Medical Service Utilization and Costs by Disease Severity, Sustained Viral Response, and Genotype in European Patients with Chronic Hepatitis C Virus

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BACKGROUND

- Hepatitis C virus (HCV) is a global public health problem, affecting approximately 3% of the world's population.[1]
- Nearly three-quarters of all HCV cases progress to chronic infections.
- Commonly used treatments for chronic HCV include peginterferon alfa-2a (PEG2A) or peginterferon alfa-2b (PEG2B) plus ribavirin (R) combination therapy.
- Variations in medical service utilization and costs by important clinical factors and by treatment status have not been widely studied in real-world HCV populations in Europe.

OBJECTIVE

- To document variations in medical service utilization and costs by disease severity, sustained viral response (SVR), and genotype in a European population with chronic HCV.

METHODS

Study Design
- Retrospective abstraction of patient chart data

Data Source
- Deidentified patient charts abstracted by physicians in five European countries: United Kingdom (UK), France, Germany, Italy, and Spain.
- Physicians recruited by Kantar Health (formerly TNS Healthcare) from their Global Access Panel, one of the largest online physician panels in the world, with a membership of over 70,000 physicians worldwide.
- Chart review approach provided:
  – Detailed demographic and service utilization data not easily available in existing databases in Europe.
  – Rich clinical information (pathology reports, genotyping, and other laboratory results) that cannot be obtained from other data sources in Europe.
  – All outcomes assessed in a standardized manner across the five countries of interest.
- Cost information not available; therefore, country-specific unit cost estimates for various types of services obtained from standard cost sources.

Inclusion Criteria

Physicians
- At least 15 chronic HCV patients seen in the practice annually
- Practice experience of 2 to 35 years

Patients
- Age ≥ 18 years
- Diagnosis of chronic HCV within the past 5 years
- No evidence of hepatitis B or HIV/AIDS
- No treatment as part of randomized clinical trial
- Presence of HCV genotype information at first observed HCV diagnosis among untreated patients or at time of treatment initiation among treated patients
  – By study construct, 80% of sample received treatment with PEG2A+R or PEG2B+R
  – 20% of sample received no HCV treatment of any kind

- Presence of HCV RNA laboratory result at time of diagnosis for untreated patients or at treatment initiation (± 30 days) for treated patients
- ≥ 1 year of follow-up postdiagnosis among untreated patients or post-treatment initiation among treated patients

Study Measures
- Baseline physician and patient characteristics
- Overall (all-cause) service utilization and costs, assessed over 12 months following patients' index date, where index date is defined by first observed HCV diagnosis for the untreated group and treatment initiation for the treated group
  – Surgical and diagnostic procedures
  – Laboratory procedures (e.g., liver function test, HCV RNA tests)
  – Hospital admissions
  – Office visits to physician managing HCV
  – Office visits to general practitioner for other reasons
  – Emergency room (ER) visits
  – Specialty referrals
- Medical costs estimated by multiplying setting-specific unit costs (sourced from existing literature[2]) by number of encounters recorded

Analysis Stratification
- Viral genotype (1, 2, 3, or 4)
- Baseline disease severity, defined by Metavir score among patients with biopsy:
  – No fibrosis (Metavir = 0)
  – Mild fibrosis (Metavir = 1, 2)
  – Bridging fibrosis (Metavir = 3)
  – Cirrhosis/severe (Metavir = 4)
- Among treated group, stratified results by SVR as defined by viral RNA <10 IU/mL at ≥ 6 months post-treatment
- Treatment status (treated vs. not treated)

Statistical Analyses
- Analyses carried out using SAS® (Version 9) statistical software
- Descriptive analyses:
  – Mean values, standard deviations (SDs), medians, and ranges of continuous variables
  – Frequency distributions of categorical variables
- Multivariable analyses implemented to estimate the incremental effect of genotype, disease severity (defined by Metavir score), SVR attainment, and treatment status on service utilization and costs when other covariates are controlled
  – Types of multivariable models estimated determined by the outcome
    – Logistic regression for dichotomous outcomes (e.g., had ≥ 1 hospitalization); odds ratios (ORs) reported
    – Poisson regression for count data outcomes (e.g., number of hospitalizations); incidence rate ratios (IRRs) reported
    – Generalized linear models (GLMs) with log link and gamma distribution (for skewness adjustment) for all cost outcomes; adjusted marginal effects reported

RESULTS

Physician Characteristics
- 240 physicians (~ 48 in each country) recruited to abstract patient charts.
- Physicians in practice for 15 years on average.
- Hepatology, gastroenterology, and internal medicine were the predominant physician specialties observed, representing 22%, 30%, and 25%, respectively, of all physicians recruited.

