Cost-utility Analysis of Second-generation Direct-acting Antivirals for Hepatitis C

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Abstract

Background: Hepatitis C virus (HCV) can lead to increased mortality, disability, and liver transplantation if left untreated, and it is associated with a possible increase in disease burden in the future, all of which would surely have a significant impact on the health system. New antiviral regimens are effective in the treatment of the disease yet expensive.

Objectives: The purpose of the present study was to assess the cost-effectiveness of three medication regimens, namely, ledipasvir/sofosbuvir (LDV/SOF), velpatasvir/sofosbuvir, and daclatasvir/sofosbuvir (DCV/SOF) for HCV patients with genotype 1 in Iran.

Methods: A Markov model with a lifetime horizon was developed to predict the costs and outcomes of the three mentioned medication therapy strategies. The final outcome of the study was quality-adjusted life-years (QALYs), which was obtained using the previously published studies. The study was conducted from the perspective of the Health Ministry; therefore, only direct medical costs were estimated. The results were provided as the incremental cost-effectiveness ratio (ICER) per QALY. Ultimately, the one-way and probabilistic sensitivity analyses were used to measure the strength of study results.

Results: The results showed that the QALYs for LDV/SOF, DCV/SOF, and VEL/SOF were 13.25, 13.94, and 14.61, and the costs were 4,807, 7,716, and 4,546$, respectively. The VEL/SOF regimen had lower costs and higher effectiveness than the LDV/SOF and DCV/SOF regimens, making it a dominant strategy. The tornado diagram results showed that the study results had the highest sensitivity to chronic hepatitis C (CHC) and compensated cirrhosis (CC) state costs. Moreover, the scatter plots showed that the VEL/SOF was the dominant therapeutic strategy in 73% of the simulations compared to LDV/SOF and 66% of the simulations compared to DCV/SOF; moreover, it was in the acceptable region in 92% of the simulations and below the threshold. Therefore, it was considered the most cost-effective strategy. Moreover, the results showed that DCV/SOF was in the acceptable region below the threshold in 69% of the simulations compared to LDV/SOF. Therefore, the DCV/SOF regimen was more cost-effective than LDV/SOF.

Conclusions: According to the present study results, it is suggested that the VEL/SOF regimen be used as the first line of therapy in patients with HCV genotype 1. Moreover, DCV/SOF can be the second-line medication regimen.

Keywords: Cost-effectiveness Analysis, Hepatitis C Virus, Genotype1, New Antiviral Regimens, Direct-acting Antiviral Agents, Markov Modeling, Probabilistic Sensitivity Analysis

1. Background

Nowadays, hepatitis C is considered a public health issue over the world (1). This disease is a type of infection that usually affects the liver. Hepatitis C virus (HCV) is the cause of this disease (2). Around 71 million people worldwide and 21.3 million in the East Mediterranean region are inflicted with hepatitis C, making a death toll of 350,000 to 700,000 individuals (3). Hepatitis C would impose a large

economic burden on the health system in decades to come due to the risk of liver transplantation, mortality, and mortality (4). Antiviral drugs could cure more than 95% of hepatitis C patients, thus, reducing the risk of mortality, liver cancer, and cirrhosis (5). However, early access to diagnosis and treatment is a major condition. Around 5% of the world's population are chronic carriers of HCV (6). According to the latest statistics published by a systematic review article, the prevalence of HCV infection is 0.3% in the gen-

eral population of Iran.

Hepatitis C has different genotypes 1 to 7, each with a prominent role in response to treatment. Sixty percent of the patients are genotype 1 (7, 8). Given that genotype 1 is very common in Iran, it is of importance to be studied (9). Hepatitis C might lead to great social and economic costs to the patient and society. In the case of inappropriate treatment and disease progression, the costs would increase exorbitantly. In fact, the cost of the complete treatment of every HCV patient is 2,084$ for diagnostic services and 242 to 8,256$ for treatment strategies (10). Therefore, early and appropriate treatment of chronic HCV would prevent disease progression and thus disability and mortality and decrease the costs to the family and society (11).

Interferon and Ribavirin are the standard medications for HCV. Around 50-80% of the patients receiving these medications are cured. Patients that develop cirrhosis or liver cancer might require liver transplantation; however, HCV recurrence usually develops after transplantation (12). Treating the disease inhibits the progression to more severe conditions such as cirrhosis and liver cancer and enhances the quality of life and survival in patients. As a regimen, RBV + peg-IFN was previously used to treat HCV patients in Iran, which is a confirmed combination worldwide to improve and prevent disease progression (13). The sustained virologic response (SVR) in patients with genotype 1 using this therapy is estimated at 40 - 50% (13). However, this combination has certain side effects urging to shift towards novel therapies for HCV (14). Novel therapeutic methods contain different metabolites of sofosbuvir (SOF), which are prescribed for the patient according to their genotype and disease stage. The advantages of these therapeutic regimens include the decreased treatment period, higher responses, and increased quality of life (15-17). In fact, the results showed that novel medication regimens could increase the SVR rates to more than 90% in different genotypes (18).

Considering the limited number of studies on the economic assessment of different compounds of SOF drugs, the present research evaluated the cost-effectiveness of three medication regimens, i.e., VEL/SOF, LDV/SOF, and DCV/SOF in HCV patients with genotype 1 for the first time in Iran. The present study findings could be applied in designing the clinical guidelines for HCV patients to help decision-makers and policy-makers better select cost-effective interventions and increase allocation efficacy in the health system.

