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COSTS OF TREATMENT FOR HEPATITIS C VIRUS INFECTION IN UKRAINE

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Contributors (in alphabetical order):

Antoniak S[a]
Antoniak S[b]
Barnard T[c]
Cavenaugh C[c]
Chasela C[ad]
Chew KW[e]
Dible J[c]
Drame N[f]
Freiman JM[g]
Gandhi MM[e]
Ivanchuk I[h]
Minior T[c]
Rosen S[fi]
Sanne I[afi]
Stopolianksa Y[a]
Tretiakov V[j]
Tsenilova Z[k]
Vitek E[c]

[a] Right to Care/EQUIP Health, Centurion, South Africa; [b]Gromashevsky Research Institute of Epidemiology and Infection Diseases, Medical Academy of Sciences of Ukraine; [c]U.S. Agency for International Development; [d]Department of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [e]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [f]Boston University School of Public Health, Boston, MA, USA; [g]Boston University School of Medicine, Boston, MA, USA; [h]Public Health Centre of Ministry of Healthcare of Ukraine; [i]Health Economics and Epidemiology Research Office, Department of Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [j]100%Life, Kyiv, Ukraine; [k]Alliance for Public Health, Kyiv, Ukraine.

Correspondence to Sydney Rosen, sbrosen@bu.edu.

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CONTENTS

BACKGROUND

Hepatitis C Virus (HCV) is a deadly but curable disease that disproportionately affects people in low and middle income countries (LMICs). There are 70-80 million people with chronic HCV globally, of whom 50-60 million live in resource-limited settings where HCV prevalence often exceeds 3.5%[1–3]. HCV prevalence and genetic diversity (genotype) vary by population and region. HCV infection remains high among certain populations even in low prevalence settings, specifically people who inject drugs (PWID) and HIV-infected men who have sex with men (MSM)[4]. Chronic HCV infection is expected in 55% to 85% of untreated cases and is associated with liver cirrhosis, liver failure, hepatocellular carcinoma, and death. Despite the development of highly effective direct-acting antiviral (DAA) treatment, which can cure HCV infection with 8-12 weeks of therapy, HCV remains a leading cause of mortality worldwide, causing more than 350,000 deaths each year[3,5] and 85,000 deaths each year in Eastern Europe[6], including Ukraine.

The WHO's Global Health Sector Strategy sets goals of a 90% reduction in new HCV infections and a 65% reduction in HCV-related mortality by 2030[7,8]. Strategies for achieving these targets are similar to those for HIV: scaling up access to affordable testing and treatment combined with interventions for infection prevention (for HCV, these are mainly harm reduction and safe blood donation and injections). Progress in HCV treatment scale-up is encouraging, with more than 3 million treated globally with direct-acting antivirals since 2015. However, testing coverage and diagnosis rates are still less than 10% in LMICs[9].

In Ukraine, roughly 3-5% of the population—as many as 2 million people—are estimated to be HCV-infected[10,11]. Those most at risk are PWID, people living with HIV (PLHIV), commercial sex workers (CSW), MSM, prisoners, members of the military, populations in conflict zones, and sexual partners of PLHIV[12]. An integrated bio-behavioral study in Ukraine found 55.8% HCV prevalence among PWID, 15% among commercial sex workers (CSW), and 4.0% in MSM. Roughly 40% of those with HCV were co-infected with HIV[13]. For those newly diagnosed with HIV, 31.38% also had detectable HCV antibody at the time of diagnosis[14]. Among the six major genotypes of HCV, the most common in Ukraine are 1 and 3[15].

Despite ongoing medical reforms, health care in Ukraine still reflects the system established during the Soviet era[16]. Hospitals and clinics are government-run and regulated. By policy, access to health care is free and available for all citizens, but salaries for physicians and nurses are low and a client-payment system is broadly accepted. A lack of adequate facilities and free-to-client services, combined with fear of prosecution for drug use and stigma suffered by key populations (particularly PWID and MSM), means that most individuals who present for treatment for HCV and HIV are already well advanced in their illness[17]. In 2018, roughly 6,000 patients—about 0.3% of those estimated to be infected—received treatment from the government, and an additional number (probably not more than 2,500 in total) were treated by nongovernmental projects of the Alliance for Public Health and Médecins Sans Frontières[18–20].