Patient Characteristics (Table 1)
- A total of 1,016 patients (804 treated, 212 untreated) were identified (~200 per country).
- The treated group was more disproportionately male (65%) compared with the untreated group (56%).
- ~40% of both treated and untreated patients were current or past intravenous (IV) drug users; higher proportion of IV drug use seen in treated group (12% vs. 3%).

Table 1. Characteristics of the Study Sample

Characteristic	Treated	Untreated
Number of patients	804	212
Gender (n, %)		
Male	523 (65.0%)	119 (56.1%)
Female	281 (35.0%)	93 (43.9%)
Age		
Mean (SD)	45.6 (10.8)	47.5 (15.2)
Median	45	46
Range	19, 77	19, 86
Nonmissing observations (n)	759	202
Age category (n, %)		
< 18	0 (0.0%)	0 (0.0%)
18-24	15 (1.9%)	8 (3.8%)
25-34	111 (13.8%)	39 (18.4%)
35-44	237 (29.5%)	45 (21.2%)
45-54	248 (30.9%)	51 (24.1%)
55-64	114 (14.2%)	27 (12.7%)
65+	34 (4.2%)	32 (15.1%)
Unknown	44 (5.5%)	10 (4.7%)
Intravenous drug use (n, %)		
Current user	25 (3.1%)	25 (11.8%)
Past user	318 (39.6%)	58 (27.4%)
Never used	366 (45.5%)	106 (50.0%)
Unknown	95 (11.8%)	23 (10.8%)

Clinical Characteristics (Figures 1, 2, and 3)
- Genotype 1 was the most common genotype for both the treated and untreated groups in all countries (Figure 1).
  – Genotype 1 was more predominant among untreated patients, ranging from 58% of untreated patients in France to 73% of untreated patients in Italy.
  – Genotype 2 was much more common among treated patients, representing ≥ 20% of treated patients in all countries.
- Disease severity was not known for large proportion of patients in all countries, due primarily to lack of biopsies performed, particularly for untreated patients.
  – For all countries combined, of treated patients for whom biopsies were performed, 53% had mild fibrosis, 27% had bridging fibrosis, and 9% had cirrhosis (Figure 2).
  – Among untreated patients, 31% had no fibrosis, 34% had mild fibrosis, and 21% had cirrhosis (Figure 2).
- Among patients in the treated group for whom SVR was measured (N = 632 across all countries), 65% attained SVR (Figure 3).
  – SVR rates ranged from 56% in the UK to 71% in Italy.
  – SVR rates were substantially higher for patients with genotypes 2 and 3 (~70%-80% across countries) compared with genotypes 1 and 4 (~35%-60%).

Figure 1. Baseline Viral Genotype (N = 1,016)
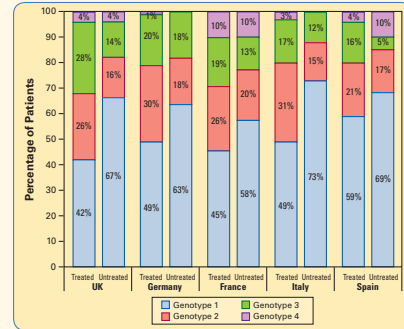
Figure 2. Baseline Disease Severity (N = 306)
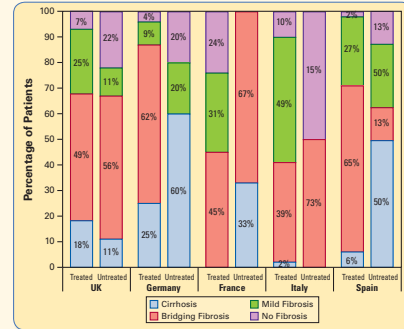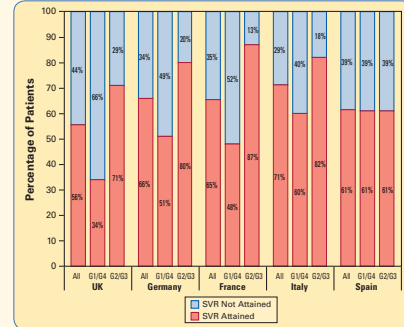
Figure 3. SVR Attainment (N = 632)
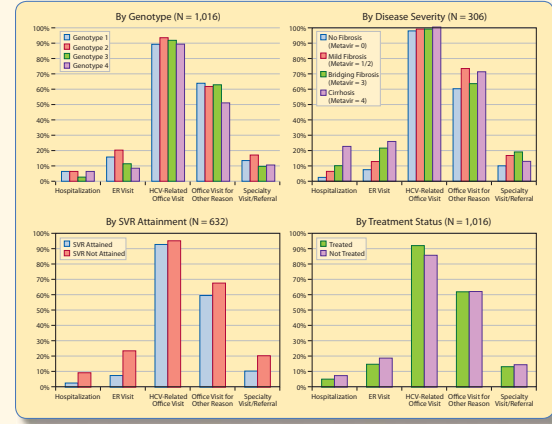
G1, G2, G3, and G4 = genotype 1, 2, 3, and 4, respectively. Genotypes 1 and 4 (G1/G4) and genotypes 2 and 3 (G2/G3) were grouped together.

