

# Risk of liver transplant in treated versus untreated hepatitis C

Ems D<sup>1</sup>, Racsa P<sup>1</sup>, Anderson C<sup>2</sup>, Gregory F<sup>2</sup>, Worley K<sup>1</sup>

1. Comprehensive Health Insights, Humana Inc., Louisville, KY; 2. Humana Pharmacy Solutions, Humana, Inc. Louisville, KY.

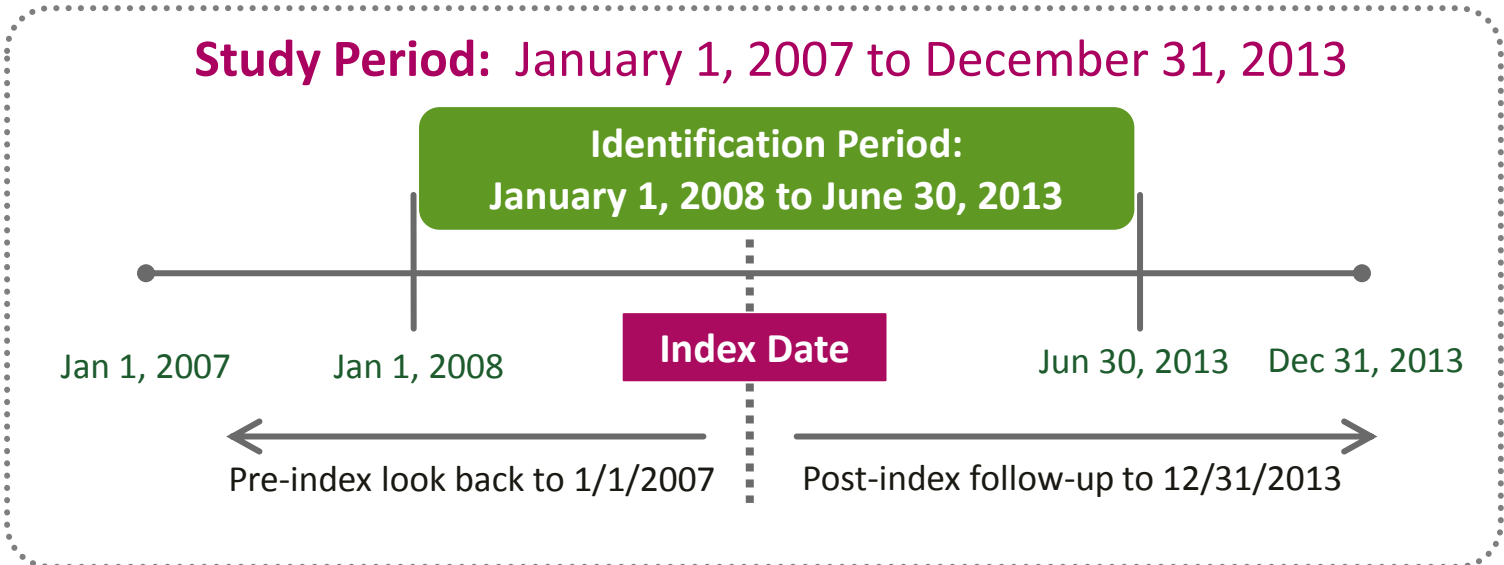
## Background

Liver failure is a major health issue, resulting in over 700,000 deaths annually.<sup>1</sup> In 2014, there were 5,723 liver transplants in the United States (US), with total per patient billed charges of over \$739,000.<sup>2</sup> Chronic hepatitis C virus (HCV) is the primary cause of liver failure leading to transplantation.<sup>1,2</sup> A recent study estimated 2.9% of patients achieving a sustained virologic response (SVR), 5.2% of those experiencing recurrent HCV after previous response, and 20.7% of non-responders had a liver transplant or died from any cause.<sup>3</sup> Achieving SVR, which has improved with the advent of newer treatment options, has been shown to reduce the risk of liver-related morbidity/mortality, all-cause mortality, and health care utilization.<sup>3-7</sup> Although there is evidence linking poor adherence with lower SVR and increased hospitalizations and costs, there is a gap in published literature examining the association between medication adherence and risk of liver transplant.<sup>8,9</sup> In addition, the impact of HCV treatment on total costs of liver transplantation is not well documented.

## Objective

To quantify liver transplant risk and mean total costs in treated versus untreated patients diagnosed with hepatitis C virus (HCV).