In July 2017, with support from USAID, EQUIP Innovation for Health (https://www.equiphealth.org/) launched a demonstration project to evaluate an integrated, simplified protocol for treating HCV and HIV among key populations in Ukraine (https://www.equiphealth.org/articles/hivhcv-co-infection). The project's purpose was to demonstrate the feasibility, acceptability, outcomes, and affordability of a clinic-based service to diagnose, treat, and monitor HCV treatment among key populations, and to integrate HCV care

with HIV testing and treatment services. A total of 868 patients were enrolled from two clinics in the Kyiv region of Ukraine, with follow up completed in April 2019. Participants were treated with a twelve-week course of sofosbuvir/ledipasvir (SOF/LDV) with or without ribavirin as determined by their HCV genotype and Metavir stage from Fibroscan testing[21].

One of the main objectives of the project was to estimate the cost of treating HCV under the protocol and, as part of this, to estimate the cost of alternative laboratory monitoring technologies. This report presents outcomes and costs of the intervention.

METHODS

Intervention description

Enrollment into the HCV/HIV demonstration project was conducted between 26 March and 02 November 2018 at two clinical facilities in Kyiv, Ukraine: the Clinic of the Gromashevsky Institute of Epidemiology and Infectious Diseases and Treatment, and Kyiv City Clinical Hospital #5. Patients were recruited to the study from HCV treatment waiting lists available at the sites, were referred by partner organisations, or had a positive HCV antibody or RNA test at one of the sites during the enrollment period. Target populations for study enrollment were people who inject drugs (PWID), men who have sex with men (MSM), sex workers (SW), and sexual partners of HCV-infected individuals.

Eligible participants included in the treatment study were HCV viremic; HCV treatment naïve or experienced (prior pegylated interferon [PegIFN] and ribavirin [RBV] only), and 18 years or older, with HCV genotype 1, 2, 3, 4, 5 or 6 and with or without HIV-1 co-infection. Patients with compensated cirrhosis (Child-Pugh Class A) and hepatitis B virus (HBV) infection were eligible; those with decompensated cirrhosis (Child-Pugh Class B or C) or prior treatment with HCV DAAs were not eligible. Patients who were ineligible for HCV treatment through the project were referred to treatment centers for care and offered enrollment in an observational arm to assess their cost, quality of life, and clinical outcomes. All participants provided written informed consent.

The intervention combined HCV and HIV testing, HCV treatment, simplified HCV treatment monitoring, and HIV treatment initiation for those with co-infection not yet on antiretroviral therapy. HCV treatment was with fixed-dose combination sofosbuvir/ledipasvir (SOF/LDV) +/- weight-based ribavirin for 12 weeks and provided by the project. Ribavirin was included in the regimen for treatment experienced cirrhotic genotype 1 and 4 participants and all participants with genotype 3 HCV. HIV treatment was per national guidelines. Participants treated with ribavirin had more frequent hemoglobin monitoring at Weeks 2, 4, and 8 on treatment. Participants with HBV co-infection and hepatitis B surface antigen positivity were concurrently treated with tenofovir. Participants with isolated hepatitis B core antibody positivity had liver function test monitoring every 4 weeks while on treatment to assess for potential HBV reactivation. Participants were followed for 24 weeks (through 12 weeks after treatment completion), including assessments of HCV and HIV treatment outcomes and safety. Intervention steps are illustrated in Figure 1.

The study is registered at ClinicalTrials.gov (NCT04038320).