Medical Service Utilization (Figure 4)
- Hospitalization, ER, HCV-related office, and specialty visit rates were slightly higher for genotype 2; otherwise, no clear resource use pattern was found by genotype.
- Resource utilization, particularly hospitalization and ER visits, generally increased with disease severity.
- Hospitalization, ER, and specialist visit rates were substantially lower for SVR attainers.
- Hospitalization and ER rates were somewhat higher for untreated patients.

Figure 4. Percentage of Patients with Service Utilization

Unadjusted Medical Service Costs (Table 2)
- For most service categories, costs were substantially higher in patients with cirrhotic disease and in patients who did not attain SVR.

Table 2. Unadjusted All-Cause Medical Service Costs (2009 €) per Patient, by Genotype, Disease Severity, SVR Status, and Treatment Status

	Hospitalizations		ER Visits	HCV-Related Office Visits	General Office Visits	Specialty Office Visits
	All Patients	Patients with Hospitalization				
Genotype (N = 1,016)						
1	428 (2,996)	7,091 (10,216)	35 (106)	479 (687)	111 (225)	14 (48)
2	312 (1,392)	5,202 (2,687)	78 (383)	419 (578)	110 (196)	21 (66)
3	83 (671)	3,077 (3,046)	27 (103)	459 (489)	126 (330)	10 (45)
4	381 (1,730)	5,968 (4,337)	10 (35)	330 (415)	35 (46)	10 (33)
Disease severity (N = 306)						
No fibrosis	47 (299)	1,892 (--)	14 (61)	792 (1,518)	89 (123)	7 (21)
Mild fibrosis	218 (1,140)	3,402 (3,215)	32 (112)	604 (562)	98 (128)	17 (47)
Bridging fibrosis	348 (1,531)	3,439 (3,739)	37 (86)	451 (408)	82 (169)	17 (40)
Cirrhosis	1,313 (3,171)	6,565 (4,118)	83 (206)	503 (582)	96 (110)	17 (49)
SVR status (N = 632)						
Attained	72 (559)	2,938 (2,174)	12 (53)	497 (661)	99 (223)	11 (42)
Not attained	456 (1,832)	4,863 (3,863)	86 (389)	578 (745)	131 (246)	20 (48)
Treatment status (N = 1,016)						
Treated	301 (2,403)	5,888 (9,059)	42 (228)	513 (667)	112 (232)	15 (51)
Not treated	461 (1,995)	6,916 (3,989)	45 (125)	226 (278)	101 (256)	15 (59)

Multivariable Regression Results
- Among patients with biopsy, severe HCV was associated with significantly higher hospital utilization and costs compared to mild disease.
  – Hospitalization was 5 times more likely in severe HCV patients compared to mild (OR = 5.39; P = 0.008).
  – Hospitalization rate was 4 times higher in patients with severe HCV patients compared to mild (IRR = 3.98; P = 0.010).
  – Per patient hospital costs were €1,380 higher in severe HCV patients compared to mild (P = 0.001).
- Genotype had little overall effect on resource utilization
- SVR attainment strongly correlated with lower resource use and moderately lower costs.
  – Odds of hospitalization in patients with SVR attainment was less than half that of those who did not attain SVR (OR = 0.22; P < 0.0001).
  – ER, HCV-related office, and specialist office utilization were all significantly lower in SVR attainers.
- Treated patients had significantly higher use of HCV-related physician office visits (IRR = 2.46; P < 0.0001) compared with untreated patients.
  – Treatment status not a significant factor in other categories of service utilization.

CONCLUSIONS

- The majority of European HCV patients have genotype 1 and are diagnosed with mild disease.
- Resource utilization and costs, particularly for hospitalizations, increase substantially with disease severity.
- After adjustment for covariates, genotype has little effect on resource use, moderate effect on hospital costs.
- SVR attainment is strongly associated with lower resource utilization.

ACKNOWLEDGMENTS

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