## Figure 1. Study Design



## Methods

- Study Design:** Observational, historical cohort study.
- Data Source:** Pharmacy and medical claims, and enrollment data, from the Humana Research Database, which is derived from approximately 17.1 million members nationwide across commercial, Medicare Advantage and prescription drug plans.
- Inclusion and Exclusion Criteria:**
- To be included, patients had to meet one of the following criteria between January 1, 2008 and June 30, 2013 (**Figure 1**):
    - At least one prescription claim for HCV treatment (boceprevir, telaprevir, ribavirin or PEG-interferon/interferon, alone or in combination )
    - At least one HCV diagnosis (ICD-9/CPT codes: V0262, 07041, 07044, 07051, 07054, 07070, 07071, G8461, G8463, 4150F, 4153F) if not treated
  - The index date was defined as either the date of liver transplant (ICD-9/CPT codes: 50.50, 50.51, 50.59, 47135, 47136), or date of first observed HCV treatment or diagnosis (if not treated).
  - Patients were then excluded for any of the following reasons:
    - Aged <19 or >89
    - Not fully insured by a commercial or Medicare plan, i.e., prescription drug coverage only
    - Hepatitis B virus (HBV) diagnosis (ICD-9/CPT codes: 070.20-070.23, 070.30-070.33, V02.61)
- Outcomes and Statistical Analyses:**
- Cox proportional-hazard regression approximated adjusted relative risk (aRR) of transplant in treated versus untreated patients, controlling for age, gender, geographic location, Deyo-Charlson Comorbidity Index, RxRisk-V Score, and pre-index medical and pharmacy costs.
    - Results were also reported by treatment adherence level based on proportion of days covered (≥80%, 50-79%, <50%).
  - Mean total costs (plan- and patient-paid) were assessed over the observation period using generalized linear models with log link and gamma distribution.

## Results

Table 1. Baseline Characteristics

	HCV			HCV and Liver Transplant		
	Untreated n=40,338	Treated n=2,708	P value	Untreated n=318	Treated n=48	P value
Age, years, Mean (SD)	58.4 (11.7)	53.8 (10.3)	<0.0001	57.0 (7.5)	55.2 (6.3)	0.12
Male Gender, No. (%)	23,447 (58.1%)	1,723 (63.6%)	<0.0001	234 (73.6%)	35 (72.9%)	0.92
*Race/Ethnicity, No. (%)			<0.0001			0.42
Caucasian	19,275 (65.0%)	1,124 (70.0%)	---	192 (78.4%)	20 (69.0%)	---
African American	4,960 (16.7%)	267 (16.6%)	---	25 (10.2%)	5 (17.2%)	---
Hispanic	713 (2.4%)	38 (2.4%)	---	6 (2.5%)	0 (0.0%)	---
Other/Unknown	4,699 (15.9%)	177 (11.0%)	---	22 (9.0%)	4 (13.8%)	---
Plan Type, No. (%)			<0.0001			0.01
Commercial	10,691 (26.5%)	1,102 (40.7%)	---	73 (23.0%)	19 (39.6%)	---
MAPD	29,647 (73.5%)	1,606 (59.3%)	---	245 (77.0%)	29 (60.4%)	---
Rx Risk-V Comorbidity Score, Mean (SD)	5.0 (3.1)	4.3 (2.9)	<0.0001	4.7 (4.0)	3.1 (3.4)	0.01
Deyo-Charlson Comorbidity Index, Mean (SD)	1.0 (2.0)	0.7 (1.9)	<0.0001	2.8 (3.3)	1.8 (2.7)	0.05
Pre-Index All-Cause Healthcare Costs, Mean (SD)	\$3,657 (35,015)	\$7,073 (56,943)	<0.0001	\$18,156 (141,411)	\$7,823 (21,392)	0.61
Pre-Index Eligibility, months, Mean (SD)	11.9 (18.0)	9.7 (16.2)	<0.0001	13.4 (20.4)	9.5 (19.9)	0.22
Post-Index Eligibility, months, Mean (SD)	14.0 (14.4)	15.1 (13.4)	0.0002	19.0 (17.0)	17.1 (16.7)	0.46
*Medicare only SD=standard deviation						

Table 3. Cost Differences Between Treated and Untreated Patients Receiving a Liver Transplant

Total mean healthcare costs were significantly higher for liver transplant patients who received HCV treatment vs. untreated.

	Transplanted, Untreated n=318	Transplanted, Treated n=48	P value	
	Mean	Mean	Unadjusted	Adjusted
Total Healthcare Costs	\$141,616	\$237,949	0.001	<.0001
Medical	\$122,362	\$165,393	0.10	0.03
HCV Related	\$78,842	\$122,138	0.04	0.03
Non-HCV Related	\$43,520	\$43,254	0.91	0.83
Pharmacy	\$20,999	\$72,557	<.0001	<.0001
Index (1st) HCV Product	-	\$28,162	-	-
Non-index (2nd) HCV Product	-	\$7,810	-	-
Non-index, Non-HCV Product	\$20,999	\$36,585	0.002	<.001

