

Absenteeism and Productivity Among Employees Being Treated for Hepatitis C

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The hepatitis C virus (HCV) is a major cause of chronic liver disease in the United States and worldwide. According to the Centers for Disease Control and Prevention, HCV infection is the most common chronic blood-borne viral infection in the United States.^{1,2} Based on the Third National Health and Nutrition Examination Survey (1988-1994), 3.9 million Americans, 1.8% of the total population, have been infected with HCV; and 2.7 million Americans are chronically infected and likely to progress to a more advanced disease.² Globally, about 170 million people are chronically infected by this virus, with 3 to 4 million new infections expected each year.³ Unlike hepatitis B infection, no vaccine is currently available to prevent HCV infections.⁴

Chronic HCV infection develops in 80% of acutely infected patients. With an incubation period ranging from 15 to 150 days, acute HCV infections commonly present with symptoms of fatigue and jaundice. However, the majority of HCV cases (60%-70%) are asymptomatic, including those that develop into chronic infections. Chronic infection results in the development of cirrhosis in between 10% and 20% of these patients, with liver cancer developing in between 1% and 5% of this population over a period of 20 to 30 years.³ HCV is estimated to cause 10,000 to 12,000 deaths annually in the United States.⁴ Wong and colleagues⁵ project as many as 16,500 deaths per year in the United States, with 27,200 total deaths from liver cancer alone between 2010 and 2019. Additionally, this model estimates 1.83 million years of life lost, with a total direct medical cost of 10.7 billion dollars and a US societal cost of premature mortality for those younger than 65 years of \$54.2 billion.⁵ Furthermore, the prevalence of HCV is increasing in some populations.⁶

HCV-infected patients have been reported to experience a lower health-related quality of life compared with the general population.⁷⁻⁹ Symptomatic HCV infection adversely impacts psychological well-being, functional health status, and general health perception of those afflicted.¹⁰ Cognitive impairment or “difficulty in thinking” has been described in approximately one-third of chronic HCV patients, independent of liver function status.¹¹ Work performance and productivity may also be diminished in these patients.^{12,13}

The majority of HCV patients in the United States are infected with genotypes 1a or 1b and treatment guidelines are genotype specific.

The current standard of care for chronic HCV infection is a combination of peginterferon plus ribavirin.^{4,14} Generally, genotype 1 infection requires higher dosages and more pro-

Objectives: To compare productivity, absence days, and absence costs for treated (HCV-Tx) and untreated (HCV-NoTx) US employees with hepatitis C virus (HCV) infection.

Study Design: Retrospective database study.

Methods: Employee records from multiple large employers in the United States with data about demographics, jobs, and healthcare use in the Human Capital Management Services database were assessed. HCV subjects were identified by *International Classification of Diseases, 9th Revision* codes. To test differences between cohorts, *t* tests and χ^2 tests were used. Regression modeling was used to compare absence days, costs, and objectively measured productivity, while controlling for confounding factors. For HCV-Tx employees, the index date was the date of the first treatment with interferon, peginterferon, and/or ribavirin. For HCV-NoTx employees, the index date was the average date by company among HCV-Tx employees. Absence and productivity were measured from each employee's index date to the last date the employee was enrolled in health benefits coverage.

Results: A total of 441 HCV-Tx and 1223 HCV-NoTx employees were evaluated. HCV-Tx workers had 0.52 more total monthly absence days and \$31.31 in additional monthly absence payments per employee than untreated employees. Treated employees' productivity was lower, with treated subjects processing 11.7% fewer units per hour and 17.4% fewer units per month than untreated employees.

Conclusions: This study quantified the substantial indirect burden of illness associated with use of current HCV treatments. New treatments are needed with improved adverse effect profiles that result in reduced absence from work and improved productivity among HCV-infected persons.

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Take-Away Points

United States employees with hepatitis C infection who did and did not undergo treatment were compared on productivity, absence days, and absence costs.

- Patients using existing medications for hepatitis C had increased absenteeism and higher indirect costs.
- As new agents become available, the impact of these agents needs to be considered, in terms of both direct and indirect costs.

