Cost Effectiveness of Early Treatment with Direct-Acting Antiviral Therapy in Adolescent Patients with Hepatitis C Virus Infection

Joehl Nguyen, MPH[1], A. Sidney Barritt IV, MD, MSCR[2], and Ravi Jhaveri, MD[3,*]

Objective To evaluate the cost effectiveness of early treatment with direct-acting antiviral therapy in adolescent patients with chronic hepatitis C virus (HCV) infection compared with treatment deferral.

Study design We constructed a Markov model to assess the cost effectiveness of treating a hypothetical cohort of 30 000 adolescent patients with chronic HCV at age 12 years compared with deferring treatment until adulthood from a societal perspective. Model inputs for transition probabilities, HCV treatment and medical care costs, and quality-adjusted life-year (QALY) utilities were derived from the literature and wholesale acquisition estimates. Deterministic sensitivity analyses varied parameters for non-HCV medical care and treatment cost, reinfection rates, treatment uptake, disease progression, liver transplant survival, and treatment with recently approved pangenotypic direct-acting antiviral agents. Discounted costs and total QALYs per person were quantified after 30 years. Cost effectiveness was evaluated as the incremental change in total medical costs per QALY gained.

Results The incremental cost effectiveness of early treatment initiation compared with deferred treatment was approximately $27 000 per QALY gained after 30 years and considered cost effective. In a scenario analysis, hypothetical treatment initiation with currently available pangenotypic agents would be even more cost effective, ranging from $10 000 to $21 000 per QALY gained. Cost-effectiveness estimates were sensitive to variations in decompensated cirrhosis progression in adolescence, adult reinfection, and treatment uptake in adults.

Conclusions Early treatment in adolescent patients with chronic HCV infection with currently available direct-acting antivirals seems to be cost effective compared with deferred treatment. Future efforts to control the HCV epidemic should include increasing the number of children treated. *(J Pediatr 2019;207:90-6)*.

Chronic hepatitis C virus (HCV) infection continues to be a global public health concern and is responsible for serious health complications including fibrosis, cirrhosis, and liver cancer.[1-3] In recent years, HCV has received significant attention owing to increases in cases attributed to injection drug use and the availability of highly curative direct-acting antiviral (DAA) therapy.[4] Adolescent patients represent a subset of the population affected by HCV, with 30 000-50 000 cases estimated in the US.[5,6] Most incident cases of pediatric HCV are attributed to vertical or perinatal transmission, although the number of adolescent HCV cases associated with substance abuse is increasing.[5-8] Although disease progression seems to be mild in childhood, without appropriate treatment, patients remain at risk for chronic liver disease, extrahepatic complications, and lower quality of life over time.[3,9-11]

The US Food and Drug Administration (FDA) has approved many new DAA therapies in recent years that are highly effective for curing HCV.[12] These medications have provided a real public health opportunity to eradicate the disease globally. However, adolescent patients with HCV were not routinely considered for therapy and are typically deferred treatment until adulthood based on previous guidelines.[6,13] The American Association for the Study of Liver Disease and Infectious Disease Society of America have recently updated guidelines for treating adolescents aged 12-17 years. Currently, only sofosbuvir/ledipasvir (SOF/LDV) and SOF/ribavirin (RBV) regimens are FDA approved for treatment of infected children ages 12-17 years old[12,14,15] Clinical trials with adult-approved pangenotypic combination DAAs, glecaprevir/pibrentasvir (GLE/PIB) and SOF/velpatasvir (VEL) are currently in progress with likely approval in the near future (www.

DAA	Direct-acting antiviral	QALY	Quality-adjusted life year
FDA	US Food and Drug Administration	RBV	Ribavirin
GLE	Glecaprevir	SOF	Sofosbuvir
HCC	Hepatocellular carcinoma	SVR	Sustained virologic response
HCV	Hepatitis C virus	VEL	Velpatasvir
ICER	Incremental cost-effectiveness ratio	WAC	Wholesale acquisition cost
LDV	Ledipasvir	WTP	Willingness-to-pay
PIB	Pibrentasvir		

From the [1]Division of Pharmaceutical Outcomes and Policy, University of North Carolina at Chapel Hill Eshelman School of Pharmacy; [2]Division of Gastroenterology and Hepatology, and [3]Division of Infectious Diseases, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

*Current affiliation: Pediatric Infectious Diseases, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

No external funder had any role in the design or conduct of this study. JN receives tuition and stipend support from a pre-doctoral fellowship funded by GlaxoSmithKline, unrelated to the present study. RJ receives grant support, unrelated to the present study, for clinical research from Gilead, AbbVie, and Merck. The other author declares no conflicts of interest.

