Incidence and Cost of Treatment-Emergent Comorbid Events in an Insured Population Receiving Treatment for Chronic Hepatitis C (CHC) Virus Infection

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Background and Objectives

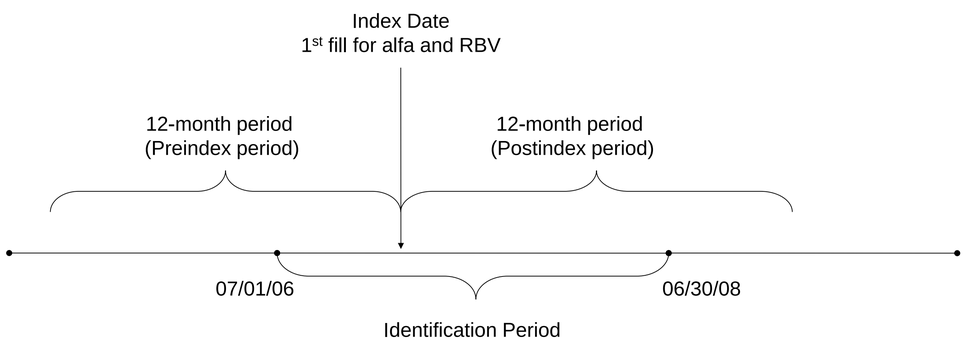
- Chronic hepatitis C (CHC) virus infection, with a worldwide prevalence of 2%-3%,[1] causes substantial loss of life and reduces quality of life in those who are infected.[2]
- For patients with CHC genotype 1, 48 weeks of pegylated interferon alfa (PEG-alfa) and ribavirin (RBV) is the standard treatment, whereas in patients with genotypes 2 and 3, 24 weeks is adequate.
- Patients who are able to maintain at least 80% adherence to their drug regimen have the highest likelihood of achieving sustained virologic response, but treatment-emergent comorbid events commonly limit adherence.[3-5]
- 47.4% -77.5% of patients discontinue therapy prematurely in clinical care settings.[6-8]
- Despite their frequency and affect on treatment, little is known about the cost associated with these adverse events.[9]

The objective of this study was to estimate the incidence of treatment-emergent comorbid events and the incremental costs of treating these events in insured patients initiating PEG-alfa and RBV treatment for CHC.

Methods

- Retrospective cohort analysis of healthcare claims from the i3 Ingenix LabRx database.
- Inclusion criteria: Treated with alfa/RBV during the identification period; AND ≥1 medical claim with an ICD-9 -CM code for CHC (070.41, 070.44, 070.51, 070.54, 070.7x) during the preindex period; AND initial prescription for both drugs filled within 14 days of one another.
- Exclusion criteria: <18 years of age; not continuously enrolled during the entire study period; not a new start or a therapy started at nonrecommended dose; diagnosis of other condition for which these drugs may have been used (e.g., hepatitis B, Hodgkin's lymphoma, multiple myeloma).
- Index date was the date of first fill for alfa/RBV within the identification period. Twelve months before was defined as the preindex period, and 12 months after was the postindex period.
- Treatment-emergent comorbid events were defined as a medical claim with a diagnosis for a condition in the postindex period that was not present in the preindex period.
- Net incremental cost was calculated as the difference between preindex and postindex costs for these comorbidities and their treatments, excluding cost of alfa/RBV.
- Age, gender, region, and treatment duration were used in an exploratory multivariate model to identify factors that may be associated with these increased costs.
- Treatment duration was calculated as time to discontinuation of <u>both</u> alfa and RBV therapy for ≥60 days