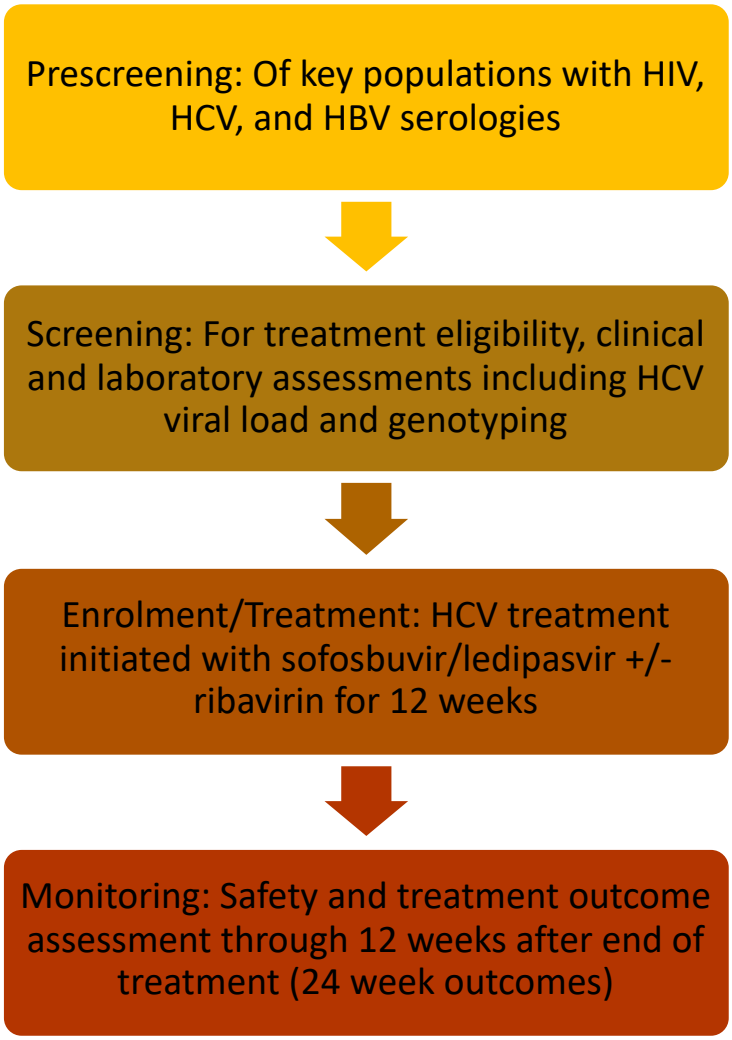

Figure 1. Intervention procedures. HIV = human immunodeficiency virus; HCV = hepatitis C virus; HBV = hepatitis B virus

Economic evaluation

The economic evaluation that we report here has two components: 1) comparison of the costs of alternative laboratory assays for HCV treatment monitoring; and 2) estimate of the cost per patient and per outcome of HCV treatment.

Costs of laboratory assays

Three alternative HCV viral assays on two platforms were compared to the two standard of care assays, as listed below:

Standard of care assays:

- RT-PCR in real time performed at the Synevo central laboratory in Kyiv detection and quantification of HCV RNA using. The reagent kit is D-0794, manufactured by "Vector Best"
- Detection and differentiation of HCV genotypes in clinical material using PCR with hybridization-fluorescence detection in the "real time" mode performed at the Synevo central laboratory in Kyiv, using the AmpliSense HCV-genotype-FL reagent kit manufactured by the Central Epidemiology Research Institute in the Russian Federation.

Alternative assays:

- GeneXpert ® (Cepheid) HCV (hereafter “Xpert”): quantitative HCV RNA assay run on the GeneXpert platform designed for point-of-care (POC) implementation;
- Advanced Biological Laboratories (“ABL”) UltraGene-HCV Assay: quantitative HCV RNA assay run on a polymerase chain reaction (PCR) platform designed for laboratory implementation;
- Advanced Biological Laboratories DeepChek® Assay and Software (“ABL combo”): combination test that provides quantitative HCV RNA, HCV genotype, and drug resistance testing run on a PCR platform in a laboratory. This test provides genotype and resistance assessment using the same sample used for quantitative viral load assessment by UltraGene-HCV assay, which is valuable for generic DAA treatment options that are not fully pan-genotypic.

We calculated the cost per test performed utilizing HE^{2}RO’s Testing Platform Cost Model (http://www.heroza.org/researchtools/testing-platform-cost-model)[22] with cost per test as the primary outcome and production cost per successful test, which accounts for costs incurred for unsuccessful tests, as the secondary outcome. The model includes material costs (consumables used in each test performed), staff costs, daily running and quality control costs, equipment costs, equipment life expectancy, and overhead costs. Activity data were derived from clinic flow observations and the lab capacity and volume recorded by the lab supervisor. Unit cost data were gathered from study invoices, laboratory invoices, and salary sheets. Overhead for each clinical site was estimated from advertisements of nearby commercial properties.

