The burden of viral hepatitis C in Europe: a propensity analysis of patient outcomes

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Objective Hepatitis C virus (HCV) affects 170 million patients worldwide and is the leading cause of liver cirrhosis and hepatocellular carcinoma. The aim of the current study is to examine the burden of HCV in the European Union (EU) from a patient perspective.

Methods Using data from the 2010 EU National Health and Wellness Survey, patients who reported a diagnosis of HCV ($n = 332$) were compared with a propensity-score-matched non-HCV control group ($n = 332$) on measures of quality of life (using the SF-12v2), work productivity, and healthcare resource utilization in the past 6 months. All analyses applied sampling weights to project to the respective country populations.

Results Projected prevalence estimates of HCV were 0.59% in France, 0.44% in Germany, 1.42% in Italy, 0.82% in Spain, and 0.35% in the UK. HCV patients reported significantly lower levels of emotional role limitations (means = 66.4 vs. 70.6, $P = 0.040$), physical functioning (means = 63.8 vs. 71.9, $P = 0.001$), general health (means = 48.3 vs. 54.4, $P = 0.004$), bodily pain (means = 64.3 vs. 70.8, $P = 0.002$), and physical component summary scores (means = 42.9 vs. 45.3, $P = 0.002$) than the matched controls. Patients with HCV also reported significantly higher levels of presenteeism (means = 27.1 vs. 21.0%, $P = 0.044$) and a greater number of physician visits in the past 6 months (means = 9.9 vs. 6.7, $P < 0.001$).

Conclusion Using a population-based survey methodology and a propensity-score matching analysis, these results add to the literature by documenting the significant effect that HCV has on a variety of both humanistic and economic outcomes in the EU. *Eur J Gastroenterol Hepatol* 24:869–877 © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.

European Journal of Gastroenterology & Hepatology 2012, **24**:869–877

Keywords: emergency room visits, health status, healthcare provider visits, hepatitis C virus, hospitalizations

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Received 5 January 2012 **Accepted** 22 April 2012

Introduction

The hepatitis C virus (HCV) is a chronic blood-borne disease, which is a leading cause of liver cirrhosis and hepatocellular carcinoma (HCC) worldwide [1]. Across Europe, an estimated 250 000 individuals die annually from HCV-related causes [2]. Although the significant risk for developing cirrhosis and HCC in the later stages of infection is well recognized, the early phases of chronic HCV infection are often asymptomatic [3]. Indeed, a number of patients in Europe are unaware that they are infected with the virus. Less than 60% of urban French residents with HCV-positive sera were aware of their status [4]. The rates of awareness for most other European countries vary between 60 and 90%, although Germany and Poland have been estimated at closer to 10% [2].

Prevalence figures range between 1.1 and 1.3% across the entire European region, although the rates of HCV infection vary substantially between and within countries [5]. According to the European Centre for Disease Prevention and Control, anti-HCV prevalence ranges from 0.4% (Germany, Sweden, the Netherlands) to 5.2% (Italy) [6]. Because of the advances in blood screening techniques in the 1990s, there has been an overall reduction in the incidence of HCV. Most HCV transmission now occurs through intravenous drug use, although tattoo and piercing needles also pose a risk of transmission [7]. However, some areas in Europe, such as central and southern Italy, are still considered to be hyperendemic [6,8]. On the basis of data from the WHO, country-specific prevalence rates for the five large European nations have been estimated to be between 0.13 and 1.10% for France, 0.10 and 0.22% for Germany, 0.5 and 3.0% for Italy, 0.7 and 2.0% for Spain, and 0.02 and 0.70% for the UK [5,9]. A recent systematic review by Cornberg *et al.* [10] reported the following estimates: 0.84% for France (with a 57% diagnosis rate), 0.40% for Germany (with a 38% diagnosis rate), 5.2% for Italy (with a 12% diagnosis rate), 2.64% for Spain (with a 17% diagnosis rate), and 0.60% for the UK (with a 36% diagnosis rate).