2. Objectives

The objective of this study was to assess the cost-effectiveness of ledipasvir/sofosbuvir (LDV/SOF) compared with velpatasvir/sofosbuvir and daclatasvir/sofosbuvir (DCV/SOF) in HCV patients with genotype 1 in Iran.

3. Methods

The present economic assessment was a cost-utility analysis study on chronic hepatitis C patients with genotype 1 to compare the effects of three medication regimens, including SOF/VEL, SOF/LDV, and SOF/DCV. The statistical population of the present study included 46 records for VEL/SOF, 400 records for DCV/SOF, and 400 records for LDV/SOF in patients with HCV in Baqiyatallah Hospital, Baqiyatallah Gastroenterology and Liver Research Center, Namazi Hospital, and Motahhari Clinic, Shiraz, in 2018. Given the limited number of records in the SOF/VEL regimen, the 46 records were assessed by the census. However, due to a large number of records for the two other strategies, i.e., DCV/SOF and LDV/SOF, 392 records were selected using the Morgan table. The Morgan table is a simple way to calculate the sample size when the population size is known. The inclusion criteria included patients having chronic hepatitis C with genotype 1 and receiving the understudy medications with available records. Moreover, the exclusion criteria were having other genotypes of hepatitis C and other types of hepatitis. The Markov model was used in this study due to the chronic and recurring nature of HCV infection (19).

The outcomes used in this study included quality-adjusted life-year (QALY) and costs for each health state and each medication strategy. The lifetime horizon was developed using Tree Age (version 2020) to predict the costs and outcomes of three medication strategies in a simulated population of 5,000 hepatitis C patients with genotype 1. Using the opinions of the experts, the study period was determined one year. Given that the time horizon of the study is more than a year, the costs and the QALYs were discounted with annual rates of 5.8% (20, 21) and 3% (22, 23), respectively.

3.1. Model Structure

Figure 1 shows the general structure of the Markov model for a simulated population of 5,000 patients with hepatitis C. The model was extracted according to the trend of the disease apparent in other diseases, and it was finalized after consulting with hepatologists. Health states of the disease were defined as chronic hepatitis C (CHC), compensated cirrhosis (CC), decompensated cirrhosis (DC),

hepatocellular carcinoma (HCC), liver transplant (LT), sustained virologic response (SVR), and death. Individuals were in the CHC state in the first place and would stay in the same state or move to a different state each year until death. Moving between different disease states and staying in the same state were determined using data from other studies and experts' opinions. Patients receiving treatment from any state could move to the HCC state and death.

It is not possible to regress to milder states from severe states of the disease in this model. Although some studies confirm the possibility of regression (24, 25), it was not clearly reported; therefore, we decided not to model these states. The designed Markov model compared the three medication strategies, and patients evaluated using this model received one of the three medication regimens. Moreover, SVR was determined as the therapeutic target and the cured state in the model. Therefore, patients not reaching SVR were at risk for the progression of hepatic disease.

3.2. Understudy Population

In this study, 846 files of hepatitis C patients with genotype 1 in Baqiyatallah Hospital, Baqiyatallah Hospital Research Center for Gastroenterology and Liver, Namazi Hospital, and Motahhari Clinic, Shiraz, entered the study. These centers are national referral centers, and patients from around the country are hospitalized there. The analysis and simulation were conducted for a hypothetical cohort group of 5,000 individuals.

3.3. Model Parameters

We used three sets of parameters in the Markov model (Tables 1-3), as follows:

(1) Transitional Probabilities: The transitional probabilities between the different study states were extracted from domestic and foreign studies on hepatitis C (26-32). All-cause mortality probabilities were obtained for age and gender data from Iran's 2018 life table (33). Finally, the probability of HCV-related mortalities was extracted from the published articles (34-37). The probabilities used in the model are reported in Table 1.

(2) Cost Inputs: The cost data in the present study were estimated from the perspective of the Ministry of Health. Therefore, only the direct medical costs (DMC) were extracted according to a designed form for health states and medication regimens ascertained in patients' medical records and expert opinions in Baqiyatallah Hospital and Baqiyatallah Hospital Research Center for Gastroenterology and Liver, Namazi Hospital, and Motahhari Clinic, Shiraz. These centers were purposefully selected due to being

referral centers. The bottom-up approach was used to calculate the costs. The components of DMC consisted of costs for hospitalization, diagnostic medical services, physician visits, and medications. Moreover, for international comparisons, the costs were estimated based on tariffs in 2019 per international dollar (purchasing power parity) with an exchange rate of 22,075 Rials per dollar (38). The cost of each health state is presented separately in Tables 2 and 3.

(3) Utility Values: As final outcomes are preferred for policy-making and decision-making, only the QALYs outcome was used for the final analysis. In this study, QALYs were considered as the health outcome. The utility values used in the model are presented in Table 4. Since the drug regimens are recently introduced and used in the country, there is a lack of sufficient evidence determining the values used in the model; thus, we used the evidence found in studies published in other countries (13, 18, 39-45).