Force (139.2 million) in terms of age and sex, and has been used in prior published research.²³⁻²⁵ Confidentiality and anonymity of subject-level data in this study were maintained in accordance with Health Insurance Portability and Accountability Act guidelines.²⁶

longed therapy than genotypes 2 or 3. Response to treatment is considered “sustained” if HCV remains undetectable for 6 months or longer after the completion of therapy.⁴ Relapses and the long-term sequelae associated with disease progression are rare at this point.⁴ It must be noted that this combination treatment is associated with significant and often dose-limiting adverse events and has been documented to negatively affect both patients’ quality of life and worker productivity using validated scales in randomized controlled clinical trials.^{12,13} Toxicity associated with ribavirin and α -interferon may require dose modification or discontinuation of therapy in 2% to 10% of patients.^{14,15}

Prior research on outcomes of HCV infection is limited, especially from the employer’s perspective.^{12,16} Little has been reported on the impact of HCV infection on productivity and the incremental impact of treatment on productivity outside of the randomized clinical trial setting.¹² Recently, Su et al¹⁶ compared controls without HCV with HCV-infected workers and found that those with HCV had lower productivity and more absence days. Reduced worker productivity due to treatment side effects during therapy has also been reported.^{12,13} Other prior studies comparing treated and untreated HCV populations have been based on small sample sizes,¹⁷ persons coinfecting with HIV,¹⁸ specialty populations such as Veterans Affairs patients,¹⁹ or individuals with substance abuse issues.²⁰⁻²²

The goal of this study was to assess the impact of HCV treatment with interferon, peginterferon, and/or ribavirin on absenteeism (lost time and costs associated with workforce absenteeism) and on worker productivity using objectively captured data from an employed population.

METHODS

This retrospective study was based on longitudinal data from the Human Capital Management Services Research Reference Database (HCMS RRDb) of multiple, geographically diverse, US-based employers. The HCMS RRDb contains adjudicated health insurance and prescription drug claims, with demographics and payroll information from more than 670,000 employees over the period from 2001 to 2008. The HCMS RRDb is representative of the 2004 US Employed Civilian Labor

Study Groups

Using medical insurance claims data, the following *International Classification of Diseases, 9th Revision (ICD-9)* codes were used to identify employees with HCV: 070.41 (acute hepatitis C with hepatic coma), 070.44 (chronic hepatitis C with hepatic coma), 070.51 (acute hepatitis C without mention of hepatic coma), 070.54 (chronic hepatitis C without mention of hepatic coma), or 070.7x (unspecified viral hepatitis C). Employees in the treatment group (HCV-Tx) were those with HCV and 1 or more prescriptions for interferon, peginterferon, and/or ribavirin. These employees were compared with HCV-infected employees who did not receive interferon, peginterferon, and/or ribavirin treatment (HCV-NoTx).

Analyses focused on the time after each subject’s index date. For the HCV-Tx cohort, the index date was defined based on the start of therapy. Because the nontreated cohort (HCV-NoTx) did not receive therapy, the index date was defined as the average index date (by company) of the HCV-Tx cohort.

Subjects in both cohorts were required to be more than 18 years old on their index date, to have a minimum of 1 month of continuous health plan enrollment after their index date, and to be retained as employees to the last date of health plan enrollment.

Outcome Measures

Outcomes included monthly average health-related work absences (absenteeism or lost time) due to sick leave, short- and long-term disability, and workers’ compensation; payments for indirect costs for health-related work absences (due to sick leave, short- and long-term disability, and workers’ compensation); and presenteeism based on electronically measured work output data (in the form of number of units of work performed per person per day and number of hours worked per day) converted to hourly productivity (number of units of work performed per hour worked) and monthly productivity (number of units of work performed per month). Sick leave time and costs were drawn from the payroll data, short- and long-term disability time and costs data came from the individual disability insurance carriers, and workers’ compensation time and costs were obtained from workers’ compensation claims data. Because the data spanned several years, all cost variables were inflated to 2007 dollars prior to the analysis using nonseason-

Table 1. Descriptive Statistics and Comparisons Between Cohorts

Variable	HCV Employees With Treatment		HCV Employees Without Treatment		Difference	P ^a
	No.	Mean (SE) or Percentage	No.	Mean (SE) or Percentage		
Age, y ^b	441	46.25 (0.31)	1223	45.54 (0.22)	0.71	.0638
Tenure, y ^b	441	10.54 (0.39)	1223	9.90 (0.23)	0.64	.1571
Annual salary ^c	441	\$48,176 (\$1118)	1219	\$50,237 (\$761)	-\$2061	.1279
Female	441	35.4%	1223	38.2%	-2.8%	.2958
Married ^c	409	57.7%	1145	50.2%	7.5%	.0093
White	336	64.6%	943	52.9%	11.7%	.0002
Black	336	14.6%	943	12.7%	1.9%	.3878
Hispanic	336	10.7%	943	8.8%	1.9%	.3001
Exempt ^c	441	20.6%	1223	26.2%	-5.6%	.0192
Full time ^c	441	93.4%	1223	93.3%	0.1%	.9259
Charlson Comorbidity Index score ^d	441	0.687 (0.688)	1223	0.671 (0.042)	0.016	.8451