Because of the potential for HCV-related complications such as cirrhosis and HCC, HCV is considered to be a

0954-691X © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/MEG.0b013e3283551dee

major public health issue in Europe [11–13]. Indeed, the recent Summit Conference of Hepatitis B and C, under the auspices of the Belgian EU presidency, has issued a call to action for enhanced surveillance of these chronic illnesses [14]. Besides additional information on incidence and prevalence rates, which have inconsistent methodologies across countries, making comparisons difficult, data are needed on its effect on health outcomes in the region. Although broad population-level measures of disease burden (e.g. 1.2 million disability-adjusted life years lost in 2002 because of HCV) have been reported by the WHO [5], these estimates largely represent the impact of late-stage infection and its associated sequelae (e.g. cirrhosis, HCC). The European Centre for Disease Prevention and Control report focused exclusively on the burden of HCV-related cirrhosis and HCC rather than on the infection itself [6]. More sensitive assessments of the impact of HCV on the patient and healthcare system are currently lacking.

A few studies have assessed the effect of HCV on health status with respect to country-specific norms. Hauser *et al.* [15] and Cillo *et al.* [16], in Germany and Italy, respectively, each found that patients with HCV reported significantly lower health status scores as measured by the Short Form 36 (SF-36). A second study in Germany reached similar conclusions using the Short Form 12 [17]. Previous studies in Spain and the UK have also compared patients with HCV with healthy controls using the SF-36, finding marked differences [18,19]. However, none of these studies were population-based and many potential confounding variables were not included in the analyses, limiting the inferences that can be drawn on the impact of HCV. Other aspects of the burden of HCV, particularly work-related and activity-related impairments, have not been assessed.

The aim of this study is to assess prevalence information about HCV, as well as its impact on health outcomes across five European countries (France, Germany, Italy, Spain, and the UK) using a standardized methodology. Detriments in health-related quality of life [20–22], and increased healthcare resource utilization [22,23], and work productivity loss [22,23] have been observed previously in the USA; however, few studies have examined these outcomes using representative European samples. Some studies have examined the impact of HCV on health-related quality of life [15–19] and healthcare resource use [24], but no single study has examined both patient-centered and economic (both indirect and direct) outcomes across multiple European countries using a consistent methodology. As reported in previous reviews, the lack of a standardized methodology in HCV research is a major obstacle to assimilating epidemiological information across the European region [5,14].

This analysis also attempts to overcome the methodological limitations of previous studies through the application of a propensity score-matching procedure. The use of propensity score matching allows for the elimination of selection biases through the inclusion of demographic, health history, and comorbid disease characteristics that may be associated with HCV disease status and patient outcomes. Using such a methodology, patients will be compared with matched controls to isolate the contribution of HCV. To quantify the disease burden of HCV on the selected European population, the current study compares the health-related quality of life, work productivity loss, and healthcare resource utilization between those with and without HCV across France, German, Italy, Spain, and the UK.

Patients and methods

National Health and Wellness Survey

Data were obtained from the 2010 European Union (EU) National Health and Wellness Survey (NHWS), which included respondents from France, Germany, Italy, Spain, and the UK ($N = 57\,805$). The NHWS is an annual, cross-sectional, self-administered Internet survey of a sample of adults (18 years and older) who are identified through a web-based consumer panel. Members of the panel are recruited through opt-in e-mails, co-registration with panel partners, e-newsletter campaigns, and online banner placements. All panelists explicitly agreed to become panel members, registered through unique e-mail addresses, and completed in-depth demographic registration profiles. Offline recruiting was used to supplement this sample source in areas of limited Internet penetration, particularly in Spain and Italy among the older subpopulations. All participants provided informed consent and the study protocol was approved a priori by the Essex Institutional Review Board (Lebanon, New Jersey, USA).

Using data from the International Database of the United States Census [25], a stratified random sampling method was implemented to ensure that the final demographic characteristics (specifically, age, and sex) of the NHWS sample matched those of the respective countries (Table A1). The International Database of the United States Census was used as it provides a uniform methodology for determining the size of the age by sex subpopulations of all European countries on an annual basis. The NHWS is a general health survey and respondents were not specifically made aware of the presence of HCV-related questions before taking part in the survey. All respondents of the NHWS were preliminarily included in the analyses ($N = 57\,805$).

Hepatitis C virus status

Respondents of the NHWS were asked whether a physician had diagnosed them with HCV. Only those who reported that they had been diagnosed ($n = 336$) were considered part of the HCV group. All others were considered part of the control group ($n = 57\,469$).

