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# Data linkage to monitor hepatitis C-associated end-stage liver disease and hepatocellular carcinoma inpatient stays in England

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**Abstract**

Persons with chronic hepatitis C (HCV) infection are at increased risk of end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC). The impact of hepatitis treatment scale-up and elimination strategies on ESLD and HCC incidence is a critical measure of progress towards WHO targets. Data from national laboratory surveillance of HCV diagnoses were linked to inpatient care records in Hospital Episode Statistics (HES). For persons first diagnosed with HCV between 1998-2016, we describe the characteristics of those with ESLD and HCC and estimate incidence. Of persons diagnosed with HCV between 1998 and 2016 (104,674), 9.1 % (9,525) had an admission for ESLD and 2.5% (2,610) for HCC. The majority of persons with ESLD and HCC were male (70.7% and 82.7%) and of white ethnicity (89.9% and 82.7%). Crude incidence of ESLD and HCC admission was 10.4 and 3.2 per 1,000 person years respectively. When compared to 2011-2013, incidence of ESLD and HCC admissions in 2014-2017 were lower [ESLD incidence rate ratio (IRR): 0.81; 95% Confidence interval (CI): 0.76-0.86; HCC IRR: 0.90; 95% CI: 0.82-1.00, p=0.045]. Data linkage showed considerable underreporting of HCV in HES coding for ESLD and HCC (16.0% and 11.3% respectively). In conclusion, we found a decline in incidence of ESLD and HCC-related inpatient admissions since 2011-2013. Linked analysis is required for the continued monitoring of ESLD and HCC inpatient incidence. However, HES data quality issues around completeness of identifiers contribute to uncertainty in linkage and may limit our ability to robustly monitor progress towards WHO elimination goals.

**Introduction**

In 2018, an estimated 0.2% (113,000) of the population in England had chronic hepatitis C virus (HCV) infection, with the main group at risk being persons who inject drugs (PWID) [1]. Chronically infected persons are at increased risk of liver cirrhosis, end-stage liver disease (ESLD) (complication of cirrhosis and decompensated cirrhosis) and hepatocellular carcinoma (HCC). The burden of liver disease in this population had been increasing prior to 2014, but following the introduction of direct acting antivirals (DAAs) to treat HCV, which are of shorter treatment duration, better tolerated and more effective than previous interferon-based regimens, there are hopes for a reversal in this concerning trend. Successful clearance of HCV, defined as the absence

of detectable HCV RNA after treatment completion and referred to as a sustained virological response (SVR), improves the outcomes in persons with HCV, including improved liver function and reduced mortality rates [2,3].

As the UK has signed up to the WHO global strategy for elimination of viral hepatitis as a significant public health threat by 2030 and the National Health Service (NHS) is ramping up HCV treatment rates nationally, it is important to benchmark the burden of HCV-associated disease in the pre-DAA era and monitor the evolution of HCV-associated liver disease following their introduction. Whilst there has been some work to show the positive initial impact of DAAs on HCV-associated burden of disease in the UK [4,5], the incidence of ESLD and HCC, based on NHS Hospital Episode Statistics (HES) inpatient care data, has continued to increase post-DAA introduction [5]. However, it is unknown whether this increase is a true reflection of the current burden or influenced by changes in reporting of HCV within HES, as this methodology relies on HCV diagnosis been recorded on a patient's record.

It is for this reason we have used data linkage of laboratory reports of new HCV diagnoses and HES inpatient care data to estimate rates of ESLD and HCC-related inpatient stay (hereafter called an admission) in persons with HCV, investigate whether these have decreased following the introduction of DAAs in 2014, to describe the characteristics of persons requiring admission for HCV-associated ESLD and HCC and to explore underreporting of HCV within HES. Through this we can provide a baseline against which we can monitor progress towards the WHO elimination goals and inform future analysis of HCV-associated ESLD and HCC incidence in England.

