BMJ Open Sick leave and disability pension in patients with chronic hepatitis C compared with a matched general population: a nationwide register study

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ABSTRACT

Objective The objective of this study was to evaluate sick leave and disability pension in patients with chronic hepatitis C virus (HCV) infection as compared with a matched general population cohort.

Design Retrospective register study.

Setting Nationwide in Sweden.

Participants This register-based study used the Swedish National Patient Register to identify working-age patients with HCV in 2012 (n=32 021) who were diagnosed between 1999 and 2007 (n=19 362). Sick leave and disability pension data were retrieved from Statistics Sweden (1994–2012), with up to five matched individuals from the general population.

Primary and secondary outcome measures The primary outcome was workdays lost due to sick leave episodes (>14 days) and disability pension overall. The secondary outcome was workdays lost per subgroup of patients with chronic HCV.

Results In 2012, 14% of the HCV patients had ≥1 registered sick leave episode compared with 10% in the matched comparator cohort. For disability pension benefits, results were 30% versus 8%, respectively. Overall, in 2012, 57% of patients with HCV did not have any registered workdays lost, whereas 30% were absent ≥360 days compared with 83% and 9% in the matched cohort, respectively. The mean total number of annual workdays lost in 2012 was 126 days in the HCV patient cohort compared with 40 days in the matched general population comparator cohort. Annual days lost increased from a mean of 86 days 5 years before diagnosis to 136 days during the year of diagnosis.

Conclusions These results show that Swedish HCV patients used more sick days and have a higher frequency of disability pension compared with a comparator cohort from the general Swedish population. Whether earlier diagnosis of HCV and treatment might impact work absence in Sweden warrants further investigation.

BACKGROUND

Hepatitis C is an infectious viral disease affecting the liver, with Western European prevalence rates estimated between 0.35% and 1.42%.¹ In Sweden, the prevalence of

Strengths and limitations of this study

- Previous studies focused on describing sick leave in a small segment of patients with chronic hepatitis C, whereas this is the first study to investigate sick leave and disability pension on a nationwide level.
- The registers contain routinely collected data, that is, limiting the risk for sampling bias.
- The diagnosis analysed was retrieved from Swedish patient register and was not validated, however, the Swedish patient register has previously shown high reliability.
- The registers do not contain information on treatment outcome, so analysis on the impact of viral eradication and workdays lost was not feasible.
- The actual number of workdays lost are underestimated since only sick leave episodes 14 days are registered.

chronic hepatitis C infection was estimated to be 0.36% in 2013.²

Patients with hepatitis C virus (HCV) infection have been shown to have increased work disabilities.³ Furthermore, models have shown a relationship between HCV and loss of productivity, increased absenteeism and higher healthcare benefit costs, which results in substantial economic burden to society.⁴⁻⁶ A retrospective database analysis showed employees in the USA with HCV infection to have a higher number of lost workdays than employees without HCV infection. In addition, they also used more sick leave, with increased use of short-term and long-term disability.⁵ The annual cost due to productivity loss in untreated patients with genotype 1 HCV infection in USA has been estimated to US\$7.1 billion.⁶ Before the introduction of the new interferon-free HCV treatment options, the HCV-associated productivity losses in UK were estimated

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to rise from £184-£367 million in 2010 to £210-£427 the data on sick leave and disability pension available until 31 December 2012; thus, the current analysis is based on The objective of the present study was to evaluate sick data from 1997 to 2012.

> Informed consent is not required for large-scale registry-based studies in Sweden.¹¹ Data from the Swedish registries are available for research after ethical and registry approval.

Patient and public involvement

No patient involved.