3.4. Cost-effectiveness Analysis

According to the results of the previous step, the Markov model was developed using Tree Age software, and the extracted data were imported into the model. The cost, effectiveness, and cost-effectiveness were calculated for all interventions by monetary units, QALYs, and cost per QALYs, respectively, according to the time horizon of the study. Furthermore, ICER was calculated using the ratio of the cost difference to QALYs difference between the compared options. Moreover, the ICER results were compared using a threshold to determine the cost-effectiveness of interventions in the country. The GDP was equal to 12,547 dollars in Iran, 2019, with which, the willingness-to-pay (WTP) threshold would be 12,547 (GDP*1) and 37,641 (GDP*3) in Iran (46).

3.5. Sensitivity Analysis

A one-way and probabilistic sensitivity analysis (PSA) was conducted on the results of the model in the present study to determine the certainty of the evidence of the results. It was attempted in one-way sensitivity analysis to change the key parameters of the model and provide it in the form of a tornado diagram; for this purpose, cost data were changed by 20%, and the effective values were changed for the dispersion obtained from other studies. Moreover, according to the probability distribution defined for the parameters imported to the model, a second-order Monte Carlo simulation was developed using 5,000 trials for sensitivity analysis, and the PSA results were displayed using cost-effectiveness acceptability curves and incremental cost-effectiveness scatter plots.
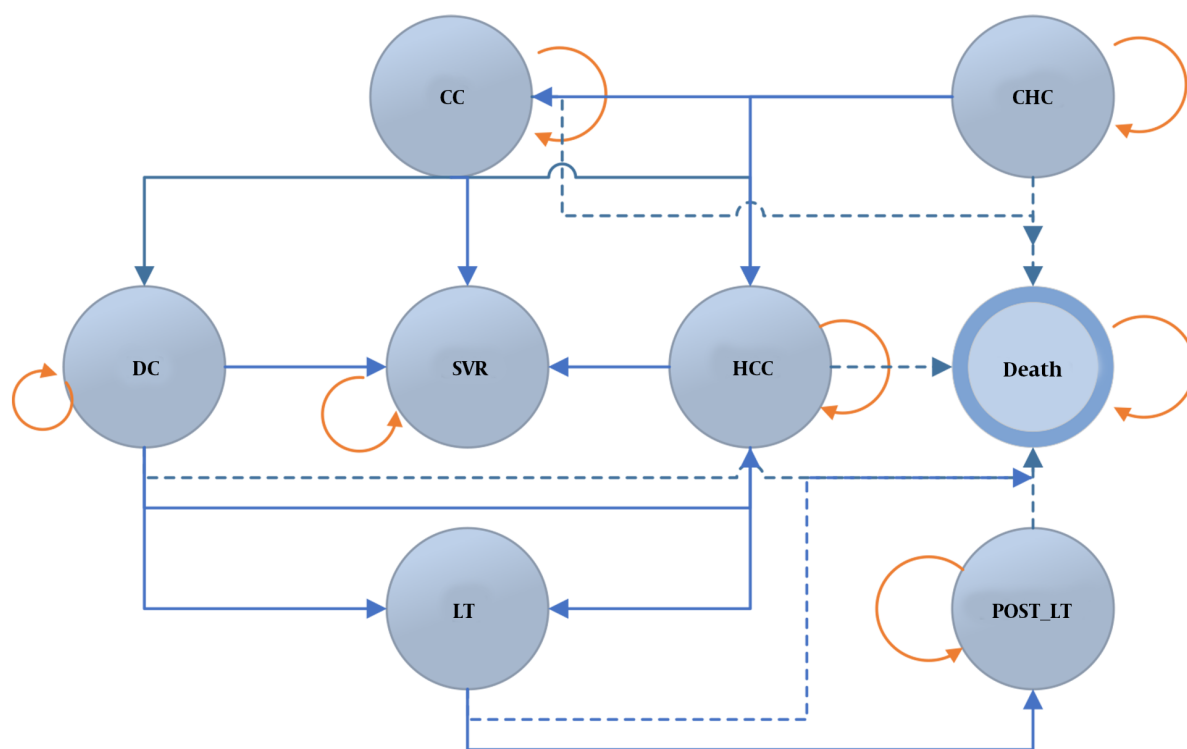
Figure 1. Health state transition diagram for the Markov model of chronic HCV infection. Abbreviations: CHC, chronic hepatitis C; CC, compensated cirrhosis; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; SVR, sustained virological response; LT, liver transplantation.

4. Results

4.1. Base-case Analysis

The results of cost-effectiveness obtained from the Markov Model estimation are provided in Figure 2 and Table 5 in the form of expected ICER, incremental QALYs, incremental cost, expected QALYs, and cost, in addition to the dominance of the three medication strategies in relation to each other in CHC patients. The results showed that the QALYs for LDV/SOF, DCV/SOF, and VEL/SOF were 13.25, 13.94, and 14.61, and the costs were 4807, 7716, and 4546 PPP$, respectively. Thus, the results of cost-effectiveness showed that LDV/SOF and DCV/SOF regimens had higher costs and lower QALYs than the VEL/SOF regimen, making it a dominant option. In fact, the ICER of VEL/SOF in relation to LDV/SOF and DCV/SOF was -192 and -4723 PPP$, respectively. Moreover, the DCV/SOF regimen had higher costs and lower QALYs than the VEL/SOF regimen, making it a dominant regimen. However, this regimen had an ICER of 4215 PPP$ compared to the LDV/SOF regimen, which was below the threshold, making it a cost-effective regimen compared to LDV/SOF.