## Methods

### *Data sources*

#### *Routine laboratory reports of HCV diagnoses*

First HCV diagnoses were obtained from routine laboratory reports of HCV, defined as the detection of HCV antibody (anti-HCV) or HCV RNA in blood, submitted by virology laboratories in England to Public Health England. The laboratory reporting system does not distinguish between anti-HCV and HCV RNA in an individual and so laboratory "confirmed" cases are a mix of current (viraemic) and ever infected individuals. Laboratory HCV reports have been submitted to PHE (previously the Health Protection Agency), through surveillance forms or electronically, since 1990 but laboratory reporting became mandatory in 2010. Reports include basic demographics (name, date of birth, sex, NHS number), and variable risk factor information. Through linkage with the Patient Demographic Service, reported information can be improved, particularly for persons reported to PHE with an NHS number, and date of birth, sex, date of death, patient address and registered General Practice (GP) can be updated. Ethnicity is poorly recorded. Name, date of birth, sex and NHS number are used to de-duplicate reports.

For this study, the routine laboratory reporting dataset was enhanced with information from additional sources. As the date of first HCV diagnosis is critical, this was updated, where possible, with information from the Sentinel Surveillance of Blood Borne Virus Testing (SSBBV). Established in 2002, SSBBV collects information on hepatitis A-E, HIV and HTLV tests, regardless of result, from 23 participating NHS laboratories in England [6,7]. SSBBV is broadly representative of testing in England, estimated to cover 40% of all HCV testing. HCV treatment with DAAs (both date and outcome) was obtained through linkage with the national HCV treatment monitoring and outcomes dataset, established in 2015.

Information on a person's first diagnosis with HCV between 1998 and 2016, as well as identifiers required for linkage (sex, date of birth and NHS number), were extracted from the database and used for linkage.

#### *Hospital Episode Statistics*

HES contains patient and clinical information for all inpatient (including day-cases), outpatient and accident and emergency episodes. Inpatient stays and day-cases (hospital admissions) have been collected since 1989 onwards and were used for the analysis. Diagnoses associated with admission are coded using International Classification of Diseases version 10 (ICD-10). Outpatient and accident and emergency data was excluded as diagnoses codes are not collected within the accident and emergency dataset, and are poorly completed in the outpatient dataset. Identifiers available for linkage include hospital number, NHS number, sex, date of birth, patient address and registered General Practice.

*Data linkage*

Between 1998 and 2017 67.6% (112,920/167,130) of persons (all ages) reported to PHE as testing positive for anti-HCV had an NHS number and we were able to obtain a patient's address and registered GP by querying the NHS Patient Demographic Service. Linkage to HES was a two-step process, (Supplementary figure), with persons first linked to all HES records using NHS number, date of birth and sex. Secondly, persons with an NHS number in the routine laboratory reports of HCV, were linked to persons without an NHS number within HES who had a record of an HCV, ESLD or liver cancer associated admission, using data of birth, sex and geographies associated within the patient (postcode, Primary Care Trust or Clinical Commissioning Group of residency at time of test) and registered General Practice address (GP code, Primary Care Trust and Clinical Commissioning Group). NHS number completion for persons with a HCV diagnosis recorded in HES was variable (60.1% overall, but with a decreasing trend since 2011).

*Inclusion/exclusion criteria*

Diagnosis codes were grouped using ICD-10 as in table 1. Earlier diagnosis dates are identified in HES if an earlier admission was recorded with HCV. This updated the date of diagnosis for 13,779 people, by a median of 3.1 years (interquartile range (IQR): 0.4-7.1 years). Using this updated HCV diagnosis date, only persons diagnosed between 1998 and 2016 and aged 15 years or over at the time of HCV diagnosis (n=104,674) were included in the analysis. Data for 2017 was excluded as during that year HCV was mistakenly included as a sensitive diagnosis code in HES,

which resulted in most HES records with an HCV code systematically being stripped of the patient's NHS number, impeding deduplication and linkage [8].