Study Timeline



Results

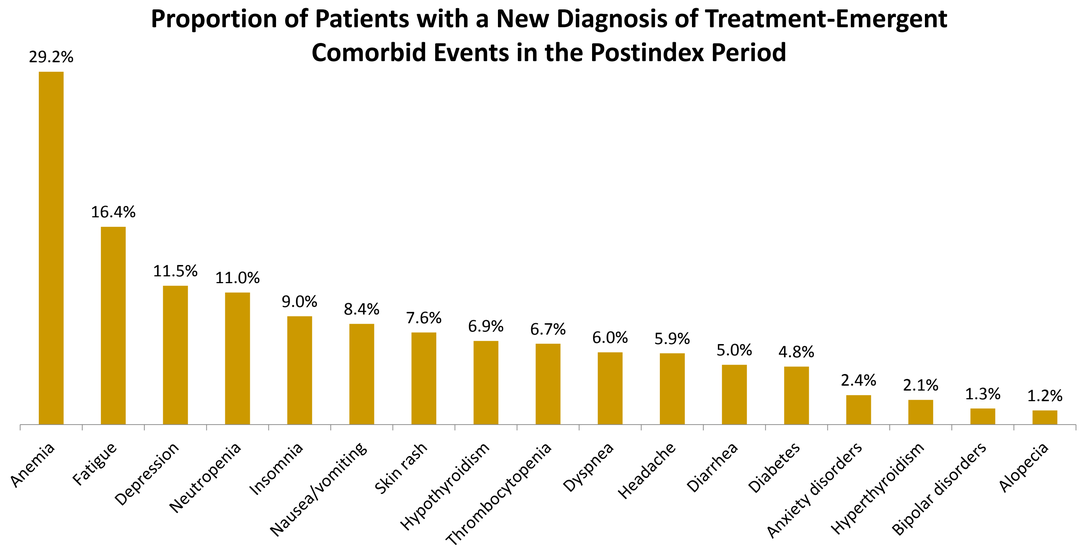
Patient Characteristics (N=1,269)

Age (y) mean (SD)	50.2 (7.7)
Age group (y) no. (%)	
18-29	31 (2.4)
30-39	61 (4.8)
40-49	405 (31.9)
50-59	675 (53.2)
60-69	91 (7.2)
70+	6 (0.5)
Female no. (%)	459 (36.2)
HIV infection no. (%)	44 (3.5)
Specialty of usual care physician no. (%)	
Gastroenterology	411 (32.4)
Family practice	362 (28.5)
Internal medicine	320 (25.2)
Infectious diseases	36 (2,8)
Other specialty*	120 (9.5)
Unknown	20 (1.6)

*All individual specialties in "Other" are <2%

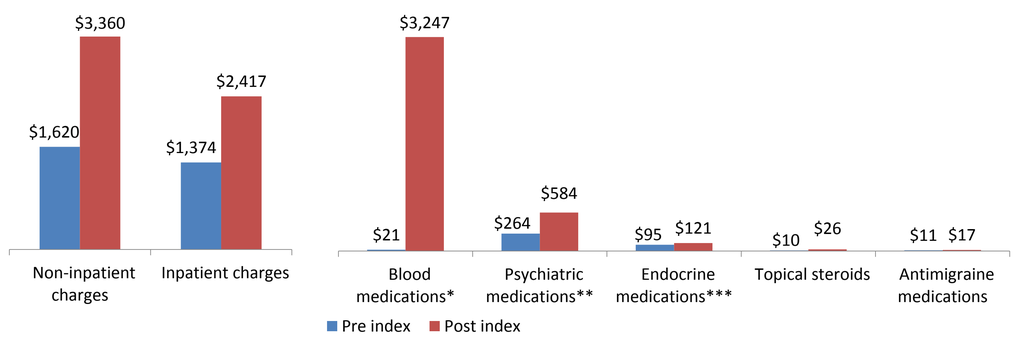
- Of 3,795 newly treated patients, 1,269 met the inclusion criteria.
- Most exclusions (2,274) were those who did not meet the continuous enrollment criteria.

Proportion of Patients with a New Diagnosis of Treatment-Emergent Comorbid Events in the Postindex Period



New treatment-emergent events were common, with 61.6% of patients having ≥1 event.