HCV indicates hepatitis C virus; SE, standard error.
^aSignificant differences ($P < .05$) are boldfaced.
^bAt index date.
^cFrom the most recent postindex data available.
^dOver the 12-month period immediately following the index date.

ally adjusted Consumer Price Indices for medical services, prescription drugs, and all consumer goods.²⁷

Statistical Analyses

Differences in descriptive characteristics between the HCV-Tx and HCV-NoTx cohorts were compared using student *t* tests for continuous variables and χ^2 tests for discrete variables ($P \leq .05$ for statistical significance).

Because of the nonnormal distributions of the data, 2-part multivariate regression models²⁸ were used for comparisons of health benefit costs and health-related work absences between the HCV-Tx and HCV-NoTx cohorts. For example, in the cost models, logistic regression was first used to predict the likelihood of subjects having any costs (part 1). Generalized linear models were used with a gamma distribution and a log link function to model costs for subjects with more than zero costs in the second part of the model. The estimated probability of having positive cost (found from the logistic regression model) was multiplied by the estimated mean cost for persons with positive cost (found from the generalized linear model) to produce an estimated mean cost for all employees in each cohort.²⁸ Only employees eligible for a specific work absence benefit were included in regression models for that benefit.

Productivity data for subjects used in this analysis were available only for a subset of the HCMS RRDb (those with values provided for number of units processed per hour). The analysis allowed for examination of productivity while at work (hourly productivity). The at-work productivity analyses were performed using only the second-part regression

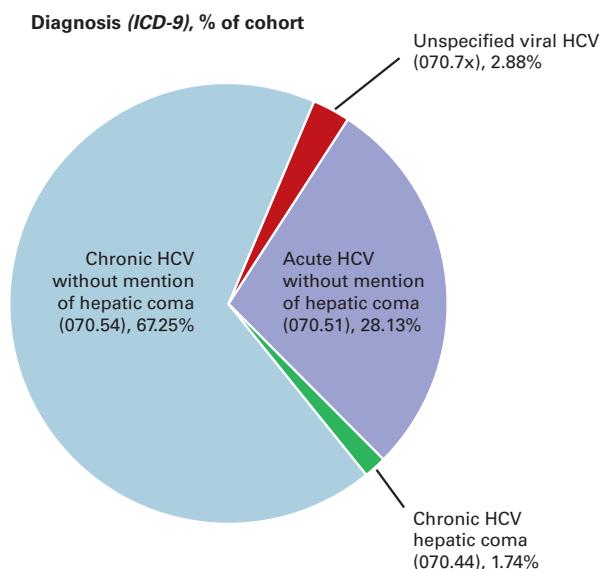
modeling described above. Subjects with hourly productivity values below the first percentile or above the 99th percentile were removed (0 employees with treatment and 1 employee without treatment) from the hourly productivity model, and subjects with monthly productivity values below the first percentile or above the 99th percentile were removed (1 employee with treatment and 1 employee without treatment) from the monthly analysis.

Separate regression models were run on the following productivity-, cost-, and absence-dependent variables: hourly productivity, monthly productivity, sick leave cost, short-term disability cost, long-term disability cost, workers' compensation cost, sick leave days, short-term disability days, long-term disability days, and workers' compensation days. In each case, the multivariate regression models controlled for the impact of confounding factors such as age, sex, marital status, race, exempt/nonexempt status, full-time/part-time status, salary, region, the Charlson Comorbidity Index score (a risk-adjusting score built from claims data indicators of serious comorbid conditions that are predictive of mortality²⁹), and the number of months of eligibility after the index date. All models and statistics were generated via version 9.1 of the SAS System for Windows (SAS Institute Inc, Cary, North Carolina).

RESULTS

The analysis identified 1664 employees with HCV: 441 employees (26.5%) with treatment (HCV-Tx) and 1223 employees (73.5%) without treatment (HCV-NoTx). **Table 1**

■ **Figure 1.** Cohort Inclusion Criteria by ICD-9 Classification^a



HCV indicates hepatitis C virus; ICD-9, *International Classification of Diseases, 9th Revision*.