Presented at the Pediatric Academic Societies Annual Meeting, May 5-8, 2018, Toronto, Canada, and at the 34th International Conference on Pharmacoepidemiology and Therapeutic Risk Management, August 22-26, 2018, Prague, Czech Republic.

https://doi.org/10.1016/j.jpeds.2018.12.012

clinicaltrials.gov: NCT03067129; NCT03022981). Treatment strategies with DAAs have previously been shown to be cost effective in various adult populations.[16-18] However, cost-effectiveness analyses of treatment for HCV in the pediatric population to date are limited and have focused on outdated guidelines with interferon-based therapies.[13] Subsequently, the cost effectiveness of treating HCV in childhood with generally costly DAAs when symptoms and progression are milder is unknown.

The goal of this study was to evaluate the cost effectiveness of early treatment initiation with approved DAA therapy in patients aged 12 years with chronic HCV infection compared with the previous standard of care of deferring treatment until adulthood.

Methods

Table I summarizes the hypothetical cohort characteristics, input variables, and assumptions used in our estimations. We evaluated treatment strategies for a hypothetical cohort of 30 000 patients aged 12 years with chronic HCV infection to reflect the known epidemiology and current treatment guidelines for HCV in children.[3,6,12] Given differences in genotype-specific treatment, efficacy, and costs, we estimated the genotype distribution to be 80% for genotypes 1, 4, 5, and 6, 10% for genotype 2, and 10% for genotype 3. We estimated this breakdown based on observed distributions in the pediatric population in real-world settings.[9]

Patients were assumed to be newly diagnosed and treatment-naïve before entering the Markov cycle. We examined 2 treatment strategies assuming that patients would receive treatment with SOF/RBV (genotypes 2 and 3) or SOF/LDV (genotypes 1, 4-6). In early treatment, all patients are treated beginning at age 12 years. In deferred treatment, patients enter the Markov cycle at age 12 years, but do not initiate DAA treatment until age 18 years. To provide a best case scenario estimate of the cost effectiveness of early compared with deferred treatment, we assumed full uptake in both strategies from a societal perspective. In general, cost-effective analyses of healthcare interventions using a societal perspective incorporate direct, indirect, and future costs, in addition to total effects of interventions, regardless of payers or intervention recipients.[19]

Markov Model

We constructed a Markov model in Microsoft Excel (Microsoft, Redmond, Washington) to quantify and evaluate the number of patients transitioning through HCV health states over a 30-year time horizon. This 30-year time horizon accounts for the natural history of HCV given that more progressive complications will occur over this time in adolescent patients.[3,9] Figure 1 illustrates how patients in this Markov model move through different HCV health states. In this model, patients occupy different health states representing either HCV, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma (HCC), liver transplantation, or death in a given year.

All patients in our analysis entered the Markov cycle in the chronic HCV state, identified at age 12 years. The number of patients in each HCV state at the beginning of each Markov cycle or calendar year was quantified using annual transition probabilities reported from published cost-effectiveness models in the HCV population. Where available, we favored annual transition probabilities reported in studies describing children and adolescents to represent progression in the early treatment strategy. In the deferred treatment strategy, we used transition probabilities reported by studies in the young adult population or general adult population, given the paucity of literature reporting reliable progression rates in the pediatric population over time. In both strategies, patients who are treated receive up to 1 course of DAA therapy per patient per year. Without treatment during adolescence, patients remain at risk of transitioning through to progressive disease states during adolescence.

In the early and the deferred treatment strategies, patients who are treated in chronic HCV or compensated cirrhosis states can achieve a sustained virologic response (SVR), representing viral clearance or essentially a transition to a healthy state.[14,15] We further accounted for susceptibility to reinfection post SVR to reflect the fact that most new cases of HCV in the US have recently been attributed to the increasing prevalence of risk behaviors for HCV infection, namely injection drug use in young adults.[8,16,20] Patients who are reinfected with HCV then reenter the Markov HCV progression cycle to the chronic HCV state. In this simulation, we assumed that the HCV reinfection rate after SVR would remain uniform at 5% per year in adults based on the previous literature.[20] Patients who are reinfected with chronic HCV after treatment then have the potential to be retreated up to the end of the 30th Markov cycle.