4.2. One-way Sensitivity Analysis

The tornado chart was used to show the sensitivity of the model to the effective variables. As shown in Figure 3, the ICERs resulted from the medication regimens LDV/SOF and LDV/SOF, DCV/SOF and VEL/SOF, and VEL/SOF and DCV/SOF were most sensitive to HCC and CC costs. Still, due to the ICER results below the threshold, these variables would not significantly impact the study results.

4.3. Probabilistic Sensitivity Analysis (PSA)

In PSA, all parameters are considered distribution instead of the single point due to the probability nature of variables. Moreover, the beta distribution was used to determine the distribution of utility values and transitional probabilities (which takes a value between 0 and 1), and the gamma distribution was used for costs. Therefore, a second-order Monte Carlo simulation was developed for PSA using 5,000 trials. The results of uncertainty are shown in the form of cost-effectiveness acceptability curves and incremental cost-effectiveness scatter plots in Figures 4 and 5.

Moreover, the scatter plot results showed that VEL/SOF was the dominant therapeutic strategy in 73% of the simulations compared to LDV/SOF and 66% of the simulations

Table 1. Results of Transition Probabilities of Different Therapies

Transition Probability Variable	α	β	Distribution	Reference
LDV/SOF				
Prob CHC to SVR	0.89	0.061	Beta	Ruggeri et al. (26), Igarashi et al. (32), Rezaee-Zavareh et al. (29)
Prob CHC to CC	0.0905	0.025	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob CHC to HCC	0.0109	0.001	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob CC to SVR	0.89	0.02	Beta	Ruggeri et al. (26), Igarashi et al. (32), Rezaee-Zavareh et al. (29)
Prob CC to DC	0.053	0.013	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob CC to HCC	0.045	0.03	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob DC to HCC	0.041	0.027	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob DC to LT	0.0125	0.009	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob DC to death	0.13	0.02	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob HCC to LT	0.04	0.011	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob HCC to death	0.43	0.059	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob LT to death	0.189	0.021	Beta	Ruggeri et al. (26), Igarashi et al. (32)
Prob Post LT to death	0.057	0.014	Beta	Ruggeri et al. (26), Igarashi et al. (32)
LDV/DCV				
Prob CHC to SVR	0.89	0.025	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob CHC to CC	0.114	0.025	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob CHC to HCC	0.0109	0.0014	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob CC to SVR	0.9	0.02	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob CC to DC	0.038	0.004	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob CC to HCC	0.018	0.004	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob DC to HCC	0.023	0.01	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob DC to LT	0.0182	0.0022	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob DC to death	0.13	0.011	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob Post LT to death	0.045	0.012	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob HCC to LT	0.03	0.012	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Prob HCC to death	0.43	0.059	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
VEL/SOF				
Prob CHC to SVR	0.92	0.006	Beta	Yun et al. (31), Buti et al. (30)
Prob CHC to CC	0.068	0.048	Beta	Yun et al. (31), Buti et al. (30)
Prob CHC to HCC	0.007	0.007	Beta	Yun et al. (31), Buti et al. (30)
Prob CC to SVR	0.94	0.035	Beta	Yun et al. (31), Buti et al. (30)
Prob CC to DC	0.039	0.039	Beta	Yun et al. (31)
Prob CC to HCC	0.018	0.006	Beta	Yun et al. (31), Buti et al. (30)
Prob DC to HCC	0.068	0.028	Beta	Yun et al. (31), Buti et al. (30)
Prob DC to LT	0.001	0.002	Beta	Yun et al. (31), Buti et al. (30)
Prob DC to death	0.169	0.05	Beta	Yun et al. (31), Buti et al. (30)
Prob HCC to LT	0.005	0.001	Beta	Yun et al. (31), Buti et al. (30)
Prob HCC to death	0.427	0.023	Beta	Yun et al. (31), Buti et al. (30)
Prob LT to death	0.116	0.018	Beta	Yun et al. (31), Buti et al. (30)
Prop Post LT to death	0.044	0.012	Beta	Yun et al. (31), Buti et al. (30)

Abbreviations: CHC, chronic hepatitis C; CC, compensated cirrhosis; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; W, withdrawal; SVR, sustained virological response; LT, liver transplant.

compared to DCV/SOF; moreover, it was in the acceptable region in 92% of the simulations and below the threshold. Therefore, it dominated other regimens and was considered the most cost-effective strategy. Moreover, the results showed that DCV/SOF was in the acceptable region below the threshold in 69% of the simulations compared to LDV/SOF. Therefore, the DCV/SOF regimen was more cost-effective than LDV/SOF. Moreover, the results of the acceptability curve showed that given the threshold determined in the study, VEL/SOF, DCV/SOF, and LDV/SOF were the acceptable strategies in 65%, 25%, and 5% of the cases, respectively.