*Statistical Analysis*

Statistical analysis was carried out in STATA SE (version 13). Persons with any admission (ie did not have to be associated with ESLD or HCC) for alcohol-associated and opioid-associated diagnoses (table 1), and suggestive of alcohol or opioid misuse, or no fixed abode (homeless) reported at admission were identified. Kaplan-Meier analysis was used to estimate the cumulative proportion of persons having had an ESLD or HCC-related admission at 1, 5, 10 and 15 years after HCV diagnosis and to describe unadjusted survival patterns following first ESLD or HCC inpatient stay. Crude incidence of first ESLD or HCC admission, by year, was calculated for all persons diagnosed with HCV between 1998 and 2016. Persons were excluded where the first ESLD or HCC admission preceded a HCV diagnosis. Follow-up started at HCV diagnosis and ended at first ESLD or HCC-related admission, death or 31st December 2016, whichever came first. 95% confidence intervals (CI) were calculated using Poisson distribution. Poisson regression was used to identify predictors of an admission for ESLD and HCC in persons diagnosed with HCV between 1998-2016 and to test for a change in incidence pre- and post-2014; factors included in these models were sex, age at diagnosis and calendar period (grouped as 1998-2001, 2002-2004, 2005-2007, 2008-2010, 2011-2013 and 2014-2016).

*Ethics*

Laboratory diagnosis data and linkage to HES are collated and processed by PHE as part of surveillance of HCV infection and disease. These data collections, and linkage to HES, are covered by Health Service (Control of Patient Information) Regulations 2002 (regulation 3) which makes provisions for the recognition, control and prevention of communicable diseases and other risks to public health.

**Results**

Between 1998 and 2016, 104,674 persons aged 15 years or older were diagnosed with HCV and included in our analysis; 68.1% were male and the median age at HCV diagnosis was 39 years (interquartile range (IQR): 31-48 years) (table 2). Over the study period 7,467 persons were treated with DAAs; among this group the median time from diagnosis to treatment initiation was 4.9 years (IQR: 1.8-9.7 years).

*ESLD*

By the end of 2016, 9.1% (9,525) of persons diagnosed with HCV had a record of an ESLD admission within HES, the majority of which were emergency admissions (88.5%) (table 2). 402 were day-case admissions. Of persons with an admission for ESLD, 70.7% were male, 89.9% were of white ethnicity and the median age was 49 years (IQR: 41-57 years) at first stay. The majority (70,5%) also had at least one admission with an alcohol-associated diagnosis, 42.6% with an opioid-associated diagnosis and 9.3% had no fixed abode recorded in HES.

Of first ESLD admission, 1,617 were prior to HCV diagnosis (median: 39 days; IQR: 3-787 days). After excluding these persons from the analysis, the cumulative proportion of persons with an ESLD-related admission was 1.3%, 4.5%, 8.3% and 11.9% at 1, 5, 10 and 15 years and 2.9%, 10.2%, 18.2% and 25.9% respectively in persons who had ever had an admission with an alcohol-associated diagnosis.

Excluding persons diagnosed with HCV after first admission for ESLD, the crude incidence of ESLD-related first admission over the study period was 10.4 (95% CI: 10.2-10.7) per 1,000 person years. Crude incidence rates (figure 1) increased between 2005 and 2012 but decreased thereafter. Using Poisson regression, ESLD admission incidence rates were higher in persons older at time of HCV diagnosis [incidence rate ratio (IRR) per 10 years older: 1.63; 95% CI: 1.60-1.66]. Incidence rates were lower in persons of Asian and black ethnicity when compared to those of white ethnicity (Asian: IRR: 0.90; 95% CI: 0.81-0.99 and black: IRR: 0.40; 95% CI: 0.32-0.51) and lower in 2002-2004 and 2005-2007 when compared to 2011-2013, (2002-2004: IRR:

0.87; 95% CI: 0.77-0.97, 2005-2007: IRR: 0.82; 95% CI: 0.76-0.90). Subsequently there was a 19% fall in incidence for 2014-2016 (IRR: 0.81; 95% CI: 0.76-0.86).

By the end of 2016, 60.4% (5,752) of persons with ESLD had died. Using Kaplan-Meier survival analysis, the proportion of persons who had survived 1, 5 and 10 years after first admission for ESLD were 64.3%, 43.2% and 32.2% respectively and median survival time was 3.2 years.

*HCC*

By the end of 2016, 2.5% (2,610) of persons diagnosed with HCV had an admission for HCC. Of persons with an admission for HCC, 80.5% were male, 82.7% were of white ethnicity and with a median age of 58 years (IQR: 53-64 years) at first admission. A similar proportion of HCC-associated admissions were elective and emergency admissions (51.1% and 47.4% respectively). 43.5% and 12.7% had ever had an admission with alcohol-associated or opioid-associated diagnoses respectively, and 2.0% had no fixed abode recorded in HES.