With respect to mortality, we assumed that the probability of dying for patients in the SVR, chronic HCV, and compensated cirrhosis states were reflective of the general US population, based on age-adjusted life expectancy derived from the 2014 National Vital Statistics Report.[21] We used state-specific estimates from the literature to estimate annual mortality rates for patients in the decompensated cirrhosis, HCC, and liver transplantation states.[13,17,18]

Costs, Outcomes, and Cost Effectiveness

At the end of each Markov cycle, patients accrue costs associated with treatment and other medical expenses. Unit costs for DAA therapy were attained from the University of Washington Hepatitis C Online resource, namely, the wholesale acquisition cost (WAC) estimates.[22] We calculated the cost for one course of DAA therapy based on these WAC estimates and approved DAA-specific treatment duration. For SOF/RBV therapy, we used the University of Washington reported range to estimate an average cost of RBV for a 12- and 24-week treatment course, where appropriate. Other HCV-related medical expenses were derived from the

Table I. Baseline model input variables for Markov model assessment

Cohort characteristics					References
Cohort size		30 000			6
Starting condition		Chronic HCV			
Starting age		12 years			12
Cycle length		30 Markov cycles			3,9
Genotype distribution					9
1, 4, 5, 6		80%			
2		10%			
3		10%			
Annual discount		3%			
Treatment uptake, ages 12-17		100%			Assumption
Probability of SVR		97%-99%			14,15
	Base case		**Lower bound**	**Upper bound**	**References**
Treatment uptake ages ≥18*	100%		10%	50%	Assumption
Post-SVR reinfection in adults*	0.05		0.019	0.267	16,20
Transition probabilities					
	Base case				
	Age 12-17	**Age ≥18**	**Lower bound**	**Upper bound**	**References**
Chronic HCV to					
Compensated cirrhosis	0.0018	0.10975	0-0.075	0.10975-0.133	9,17
Decompensated cirrhosis*	0.0018	0.10975	0-0.075	0.10975-0.133	9,17
HCC*	0.001	0.001	0.0005	0.002	13
Compensated cirrhosis to					
Decompensated cirrhosis	0.039	0.04	0.03-0.035	0.043-0.05	13,18
HCC	0.015	0.025	0.01-0.022	0.028-0.03	13,18
Decompensated cirrhosis to					
HCC	0.03	0.068	0.015-0.03	0.05-0.083	13,18
Liver transplantation	0.03	0.031	0.01-0.029	0.1-0.033	13,18
Death	0.1	0.182	0.05-0.065	0.15-0.19	13,18
HCC to					
Liver transplantation	0.03	0.031	0.029	0.033	18
Death	0.409	0.409	0.368	0.450	18
Liver transplantation*					
Death after transplantation, first year	0.14	0.14	0.126	0.154	18
Death after, transplantation second year and beyond	0.025	0.025	0.023	0.027	18
Costs in 2017 US dollars					**References**
Treatment costs per recommended course					
SOF + LDV—12 weeks (genotypes 1, 4-6)	$94 500				16,22
SOF + RBV—12 weeks (genotype 2)	$84 700				18,22
SOF + RBV—24 weeks (genotype 3)	$169 400				18,22
SOF + VEL—12 weeks (pangenotypic)	$74 760				22
GLE + PIB—8 weeks (pangenotypic)	$26 400				22
	Base case		**Lower bound**	**Upper bound**	**References**
Annual costs of HCV-related medical care					18
Chronic HCV	$795		$615	$1026	
Compensated cirrhosis	$1513		$1171	$1953	
Decompensated cirrhosis	$20 390		$1217	$35 316	
HCC	$42 921		$24 780	$74 341	
Liver transplantation	$200 869		$115 973	$347 913	
Liver transplantation monitoring	$36 278		$20 945	$62 834	
Annual costs of non-HCV medical care*					17
Ages 12-14	$2177		$1776	$2639	
Ages 15-19	$2122		$1907	$2352	
Ages 20-24	$1911		$1618	$2240	
Ages 25-29	$2644		$2193	$3158	
Ages 30-34	$3463		$2963	$4024	
Ages 35-39	$3442		$3000	$3930	
Ages 40-44	$4007		$3465	$4608	
Utilities (QALY)					18
Markov Health State					
SVR	1.0		–	–	
Chronic HCV	0.85		0.78	0.94	
Compensated cirrhosis	0.81		0.67	0.90	
Decompensated cirrhosis	0.70		0.55	0.80	
HCC	0.67		0.55	0.79	
Liver transplantation	0.50		0.72	0.84	
Liver transplantation monitoring	0.78		0.72	0.84	

*Input variable modified in 1-way sensitivity analysis. Ranges in reported lower and upper bound estimates reflect differences between probabilities of transition between HCV progression in adolescence (12-17) and adulthood (≥18). Costs were inflated to 2017 USD using Consumer Price Indices reported for medical care in 2017; costs and utilities were discounted at 3% annually.