We also performed sensitivity analyses for the Xpert and ABL platforms, varying the laboratory capacity, volume per day, and equipment life expectancy.

- The expected or base case utilized the average number of tests performed per day during the study period with 10% downtime for a total of 225 working days per year. We used manufacturer information and warranty periods to determine equipment life expectancy.
- The worst case utilized the lowest number of tests performed per day during the study period with 20% downtime for 200 working days per year. We decreased the equipment life expectancy 20% from the base case.
- The best case utilized the maximum capacity of the laboratory platform of interest with 250 working days per year. We increased the equipment life expectancy 20% from the base case.

Best and worst case scenarios were calculated only for the alternative laboratory assays, not for those used in standard of care.

Lastly, for the ABL assay, we modeled utilization of an automated sample preparation platform (MagNA Pure Compact: Roche) to increase the daily processing capacity two-fold.

We performed all cost analyses in 2018 Ukrainian hryvnia (UAH) converted to United States dollars (USD) at the average exchange rate in 2018 of 27.31:1 (UAH:USD).

Costs of HCV treatment

Costs were estimated from the provider perspective from initial screening date until assessment of cure 12 weeks after HCV treatment completion (24 weeks total) using standard economic methods described previously[23,24]. Resources incurring costs included: laboratory testing, imaging studies, HCV, HBV, and HIV medications, clinic staff, clinic space and overhead, equipment and supplies, education and outreach. We determined variable patient resource utilization from a de-identified dataset compiled from study participant case reporting forms, and estimated resource utilization from average clinic site capacity and total annual visits. We then multiplied the quantity of each resource used by each patient by the associated unit cost to determine a total cost per patient.

We evaluated the average resource utilization per patient by cost category, HCV treatment outcome, and HIV status and determined 95% confidence interval by outcome category. Each patient was assigned one of the following four outcomes at 24 weeks after treatment initiation:

- Treatment success (sustained virologic response 12 weeks after therapy completion (SVR12)
- Treatment failure (HCV viremia greater than the lower limit of quantification 12 weeks after therapy completion)
- Loss to follow up (did not return to clinic for 24 week evaluation)
- Death within 24 week study period

We calculated the production cost of a successful outcome by dividing the sum of all costs by the number of successful outcomes. We then report the difference between the production cost and cost per patient treated as a proportion of the cost per patient treated and add a “tax” proportion to successful outcomes to pay for non-successful outcomes.

For this analysis, we considered six scenarios:

1) Observed costs excluding research related expenses (proxy for cost for scale-up in routine care using generic pricing of SOF/LDV ($1.06 USD/pill))
2) Observed costs including research expenses (SOF/LDV pricing $10.61/pill)
3) Replaced standard HCV RNA with GeneXpert HCV RNA testing, excluding research expenses
4) Replaced standard HCV RNA with ABL RNA testing, excluding research expenses
5) Replaced standard HCV RNA and genotype testing with ABL combination RNA/genotype/resistance testing, excluding research expenses; and

6) Increased the treatment failure rate to 10% to simulate poor treatment adherence in a real-world setting, excluding research expenses.

The patient resource utilization matrix for this study was generated using SAS software, Version 9.3 (SAS Institute Inc., Cary, NC, USA). Study CRFs and patient data were managed with HepatiC® (ABL SA, Luxembourg). Estimates per patient treated and per successful outcome were made using the HE^{2}RO Healthcare Costs and Outcome Model (http://www.heroza.org/researchtools/the-healthcare-cost-and-outcomes-model-hcom) (HE^{2}RO, Johannesburg, South Africa). Economic models were generated with Excel 2011.

The study was reviewed by the Ukrainian Institute on Public Health Policy IRB #1, Institutional Review Board (00007612) and the University of the Witwatersrand Human Research Ethics Committee (M17078). The Boston University Institutional Review Board approved analysis of a de-identified analytic dataset (H-37820).

RESULTS

Patient characteristics and treatment outcomes

The economic sample evaluation included the 522 participants who had reached the SVR12 stage of the study at the time of analysis.