Of first HCC-related admission, 107 were admitted prior to HCV diagnosis (median 6 days, IQR: 3-27 days) (table 2). Excluding these persons, the cumulative proportion of persons with an HCC-related admission was 0.6%, 1.5%, 2.7% and 3.9% at 1, 5, 10 and 15 years after HCV diagnosis. The corresponding figures for persons who had ever had an admission with alcohol-associated diagnoses were 0.8%, 2.1%, 3.8% and 5.6%.

Excluding persons with a HCC-related admission prior to HCV diagnosis, the crude incidence of first HCC-related admission over the study period was 3.2 (95% CI: 3.1-3.3) per 1,000 person years. Crude incidence rates (figure 1) remained constant between 1998 and 2007, increased between 2007 and 2013 and then fell thereafter. Using Poisson regression, HCC admission incidence rates were higher in older persons at HCV diagnosis (IRR per 10 years older: 2.46; 95% CI: 2.39-2.52) and incidence was lower in persons of black ethnicity when compared to white ethnicity (IRR: 0.68; 95% CI: 0.53-0.87) and in females when compared to males (IRR: 0.40; 95% CI: 0.36-0.44). When compared to 2011-2013, incidence rates for all earlier years were lower (1998-2001: IRR: 0.54; 95% CI: 0.39-0.76, 2002-2004: IRR: 0.68; 95% CI: 0.56-0.83, 2005-2007:

IRR: 0.68; 95% CI: 0.59-0.79, 2008-2010: IRR: 0.83; 95% CI: 0.74-0.94). Subsequently, there was a 10% fall in incidence rates for 2014-2016 (IRR: 0.90; 95% CI: 0.82-1.00 p=0.045).

By the end of 2016, 66.1% (1,724) of persons with HCC had died. Using Kaplan-Meier survival analysis, the proportion of persons who had survived 1, 5 and 10 years after first admission for HCC were 53.6%, 32.1% and 26.5% respectively, with a median survival rate of 1.3 years.

*Underreporting of HCV in HES*

Overall, 47.7% (49,883) of people with a laboratory report of HCV infection and included in our analysis had a record of any admission associated with a HCV code in HES. For linked persons, the proportion with a HCV diagnosis code in HES was 84.0% (8,001) for persons with ESLD and 88.7% (2,314) for persons with HCC.

**Discussion**

Among persons diagnosed with HCV, the cumulative proportion of persons with an ESLD or HCC-related admission 10 years after HCV diagnosis was 8.2% and 2.7% respectively. Incidence of ESLD and HCC increased between 2006 and 2013 but has fallen in more recent years. Survival following first admission for ESLD or HCC was poor, with 50% of persons surviving 3.1 years and 1.3 years respectively. Under reporting of HCV within HES was 16.0% for persons with an ESLD-associated admission and 11.3% for persons with an HCC-associated admission.

Our incidence estimates suggest ESLD and HCC-related admission incidence was increasing prior to 2011-2013, but has since decreased. These results conflict with recent analysis of unlinked data, that used HCV records in HES to look for new ESLD and HCC-associated admissions and found a 15% increase between 2015 and 2016 [5]. As our linkage of HCV diagnosed persons to records of ESLD and HCC did not rely on the reporting of HCV itself, we were able to identify HCV in 16% of cases which would not have been included in the previous estimates. A fall in ESLD and HCC incidence was expected, as progression to liver disease is prevented by successful HCV treatment, the rates of which have increased since the phasing out of interferon-based

treatments and the introduction of DAAs in 2014, and as Operational Delivery Networks (who are responsible for local treatment decisions for persons with HCV) have increased case finding to achieve treatment quotas. Similar declines have been observed in liver transplant rates in persons with HCV, and although not significant a reduction in liver disease mortality rates has also been observed [4,9]. The lag in HCC admission incidence reduction, when compared to ESLD admission incidence, could be due to the former having more advanced liver disease. Successful treatment of HCV may have relatively greater impact on regression of fibrosis and improvement in liver function in patients with cirrhosis, than removing the risk of progression to liver cancer, despite SVR and viral clearance. This delay was observed by Simmons et al. in linked analysis of mortality data [10]. It is important to recognise that DAA treatment in England was initially prioritized for patients with advanced or decompensated cirrhosis.