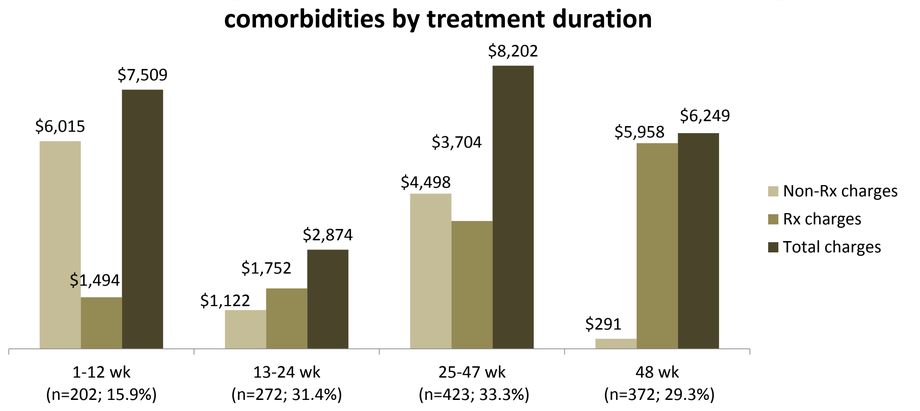
Increase in non-medication-related and medication-related charges for treatment-emergent comorbid events between preindex and postindex periods



*epoetin alfa, darbepoetin, filgrastim, and eltrombopag , **anxiolytics, antidepressants, antipsychotics/antimanics, and hypnotics, ***antidiabetes medications (including dextrose) and thyroid agents

- The mean incremental cost for treatment-emergent comorbid events in the postindex period was $6,377 (SD $22,326), $2,782 for medical and $3,595 for pharmacy claims.
- In the multivariate model, age ≥60 (P<0.01) and female gender (P<0.05) were significantly associated with higher charges .

Increase in charges from pre- to postindex for treatment-emergent comorbidities by treatment duration



Alfa/RBV charges* by treatment duration

	1-12 weeks	13-24 weeks	25-47 weeks	48 weeks**
Mean (SD)	$9,941 (8,696)	$16,249 (5,039)	$25,454 (7,753)	$41,041 (6,248)

*Total charges of alfa/RBV claims **Completed treatment

- 14.2% discontinued treatment before week 12, 32.8% before week 24. Among patients who were treated for >24 weeks (e.g., patients with genotype 1, 4, or 6), 46.8% discontinued treatment by week 48.
- Increase in non-drug-related charges were the highest ($6,015; SD 28,057) in patients who completed only 12 weeks of treatment and the lowest ($291; SD 17,308) in patients who completed the 48-week treatment.

Conclusions

- In an insured US cohort with CHC virus infection treated with alfa/RBV, treatment-emergent comorbidities are common, with anemia, neutropenia, and depression being the most common.
- Treatment-emergent comorbid events increase direct treatment costs by 25% ($6,377). This study did not assess indirect costs, and these estimates may therefore be conservative.
- The cost of treatment-emergent comorbid events may rise with the use of triple therapy (alfa/RBV and a protease inhibitor) as gastrointestinal events, skin rash, and anemia are more common with triple therapy than with alfa/RBV alone.[10]
- Our treatment discontinuation rate of 46.8% is consistent with previous estimates that range from 47.4% to 77.5%.[6-8] Dissimilarities in data sources, clinical care settings, and data analysis techniques may explain some of the differences in the treatment discontinuation estimates.
- Overall, these findings consistently indicate that a substantial proportion of patients discontinue therapy. Although we could not distinguish between patients discontinuing therapy due to adverse events and those discontinuing because of lack of virologic response, our findings support the concept that adverse events lead to therapy discontinuation.[9]
- Better-tolerated therapies that reduce healthcare system costs and improve patient experience are desirable.
- Limitations: A commercially insured population may not be representative of the entire US population nor of treatment patterns in other countries. Claims do not provide data on genotype, so patients treated beyond 24 weeks were presumed to have genotype 1, 4, or 6. Miscoding or undercoding of claims may affect the accuracy of cost estimates.