Table 2. Annual Costs of Patients with Chronic Hepatitis C Genotype 1 in Early Stages by Medication Strategy

Direct Medical Cost	SOF/VEL (12 wk)		SOF/DCV (12 wk)		SOF/LDV (12 wk)	
	%	PPP$	%	PPP$	%	PPP$
Visit	1.56	75.32	1.66	75.32	1.77	75.32
Main Drug	51.79	2500	52.15	2362	51.14	2169
Laboratory	35.84	1730.37	35.18	1593.49	35.79	1517.88
Radiology	10.8	521.31	11	498.19	11.29	478.8
Total	100	4827	100	4529	100	4241

Table 3. Components of Annual Direct Costs of Patients with Chronic Hepatitis C Genotype 1 by Medication Strategy

Variable Cost	Mean (PPP$)	SD	Distribution	SD Reference
SOF/LDV (12 weeks)				
CHC	4241	293	Gamma	Calculated
CC	4919	321	Gamma	Calculated
DC	6994	265	Gamma	Calculated
HCC	17498	289	Gamma	Calculated
SOF/DCV (12 weeks)				
CHC	4529	293	Gamma	Calculated
CC	5498	321	Gamma	Calculated
DC	7283	265	Gamma	Calculated
HCC	17832	289	Gamma	Calculated
SOF/VEL (12 weeks)				
CHC	4827	293	Gamma	Calculated
CC	5449	321	Gamma	Calculated
DC	7524	265	Gamma	Calculated
HCC	18074	289	Gamma	Calculated
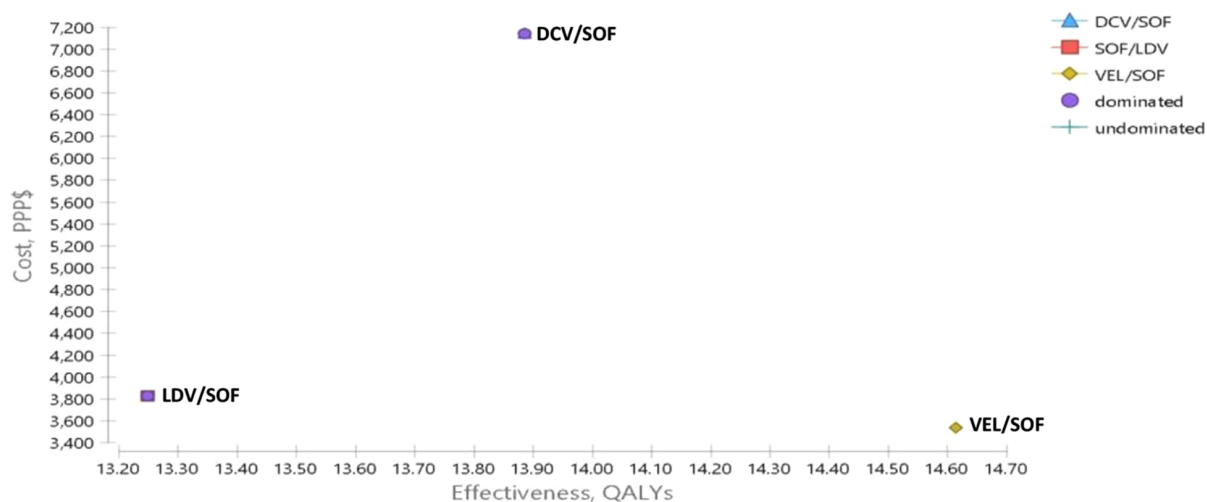
Figure 2. Base-case analysis results (ICERs) of new antiviral regimens in patients with chronic hepatitis C virus genotype 1 shown on cost-effectiveness plane.

Table 4. Utility of Different Health Conditions in Patients with Hepatitis C by Medical Strategy

Utility Variable	Mean	SD	Distribution	Reference
SOF/LDV				
Utility CHC	0.76	0.023	Beta	Buti et al. (30), Igarashi et al. (32)
Utility CC	0.74	0.02	Beta	Buti et al. (30), Igarashi et al. (32)
Utility DC	0.68	0.01	Beta	Buti et al. (30), Igarashi et al. (32)
Utility HCC	0.57	0.041	Beta	Buti et al. (30), Igarashi et al. (32)
Utility LT	0.55	0.032	Beta	Buti et al. (30), Igarashi et al. (32)
Utility Post LT	0.65	0.05	Beta	Buti et al. (30), Igarashi et al. (32)
Utility SVR	0.86	0.04	Beta	Buti et al. (30), Igarashi et al. (32)
SOF/DCV				
Utility CHC	0.74	0.03	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Utility CC	0.73	0.043	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Utility DC	0.64	0.21	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Utility HCC	0.52	0.023	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Utility SVR	0.87	0.071	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Utility Post LT	0.72	0.054	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
Utility LT	0.52	0.06	Beta	Saint-Laurent et al. (28), Moshyk et al. (27)
SOF/VEL				
Utility CHC	0.81	0.03	Beta	Yun et al. (31), Ruggeri et al. (26)
Utility CC	0.74	0.05	Beta	Yun et al. (31), Ruggeri et al. (26)
Utility DC	0.69	0.04	Beta	Yun et al. (31), Ruggeri et al. (26)
Utility HCC	0.58	0.04	Beta	Yun et al. (31), Ruggeri et al. (26)
Utility LT	0.56	0.032	Beta	Yun et al. (31), Ruggeri et al. (26)
Utility Post LT	0.71	0.02	Beta	Yun et al. (31), Ruggeri et al. (26)
Utility SVR	0.87	0.087	Beta	Yun et al. (31), Ruggeri et al. (26)