Table 1. Participant characteristics

Characteristic	N	Column %
Enrolled	522	100%
Male	333	63.8%
Median (IQR) age (years)	39 (35-44)	
HCV risk category		
MSM only	3	0.6%
CSW only	6	1.1%
PWID	446	85.4%
PWID only	*190*	*36.4%*
PWID/PLHIV	*221*	*42.3%*
PWID/CSW	*3*	*0.6%*
PWID/partner +	*31*	*5.9%*
PWID/MSM	*1*	*0.2%*
Partner + only	24	4.6%
PLHIV only	1	0.2%
PLHIV/CSW	10	1.9%
PLHIV/partner +	27	5.2%
PLHIV/MSM	5	0.9%
HCV genotype		
Genotype 1	411	78.7%
Genotype 2	7	1.3%
Genotype 3	98	18.8%
Genotype 4	1	0.2%
Mixed	1	0.2%
Indeterminate	4	0.8%
Comorbidities		
HIV co-infection	271	51.9%
New HIV diagnosis identified by project	*66*	*24.4%*
HBV co-infection	2	0.4%

Characteristic	N	Column %
HIV/HBV/HCV co-infection	1	0.2%
Compensated cirrhosis	48	9.2%

HCV = hepatitis C virus, MSM = men who have sex with men, CSW = commercial sex worker, PWID = people who inject drugs, Partner + = sexual partner of HCV infected person, PLHIV = people living with human immunodeficiency virus (HIV) infection

Clinical outcomes at 24 weeks after treatment initiation are shown in Table 2.

Table 2. Study outcomes for 522 participants who completed or were expected to complete HCV treatment with sofosbuvir/ledipasvir +/- ribavirin and 12 weeks of post-treatment follow-up by January 31, 2019.

Outcome	N=522	Column %
Treatment success (cure)	511	97.8%
Treatment failure	7	1.3%
Lost to follow-up*	3	0.6%
Died	1	0.2%

*Three participants completed 12 weeks of HCV treatment but were lost to follow-up prior to 24-week evaluation.

Three participants did not return for the 24-week visit, though they completed the 12-week treatment course. One participant died from a myocardial infarction unrelated to the study after completion of HCV treatment.

Cost of laboratory assays

We first estimated and modeled the cost/test of implementing the laboratory platforms described above.

Table 4. Cost per successful test, by assay/platform

Test	Base case USD	Best case USD	Worst case USD
Xpert HCV	40.03	27.54	69.61
ABL, manual	52.48	37.17	79.39
ABL, auto	47.91	34.50	67.72
ABL combo, manual	107.82	86.89	139.27
ABL combo, auto	103.38	84.30	129.08
SOC Synevo HCV RNA*	33.71	n.a.	n.a.
SOC Synevo HCV genotype*	25.31	n.a.	n.a.

*Best and worst case costs were not calculated for standard of care assays. USD = United States Dollars, HCV = hepatitis C virus, ABL = Applied Biosystems, SOC = standard of care assays performed at the Synevo centralized laboratory

For the base case, HCV tests performed at the centralized Synevo lab (SOC) were least expensive per successful test. Among the alternatives evaluated, Xpert was least expensive in the base and best cases. In the low-volume, worst-case scenario, Xpert was slightly more expensive than the automated ABL test. With the exception of Xpert in the best case, the cost per successful test for all alternatives in all cases exceed those in the SOC base case. A detailed breakdown of the cost/test is provided in the Appendix.

Cost of HCV treatment

All scenarios

Table 5 presents key results for all six scenarios modeled and for the relevant lab assay costs. A more detailed presentation of scenarios 1 and 2, which represent expenses incurred in implementation of the pilot project, is provided later in this section.