Identification of patients with HCV and matched general population comparators

Patients were identified in the NPR using healthcare visits with a chronic HCV diagnosis (ICD-10: B18.2),¹² as described previously for this cohort.² Only patients of working age (ie, between 19 and 65 years) were included. Subgroup analyses by age (19-29, 30-39, 40-49, 50-59, 60-65 years), gender (male/female), education (<9, 10–12 and \geq 12 years), disease status (eg, DCC, liver cancer (HCC), liver transplantation; online supplementary table S1 and S2), treatment status (HCV treatment or opioid substitution therapy (OST); online supplementary table S3) and co-infection (HIV or hepatitis B virus; online supplementary table S4), were performed. Up to five general population controls were matched by age, sex and county of residence to each patient with HCV at the time of diagnosis.

Definition of outcomes

The outcome was the annual number of days of sick leave and disability pension (maximum of 365 per year).

Sick leave

As of 1998 the first day of sick leave is not compensated ('waiting period') in Sweden, with day 2-14 being paid by employers. Thus, only sick leave episodes >14 days were recorded in the LISA database, as those were paid by the Social Insurance Agency. Any episode occurring within 5 days of a previous episode does not require a new 'waiting period' or 'sick pay period', thus multiple shortterm episodes could waive these periods. That is, individuals with 0 days registered may, in fact, have had sick leave episodes ≤ 14 days, hence that group was denoted '0' registered days to acknowledge this uncertainty.

Disability pension

Disability pension refers to either disability pension (1990-2002) or sickness/activity compensation (2003-2012). In Sweden, disability pension can be either part-time (25%, 50%, 67% or 75%) or full-time (100%) based on the type and severity of the medical condition. As of 2003, the disability pension was replaced by two types of compensation depending on age. 'Activity compensation' was introduced for younger individuals (19-29 years old) whereas older individuals were eligible for 'sickness compensation'. Both sickness and activity compensation were either timelimited or permanent but required at least $\geq 25\%$ reduction in work capacity that was expected for at least 1 year. Gross

METHODS

Setting

The population in Sweden was 9.6 million people in 2012 (Statistics Sweden; www.scb.se). Sweden has a universal tax-funded healthcare system where the Swedish Social Insurance Agency captures information on full or partial sick leave and disability compensations. In 2012 the common retirement age in Sweden was 65 years with people having the right to retire at 61 years of age or choose to continue working until 67 years of age.

leave and disability pension in patients with chronic HCV

compared with matched general population comparators using the Swedish National Patient Register (NPR). A

secondary objective was to examine sick leave and disability

pension within certain subgroups (eg, patients with decom-

pensated cirrhosis (DCC), cirrhosis, hepatocellular carci-

noma (HCC) or liver transplantation) or prevalent patients,

as well as sick leave in relation to diagnosis.

Information on Swedish citizens are collected in the nationwide registers using the Swedish unique personal identity number.⁸ In the present study the following registries were used; the NPR, the Cancer Register, the Prescribed Drug Register (PDR), the Cause of Death Register (CDR), the Total Population Register (TPR) and the Longitudinal Integrated Database for Health Insurance and Labour Market studies (LISA). The NPR contains all inpatient (1987-2013) and non-primary outpatient care (2001-2013) visits, but it does not capture any primary care visits.⁹ The NPR includes information on both main and contributory diagnoses based on the International Classification of Diseases (ICD-9, 1987–1996; ICD-10, 1997–2013). The Cancer Registry covers medical data such as the site of tumour, histologic type, basis and date of diagnosis (1958-2013). It is mandatory to report all newly detected cancers to the registry. However, some cases are only reported to the CDR (ie, cases denoted as death certificate only and death certificate notification) and are not necessarily included in the Cancer Registry. The PDR includes all prescribed drug use in ambulatory care (2005-2013), although in-hospital drug use is captured to a much lesser extent.¹⁰ It contains information on dates, drugs and costs for all pharmacy dispensed prescriptions in Sweden using Anatomical Therapeutic Chemical codes. The CDR contains information on the cause of death with information on the year and month of death. The TPR provides information on place of residence, age, sex, country of origin and emigration status. LISA includes data on sick leave and disability pension for all residents in Sweden ≥16 years of age with information on work-related and socioeconomic variables (eg, education level, marital status and days per year of sick leave and disability pension (annual data retrieved for 1994–2012)).