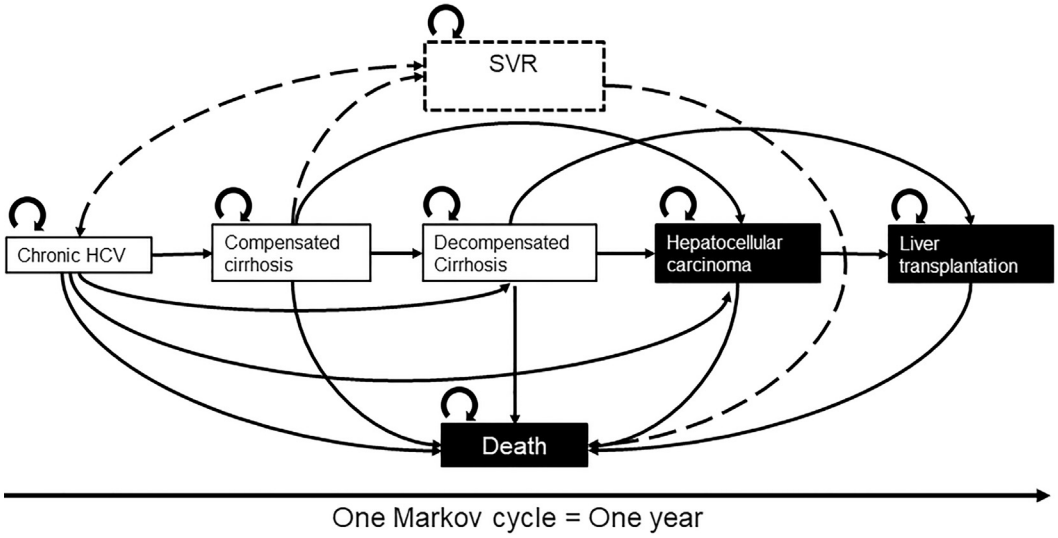

Figure 1. Markov model of chronic HCV infection and liver disease progression with DAA therapy. Patients aged 12 years with HCV infection begin in the chronic HCV state and progress to compensated cirrhosis, decompensated cirrhosis, HCC, liver transplantation, or death states, regardless of treatment strategy, and accrue costs and utilities at the end of each Markov cycle. Patients who initiate early treatment are treated at age 12 years; patients who defer treatment are treated at age 18 years. Patients with chronic HCV or compensated cirrhosis who are treated with DAA therapy (dashed transition arrows) can achieve SVR. Bidirectional arrows between chronic HCV and SVR states reflect potential for reinfection after treatment. Circular arrows indicate retention within respective HCV states or no transition. Death was modeled as an absorbing state.

literature to account for direct medical costs of HCV and future costs of untreated HCV outcomes.[16,18] To capture indirect costs, we included non-HCV-related medical costs based on previously reported, age-adjusted costs in the general population. This number represents costs accrued by healthy patients who achieve SVR after successful treatment.[17]

Annual costs were adjusted for inflation to 2017 US dollars using the ratio of the US Consumer Price Index for prescription drugs and medical care reported in December 2017 to that of the originally reported year in the reference publication.[23] We estimated the total costs associated with HCV treatment, HCV-related medical care, and non-HCV-related medical care by multiplying the number of patients in each HCV state at the end of each Markov cycle with the annual costs of treatment, state-specific HCV medical care, and non-HCV-related medical care, where appropriate. Depending on their HCV disease state during a given Markov cycle, patients also accrue differential quality-adjusted life year (QALYs) utility values. We estimated the utility for each HCV state using previously published literature and quantified annual QALYs based on the number of patients in each HCV state in a given year. Total costs and QALYs accrued were quantified after 30 years for both strategies and discounted at an annual rate of three percent to account for time preferences. The total cost and QALYs per person were then calculated by dividing the estimates by the cohort size.