Table 5. Comparing Cost-effectiveness of New Antiviral Regimens in Patients with Chronic Hepatitis C Virus Genotype 1 Based on the Number of QALY Using Markov Microsimulation Model

Strategy	Cost (PPP$)	Utility	Incremental Cost (PPP$)	Incremental QALYs	ICER (Incremental Cost per QALY Gained) PPP$
Cost-effectiveness analysis					
LDV/SOF	4807	13.25	262	-1.37	-192
DCV/SOF	7716	13.94	3170	-.67	-4723
VEL/SOF	4546	14.61	-	-	Dominant

Abbreviations: LDV/SOF, ledipasvir + sofosbuvir; VEL/SOF, velpatasvir + sofosbuvir; DCV/SOF, daclatasvir + sofosbuvir; QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio.

5. Discussion

Considering the minimal improvement of hepatitis C patients with genotype 1 using the available first-line medications and introducing novel medications, an economic assessment to determine the most cost-effective strategy among the available strategies seemed necessary. There-fore, the present study aimed to determine the most appropriate medication therapy protocols for hepatitis C patients while taking into account the cost-effectiveness and economic considerations, in addition to evaluating the cost-effectiveness of these medication therapies in these patients in the perspective of the Ministry of Health. Con-
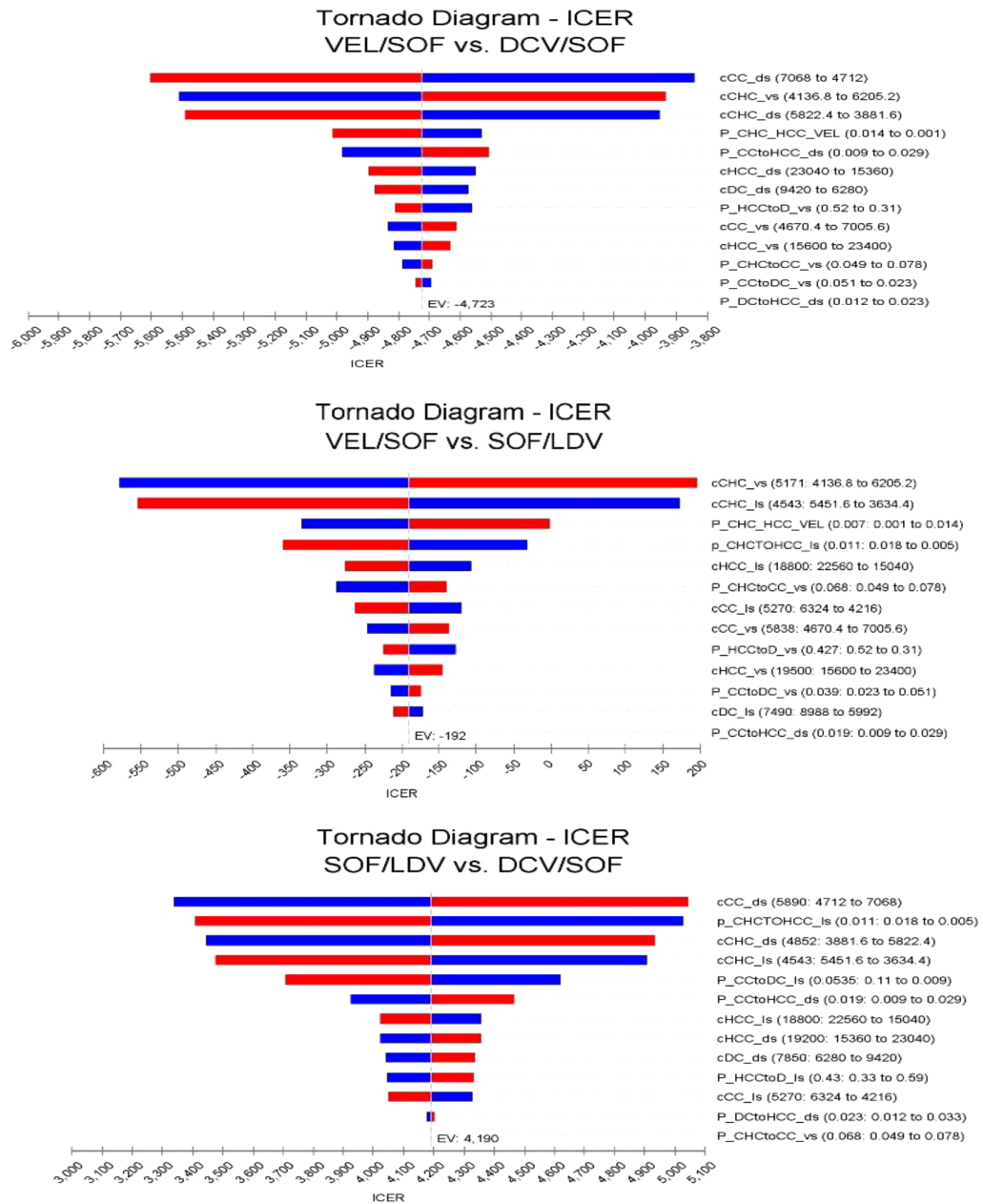
Figure 3. Tornado chart of the one-way deterministic analysis. The blue bar indicates that the high value of the parameter has been used, and the red bar indicates the low value of the parameter has been used. Abbreviations: LDV/SOF, Ledipasvir/Sofosbuvir; VEL/SOF, Velpatasvir/Sofosbuvir; DCV/SOF, daclatasvir/sofosbuvir.