Table 5. Summary of treatment cost/successful outcome for all cases

Scenario	Production cost per successful outcome*		
	Base case	Best case+	Worst case+
1) Observed costs without research expenses	693		
2) Observed cost with research expenses	1,572		
3) Xpert HCV RNA testing	706	680	766
4) ABL assay HCV RNA, auto prep	722	695	762
5) ABL combination assay, auto prep	809	770	862
6) Increased treatment failure rate to 10%	758		

*Production cost per successful outcome = all costs for cohort/number of successful outcomes
+Best case and worst case values are presented only for the scenarios comparing alternative laboratory assays, with cost varying with lab capacity,equipment downtime, and equipment life expectancy.
SOF/LDV = sofosbuvir/ledipasvir, ABL = Applied Biosystems, auto = automated, prep = sample preparation

Treatment resource utilization

For the 522 participants with resource utilization data, we tabulated the number of physical exams, counseling visits, laboratory assessments, Fibroscan evaluations, and medications for HCV, HBV, and HIV utilized by each patient). The first 150 participants in the study had baseline and SVR12 evaluation for HCV RNA with three separate assays as part of the study investigation protocol: the standard centralized lab assay, Xpert HCV, and ABL. We counted only one of these at each time period for cost purposes, however. As shown in Table 6, Actual resource utilization was equivalent to expected utilization outlined in the study protocol.

Table 6. Median resource utilization and mean HIV and HCV medication cost (USD) per participant during the 24-week study period

Resource	Median per patient
Physical exam	2
Counseling visit	4
Fibroscan	1
HCV RNA	2
HCV genotype	1
Liver tests (ALT, AST, albumin, bilirubin)	3
CBC (Hb, Plt)	3
Creatinine	3
INR/PT	2
HIV screening antibody (OraQuick)	1
HBV testing (Surface Ab, Core Ab, Surface Ag)	1
HIV medication cost (mean/HIV+ participant per 24-week study period)	$298.96
HCV medication cost using generic pricing (mean per 24-week study period)	$101.69
HCV medication cost as procured in the study (mean per 24-week study period)	$912.29

HCV = hepatitis C virus, RNA = ribonucleic acid, ALT = alanine aminotransferase, AST = aspartate aminotransferase, CBC = complete blood count, Hb = hemoglobin, Plt = platelet count, INR = international normalized ratio, PT = prothrombin time, HIV = human immunodeficiency virus, HBV = hepatitis B virus, Ab = antibody, Ag = antigen

Scenario 1

Scenario 1, which reflects observed costs minus expenses related to research and uses generic SOF/LDV drug pricing ($1.06 USD per pill), represents the most likely "real world" scenario. Costs under Scenario 1 by outcome, with average component costs and production cost of a successful outcome, are shown in Table 7. Indirect costs include support staff/personnel, building costs, and office supplies. Events include physical exams (physician visit), counseling visits, and Fibroscans. Lab tests include HCV RNA modeled using the centralized laboratory pricing (Synevo lab), HCV genotyping, HIV and HBV testing, pregnancy testing if applicable, PT/INR, blood counts, and chemistries.

Table 7. Cost/patient by outcome in Scenario 1 in USD

Outcome	N	%	Indirect costs	Events	Labs	Drugs	Mean (SD) cost per outcome
Success	511	98%	174	69	178	257	678 (305)
Failure	7	1%	174	58	193	206	630 (139)
Loss	3	1%	141	69	153	243	606 (157)
Death	1	0%	124	69	118	1,188*	1,498 (N/A)
All outcomes	522	100%	173	69	178	258	678 (304)

*The patient who died was an HIV infected individual with Nevirapine (6 USD per pill) as a component of the antiretroviral regimen, incurring very high drug costs.

For the full sample, drugs comprised 38% of average cost/patient, laboratory tests 26%, events 10%, and indirect costs 26%. In this scenario, in which generic HCV medication prices were used, HIV drugs accounted for 60% of all drug costs and HCV and other drugs 40%. When costs for non-successful outcomes are taken into account, the production cost per successful outcomes was $693/patient, or about 2% more than the average cost per patient. The small difference between these two values reflects the very good outcomes of treatment, with 98% of patients cured.

Scenario 2

Scenario 2 also reflects observed costs but includes all in-country expenses for the project, not just those likely to be incurred under routine care (Scenario 1), and uses brand pricing for SOF/LDV ($10.61/pill). The cost per patient under Scenario 2, by outcome and component, is shown in Table 8. Indirect costs include support staff, research staff, building costs, office supplies, and patient education and outreach (meals, fliers). Events include physical exams (physician visit), counseling visits, and Fibroscans. Labs include HCV RNA modeled using the centralized laboratory pricing (Synevo lab), HCV genotyping, HIV and HBV testing, pregnancy testing if applicable, PT/INR, blood counts and chemistries.