Figure 2. Risk of Transplant by Adherence Level

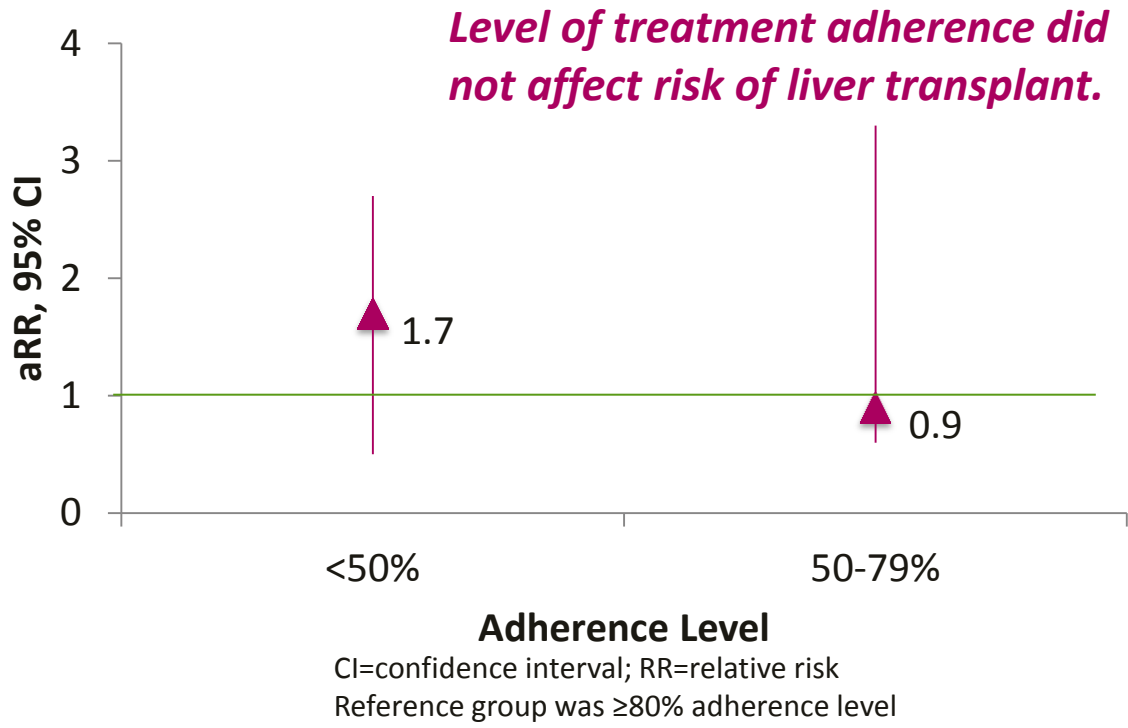


Table 2. Risk of Transplant by Treatment Status

	Total N	Liver Transplant, N (%)	aRR of Liver Transplant	P value (adjusted)
Treated	2,708	48 (1.77)	1.01	0.56
Untreated	40,338	318 (0.79)	1.00	-----
There were no significant differences in liver transplant risk according to treatment status.				

## Conclusions

- Despite adjusting for covariates, there was no evidence that HCV treatment reduced the risk of liver transplant, suggesting that treated patients may be sicker and have unmeasured confounders.
- Within the treated group, there was no change in risk of liver transplant by level of treatment adherence, underscoring the need for further evidence on liver transplant outcomes.
- HCV-treated patients who required a liver transplant incurred significantly higher total healthcare costs than those who did not receive treatment for HCV prior to transplant.

## References

- Vilariño S, Liffon RP. Liver Transplantation: from inception to clinical practice. *Cell*. Sep 2012;150(6):1096-1099.
- Bentley TS. 2014 U.S. organ and tissue transplant cost estimates and discussion. Milliman Research report. 2014. Available at [http://www.milliman.com/insight/research/health/2014-U\\_S\\_-organ-and-tissue-transplant-cost-estimates-and-discussion](http://www.milliman.com/insight/research/health/2014-U_S_-organ-and-tissue-transplant-cost-estimates-and-discussion). Accessed on March 3, 2014.
- Morgan T, Ghany M, Kim H, Snow K, Shiffman M, De Santo J, et al. Outcome of sustained virological responders with histologically advanced chronic hepatitis C. *Hepatology*. September 2010;52(3):833-844.
- Manos MM, Darbinian J, Rubin J, et al. The effect of hepatitis C treatment response on medical costs: a longitudinal analysis in an integrated care setting. *Journal of managed care pharmacy: JMCP*. Jul-Aug 2013;19(6):438-447.
- Singal, A, Volk M, Jensen D, Di Bisceglie A, Schoenfeld P. A sustained viral response is associated with reduced liver-related morbidity and mortality in patients with hepatitis C virus. *Clin Gastroenterol Hepatol*. March 2010;8(3):280-288.
- Backus L, Boothroyd D, Phillips B, Belperio P, Halloran J, Mole L. A sustained virologic response reduces risk of all-cause mortality in patients with hepatitis C. *Clin Gastroenterol Hepatol*. June 2011;9(6):509-516.
- Younossi Z, Singer M, Mir H, Henry L, Hunt S. Impact of interferon free regimens on clinical and cost outcomes for chronic hepatitis C genotype 1 patients. *J Hepatol*. Mar 2014;60(3):530-537.
- Lo Re III V, Amorosa V, Localio A, O'Flynn R, Teal V, Dorey-Stein Z, et al. Adherence to hepatitis C virus therapy and early virologic outcomes. *Clin Infect Dis*. Jan 2009;48(2):186-193.
- Mitra D, Davis K, Beam C, Medjedovic J, Rustgi V. Treatment patterns and adherence among patients with chronic hepatitis C virus in a US managed care population. *Value in Health*. Nov 2010;13:479-486.

