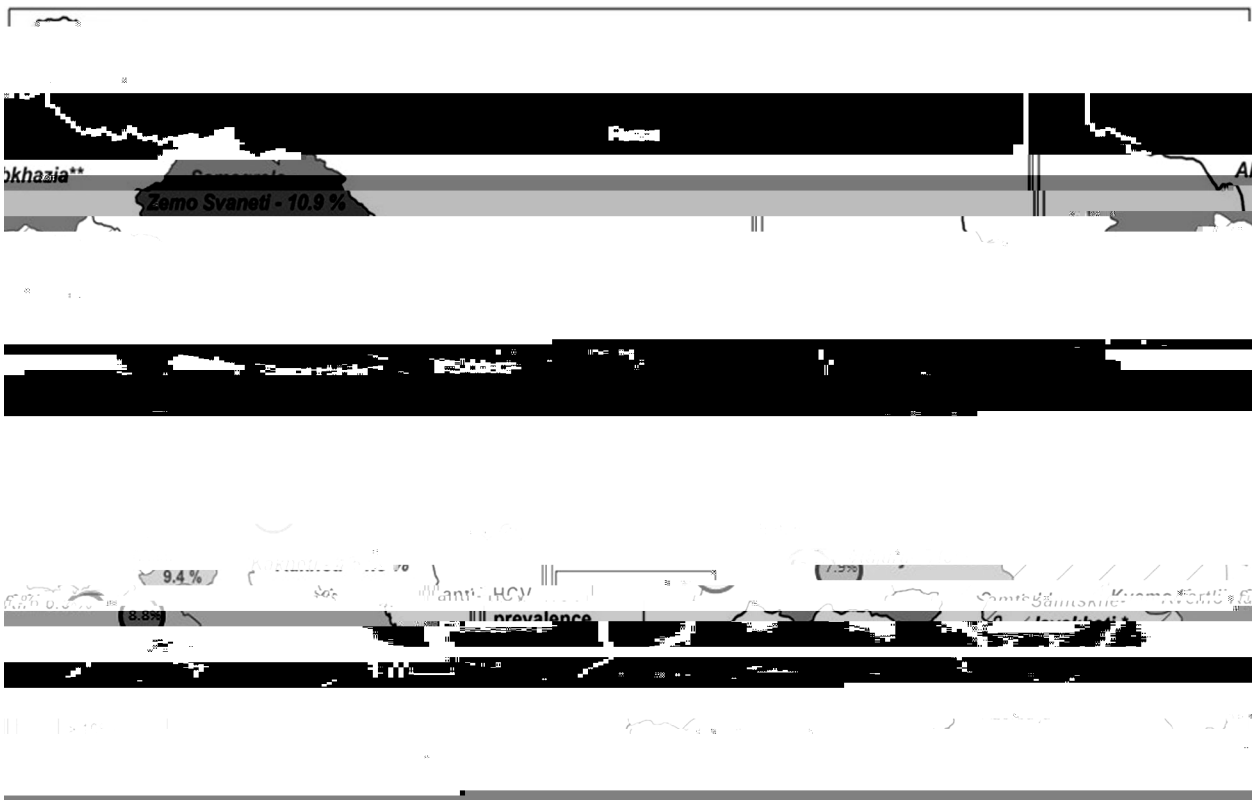
In bivariate analysis, anti-HCV positivity was significantly associated with male sex, unemployment, and urban residence, as well as history of IDU, incarceration, blood transfusion, tattoos, frequent dental cleanings, medical injections, dialysis, and having multiple lifetime sexual partners (Table 2). Among participants who reported a history of blood transfusion, no significant difference in anti-HCV prevalence was detected between those who reported receiving a transfusion before vs. in/after 1997 (when Georgia began testing donated blood for HCV) (Table 2). Other medical and community exposures including hospitalization, surgery, body piercings, and manicures/pedicures were not significantly associated with anti-HCV positivity (data not shown).

In the adjusted model, history of IDU (adjusted odds ratio (AOR) = 21.4, 95% CI = 12.3, 37.4) and receipt of a blood transfusion at any date (AOR = 4.5, 95% CI = 2.8, 7.2) were the only risk factors that were significantly, independently associated with anti-HCV positivity, controlling for sex, age, urban vs. rural residence, and history of incarceration (Table 2). [Note: A dichotomous blood transfusion variable (ever vs. never received transfusion) was used in the multivariate model.] There were no significant interactions in the final model.