Outcome variables

Health-related quality of life

The Medical Outcomes Study 12-Item Short Form Survey Instrument version 2 (SF-12v2) is a validated instrument used to assess health-related quality of life [26]. The SF-12v2 instrument measures eight health domains: physical functioning, physical role limitations, bodily pain, general health, vitality, social functioning, emotional role limitations, and mental health. Along with these eight domains, two summary scores [physical (PCS) and mental component summary scores] and a health utility index (SF-6D) are also computed. PCS and mental component summary scores each have a population mean of 50, along with an SD of 10 (higher scores indicated greater quality of life). The health utility index has interval scoring properties and yields a summary score on a theoretical 0–1 scale.

Work productivity

The Work Productivity and Activity Impairment questionnaire was used to measure the impact of health on work productivity loss and impairment in daily activities [27]. The Work Productivity and Activity Impairment questionnaire is a six-item validated instrument that consists of four metrics: absenteeism (the percentage of work time missed because of one's health in the past 7 days), presenteeism (the percentage of impairment experienced while at work in the past 7 days because of one's health), overall work productivity loss (an overall impairment estimate that is a combination of absenteeism and presenteeism), and activity impairment (the percentage of impairment in daily activities because of one's health in the past 7 days). Only respondents who reported being employed full-time, employed part-time, or self-employed provided data for absenteeism, presenteeism, and overall work impairment. All respondents provided data for activity impairment. The validity and accuracy of the instrument have been established in a number of disease states [28] and has been used previously among patients with HCV [29,30].

Absenteeism was calculated by dividing the number of work hours a patient missed in the past week because of his or her health by the total number of hours a patient could have worked (the number of hours he/she did work plus the number of hours missed because of his/her health) and converting this proportion into a percentage. Presenteeism was measured by a patient's rating of his or her level of impairment experienced while at work in the past 7 days (from 0 to 10, with higher numbers indicating greater impairment), which was then multiplied by 10 to create a percentage, with a range from 0 to 100%. Overall work impairment was measured by adding absenteeism and presenteeism to determine the total percentage of lost work time. Activity impairment was measured by a patient's rating of the level of impairment experienced in daily activities in the past 7 days (from 0 to 10, with higher numbers indicating greater impairment), which was then multiplied by 10 to create a percentage, with a range from 0 to 100%.

Healthcare resource utilization

Healthcare resource use was assessed by the number of visits in the last 6 months to healthcare providers, the emergency room, and the hospital for the patient's own medical condition. Healthcare providers included the following list: general practitioner/family practitioner, internist, allergist, cardiologist, dentist, dermatologist, diabetologist, endocrinologist, gastroenterologist, gynecologist, neurologist, nephrologist, nurse practitioner, oncologist, ophthalmologist, orthopedist, otolaryngologist, plastic surgeon, podiatrist, psychiatrist, psychologist/therapist, pulmonologist, rheumatologist, and urologist.

Predictor variables

Several variables were accounted for in the propensity score-matching process, including demographic, health history, and comorbidity information. Demographic variables included country of residence, age, sex, marital status (married/living with partner vs. all else), educational attainment (University degree vs. all else), and employment status (currently employed vs. not employed). Because of disparate healthcare systems across the five countries, insurance coverage was categorized as public health insurance, private health insurance, or unknown insurance. For similar reasons, annual household income was categorized as low income (< €20 000), moderate income (€20 000 to ≤ €50 000), high income (> €50 000), or decline to answer on the basis of the distributions of these variables. Health history variables included tobacco smoking (current smoker vs. nonsmoker), alcohol consumption (consume alcohol vs. abstain from alcohol), BMI, and physical exercise (exercise once or more per month for 20 min vs. no exercise in the past month). Comorbidity variables included the Charlson comorbidity index (CCI) [31], a single score that captures the overall comorbidity burden of each patient, and, separately, the presence of hepatitis B virus (HBV) and HIV/AIDS. Although HCV is a traditional component of the CCI ('liver disease'), it was excluded from our calculation of the CCI in the current study to ensure that the CCI was independent of HCV status.