^aNo subjects in the study were identified as having acute HCV with hepatic coma (ICD-9 code 070.41).

shows descriptive statistics for both cohorts. Both groups were similar ($P > .05$) in average age (about 46 years); had a mean tenure (time with current employer) close to 10 years; earned about \$50,000 in salary; were about one-third female; had similar regional dispersion; and had similar Charlson Comorbidity Index scores. The treated population was 7.5% more likely to be married, 11.7% more likely to be white, and 5.6% less likely to be exempt employees (those not eligible for overtime pay).

Figure 1 shows that most of the subjects with HCV did not have mention of hepatic coma and were classified as chronic (67.25%) or acute (28.13%).

Comparisons of Absence and Health Benefit Costs

Treated employees (HCV-Tx) had 0.52 more health-related work absence days than those in the HCV-NoTx cohort, missing an average of 1.27 workdays monthly, while employees without treatment missed 0.75 days per month (**Figure 2**). Most of the additional time lost by employees with treatment occurred under the long-term disability benefit and most lost-time differences were significant ($P < .05$), except the difference in short-term disability days (0.46 vs 0.31, $P = .0758$).

Analysis of indirect costs due to absences found that treated employees (HCV-Tx cohort) incurred significantly greater expenditures for sick leave ($P < .0001$) and short-term disability ($P = .0309$), but nonsignificantly lower costs for long-term disability ($P = .7200$) and workers' compensation ($P = .1437$) (**Table 2**). Mean monthly total indirect costs per treated em-

ployee were \$31.31 greater than those for employees without treatment.

Objective Productivity Measurements

The analysis identified 94 employees with HCV and objective productivity data: 31 employees (33%) with treatment (HCV-Tx) and 63 employees (67%) without treatment (HCV-NoTx). **Table 3** shows descriptive statistics for both subcohorts, which were similar ($P > .05$) in all metrics.

Table 4 displays the objectively measured productivity comparison of units processed per hour worked and units processed per month (with 95% confidence limits). Treated HCV employees averaged 11.7% fewer units processed per hour worked than those without treatment, but this difference was found to be nonsignificant ($P = .2001$). The difference in units processed per month (17.4% fewer units for employees with treatment) was also nonsignificant ($P = .2069$).

DISCUSSION

Published studies of indirect costs and health-related work absences for treated persons with HCV are limited. Few studies report costs or lost time, and most are based on patient self-reports. Based on observational employee data, employees with HCV infection were shown to have more total absence days per employee, lower productivity, and significantly elevated overall health benefit costs compared with noninfected employees.¹⁶

Currently available treatments have a considerable impact on employed HCV patients. Pharmacologic management of HCV may cause significant adverse reactions during the treatment period, resulting in reduced work productivity and performance. McHutchison et al¹³ found a significant number of subjects had decreased worker productivity during therapy based on self-reported data (46% of sustained responders and 59% of nonresponders). Using the Work Productivity and Activity Impairment questionnaire, Perrillo et al¹² reported that despite baseline similarities, patients randomized to peg-interferon (the less toxic treatment) showed less impairment than the group treated with interferon plus ribavirin across all measures of work functioning and productivity at each visit ($P < .05$).

Studies following patients after completion of treatment report improved health-related quality of life and work functioning and productivity.^{8,13} Davis et al⁸ found significant ($P \leq .05$) improvement in work, sleep and rest, and recreation and pastimes scores following treatment with interferon α -2b. Numerical improvement was observed in total score, physical and psychosocial dimension scores, and most individual category scores. Mean Sickness Impact Profile scores were

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unchanged or slightly worsened in untreated control patients.