We estimated the cost effectiveness of early vs deferred treatment using an incremental cost-effectiveness ratio (ICER) that represents the difference in costs per person relative to the difference in QALYs per person. To be considered cost effective, we assessed ICER estimates for early compared with deferred treatment against the commonly cited conservative willingness-to-pay (WTP) threshold of $50 000 per QALY under differential scenario and sensitivity analyses.[24]

Sensitivity and Scenario Analyses

To assess the model's sensitivity to uncertainty of certain input parameters in estimating the cost effectiveness, we conducted 1-way sensitivity analyses. The reported lower and upper bound estimates were varied for the annual cost of non-HCV care, reinfection rates, childhood progression to decompensated cirrhosis and HCC, and survival after liver transplantation. Additionally, treatment uptake for adults was varied at 10% and 50% per year in a scenario analysis to evaluate the effect of assumed treatment uptake in real-world settings on estimates in our model. We also estimated the cost effectiveness of treatment in the adolescent population with recently approved pangenotypic DAA to account for a possible shift in future HCV treatment owing to recent decreases in treatment costs for GLE/PIB.[22] In these scenario analyses, we assumed that all patients would be treated with either SOF/VEL or GLE/PIB, with an average SVR of 95% to reflect differences among patients with genotype 3 and 4 observed in clinical trials.[25-28]

Results

Table II summarizes the results of our base case estimations comparing the costs and outcomes associated with early and deferred treatment initiation with SOF/LDV and SOF/RBV

treatments in adolescent patients with chronic HCV infection. We found that early treatment results in an estimated 1.05 additional QALYs per person after 30 years compared with deferred treatment. The total cost per person after 30 years in the early treatment strategy was approximately $216 000 compared with around $188 000 in the deferred treatment strategy. Under a $50 000 per QALY gained WTP, early treatment was considered cost effective, yielding an ICER value of approximately $27 000 per QALY gained.

Figure 2 illustrates the results of our sensitivity analysis. Cost-effectiveness estimates in our model were most sensitive to model adjustments for reinfection rates in adults, childhood decompensated cirrhosis progression, treatment uptake in adults, and treatment with pangenotypic DAAs. Our model estimations were least sensitive to modifications in incident and overall liver transplant mortality, yielding minimal ICER changes from our reference case analysis. Variations to childhood HCC progression and costs of non-HCV-related medical care resulted in ICER estimates below our WTP threshold, ranging from $25 000 to $28 000 per QALY gained.

In our scenario analysis varying treatment uptake in adults, we found that estimated ICER values ranged from $31 500 to $42 800 per QALY gained when varying treatment uptake from 50% and 10% of the total infected population per year, respectively. We also found that cost effectiveness was retained in our hypothetical cohort when patients were treated with GLE/PIB and SOF/VEL. When compared with deferred treatment, ICER estimates were approximately $10 000 per QALY gained for early treatment with GLE/PIB and $21 000 per QALY gained for early treatment with SOF/VEL.

Discussion

We aimed to estimate whether treatment for chronic HCV infection in early adolescence would be cost effective from a societal perspective by using a Markov model to estimate HCV progression. In our base scenario, we found that early treatment at age 12 years resulted in an additional 1.05 QALYs per person and was cost effective at $27 000 per QALY gained. The higher per person total cost of an early treatment strategy in this simulation is expected because treatment is initiated in all patients at age 12 years. In the deferred treatment strategy, fewer patients in the hypothetical cohort accrue the upfront costs of DAA initiation at age 18 years because they remain at risk of transitioning to other HCV Markov states or death without treatment between ages 12 and 17 years. However, under a conservative WTP threshold of $50 000 per QALY gained, these results suggest that increasing the number of treated patients with HCV in earlier disease stages is cost effective in the long term from a societal perspective when accounting for additional QALYs gained from earlier treatment. Although progression in childhood is generally slower, the increasing incidence of HCV among adolescents and young adults in recent years needs to be appropriately addressed.

In both treatment strategies, our base case model assumes that treatment uptake would be 100%, that is, all patients with chronic HCV and compensated cirrhosis would be eligible and receive treatment in a given year. This scenario is likely to be more reflective of treatment in the adolescent population, where patients are more likely to be considered a "captive audience" owing to parental insurance access, for example. However, full treatment uptake is unlikely in adult populations, particularly in settings with limited resources or higher proportions of historically underserved patients. In our scenario analysis, a conservative estimate of 10% treatment uptake per year among eligible adult patients resulted in an ICER estimate of $43 000 per QALY gained. This estimate is greater than our original analysis but still under our WTP threshold of $50 000 per QALY gained, assuming that uptake among adolescent patients remains at 100%. As the incidence of new HCV increases among young adults and the prevalence of disease matches that of the baby boomers, efforts to increase treatment uptake will be critical to curb the epidemic as well as retain treatment benefits from a societal perspective.[29]