HCV as a diagnosis was introduced with the ICD-10 in 1997 and at the time of data collection (April 2014) was disability pension refers to the number of days away from work, whereas net disability pension refers to the net time away, for example, 50% sick leave for 14 days would be equal 14 days gross disability pension and 7 days net disability pension (ie, 182.5 days a year).¹³

Follow-up of patients with HCV and matched general population comparators

Patients with HCV were followed from the date of first visit with an HCV diagnosis during the observation time (index date) until emigration, death, retirement (age 65 years) or study end (31 December 2012), whichever occurred first. The matched comparators were followed from index date until emigration, death, retirement, until HCV diagnosis or 31 December 2012, whichever occurred first. The prevalent cohort included patients alive and living in Sweden as of 31 December 2012.

For the longitudinal analyses of work loss due to sick leave and disability pension, the patients with HCV were followed from 5 years before to 5 years after diagnosis. Patients were included if diagnosed between 1999 and 2007 to allow a \pm 5 year follow-up time. In addition, patients had to be between 24 and 59 years of age at the time of diagnoses in order to be eligible for benefits during the full follow-up. All codes used are available in the online supplementary tables S1–S4.

Statistics

The annual days of sick leave and disability pension were in the descriptive statistics grouped by categories ('0', 1–90, 91–180, 181–359 and ≥360 days) and presented using arithmetic means.¹⁴ The study calculated the total annual number of days of sick leave and disability pension in 2012 for both cohorts. The difference in workdays lost between the groups was also evaluated using multivariable regression models. The analyses were adjusted for age, sex and educational level, as well as occurrence of psychiatric diseases and/or liver-related outcomes (defined as history of cirrhosis, mental and behavioural disorders, and/or liver transplantation), if the goodness of fit was R^2 >0.6.

The longitudinal analysis followed the patients with HCV and their comparators from 5 years ahead of index date until 5 years after the index date. The impact of interferon-based treatment was analysed for patients with HCV treated with interferon 2 years before until 2 years after first treatment during 2005 and 2010.

SAS V.9.4 (SAS Institute) was used for all statistical analyses. All p values are two-sided.

RESULTS

Overall, 32 021 patients aged 19–64 years were diagnosed with HCV and were living in Sweden on 31 December 2012 (HCV prevalent cohort; table 1).

Prevalence and days of sick leave and disability pension in 2012

Fourteen percent of patients with HCV had ≥ 1 registered sick leave episode(s) in 2012 compared with 10% in the

matched general population comparator cohort. Eight percent of individuals in the matched general population received disability pension benefits, compared with 30% of patients with HCV. In total, 43% of patients with HCV and 17% of individuals in the matched general

| Table 1 Characteristics of register-identified patients with |
|--|
| prevalent HCV aged 19–64 years on 31 December 2012, in |
| Sweden and their matched general population comparators |

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|---|--|--|--|--|
| | Patients with HCV in 2012; 19–64 years (n=32 021*) | Matched GenPop comparators in 2012 (n=149 688) | | |
| Men, n (%) | 20 654 (65) | 95 546 (64) | | |
| Mean (SD) age, years | | | | |
| At identification/ diagnosis | 39 (11) | | | |
| In 2012 | 47 (11) | 47 (11) | | |
| Highest attained education, n (%) | | | | |
| <9 years | 11 509 (36) | 21 600 (14) | | |
| 10–12 years | 16 021 (50) | 72 946 (49) | | |
| ≥12 years | 4159 (13) | 53 866 (36) | | |
| Missing | 332 (1) | 1276 (1) | | |
| Marital status at the time of identification, n (%) | | | | |
| Unmarried | 19 725 (62) | 75 011 (50) | | |
| Married | 6074 (19) | 57 376 (38) | | |
| Divorced | 6111 (19) | 16 539 (11) | | |
| Widow | 0 | 5 (<0.1) | | |
| Missing | 111 (0.3) | 757 (1) | | |
| Co-infection, n (%) | | | | |
| HIV | 672 (2) | 210 (0.1) | | |
| HBV | 3222 (10) | 377 (0.3) | | |
| Registered HCV-related outcome, n (%)† | | | | |
| Liver cirrhosis | 2346 (7) | 213 (0.1) | | |
| Decompensated cirrhosis | 1041 (3) | 31 (0) | | |
| Hepatocellular carcinoma | 408 (1) | 125 (0.1) | | |
| Liver transplantation | 289 (1) | 48 (<0.1) | | |
| HCV treatment since 2005 | 6234 (19) | | | |
| OST treatment since 2005 | 3735 (12) | 1102 (1) | | |