Statistical analysis

As shown in previous research, patients with HCV have significantly different characteristics compared with those without HCV, including higher age and greater comorbidity burden as assessed with the CCI [22,30]. To more appropriately address the potential issue of selection bias, a propensity score matching methodology was implemented. Specifically, country of residence, sex, age, marital status, education, household income, employment status, insurance coverage, tobacco smoking, alcohol consumption, BMI, physical exercise, HBV, and

HIV/AIDS and comorbidity status using the CCI were entered into a single logistic regression model to predict HCV status (self-reported physician diagnosis of HCV vs. all others). Propensity score values from the logistic regression model were saved and used as part of the matching process. Each HCV patient was matched with a control whose propensity score was nearest using a greedy-matching algorithm. The greedy-matching algorithm allows for each case to be matched with the most suitable control available at that point in the matching process [32]. This is done by performing up to seven passes to find one matched control for each case. First, the algorithm searches for a control with a propensity score within 0.0000001 of a case's propensity score value. If none is found, the algorithm searches for a control within 0.000001 and continues searching for a suitable control with decreasingly restrictive criteria (0.00001, 0.0001, 0.001, and 0.01) until a control is found [32].

Differences between the HCV group and the control groups (both before and after the matching process) were analyzed using χ^2-tests for categorical variables and t-tests for continuous variables. Because the HCV group reported significantly higher rates of HBV even after the matching process, sensitivity analyses were carried out to ensure that HBV was not the reason for the difference in health outcomes. Multiple regressions were conducted controlling for HBV status on all outcomes. All analyses were carried out using SAS v9.1 (SAS, Cary, North Carolina, USA). Sampling weights from the NHWS were applied to all analyses to mitigate any sampling bias. Statistical significance was set a priori to a two-tailed P less than 0.05.

Results

A total of 336 patients across France ($n = 78$), Germany ($n = 65$), Italy ($n = 97$), the UK ($n = 52$), and Spain ($n = 44$) reported being diagnosed with HCV. Applying sampling weights, these correspond to prevalence estimates of 0.59% in France, 0.44% in Germany, 1.42% in Italy, 0.82% in Spain, and 0.35% in the UK. Patients with HCV were predominantly men (54.2%) and had a mean age of 55.1 years (SD = 15.4). Several demographic and patient characteristics were observed between HCV patients and those not diagnosed with HCV (Table 1). Specifically, patients with HCV were significantly more likely to have public health insurance (84.5 vs. 75.2%) and currently smoke (46.7 vs. 27.5%) (all P's < 0.05). Conversely, patients with HCV were significantly less likely to be women (45.4 vs. 51.4%), be employed (44.2 vs. 53.5%), to have private insurance (11.8 vs. 17.6%), and consume alcohol (67.8 vs. 76.8%) (all P's < 0.05). Although 32.2% of patients with HCV reported not drinking alcohol, 39.3% still continued to drink at least once a week (10.9% reported drinking daily, 5.1% reported drinking 4–6 times per week, 12.3% reported drinking 2–3 times per week, and 10.8% reported drinking once a week).

The rates of HBV (14.7 vs. 0.9%, $P < 0.05$) and HIV/AIDS infection (4.3 vs. 0.2%, $P < 0.05$) were higher among patients with HCV as was an overall greater comorbidity burden as assessed using the CCI (mean = 1.1 vs. 0.3, $P < 0.05$). Only 2.2% of patients with HCV reported a diagnosis of cirrhosis. Table 2 lists the 15 most common comorbidities reported by patients with HCV.

During the matching process, four patients with HCV could not be matched with suitable controls because of their unique pattern of covariates. As a result, these four patients were excluded from the analyses. After the matching process, patients with HCV were equivalent to matched controls on all demographic and health history variables (Table 3). Although the overall comorbidity burden was also equivalent between groups, patients with HCV did report higher rates of HBV than the matched controls (14.3 vs. 7.1%, $P = 0.013$).

Several health-related quality-of-life differences were observed between patients with HCV and the matched controls, as assessed using the domain scores of the SF-12v2 instrument (Fig. 1). Patients with HCV reported significantly lower levels of emotional role limitations (means = 66.4 vs. 70.6, $P = 0.040$), physical functioning (means = 63.8 vs. 71.9, $P = 0.001$), general health (means = 48.3 vs. 54.4, $P = 0.004$), bodily pain (means = 64.3 vs. 70.8, $P = 0.002$), and PCS scores (means = 42.9 vs. 45.3, $P = 0.002$). Although no other significant differences were observed, patients with HCV reported lower scores in all other domains of the SF-12v2 as well. Because the HBV rates were higher among those with HCV, a sensitivity analysis was carried out to determine whether controlling for differences in HBV accounted for the observed effects. In all cases, adjusting for HBV did not reduce the health-related quality-of-life detriments (emotional role limitations: adjusted means = 66.0 vs. 70.6, $P = .023$; physical functioning: adjusted means = 65.6 vs. 72.6, $P = 0.004$; general health: adjusted means = 48.4 vs. 54.6, $P = 0.004$; bodily pain: adjusted means = 64.1 vs. 70.0, $P = 0.007$) and PCS scores (adjusted means = 43.3 vs. 45.6, $P = 0.004$).