Table 8. Cost/patient by outcome in Scenario 2 in USD

Outcome	N	%	Indirect costs	Events	Labs	Drugs	Mean (SD) cost per outcome
Success	511	98%	233	69	178	1,059	1,539 (305)
Failure	7	1%	233	58	193	1,008	1,492 (139)
Loss	3	1%	188	69	153	867	1,277 (223)
Death	1	0%	166	69	118	1,990	2,343 (N/A)
All outcomes	522	100%	232	69	178	1,059	1,539 (305)

For the full sample, drugs comprised 69% of average cost/patient, laboratory tests 12%, events 4%, and indirect costs 15%. The large share of cost/patient accounted for by drugs is due to the non-generic HCV drug pricing used in this scenario. In contrast to Scenario 1, HIV drugs accounted for just 15% of overall drug costs, and HCV and other medications 85%. Indirect costs/patient, which capture the research costs included in Scenario 2, are also substantially higher than in Scenario 1.

When costs for non-successful outcomes are taken into account, the production cost per successful outcome was $1,572 /patient, again about 2% more than the average cost per patient treated.

CONCLUSIONS

In a demonstration project of an integrated, simplified protocol for treating HCV and HIV among key populations in Ukraine, the estimated average cost of treatment per patient initiated on HCV therapy and achieving SVR12, including both HCV and HIV treatment, was $678. The small handful of patients who did not achieve sustained virologic response or did not return for the 24-week evaluation (LTFU) cost slightly less per patient, while the single patient who died cost substantially more, due largely to expensive HIV drugs.

The production cost for a successful outcome reported here ($693/patient) is dependent on utilizing the lowest cost testing platform to confirm HCV viremia and treatment response (the status quo Synevo labs), and securing generic pricing for HCV medications. Other laboratory platforms will cause the cost/patient to go up or down depending on patient volume. If generic drugs cannot be obtained, the cost of treatment will be substantially higher. If HCV treatment is scaled up in large centers in Ukraine, allowing efficient use of equipment, Xpert on site may prove to be the least expensive scenario for the country. As HCV treatment moves towards the use of pan-genotypic drugs, further reductions in the laboratory cost component are possible with elimination of genotype testing, though the cost of the medications will likely be higher than generic SOF/LDV.

In our study cohort, 98% achieved SVR and remained engaged in care for the duration of the 24 week follow up period. This is unusual success in not only a high risk population, but also for the efficacy of SOF/LDV +/- ribavirin particularly for genotype 3 infection. A prior US trial without ribavirin reported 89% SVR among genotype 3 patients without cirrhosis[25], while a European study using ribavirin combination treatment reported and overall SVR of 94%[26]. To estimate real-world effectiveness of our intervention, we performed a sensitivity analysis decreasing SVR to 90%. This resulted in a 9% increase in the production cost of a successful outcome.

For budgeting purposes, under the assumption of generic drug pricing and decreased real-world effectiveness (lower SVR and retention rates), an average cost of $750/patient is likely a reasonable estimate for this intervention. This does not include costs for scaling up or maintaining the treatment program, such as procurement, training, management, and oversight.

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APPENDIX: BREAKDOWN OF LABORATORY COSTS

1. Cepheid GeneXpert

Category	Unit	Best Case		Expected Case			Worst Case	
		$	$	$	$	%	$	$
Materials	For specific test	18.08	18.08	20.09	20.09	*51%*	22.10	22.10
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Staff	For specific test	2.59	2.59	7.28	7.28	*19%*	11.63	11.63
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Quality control	For specific test	0.00	0.11	0.00	0.20	*0%*	0.00	0.36
Equipment	For specific test	0.71	0.71	1.89	1.89	*5%*	15.37	15.37
	Shared	0.07	0.07	0.27	0.27	*1%*	1.65	1.65
Other	For specific test	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Overhead	Shared	4.76	4.76	9.52	9.52	*24%*	17.13	17.13
TOTAL	**Cost per test**	**26.21**	**26.32**	**39.05**	**39.25**	***100%***	**67.88**	**68.24**
TOTAL	**Cost per successful test**	**26.73**	**26.84**	**39.83**	**40.03**		**69.24**	**69.61**