*One hundred sixty-nine patients with HCV were excluded, as there was no data available in the Longitudinal Integrated Database for Health Insurance and Labour Market Studies Dataset. †Interpretation of data should be done with caution, as certain outcomes such as liver cirrhosis were likely underreported in the National Patient Register; all codes used todefine outcomes are provided in online supplementary tables S1–S4. HBV, hepatitis B virus; HCV, hepatitis C virus; OST, opioid substitution therapy. population comparator cohort had at least one registered sick leave episode or received disability pension benefits in 2012 (table 2).

The proportion of receiving a disability pension was similar among men and women, but was higher among older individuals, those with co-infection (HCV and HIV or hepatitis B virus), and those receiving OST (see online supplementary figure S1). It was lower among those with a higher educational level and those who previously had been treated for HCV infection. The proportion of sick leave was higher among women and those with higher education, with minor variations by age. Proportion of sick leave or disability pension use was always higher among patients with an HCV-related complication, such as cirrhosis, DCC, HCC or liver transplantation.

Overall, fewer patients with HCV did not have any registered workdays lost in 2012 compared with the matched general population comparator cohort (57% vs 83%). A greater proportion (30%) of patients with HCV were absent \geq 360 days than in the matched general population comparator cohort (9%, p<0.001; figure 1). The median number of workdays lost was '0' in both cohorts, thus the distribution of workdays lost in 2012 was non-normal.

Among prevalent patients, the annual number of workdays lost was generally higher among older patients, patients with lower education, patients with coinfection and among patients with liver complications, such as DCC, HCC and liver transplantation (figure 2). The average total annual number of workdays lost in 2012 was 126 in the HCV patient cohort and 40 in the matched general population comparator cohort (table 2). When only those with a registered episode were analysed, the mean total annual number of workdays lost rose to 296 days among patients with HCV, a trend that was observed among all subgroups (figure 2).

The multivariable regression model was adjusted for age, sex and educational level, showed patients with HCV

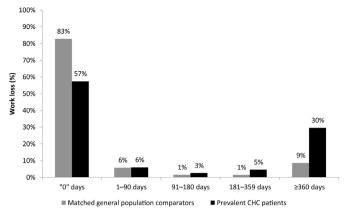


Figure 1 Distribution of days on sick leave and disability pension in 2012 in the Swedish register-identified HCV; population (n=32 021) and matched general population comparators (n=1 49 688). '0' days may include sick leave episodes ≤14 days. General population comparators were matched 5:1 by age, sex and place of residency at the time of diagnosis (index date). CHC, chronic hepatitis C; HCV, hepatitis C virus.

to have on average 75 more workdays lost compared with the general population. The number of workdays lost decreased to 60 days when considering psychiatric diseases. When also adjusting for any history of either cirrhosis, HCC or liver transplantation the estimate was reduced to 55 days. The independent factors associated with a greater number of workdays lost were older age, lower level of education, female sex, psychiatric diseases and history of liver-related outcomes were all independently and significantly (p<0.001).