Patients with HCV also reported significantly higher levels of presenteeism than the matched controls (means = 27.1 vs. 21.0%, $P = 0.044$). Absenteeism (means = 7.1 vs. 6.7%, $P = 0.87$), overall work impairment (means = 31.1 vs. 25.6%, $P = 0.11$), and activity impairment (means = 34.1 vs. 31.8%, $P = 0.32$) were all higher among patients with HCV, but not significantly so. As with health-related quality of life, a sensitivity analysis was carried out to control for HBV. The effect of HCV status on presenteeism became slightly more pronounced after this adjustment (adjusted means = 26.3 vs. 19.8%, $P = 0.031$).

Table 1 Demographic, health history, and comorbidity differences between those diagnosed with hepatitis C virus and those not diagnosed with hepatitis C virus

	Unmatched control group (n=57 469)			HCV group (n=336)			
Variables	n	Weighted n	Weighted (%)	n	Weighted n	Weighted (%)	P
France	14 973	49 792 579	19.77	78	296 727	16.55	0.11
Germany	15 005	68 097 942	27.03	65	303 111	16.91	< 0.0001
Italy	7483	50 572 035	20.08	97	730 766	40.77	< 0.0001
Spain	4995	35 102 555	13.94	44	290 026	16.18	0.3193
UK	15 013	48 332 798	19.19	52	171 990	9.59	< 0.0001
Female	29 567	129 437 157	51.38	141	813 971	45.41	0.0513
Married	36 528	157 635 742	62.58	195	1 055 055	58.86	0.218
University educated	33 698	144 718 147	57.45	205	1 102 452	61.50	0.1721
Employed	32 550	134 659 246	53.46	162	791 386	44.15	0.003
Have public health insurance	41 993	189 329 230	75.16	274	1 514 617	84.49	< 0.0001
Have private health insurance	10 844	44 240 907	17.56	47	211 833	11.82	0.0023
Unknown insurance	4632	18 327 772	7.28	15	66 170	3.69	0.0006
Household income: <€20 000	16 040	68 343 285	27.13	112	591 430	32.99	0.0466
Household income: €20 000 to <€50 000	24 399	108 757 516	43.18	145	794 886	44.34	0.7037
Household income: €50 000 or more	8931	37 546 621	14.91	46	234 408	13.08	0.3537
Household income: decline to answer	8099	37 250 487	14.79	33	171 896	9.59	0.0036
Currently smoke	16 268	69 232 480	27.48	163	836 241	46.65	< 0.0001
Use alcohol	45 272	193 387 394	76.77	232	1 215 861	67.83	0.0025
Currently exercise	32 697	143 169 006	56.84	177	971 381	54.19	0.3848
Presence of HBV	467	2 362 725	0.94	40	263 589	14.70	< 0.0001
Presence of HIV/AIDS	105	445 806	0.18	17	77 773	4.34	0.0002
	Weighted mean		Weighted SD	Weighted mean		Weighted SD	P
Age	49.19		16.68	55.08		15.35	< 0.0001
BMI	26.3		5.44	26.16		5.58	0.5994
CCI	0.29		0.73	1.13		2.74	< 0.0001

Weighted statistics reflect values after the application of the sample weights.
CCI, Charlson comorbidity index; HBV, hepatitis B virus; HCV, hepatitis C virus.

Table 2 The most prevalent comorbidities among patients with hepatitis C virus

Comorbidity	n	Weighted n	Weighted (%)
Insomnia/sleep difficulties	128	649 416	36.23
Pain	109	571 045	31.86
Anxiety	100	495 557	27.64
Hypertension	84	458 550	25.58
Migraine	80	385 283	21.49
Depression	79	385 006	21.48
Heartburn	67	334 928	18.68
Hypercholesterolemia	55	309 783	17.28
Chronic liver disease	53	289 439	16.15
Arthritis	52	267 368	14.91
HBV	40	263 589	14.70
Headache	53	230 381	12.85
Thyroid condition	45	222 671	12.42
Chronic bronchitis	44	220 152	12.28
Diabetes	43	216 819	12.10

Weighted statistics reflect values after the application of the sample weights.
HBV, hepatitis B virus.