sidering the conditions of the disease, the analysis was conducted using the Markov Model and a 5,000-individual simulation. The results showed that the VEL/SOF regimen was more cost-effective than the two other medication regimens. The study of Yashika Chugh (2019) evaluated the effectiveness of VEL/SOF in comparison with LDV/SOF and DCV/SOF in different scenarios. The results showed

that VEL/SOF was more cost-effective than other therapeutic strategies, leading to cost-saving in treatments. The results of this study are in line with our study. It should be noted that the research was conducted on CHC patients with genotype 1, while our study population consisted of CHC patients with genotype 1. Moreover, utility scores in the present study were calculated locally, while in other
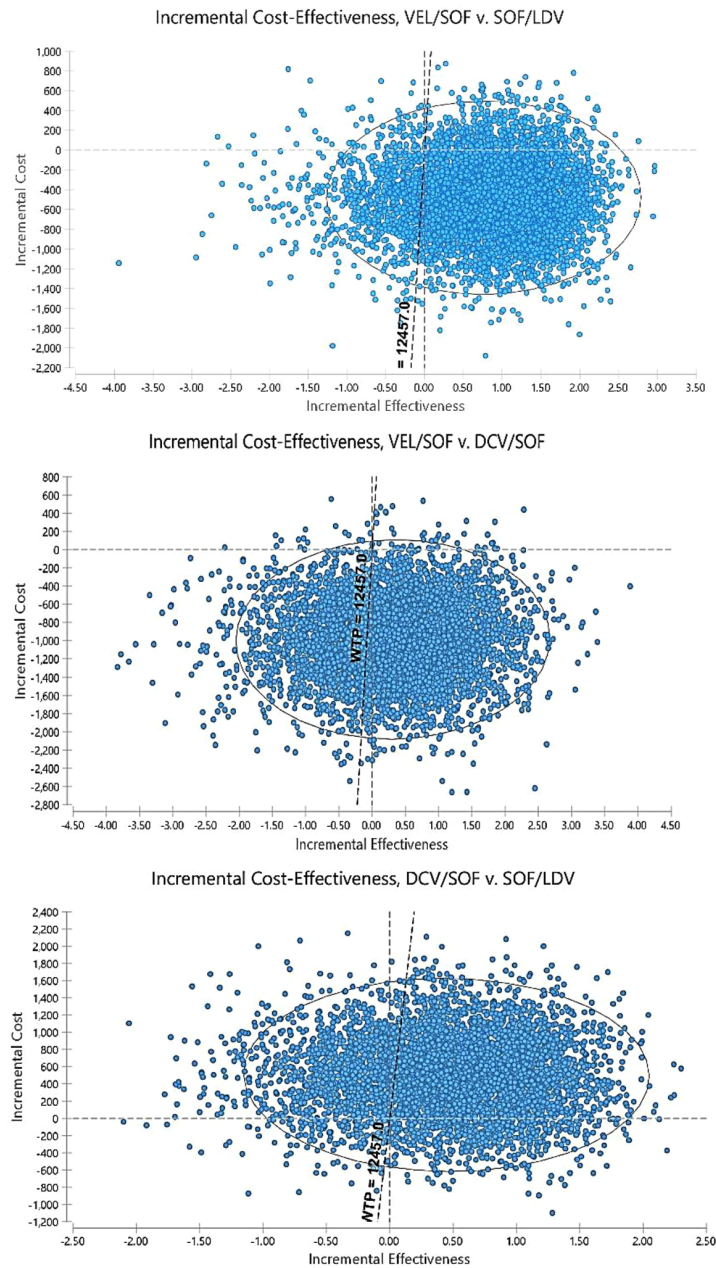
Figure 4. Scatter plot of incremental cost-effectiveness obtained from Monte Carlo Simulation for new antiviral regimens in patients with chronic hepatitis C virus genotype 1 (The scatter plots show the difference in cost and QALY results of 5,000 simulations). Abbreviations: LDV/SOF, Ledipasvir/Sofosbuvir; VEL/SOF, Velpatasvir/Sofosbuvir; DCV/SOF, Clatasvir/sofosbuvir.

studies, it was obtained by reviewing the evidence (47). Moreover, in another study by Corman et al. (2017) in the USA, comparing different antiviral medications in CHC patients, the results showed that VEL/SOF was more cost-effective than the two other strategies. This finding is in line with our study (48).