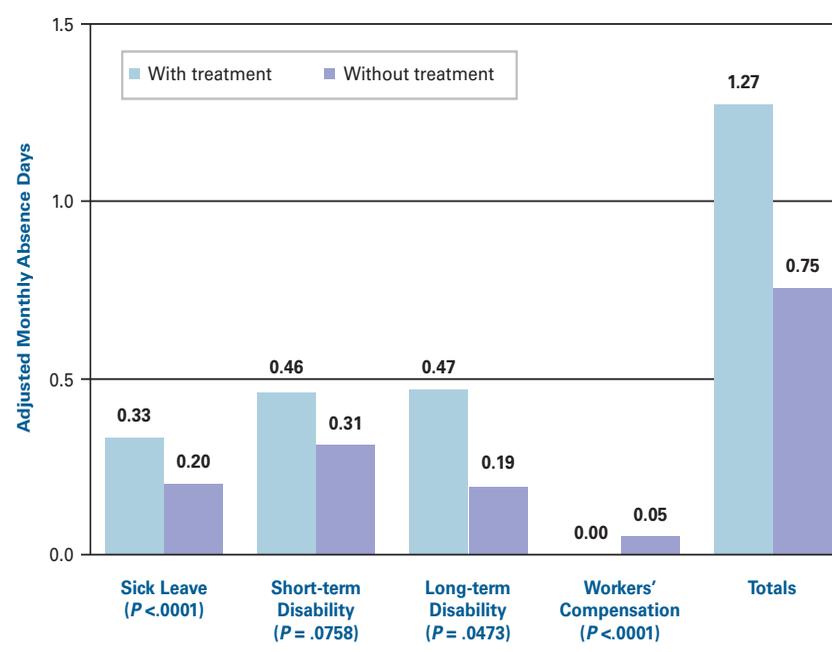
The current analysis used a comprehensive source of data that included medical and pharmaceutical claims as well as productivity data and employee benefit claims for sick leave, short- and long-term disability, and workers' compensation. As such, it adds to the limited literature on the impact of treatment for HCV—in particular, treatment of the employed population with HCV. Access to such a population database uniquely permits an analysis of indirect costs and absences associated with treatment of a medical condition. Present results indicate that HCV-infected employees who receive treatment incur higher absences and indirect costs and have more time lost in nearly every outcomes measure identified when compared with HCV-infected employees who do not receive treatment.

With the exception of workers' compensation, all absence categories in the current study were higher in the treated cohort than in the nontreated cohort. Indirect costs for sick leave and short-term disability were significantly higher for the treated population, whereas costs for long-term disability and workers' compensation were nonsignificantly higher for the nontreated population. Long-term disability absences were higher for the treated population and long-term disability costs were lower—probably reflecting differences in the salaries for the subjects. While an absence day is constant across all subjects, the absence payments are impacted by salary and benefit designs. Although Table 2 shows no workers' compensation absence days for the treated cohort,

this was due to rounding, as there were actually 0.0038 workers' compensation absence days for the treated and 0.0466 days for the nontreated populations. These minimal absence days and the inclusion of workers' compensation medical payments contributed to the workers' compensation costs (Table 3).

A major strength of the current study is the utilization of the 2-part multivariate regression methodology, which enabled examination of the adjusted probabilities of having more than zero costs or absences and subsequently focused on those employees who had more than zero costs or absences. This methodology also has advantages (compared with matched case-control analysis) in quantifying the impact

Figure 2. Adjusted Monthly Absence Days for HCV-Infected Employees With and Without Treatment



HCV indicates hepatitis C virus.

Table 2. Monthly Absence Costs for HCV-Infected Employees With and Without Treatment^a

Absence Cost Category	HCV Employees With Treatment		HCV Employees Without Treatment		Difference	P ^b
	No.	Adjusted Mean Cost	No.	Adjusted Mean Cost		
Sick leave	220	\$53.53	491	\$34.32	\$19.21	<.0001
Short-term disability	249	\$55.16	691	\$33.33	\$21.83	.0309
Long-term disability	369	\$11.98	994	\$13.88	-\$1.90	.7200
Workers' compensation	408	\$22.34	1086	\$30.17	-\$7.83	.1437
Total absence costs		\$143.01		\$111.70	\$31.31	

HCV indicates hepatitis C virus.

^aOnly employees eligible for each specific benefit were included in the regression models for that benefit.

^bSignificant differences ($P < .05$) are boldfaced.

■ **Table 3.** Descriptive Statistics for Productivity Data Subset of HCV-Infected Employees With and Without Treatment

Variable	Mean (SE) or Percentage		Difference	P ^a
	HCV Employees With Treatment (n = 31)	HCV Employees Without Treatment (n = 63)		
Age, y ^b	44.00 (1.03)	46.21 (0.73)	-2.21	.0854
Tenure, y ^b	10.39 (1.09)	11.51 (0.81)	-1.12	.4213
Annual salary ^c	\$34,946 (\$720)	\$34,482 (\$539)	\$464	.6152
Female	19.4%	14.3%	5.1%	.5281
Married ^c	67.7%	66.7%	1.1%	.9170
White	80.6%	71.4%	9.2%	.3353
Black	9.7%	11.1%	-1.4%	.8322
Hispanic	6.5%	14.3%	-7.8%	.2666
Full time ^c	87.1%	77.8%	9.3%	.2803
Charlson Comorbidity Index score ^d	0.484 (0.160)	0.413 (0.125)	-2.21	.0854