Of the 433 anti-HCV positive participants, 38.2% reported IDU, and 19.7% reported receiving a blood transfusion. Nearly half of anti-HCV positive participants (46.7%) did not report either of these risk factors. Overall, 66.5% of anti-HCV positive participants were male, and 43.4% were ≥ age 50. The sex and age breakdown was similar among anti-HCV positive participants reporting a blood transfusion (63.2% male and 55.7% ≥ age 50) and among anti-HCV positive participants who



Anti-HCV prevalence in major cities and regions of Georgia. The highest regional anti-HCV prevalence was found in Samegrelo-Zemo Svaneti region in northwest Georgia (10.9%), particularly in the city of Zugdidi (14.0%, nearly double the national prevalence of 7.7%). In general, anti-HCV prevalence was higher in cities than in the surrounding rural areas. [Notes: *Anti-HCV prevalence estimates were not calculated for Guria

among anti-HCV positive participants reporting IDU compared to those not reporting IDU (55.3% vs. 28.5%, $p = 0{\cdot}0002$). Among participants aware of their HCV infection, 50 (32.1%) reported initiating treatment prior to the survey, 32 (64.0%) of those who reported initiating treatment reported completing it, and 6 (18.8%) of those who reported completing treatment reported being cured (Fig. 3). A cross-check of self-reports against laboratory test results revealed that 14 participants reporting treatment completion tested HCV RNA negative

(more than twice the number who reported being cured); however only three of the six who reported a cure actually tested HCV RNA negative.

Among anti-HCV positive participants aware of their infection and reporting no treatment, reasons cited for non-treatment included lack of treatment availability (56.6%), high cost (33.0%), and anticipated side effects (12.3%).

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A majority of participants (56.1%) were aware that HCV can be transmitted through exposure to infected blood; when asked about specific transmission modes, 52.3% identified sharing needles/syringes, 43.6% identified sharing household objects that have had contact with blood, and 31.9% identified sexual contact as possible HCV transmission modes. More than half of participants

country to undertake HCV elimination and has set ambitious targets including a 90% reduction in chronic HCV prevalence by 2020 [10, 18].

This survey confirms that Georgia has a high burden of HCV infection and identifies risk factors that will be essential to address in Georgia's HCV elimination strategy. Applying the 5.4% HCV RNA prevalence found in this survey to Georgia's adult population of 2.78 million results in an estimated 150,340 (95% CI = 128,060, 173,060) people aged ≥18 years living with chronic HCV infection. Because this sample did not include incarcerated or homeless persons, groups known to have high HCV prevalence [19–22], this survey likely underestimates the true HCV burden. Two risk factors measured in this survey were significant, independent predictors of anti-HCV positivity: reported history of IDU and reported receipt of a blood transfusion. However, half of anti-HCV positive participants reported neither exposure, illustrating that screening based on reported risk factors alone will be insufficient to identify most chronically infected persons and eliminate HCV.

Communication about HCV transmission modes and disease course will be important components of efforts to increase screening. Half of all participants were unaware that they could have an HCV infection without experiencing any symptoms, and half were unaware that HCV is transmitted through exposure to infected blood. HCV-related knowledge was highest among participants reporting a history of IDU, possibly due to familiarity with the risks of injecting drugs. Although media coverage of the HCV elimination program within Georgia has likely increased the general public's knowledge about HCV since this survey, these findings highlight the need to further intensify public education efforts to drive screening, particularly in groups less familiar with HCV transmission risks such as injecting drugs. However, identifying effective messaging and modes of communication could be challenging, given that only one-third of participants expressed trust in healthcare professionals as sources of health-related information, and even fewer reported trust in other sources including friends, family, radio, television, or the internet.

History of IDU was the strongest predictor of HCV infection in this survey and was reported by 38.2% of anti-HCV positive participants. IDU was most common among men, likely driving the three-fold difference in anti-HCV prevalence between men vs. women. In particular, men ages 40–49 years had the highest prevalence of both reported IDU (17.4%, data not shown) and anti-HCV (22.7%). (This cohort came of age during a drug trafficking and IDU epidemic in Georgia during the 1990s/early 2000s following the collapse of the former Soviet Union [23]). However, injecting behavior poses an important challenge for HCV elimination regardless of the age of persons injecting, and those actively injecting drugs will be a key target to curb transmission. Increasing access to harm reduction programs, including needle and syringe programs and medication for opioid use disorder, will be essential. In addition, a follow-up study among persons actively injecting drugs would further clarify HCV prevalence and risk behaviors in this sub-group to guide prevention efforts.