Longitudinal work loss in relation to diagnosis

Among all patients with HCV 19362 patients were diagnosed between 1999 and 2007, thus qualified for the longitudinal analysis that followed work loss for up to 5 years

| matched general population comparators | | | | | |
|--|---|--|----------------------|--|--|
| | Patients with HCV in 2012; 19–64 years (n=32 021*) | Matched GenPop comparators in 2012 (n=149 688) | Difference (days) | | |
| Mean (SD) total annual number of days during follow-up | 106 (155) | 34 (97) | 72 | | |
| Sick leave | 27 (78) | 13 (55) | 14 | | |
| Disability pension, gross | 80 (148) | 21 (84) | 59 | | |
| Disability pension, net | 76 (143) | 18 (75) | 58 | | |
| Mean (SD) total days in 2012 | 126 (166) | 40 (107) | 86 | | |
| Sick leave | 22 (72) | 11 (88) | 11 | | |
| Disability pension, gross | 106 (164) | 29 (98) | 77 | | |
| Disability pension, net | 101 (159) | 25 (88) | 76 | | |

Table 2 Annual number of days of sick leave and disability pension in 2012 in patients with register-identified HCV and

Some sick leave episodes ≤14 days were not captured due to the 1 day waiting period and the 13-day sick pay period (waived only under certain circumstances).

*Matched general population comparators were matched on age, sex and place of residency at the time of diagnosis. HCV, hepatitis C virus.

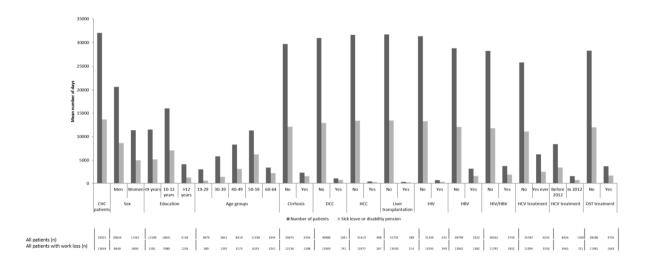


Figure 2 Mean total annual number of days of work loss in 2012 in the Swedish register-identified HCV population (n=32 021); among all patients and those with registered sick leave or disability pension. The bars represent a mix of full-time and part-time sick leave and disability pension days. Some sick leave episodes \leq 14 days were not captured due to the 1 day waiting period and the 13-day sick pay period, which could be waived only under certain circumstances. General population comparators were matched 5:1 by age, sex and place of residency at the time of diagnosis (index date). CHC, chronic hepatitis C; DCC, decompensated cirrhosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; OST, opioid substitution therapy.

before and after diagnosis. Five years before diagnosis, the percent of patients with HCV that had registered workdays lost were 37%, which increased to 51% in the year of diagnosis and thereafter remained constant. The workdays lost for the matched general population comparators for these 19 362 patients remained between 16% and 21% throughout the longitudinal analysis (figure 3). More than 30% of patients with HCV were almost fully work disabled already 1 year after diagnosis compared with approximately 10% in the matched general population comparators. Thus, patients with HCV were three times as likely to be fully work disabled compared with the matched general population cohort.

The mean annual workdays lost increased from 86 days to 146 days from 5 years before HCV diagnosis to 1 year after diagnosis. The number of workdays lost were always considerably higher among patients with HCV (5 years before HCV diagnosis: 86 vs 28 days=difference of 59 days; at the year of HCV diagnosis: 136 vs 43 days=difference of 92 days; 5 years after HCV diagnosis: 148 vs 50 days=difference of 97 days; figure 3).

Among the 5177 patients treated with interferon-based treatments between 2005 and 2010, the mean annual number of sick leave days was approximately 30 days before the start of treatment. Sick leave days increased to 60 days during the year of treatment initiation followed by a decrease to pre-treatment levels (approximately 30 days) 2 years after treatment initiation (see online

16%
e 3).
Fully DISCUSSION
Hepatitis C infection is a slowly developing disease that often begins with vague symptoms, such as fatigue, loss of

supplementary figure S2). No large differences were

observed in mean annual disability pension days in rela-

tion to interferon-based treatment. The trend that showed

an increase in mean disability pension days before treat-

ment initiation was no longer evident after treatment.