HCV indicates hepatitis C virus; SE, standard error.
^aAll differences are nonsignificant ($P > .05$).
^bAt index date.
^cFrom the most recent postindex data available.
^dOver the 12-month period immediately following the index date.

of each confounding factor on the dependent variable being modeled. Two-part multivariate regression methodology is also more appropriate for data that are not normally distributed. As such, the incremental monthly absence cost difference of \$31.31 from the combined model, comparing treated and nontreated HCV cohorts, is the relevant cost for treatment decisions regardless of health utilization behaviors. Removing the outliers from the productivity models is consistent with prior work¹⁶ and limited the possibility that a few employees were in a situation that enabled them to produce at a much higher or lower rate for which we may not have been able

to control and made the results more precise, but not significant. While the study controlled for the number of months of eligibility, the treated subjects had a significantly lower mean of 16.7 months of data compared with 19.9 months for the nontreated subjects ($P < .0001$).

Other limitations of this study include the retrospective database analysis design that lacks information on genotype or disease severity.³⁰ A Pareto-based subanalysis of the populations is available in **eAppendices A and B** at www.ajmc.com. Also, entry into the study was restricted to individuals with ICD-9 diagnosis codes of HCV, and the findings may not be

■ **Table 4.** Objective Hourly and Monthly Productivity Output^a of HCV-Infected Employees With and Without Treatment, During the Eligibility Period After Each Person's Index Date^b

Variable	HCV Employees With Treatment	HCV Employees Without Treatment	Difference	P ^c
No.	31	62		
Adjusted units processed per hour (SE)	13.52 (1.11)	15.32 (0.86)	-1.80	.2001
95% Lower confidence limit	11.34	13.64		
95% Upper confidence limit	15.70	17.00		
No.	30	62		
Adjusted units processed per month (SE)	1734 (226)	2100 (182)	-366	.2069
95% Lower confidence limit	1291	1742		
95% Upper confidence limit	2176	2457		

HCV indicates hepatitis C virus; SE, standard error.
^aProductivity output measurements came from real worker output data. These data provided the number of units processed (units of work performed) for each employee on a daily basis.
^bProductivity output measurements were taken during the eligibility period following the employee's index date.
^cDifferences in adjusted units processed per hour and month were not statistically significant ($P > .05$).

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representative of persons with HCV who are not diagnosed, who are misdiagnosed, or who do not have a diagnosis in their medical records. The treatments received by the individuals in this analysis were all interferon based. Although we did not investigate the differential impact of pegylated interferon versus regular interferon-based regimens, the observation period for this population (2001-2008) covered a substantial period of time after pegylated interferon was initially approved for use in the United States (peginterferon alfa-2b in January 2001 and peginterferon alfa-2a in October 2002). The economic burden of undiagnosed and untreated HCV may be greater than it is among those who have a formal diagnosis and receive an appropriate intervention.

The extended study duration may be considered a limitation, as both the American Association for the Study of Liver Diseases guidelines¹⁴ and NIH consensus statements³¹ only report on therapy through the end of 48 weeks (~1 year) and the longer study period may dilute the impact of therapy on some metrics.

This analysis found that treated HCV employees have greater indirect costs (salary replacement costs for absences) in the short term than HCV employees without treatment. However, the present research also quantifies the cost burden of treatment and provides insight to guide employer decision making regarding interventions aimed at managing these patients in a cost-effective manner. It remains for future research to determine the impact of treatment on study outcomes using a pre/post design.

CONCLUSIONS

In conclusion, the present approach found that current HCV treatment is associated with increased employee absences and indirect costs. Emerging therapies that potentially minimize treatment durations and treatment-related side effects will likely have an impact on the costs and need to be evaluated as the treatment standards evolve. The evolving treatment regimens should seek to maintain or improve the mortality gains of the current regimens, while improving on the quality of life of the treated patients and ultimately reducing the associated indirect costs. The results presented here provide employers, insurers, and clinicians with the incentive to work together to develop programs and make treatment choices that more effectively manage patients' healthcare and drug treatment needs, and maintain their work productivity.

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