In our sensitivity analyses, ICER estimates from our model were sensitive to variations in reinfection rates in adults. Inputs for upper and lower bound estimates for reinfection resulted in ICERs ranging from $23 000 to $48 000 per QALY gained, respectively. These results are reasonable observations, given that a lower estimated reinfection in adults would likely decrease the likelihood of HCV progression at a population level while increasing the cost per additional QALY in earlier treatment. In contrast, these results also suggest that earlier treatment for HCV may be also be a cost-effective strategy at decreasing reinfection rates owing to rising incidence of injection drug observed in recent years.[8]

Treatment costs for HCV have been debated given the very high initial price point after the approval of curative second-generation DAAs. Our base case model assumes treatment costs associated with SOF/LDV and SOF/RBV therapies

Table II. Discounted costs, outcomes, and cost-effectiveness of early vs deferred treatment initiation in adolescent patients with chronic HCV infection

Treatment strategies by DAA	Total QALYs/ person	Total cost/ person	ICER - Δ$/ ΔQALYs
Base case analysis: treatment with DAAs currently FDA approved for children			
SOF/LDV or SOF/RBV			
Early treatment (12-17)	19.34	$216 390	$26 802
Deferred treatment (≥18)	18.29	$188 135	
Scenario analysis: treatment with pangenotypic DAAs			
GLE/PIB			
Early treatment (12-17)	19.32	$98 343	$10 088
Deferred treatment (≥18)	18.24	$87 107	
SOF/VEL			
Early treatment (12-17)	19.32	$177 697	$20 604
Deferred treatment (≥18)	18.21	$154 748	

Treatment strategy considered cost-effective if ICER estimates fall below WTP threshold of $50 000 USD/QALY. Costs and QALYs quantified after 30 Markov cycles. Per person costs calculated as total costs divided by cohort size (n = 30 000). Costs are inflated to 2017 USD; costs and outcomes are discounted at 3% annually.

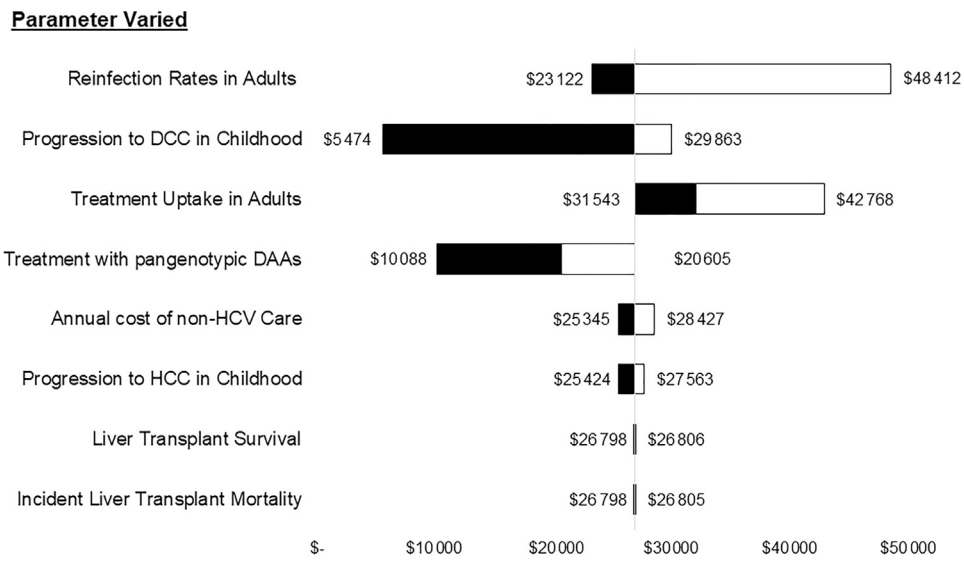

Figure 2. Deterministic sensitivity and scenario analyses of ICER estimates of early vs deferred treatment for chronic HCV in adolescence. Deterministic sensitivity analyses varied variables using estimated lower and upper bounds for model inputs. Hypothetical treatment with pangenotypic DAAs evaluated using a 95% average SVR under treatment with GLE/PIB or SOF/VEL therapies. Data presented depicts ICER values under each variable variation. Cost effectiveness evaluated using a $50 000 per QALY gained willingness to pay threshold. Data are presented relative to deviations from base case ICER value ($26 800 per QALY gained). DCC, decompensated cirrhosis.

based on current guidelines that are aligned with current FDA approvals. In the short term, we expect that total treatment costs for HCV will vary across institutions depending on differential payer reimbursement. The treatment landscape for HCV is also very likely to change in the near future. Based on recently obtained WAC estimates, our scenario analysis found that early treatment with SOF/VEL or GLE/PIB was even more cost effective. Although pangenotypic DAAs are not yet approved for treating pediatric patients, the lower prices should provide additional opportunities to address the HCV epidemic by increasing access for young adult patients.