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2. Partnership for Health Analytic Research, LLC
3. Yale University School of Medicine

Word count: 297

OBJECTIVES: To estimate the incidence of treatment-emergent comorbid events and incremental costs of treating these events in insured patients initiating pegylated interferon alfa (peg-alfa) and ribavirin (RBV) treatment for CHC.

METHODS: In a retrospective cohort analysis of healthcare claims from a US insurer, we studied CHC patients newly treated with peg-alfa/RBV between 2006-2008 and continuously eligible for 12 months before/after treatment initiation. Treatment-emergent comorbid events were defined by new medical/pharmacy claims for predefined conditions in the 12 months after treatment initiation. The net incremental cost of treatment-emergent comorbidities was calculated as the difference between baseline and follow-up costs for these comorbidities and their treatment, excluding cost of peg-alfa/RBV. Baseline measures including age, gender, and region were used in a multivariate model to identify factors associated with treatment-emergent comorbid event charges.

RESULTS: Of 3,795 newly treated patients, 1,269 (mean age=50.2 [SD 7.7], 36.2% female) met the selection criteria. The mean cost of peg-alfa/RBV treatment was $25,612 (SD $13,289). New treatment-emergent events were common, with 61.6% of patients having ≥ 1 event. Anemia was identified in 29.2% of patients, fatigue in 16.4%, depression in 11.5%, and neutropenia in 10.9%. The mean incremental cost for the pre-defined treatment-emergent comorbid events in the post-index period was $6,377 (SD $22,326); $2,783 for medical and $3,595 for pharmacy claims. Age ≥ 60 and female gender were significantly associated with higher charges in the multivariate model.

CONCLUSIONS: In an insured US cohort with CHC, treatment-emergent comorbidities with peg-alfa/ RBV were common and increased cost by $6,000/treated patient. This excludes indirect costs and is therefore a conservative estimate. Costs might increase with the use of triple therapy with peg-alfa/RBV and a protease inhibitor, as additional treatment-emergent co-morbid events may be expected. Better-tolerated therapies that reduce the financial burden on the healthcare system costs and improve patient experience are desirable.

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From: "Sapra, Sandhya" <Sandhya.Sapra@bms.com>
Date: August 16, 2011 10:12:02 AM GMT-07:00
To: michael broder <mbroder@pharllc.com>
Subject: FW: ISPOR 14th Annual European Congress: Poster Presenter Reminder
FYI- see below
Gil is going so he will present

-----Original Message-----
From: Sapra, Sandhya
Sent: Tuesday, August 16, 2011 12:55 PM
To: 'stuckerson@ispor.org'
Cc: LItalien, Gilbert
Subject: RE: ISPOR 14th Annual European Congress: Poster Presenter
Reminder

Hi Steve,
Please note that I will not be able to present this poster but Dr.L'Italien (cc'ed) here and a co-author on the poster will be presenting instead.

Please let me know if you have any questions.

Thanks,
Sandhya

-----Original Message-----
From: stuckerson@ispor.org [mailto:stuckerson@ispor.org]
Sent: Thursday, August 11, 2011 5:41 PM
To: Sapra, Sandhya
Subject: ISPOR 14th Annual European Congress: Poster Presenter Reminder

To: Sandhya Sapra

Congratulations once again on the acceptance of your research abstract:

PGI1: INCIDENCE AND COST OF TREATMENT-EMERGENT COMORBID EVENTS IN AN INSURED POPULATION RECEIVING TREATMENT FOR CHRONIC HEPATITIS C (CHC) VIRUS INFECTION

for poster presentation at the ISPOR 14th Annual European Congress to be held 5-8 November 2011 at the Hotel Auditorium Madrid in Madrid, Spain.

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Best regards,

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