Healthcare resource utilization was also compared between patients with HCV and the matched controls. No differences were observed in the number of emergency room visits in the past 6 months (means = 0.38 vs. 0.32, $P = 0.50$) or the number of hospitalizations in the past 6 months (means = 0.25 vs. 0.28, $P = 0.80$). However, there was a significant effect of HCV status on the number of physician visits in the past 6 months (means = 9.9 vs. 6.7, $P < 0.001$). This effect remained even after controlling for the presence of HBV (adjusted means = 10.2 vs. 6.9, $P < 0.001$).

Discussion

The aim of the present study was to assess the impact of the presence of HCV on health-related quality of life, work productivity loss, and healthcare resource utilization in France, Germany, Italy, Spain, and the UK. Although a few studies have examined the burden of HCV in Europe [5,14,19], no study has carried out such a comprehensive assessment of the health outcome burden of HCV across multiple European countries with a standardized methodology. Indeed, the lack of a standardized assessment of HCV and its effects has been identified as a major limitation in previous review papers [5].

Several European pricing and reimbursement decision-makers consider the public health impact of diseases as an integral part of a new medicine's therapeutic value assessment. More specifically, the French National Authority for Health, the German Institute for Quality and Efficiency in Health Care, and the recent UK Department of Health discussion paper on the UK value-based pricing all highlight the value of assessing disease severity, disease burden, and patient-relevant outcomes [33]. Our research contributes to evidence generation of the burden associated with HCV in Europe.

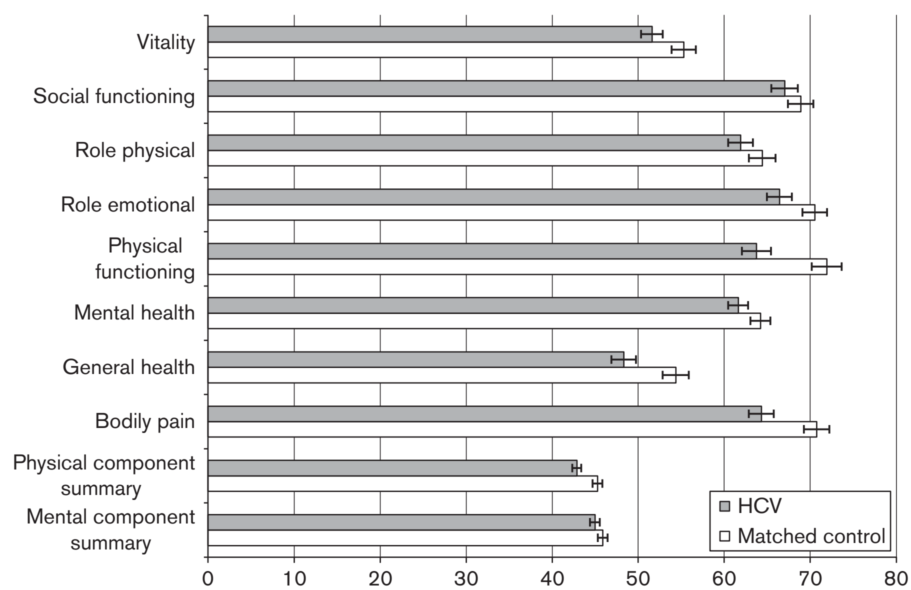
The prevalence estimates reported using NHWS are consistent from those reported by the WHO, the Hepatitis C European Network for Co-operative Research, and Cornberg and colleagues, particularly when factoring in the diagnosis rate, which would be the most

Table 3 Demographic, health history, and comorbidity differences between those diagnosed with hepatitis C virus and matched controls