2. ABL with manual sample preparation

Category	Unit	Best Case		Expected Case			Worst Case	
		$	$	$	$	%	$	$
Materials	For specific test	27.95	27.95	31.05	31.05	*60%*	34.16	34.16
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Staff	For specific test	4.34	4.34	12.53	12.53	*24%*	19.51	19.51
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Quality control	For specific test	1.20	1.20	2.11	2.11	*4%*	4.22	4.22
Equipment	For specific test	0.30	0.30	0.95	0.95	*2%*	8.09	8.09
	Shared	0.20	0.20	0.53	0.53	*1%*	3.30	3.30
Other	For specific test	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Overhead	Shared	2.45	2.45	4.28	4.28	*8%*	8.57	8.57
TOTAL	**Cost per test**	**36.44**	**36.44**	**51.46**	**51.46**	***100%***	**77.84**	**77.84**
TOTAL	**Cost per successful test**	**37.17**	**37.17**	**52.48**	**52.48**		**79.39**	**79.39**

3. ABL with automated sample preparation

Category	Category	Best Case		Expected Case			Worst Case	
		$	$	$	$	%	$	$
Materials	For specific test	27.95	27.95	31.05	31.05	*66%*	34.16	34.16
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Staff	For specific test	4.34	4.34	12.53	12.53	*27%*	19.51	19.51
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Quality control	For specific test	0.44	0.44	0.88	0.88	*2%*	2.11	2.11
Equipment	For specific test	0.13	0.13	0.45	0.45	*1%*	4.69	4.69
	Shared	0.07	0.07	0.27	0.27	*1%*	1.65	1.65
Other	For specific test	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Overhead	Shared	0.89	0.89	1.78	1.78	*4%*	4.28	4.28
TOTAL	**Cost per test**	**33.82**	**33.82**	**46.97**	**46.97**	***100%***	**66.39**	**66.39**
TOTAL	**Cost per successful test**	**34.50**	**34.50**	**47.91**	**47.91**		**67.72**	**67.72**

4. ABL combination RNA/Genotype/Resistance test with manual sample preparation

Category	Category	Best Case		Expected Case			Worst Case	
		$	$	$	$	%	$	$
Materials	For specific test	75.18	75.18	83.53	83.53	*81%*	91.89	91.89
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Staff	For specific test	4.34	4.34	12.53	12.53	*12%*	19.51	19.51
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Quality control	For specific test	1.20	1.20	2.11	2.11	*2%*	4.22	4.22
Equipment	For specific test	0.30	0.30	0.95	0.95	*1%*	8.09	8.09
	Shared	0.07	0.07	0.27	0.27	*0%*	1.65	1.65
Other	For specific test	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Overhead	Shared	2.45	2.45	4.28	4.28	*4%*	8.57	8.57
TOTAL	**Cost per test**	**83.55**	**83.55**	**103.67**	**103.67**	***100%***	**133.91**	**133.91**
TOTAL	**Cost per successful test**	**86.89**	**86.89**	**107.82**	**107.82**		**139.27**	**139.27**

5. ABL combination RNA/Genotype/Resistance test with automated sample preparation

Category	Category	Best Case		Expected Case			Worst Case	
		$	$	$	$	%	$	$
Materials	For specific test	75.18	75.18	83.53	83.53	*84%*	91.89	91.89
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Staff	For specific test	4.34	4.34	12.53	12.53	*13%*	19.51	19.51
	Shared	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Quality control	For specific test	0.44	0.44	0.88	0.88	*1%*	2.11	2.11
Equipment	For specific test	0.13	0.13	0.45	0.45	*0%*	4.69	4.69
	Shared	0.07	0.07	0.27	0.27	*0%*	1.65	1.65
Other	For specific test	0.00	0.00	0.00	0.00	*0%*	0.00	0.00
Overhead	Shared	0.89	0.89	1.78	1.78	*2%*	4.28	4.28
TOTAL	**Cost per test**	**81.05**	**81.05**	**99.45**	**99.45**	***100%***	**124.12**	**124.12**
TOTAL	**Cost per successful test**	**84.30**	**84.30**	**103.42**	**103.42**		**129.08**	**129.08**