History of a blood transfusion also emerged as an independent risk factor for HCV infection and was reported by 20% of anti-HCV positive participants. Although Georgia began testing its donated blood supply for HCV in 1997, there was no detectable difference in anti-HCV prevalence between participants who received a transfusion before vs. after the blood testing program began. To halt HCV transmission and support elimination, it is imperative that Georgia evaluate and improve its blood safety program.

Nearly half of anti-HCV positive participants reported neither IDU nor blood transfusion. Possible explanations include underreporting of risk factors due to stigma, legal

initiated treatment, and efforts are ongoing to continue to improve access for those who are aware of their HCV infection [18, 24]. With treatment infrastructure now in place, the greatest opportunity to boost progress toward HCV elimination lies in screening and diagnosing more infected individuals.

This survey has several limitations. Its cross-sectional design limits the ability to draw causal associations between possible exposures and HCV, a chronic infection that could have been acquired at any time before the survey. Further, the necessary reliance on self-reported risk factor data could result in information bias that is unmeasurable. The fact that IDU is illegal in Georgia and is the leading reason for incarceration [25] likely discourages self-reports of injecting behavior; similarly, high levels of MSM stigmatization likely explain the complete absence of self-reported MSM among participants in this survey. Finally, HCV prevalence among participants reporting a history of IDU at some point in their lifetime may not reflect HCV prevalence among persons actively injecting drugs, due to changes in infection dynamics in injecting populations over time.

Georgia is working toward ambitious HCV elimination goals, aiming to screen and diagnose 90% of the estimated 150,000+ Georgians with chronic HCV infection, treat 95% of those identified, and reduce national prevalence of chronic HCV by 90% by 2020 [18]. This survey has provided nationally representative data to guide Georgia's comprehensive HCV elimination strategy, as well as baseline HCV prevalence to evaluate progress toward HCV elimination in the coming years. In addition, conducting the survey provided an important opportunity to strengthen Georgia's public health capacity and thereby enhance global health security

Abbreviations

anti-HCV: antibodies to hepatitis C virus; AOR: adjusted odds ratio; CDC: United States Centers for Disease Control and Prevention; CI: confidence interval; DAA: direct-acting antiviral; Geostat: Georgia National Statistics Office; HCV RNA: hepatitis C virus ribonucleic acid; HCV: hepatitis C

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and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2095–128.
6. World Health Organization. Hepatitis C Fact Sheet N 164 2015 [Available from: http://www.who.int/mediacentre/factsheets/fs164/en/. Accessed 9 Feb 2016.]
7. Perz JF, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. J Hepatol. 2006;45(4):529–38.
8. National Statistics Office of Georgia. Key Indicators 2015 [Available from: http://www.geostat.ge/index.php?action=0&lang=eng. Accessed 12 Feb 2016.]
9. Stvilia K, Tsertsvadze T, Sharvadze L, Aladashvili M, del Rio C, Kuniholm MH, et al. Prevalence of hepatitis C, HIV, and risk behaviors for blood-borne infections: a population-based survey of the adult population of T'bilisi, republic of Georgia. J Urban Health. 2006;83(2):289–98.
10. Mitruka K, Tsertsvadze T, Butsashvili M, Gamkrelidze A, Sabelashvili P, Adamia E, et al. Launch of a Nationwide hepatitis C elimination program--Georgia, April 2015. MMWR Morb Mortal Wkly Rep. 2015;64(28):753–7.
11. Kish L. A procedure for objective respondent selection within the household. J Am Stat Assoc. 1949;44(247):380–7.
12. National Statistics Office of Georgia. Household Income 2015 [Available from: http://www.geostat.ge/index.php?action=page&p_id=182&lang=eng. Accessed 5 Jul 2016.]
13. European Union HCV Policy Summit. HCV elimination manifesto: The beginning of the end Brussels, Belgium2016 [Available from: http://www.

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