	Matched control group (*n*=332)			HCV group (*n*=332)			
Variables	*n*	Weighted *n*	Weighted (%)	*n*	Weighted *n*	Weighted (%)	*P*
France	69	244 523	14.41	78	296 727	16.73	0.3861
Germany	60	306 001	18.03	65	303 111	17.09	0.771
Italy	96	638 082	37.60	96	725 104	40.89	0.4595
Spain	42	307 195	18.10	43	282 927	15.95	0.536
UK	65	201 374	11.87	50	165 650	9.34	0.2077
Female	131	724 640	42.70	139	805 072	45.39	0.5439
Married	191	939 109	55.33	192	1 041 616	58.73	0.4352
University educated	200	1 017 400	59.95	203	1 093 687	61.67	0.6827
Employed	154	725 230	42.73	158	772 285	43.55	0.8475
Have public health insurance	253	1 360 797	80.18	271	1 501 178	84.64	0.1383
Have private health insurance	61	266 962	15.73	47	211 833	11.94	0.1665
Unknown insurance	18	69 416	4.09	14	60 508	3.41	0.6301
Household income: <€20 000	110	556276	32.78	112	591 430	33.35	0.8909
Household income: €20 000 to <€50 000	141	749 467	44.16	143	784 550	44.24	0.9858
Household income: €50 000 or more	51	237 478	13.99	45	231305	13.04	0.731
Household income: decline to answer	30	153 954	9.07	32	166 234	9.37	0.9041
Currently smoke	163	799 600	47.11	159	817 140	46.07	0.8111
Use alcohol	220	1 072 018	63.16	228	1 196 760	67.48	0.3092
Currently exercise	178	928 855	54.73	174	959 379	54.09	0.8837
Presence of HBV	26	120 201	7.08	38	253 387	14.29	0.0129
Presence of HIV/AIDS	16	71 012	4.18	13	58 672	3.31	0.5442
	Weighted mean		Weighted SD	Weighted mean		Weighted SD	*P*
Age	55.08		18.82	55.24		15.35	0.8976
BMI	26.36		5.73	26.16		5.57	0.6288
CCI	0.99		2.01	0.82		1.71	0.2065

Weighted statistics reflect values after the application of the sample weights.
CCI, Charlson comorbidity index; HBV, hepatitis B virus; HCV, hepatitis C virus.

Fig. 1



Health-related quality-of-life differences between those diagnosed with HCV and the matched controls. HCV, hepatitis C virus. Bars represent SE.

relevant comparison with the NHWS data [5,9,10]. Both Italy and Spain reported the highest rates of HCV compared with those in France, Germany, and the UK. It is important to emphasize that given the self-reported methodology, the prevalence figures from NHWS represent only those who are aware of their HCV status. As shown in previous studies, many patients in Europe are unaware that they are infected [2,4]. As such, the actual population levels may be underestimated. Nevertheless, the standardized representative methodology of NHWS provides valuable information on the relative prevalence figures across the five European countries. It also allows for a different perspective than previous studies, which have often recruited patients only from medical centers.

Such a methodology may over-represent patients who are active in their healthcare.

A significant and pervasive burden of HCV was identified across the three health outcome domains, although the effects on health-related quality of life were the strongest. Patients with HCV, even when compared with the controls matched on a wide array of demographics, health history, and comorbidity information, reported significantly lower levels of several domain scores, including overall physical health (as assessed by PCS). Although the effects were not as strong as those observed in previous German studies, this is likely because of the more comprehensive set of covariates included in the present study. It is important to note that, because of its broad population focus, few of the HCV patients in NHWS were in the later stages of infection (the prevalence of cirrhosis was quite low). Nevertheless, a significant burden was observed even before these patients suffer from the severe sequelae associated with HCV. Complicating the management of these patients, several comorbidities were particularly prevalent including insomnia/sleep difficulties, pain, and anxiety. It is also interesting to note the continued frequency with which patients with HCV continued to consume alcohol; over a third drank more than once a week.

HCV status was also associated with higher levels of presenteeism. Although patients with HCV were no more likely to miss work than the matched controls, they were significantly less productive while at work because of their health. Patients also reported significantly more visits (almost 50% more) to their healthcare providers than the matched controls. Both of these effects have clear economic implications from a societal perspective. Patients with HCV use more healthcare resources because of their infection and, among those in the labor force, are less able to function in their employment. To our knowledge, this is the first study of its kind to examine the effect of HCV on workplace productivity in Europe, which contributes toward a better understanding of the societal-level impact of the virus.