The field has also long debated the timing of treating HCV-infected children. We chose 12 years old as a threshold because as this is the youngest age included within the current FDA approval in 2018. DAA regimens are being studied for use in children as young as 3 years of age, and it is likely that FDA approval will be gained for children of this age. There are tangible benefits to treating before the risk-taking behavior of adolescence begins, when transmission is most likely to occur. Although the DAA dosing strategy for younger children will require lower doses, it is unclear whether this will lead to a lower price for pediatric formulation. We suspect that this will not be the case, given the short duration of administration and high likelihood of cure.

Our study has several limitations that warrant careful consideration. We used a Markov model to quantify patients transitioning between HCV health states per year. As with all economic models, uncertainty is inevitable, and we account for uncertainty with our sensitivity and scenario analyses. This model was adapted from other previously published models, which reflects a simplification of disease progression and treatment decisions that may not be precisely observed in real-world settings. Although estimates for transition probabilities in HCV progression were generally limited in describing progression in children, we found in our sensitivity analyses that the model was least sensitive to estimates for HCC progression in describing cost effectiveness. Future studies depicting more age-specific transition probabilities of chronic HCV progression to more severe disease states will help improve generalizability and utility of similar cost-effectiveness models.

Although we modeled treatment for patients aged 12 years in this study, it is likely that DAA therapy will be approved for even younger populations in the future. Treatment uptake in our model was optimistic at 100%. As this is currently unlikely to be the case, additional resources will be needed to provide the clinical infrastructure and training necessary to scale up pediatric providers' ability to treat HCV in the pediatric population. We also used WAC estimates for treatment costs, which appropriately aligns with the societal perspective of our analysis, but is unlikely to reflect the variable cost of treatment to individual patients depending on which payers are involved. In addition, we allowed retreatment among those reinfected with HCV after attaining an SVR in our model. This assumption is unlikely to hold in resource-capped settings. We show in our analysis that cost effectiveness is retained in a best case scenario where SVR is maximized on a population level. Thus, the rationale for treatment in adolescents relies on the long-term benefits

against occurrence of disease progression over time, which is reflected in our estimations.

Early treatment initiation in adolescent patients with chronic HCV infection with currently available DAAs seems to be cost effective compared with deferred treatment. Future efforts to control the HCV epidemic include strategies that include adolescent populations as a part of routine treatment. In addition, increased substance abuse linked to increased HCV infections present opportunities and challenges for identifying new populations with associated risk factors. Eradicating HCV will subsequently require more effective case identification for proper care linkage and treatment that includes the pediatric and young adult population. ■

Submitted for publication Aug 13, 2018; last revision received Nov 12, 2018; accepted Dec 5, 2018.