often begins with vague symptoms, such as fatigue, loss of appetite and headache. These symptoms often begin to manifest well before the patient is diagnosed with HCV. The comorbidities are believed to affect the general wellbeing of the patients with an accompanying increased need for sick leave and disability pension. However, the use of sick leave/disability has only been investigated in a few studies, with the largest examining data from 1664 patients with HCV diagnoses who were employed in the USA. In order to get the full picture of the sick leave and disability pension use for patients with HCV in an entire country and to avoid the bias of only analysing employed patients with HCV, the present study set out to investigate the sick leave and disability pension for all diagnosed patients with HCV of working age in Sweden. The diagnosis rate of HCV differs between regions, with an estimated 75% of the cases of HCV in USA remaining undiagnosed.¹⁵ In contrast, the diagnosis rate in Sweden is fairly high with an estimated 20% of patients remaining

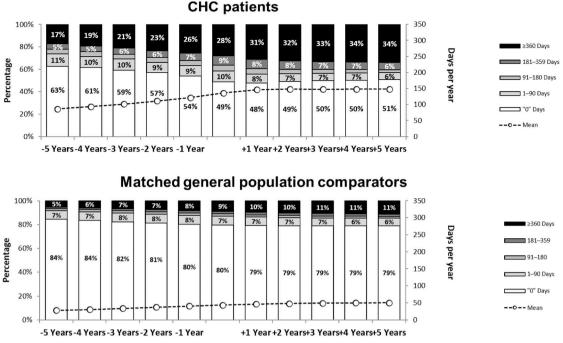


Figure 3 Annual days of sick leave and disability pension 5 years before to 5 years after HCV diagnosis. Patients with register-identified HCV who were diagnosed between the age of 24 and 59 years (n=19 362) and matched general population comparators (n=92 697) in a longitudinal analysis of annual days of sick leave and disability pension from 5 years before to 5 years after diagnosis during 1999–2007. Some sick leave episodes \leq 14 days were not captured due to the 1 day waiting period and the 13-day sick pay period, which could be waived only under certain circumstances. General population comparators were matched 5:1 by age, sex and place of residency at the time of diagnosis (index date). The figures show the full distribution of days in categories and annual mean number of total days. CHC, chronic hepatitis C; HCV, hepatitis C virus.

undiagnosed.¹⁶ This, in combination with the virtually complete national coverage of the Swedish registers, makes Sweden a country well-suited for the investigation of the burden of HCV on the welfare system.

Most importantly, the study showed that 43% of the patients with HCV received compensation from the Social Insurance Agency in the form of sick leave or disability pension in 2012 compared with 17% of the comparators. In total, the patients with HCV lost an average of 87 extra workdays per year compared with matched comparators. One caveat is that the analysis only included individuals alive as of 31 December 2012, which introduces survivorship bias in both groups. The difference in the number of sick leave days, as well as disability pension, could be explained by the inherent differences between patients with and without HCV infection, with riskier lifestyle and psychiatric disorders being more common in patients in the HCV cohort.^{17 18} This could explain the greater frequency of disability pension and higher mean sick leave days noted 5 years before HCV diagnosis. Interestingly, the annual number of days lost increased from a mean of 86 days, 5 years before diagnosis to 136 days during the year of diagnosis. In contrast, there was only an increase of 15 days in the comparator cohort during the 5-year time frame (figure 3). Thus, despite those patients with HCV started with a higher number of workdays lost, the analysis showed a rapid increase in both mean sick leave and disability pension in the years leading up to HCV diagnosis. In contrast, no such rapid

increase was seen for the match comparators. It suggests that patients did most likely experience increased symptoms as the disease progress. This increase in symptoms lead to a greater utilisation of sick leave, as well as more visits to both primary care physicians and specialists until the HCV diagnosis. In addition, after adjusting for psychiatric disease, the difference in sick leave between the two groups remained, thus suggesting that HCV impacts the general health status of patients. It is tempting to hypothesise that earlier diagnosis and treatment of patients with HCV would slow down the increasing need for sick leave and disability pension; however, the present study was not designed to investigate this. Nevertheless, other studies have suggested that earlier treatment benefits both society and the individual patient.^{19–21}

In line with previous studies, there was an increase in mean sick leave days noted during the first year of treatment, which is likely due to the side effects associated with the old interferon-based treatment.^{22 23} The newly introduced interferon-free regimens for patients with HCV infection have a more favourable safety profile compared with interferon-based regimens.²⁴ This would most likely reduce the number of sick leave days needed during treatment. The difference between interferon-based and interferon-free regimens will need to be analysed further when data from interferon-free treatments become available in the registers.