Limitations

All HCV diagnoses, work productivity, and healthcare resource-use measures were patient-reported and may have introduced measurement error. As discussed above, many patients may be unaware that they are currently infected with HCV. It is possible that members of the control group were, in fact, infected with HCV without their knowledge. Patient report is a limitation from an epidemiological perspective, but it does allow for the analysis of variables such as health status and work productivity, which are best assessed from the patient directly. Although the propensity score-matching procedure included a wide array of demographic, health history, and comorbidity information, it is possible that additional variables may not have been included, which could explain the observed differences in health outcomes. For example, illicit drug use was not assessed in the NHWS. Of course, the most important confounders (HBV, HIV/AIDS, age, etc.) were included in the analyses. The NHWS uses a stratified random sample to ensure that the final sample is representative to the individual countries in terms of age and sex. However, because of the Internet survey methodology, it is possible that other differences between our sample and the population exist. Our methodology is unlikely to capture a truly representative mix of the HCV population, as disenfranchised groups (particularly injection drug users and those in poverty) and those in end stages of infection are unlikely to be adequately represented. Those differences may have an effect on the results, but, given the close match between the epidemiology of HCV in the NHWS and that of other sources (using completely different methodologies), the effect, if it exists, is likely not marked. The scope of this study was limited to France, Germany, Italy, Spain, and the UK; these results should not necessarily be extrapolated to other countries in Europe. For example, the evolving immigration patterns from the Middle East and Asia make each country unique with respect to epidemiology and disease burden.

Conclusion

Using a standardized methodology across France, Germany, Italy, Spain, and the UK, the presence of diagnosed HCV in the EU population has been shown, utilizing a propensity scoring model, to have a significant impact on several domains of health-related quality of life, presenteeism, and the number of visits to traditional healthcare providers. These analyses accounted for an exhaustive array of demographic, health history, and comorbidity information that is known to burden the HCV population and to be associated with health outcomes. In sum, these results add to the literature by documenting the population-level effect of HCV on a variety of patient-reported outcomes. This information is increasingly relevant in the context of pricing and reimbursement reforms of new medicines as well as the recent call to action for increased surveillance of HCV throughout the EU.

Acknowledgements

This study was funded by Bristol-Myers Squibb.

Conflicts of interest

The National Health and Wellness Survey (NHWS) was conducted by Kantar Health. M.D. and J.S.W. are full-time employees of Kantar Health and P.L. serves as a consultant to Kantar Health. Bristol-Myers Squibb purchased access to the NHWS dataset and funded the analysis and writing of this manuscript. Y.Y. and G.L. are full-time employees of Bristol-Myers Squibb and B.L. is a

former employee of, and current consultant to, Bristol-Myers Squibb.

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Appendix

Table A1 Demographic characteristics of the National Health and Wellness Survey sample (before and after applying sample weights) and the International database of the US census

	NHWS			
	N	Unweighted (%)	Weighted (%)	International database of the US Census (2009)
France				
Male	6668	44.3	48.2	48.2
Female	8383	55.7	51.8	51.8
18–29	3265	21.7	19.5	19.5
30–39	3014	20.0	17.3	17.3
40–49	2748	18.3	17.9	17.9
50–64	3918	26.0	24.3	24.3
65 +	2106	14.0	21.1	21.1
Germany				
Male	7346	48.7	48.7	48.7
Female	7724	51.3	51.3	51.3
18–29	3007	20.0	16.9	16.9
30–39	2859	19.0	14.9	14.9
40–49	3015	20.0	20.7	20.7
50–64	4086	27.1	23.1	23.1
65 +	2103	14.0	24.4	24.4
UK				
Male	7512	49.9	49.1	49.1
Female	7553	50.1	50.9	50.9
18–29	2880	19.1	20.0	20.0
30–39	2256	15.0	16.6	16.6
40–49	3003	19.9	19.5	19.5
50–64	3752	24.9	23.5	23.5
65 +	3174	21.1	20.4	20.4
Italy				
Male	3996	52.7	48.7	48.7
Female	3584	47.3	51.3	51.3
18–29	1143	15.1	13.2	13.2
30–39	1154	15.2	14.4	14.4
40–49	1510	19.9	19.1	19.1
50–64	2194	28.9	23.6	23.6
65 +	1579	20.8	29.7	29.7
Spain				
Male	2575	51.1	48.5	48.5
Female	2464	48.9	51.5	51.5
18–29	858	17.0	13.8	13.8
30–39	873	17.3	17.3	17.3
40–49	1006	20.0	19.0	19.0
50–64	1301	25.8	22.8	22.8
65 +	1001	19.9	27.1	27.1

NHWS, National Health and Wellness Survey.