References

1. Chak E, Talal AH, Sherman KE, Schiff ER, Saab S. Hepatitis C virus infection in USA: an estimate of true prevalence. Liver Int 2011;31:1090-101.
2. El Khoury AC, Vietri J, Prajapati G. The burden of untreated hepatitis C virus infection: a US patients' perspective. Dig Dis Sci 2012;57:2995-3003.
3. Squires JE, Balistreri WF. Hepatitis C virus infection in children and adolescents. Hepatol Commun 2017;1:87-98.
4. Grebely J, Dore GJ, Morin S, Rockstroh JK, Klein MB. Elimination of HCV as a public health concern among people who inject drugs by 2030—what will it take to get there? J Int AIDS Soc 2017;20:22146.
5. Khaderi S, Shepherd R, Goss JA, Leung DH. Hepatitis C in the pediatric population: transmission, natural history, treatment and liver transplantation. World J Gastroenterol 2014;20:11281-6.
6. Jhaveri R, Grant W, Kauf TL, McHutchison J. The burden of hepatitis C virus infection in children: estimated direct medical costs over a 10-year period. J Pediatr 2006;148:353-8.
7. Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. Clin Infect Dis 2014;59:1411-9.
8. Barritt AS 4th, Lee B, Runge T, Schmidt M, Jhaveri R. Increasing prevalence of hepatitis C among hospitalized children is associated with an increase in substance abuse. J Pediatr 2018;192:159-64.
9. Bortolotti F, Verucchi G, Camma C, Cabibbo G, Zancan L, Indolfi G, et al. Long-term course of chronic hepatitis C in children: from viral clearance to end-stage liver disease. Gastroenterology 2008;134:1900-7.
10. Rodrigue JR, Balistreri W, Haber B, Jonas MM, Mohan P, Molleston JP, et al. Impact of hepatitis C virus infection on children and their caregivers: quality of life, cognitive, and emotional outcomes. J Pediatr Gastroenterol Nutr 2009;48:341-7.
11. Younossi Z, Park H, Henry L, Adeyemi A, Stepanova M. Extrahepatic manifestations of hepatitis C: a meta-analysis of prevalence, quality of life, and economic burden. Gastroenterology 2016;150:1599-608.
12. American Association for the Study of Liver Diseases. Infectious Diseases Society of America. HCV guidance: recommendations for testing, managing, and treating hepatitis C. HCV in Children. https://www.hcvguidelines.org/unique-populations/children. Accessed October 12, 2017.
13. Sinha M, Das A. Cost effectiveness analysis of different strategies of management of chronic hepatitis C infection in children. Pediatr Infect Dis J 2000;19:23-30.
14. Wirth S, Rosenthal P, Gonzalez-Peralta RP, Jonas MM, Balistreri WF, Lin C-H, et al. Sofosbuvir and ribavirin in adolescents 12-17 years old with hepatitis C virus genotype 2 or 3 infection. Hepatology 2017;66:1102-10.
15. Balistreri WF, Murray KF, Rosenthal P, Bansal S, Lin C-H, Kersey K, et al. The safety and effectiveness of ledipasvir-sofosbuvir in adolescents 12-17 years old with hepatitis C virus genotype 1 infection. Hepatology 2017;66:371-8.
16. Corman S, Elbasha EH, Michalopoulos SN, Nwankwo C. Cost-utility of elbasvir/grazoprevir in patients with chronic hepatitis C genotype 1 infection. Value Health 2017;20:1110-20.
17. Rattay T, Dumont IP, Heinzow HS, Hutton DW. Cost-effectiveness of access expansion to treatment of hepatitis C virus infection through primary care providers. Gastroenterology 2017;153:1531-43.
18. Rein DB, Wittenborn JS, Smith BD, Liffmann DK, Ward JW. The cost-effectiveness, health benefits, and financial costs of new antiviral treatments for hepatitis C virus. Clin Infect Dis 2015;61:157-68.
19. Neumann PJ. Costing and perspective in published cost-effectiveness analysis. Med Care 2009;47:S28-32.
20. Assoumou SA, Tasillo A, Leff JA, Schackman BR, Drainoni M-L, Horsburgh CR, et al. Cost-effectiveness of one-time hepatitis C screening strategies among adolescents and young adults in primary care settings. Clin Infect Dis 2018;66:376-84.
21. Arias E, Heron M, Xu J. United States Life Tables, 2014. Natl Vital Stat Rep 2017;66:1-64.
22. Hepatitis C Online. Hepatitis C treatments. University of Washington and the University of Alabama at Birmingham. https://www.hepatitisc.uw.edu/page/treatment/drugs. Accessed July 20, 2018.
23. Consumer Price Index (CPI) Databases. Bureau of Labor Statistics. US Department of Labor, https://www.bls.gov/cpi/data.htm. Accessed March 20, 2018.
24. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness: the curious resilience of the $50,000-per-QALY threshold. N Engl J Med 2014;371:796-7.
25. Feld JJ, Jacobson IM, Hézode C, Asselah T, Ruane PJ, Gruener N, et al. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. N Engl J Med 2015;373:2599-607.
26. Foster GR, Afdhal N, Roberts SK, Bräu N, Gane EJ, Pianko S, et al. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. N Engl J Med 2015;373:2608-17.
27. Asselah T, Kowdley KV, Zadeikis N, Wang S, Hassanein T, Horsmans Y, et al. Efficacy of glecaprevir/pibrentasvir for 8 or 12 weeks in patients with HCV genotype 2, 4, 5, or 6 infection without cirrhosis. Clin Gastroenterol Hepatol 2018;16:417-26.
28. Zeuzem S, Foster GR, Wang S, Asatryan A, Gane E, Feld JJ, et al. Glecaprevir-pibrentasvir for 8 or 12 weeks in HCV genotype 1 or 3 infection. N Engl J Med 2018;378:354-69.
29. Morse A, Barritt AS IV, Jhaveri R. Individual state hepatitis C data supports expanding screening beyond baby boomers to all adults. Gastroenterology 2018;154:1850-1.