In this study, the QALYs and costs of the DCV/SOF regimen were more than those of LDV/SOF; however, by comparing the ICER obtained with the threshold, DCV/SOF was more cost-effective than LDV/SOF. Confirming these results, Ruggeri et al. (2019) conducted a study to assess the cost-effectiveness of two regimens DCV/SOF and LDV/SOF,

CE Acceptability Curve
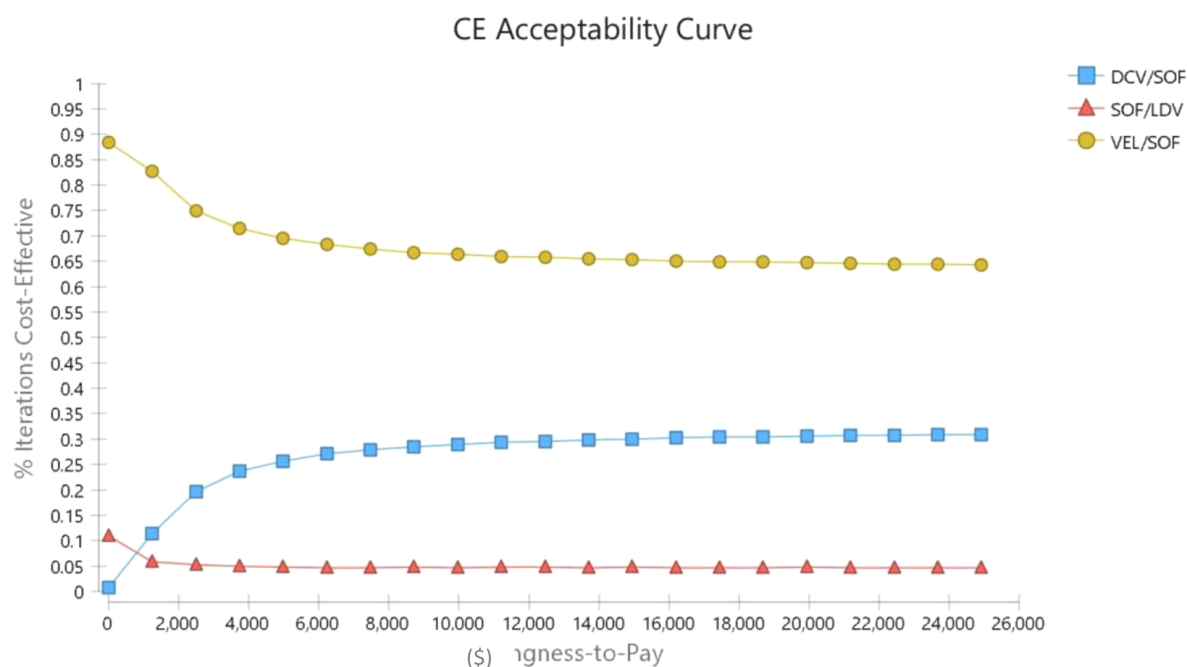
Figure 5. Cost-effectiveness acceptability curve obtained from Monte Carlo Simulation for new antiviral regimens in patients with chronic hepatitis C virus genotype 1. WTP: willingness to pay.

in which the DCV/SOF regimen had higher costs and QALY than LDV/SOF and was considered more cost-effective compared to the threshold (26). Moreover, the results of our study are in line with those of Feld et al., Ahmed et al., and Mir et al. (45, 49, 50). The highest cost, which belonged to the DCV/SOF regimen, was 7,762 PPP$. In the study by Ferreira et al. (2019) on the desirability of five medication strategies VEL/FOF, ELB/GRA, DCV/SOF, LDV/SOF, and GLB/PIB, the QALYs of VEL/FOF, LDV/SOF, and DCV/SOF were the same, and the lowest costs belonged to VEL/SOF, LDV/SOF, and DCV/SOF. The cost results of the three medication strategies in this study are in line with the present research results (51). Moreover, the results of the one-way sensitivity analysis showed that the VEL/SOF regimen was more cost-effective than the two other medical strategies, which were placed in the acceptable range below the threshold and obtained the best results considering the costs. Therefore, the results showed that conducted sensitivity analysis did not change the VEL/SOF as the most effective medication regimen and DCV/SOF as the second treatment strategy compared to the LDV/SOF regimen, showing the robustness of the study results. Then, VEL/SOF with lower costs, higher effectiveness, and higher SVR was selected as the dominant therapeutic method. Therefore, to increase SVR, decrease the treatment period, increase patient's quality of life, increase efficiency during the treat-

ment and afterward, and decrease disease complications and costs, it is suggested that this medication regimen be used (15, 37, 52, 53).

5.1. Study Limitations

The limitation of our study mainly concerned uncertainty in the dissemination of utility data that were obtained from foreign studies. Also, there were insufficient data on the mortality of CHC diseases for different health conditions in Iran. Moreover, given that our study was from the perspective of the health system, the patients' costs and their diminished efficacy were not considered. Also, in the model, according to the lack of sufficient information resources, we did not consider the side effects of medications.

5.2. Generalizability

As new antiviral medicine regimens can be used in referral centers in Iran, the results of this study can be generalized to the Iranian setting. As to other countries, other factors such as the threshold, payments system, and incidence and prevalence of HCV need to be considered.

5.3. Conclusions

In conclusion, according to the study results, it can be said that using the VEL/SOF regimen as the most effective

treatment strategy and DCV/SOF as the second most effective treatment strategy in patients with hepatitis C, particularly those with genotype 1, could decrease the relevant complications, including DC, HCC, and mortality, and also decrease the disease costs and time, particularly if the patients are visited in early stages without cirrhosis and previous treatments. These medications could also be used as the first line in patients with previous treatment.

Acknowledgments

Footnotes

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