One strength of the study was the use of nationwide register data that contained the actual number of days the social insurance pays for per person. This is in contrast to other studies relying on self-reported information, which are more prone to bias. While the data is only as valid as the information entered, the nationwide Swedish registers are considered to be >99% complete. Nationwide large-scale registries allow assessment of subgroup variations and the use of up to five matched comparators from the general population.

One main limitation of the study is that patients were identified in the NPR using physician entered diagnoses from inpatient and non-primary outpatient care (previously discussed for this cohort²⁵) thus any mistake entering a diagnosis led to misclassification in the study. Another limitation is that the first visit during the study period may not necessarily be the first HCV diagnosis given that the specific ICD code for HCV (B18.2 ICD-10) has only been available since 1997, thus the time of diagnosis must be interpreted with caution. As mentioned in the methods, the Social Insurance Agency data only includes sick leave episodes >14 days, as the first episodes are covered by the employer. This will result in an underestimation of the actual number of workdays lost; however, this applies to both cohorts. Interestingly, the main difference in work absence for US employees with HCV was driven by the short-term disability (defined as sick leave between 14 days and 6 months^{5 26}), thus suggesting the present study would capture the HCV-mediated impact on sick leave. The main route for HCV transmission in Europe is through the use of non-sterile drug paraphernalia²⁷ and since drug use is associated with absenteeism²⁸ it reasonable to think that the higher number of workdays lost among patients with HCV is at least partly due to behavioural differences between the groups. However, the study was not designed to address this confounder.

CONCLUSIONS

To our knowledge, this is the largest study on sick leave and disability pension in patients with HCV to date and the first longitudinal study that investigated this in relation to the time of diagnosis. These results indicate that patients with HCV use more sick days and have a higher frequency of disability pension compared with a comparator cohort from the general population. However, whether earlier hepatitis C diagnosis or virologic cure reduces work absence is not addressed by this study and this needs to be further investigated. Finally, the results may be less generalisable to countries where private health insurance is more common.

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Contributors The concept of the study was designed by KB and JS. FH and KB managed the database. KB, FH, MH and JS interpreted the data with support from ML, JK, JW and MS. KB and JS were the major contributors in writing the manuscript. All authors critically revised the manuscript and approved the final version that was submitted.

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Competing interests ML has consultancies with AbbVie, Gilead and MSD/Merck and is a member of the speakers' bureau for AbbVie, Gilead and MSD/Merck. MS is founder and owner of Svenska Vaccinfabriken AB. FH reports no conflicts of interest. MH is President of Lorimer Enterprises, a company that has consulted for AbbVie. JW has had paid teaching assignments for AbbVie, Gilead and MSD/Merck. JS and JK are employees of AbbVie and may hold AbbVie stocks or stock options. KB was an employee of AbbVie at the time of the study and may hold AbbVie stocks or stock options.

Patient consent for publication Not required.

Ethics approval The study was approved by the Regional Ethics Committee, Karolinska Institutet, Stockholm, Sweden (Dnr 2014/746-31). Informed consent is not needed for large registry-based studies in Sweden.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. Availability of data and materials: The datasets generated and/or analysed during the current study where retrieved from the National Patient Register (NPR), the Cancer Register, the Prescribed Drug Register (PDR), the Cause of Death Register (CDR), the Total Population Register (TPR) and the Longitudinal Integrated Database for Health Insurance and Labor Market studies (LISA) are available for research after ethical approval. The ethical approval for the present study does not allow for sharing data to persons.

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