We also found that over two-thirds (71.2%) of persons admitted for ESLD and two-fifths (43.5%) of persons admitted for HCC had ever had an admission for alcohol-associated diagnosis, and we saw higher rates of ESLD and HCC in these persons. For opioid-associated diagnosis codes the corresponding figures were 42.9% and 12.7%. Thus, whilst DAAs may eliminate HCV infection, other risk factors, such as alcohol misuse and obesity, could continue to drive liver disease progression and offset the beneficial impact of DAAs on ESLD and HCC burden [11]. A history of alcohol abuse is associated with a high incidence of ESLD, regardless of whether patients are chronically infected with HCV or have cleared their infection and non-alcoholic fatty liver disease prevalence is increasing globally [12,13]. Sustained provision of drug and alcohol treatment services alongside HCV treatment cannot be overemphasised.

Whilst almost all (92%) of first ESLD-related admissions were emergency admissions, this was the case for only 47% of HCC-related admissions. As ESLD is characterised by clinical symptoms that commonly result in emergency presentations rather than elective admissions, this high rate of emergency admissions would be expected for ESLD. The inclusively grouped ICD-10 codes (table 1) would capture but do not necessarily distinguish admissions for complications such as variceal haemorrhage, ascites, hepatic encephalopathy or spontaneous bacterial peritonitis for example. The relatively high rate of emergency HCC admissions may reflect late diagnoses of HCV or HCC or lack of engagement in liver disease care, surveillance by regular imaging and monitoring.

Indeed, in the National Cancer Intelligence Network Routes to Diagnosis analysis 39% of liver cancers diagnosed between 2006 and 2016 followed an emergency presentation, thus there is some work to improve earlier diagnoses of asymptomatic HCC in patients at risk, enhance elective treatment options and prevent emergency admissions [14].

Post-admission survival for ESLD and HCC was low, with 50% of persons surviving 3.1 years and 1.3 years respectively. Mar et al. (2017), using hospital discharge data in northern Spain, found mean survival for decompensated cirrhosis and HCC in persons with HCV to be 4.1 years and 1.75 years respectively [15], which were similar to our results, but 5-year survival estimates for all persons with HCC (regardless of HCV infection) in England were lower (10.9% vs 32.1%)[16].

PHE are required to monitor progress towards WHO elimination goals and one of the burden indicators is incidence of HCV-related ESLD and HCC. Whilst there are no other routine surveillance datasets through which ESLD incidence and survival can be monitored, the English Cancer Registry may provide another route to monitor HCC burden and survival in persons with HCV, would enable outcomes to be linked to HCC diagnosis date rather than first admission and may help us better understand the differences in HCC survival for persons with and without HCV infection.

An unintended finding of this work was the detection of poor completeness of patient identifiers, in particular NHS number, in HES. We discovered that the proportion of persons with a HCV diagnosis having an NHS number reported had decreased since 2011 (60% overall but falls to 40% in 2016). To enable data linkage among those records within HES without an NHS number, persons in routine laboratory reports of HCV who had an NHS number recorded (67.6%) were also run through the Patient Demographic Service (NHS spine) to add patient postcode, and registered GP for additional linkage fields which were available within HES. This resulted in a two-step process for linking, first linking on NHS number and second using geographies associated with the patient. By expanding the linkage criteria in this way, only 0.7% of all persons with ESLD/HCC, and 2.8% of persons with HCV and ESLD/HCC in HES did not have sufficient identifiers for linkage. In 2017, PHE also identified that HES HCV codes had been incorrectly interpreted as legally restricted codes – this resulted in records from that year being stripped of NHS number [8], which prevents the linkage of multiple admissions for the same person. As a result, we were

unable to estimate ESLD/HCC incidence using HES for 2017 – this error will continue to be a limitation in the future unless complete data can be re-submitted from all Trusts.

In addition to the HES data quality issues detailed above, we do not know how people with versus without an NHS number recorded within routine laboratory reports of HCV differ. It is likely that many of these persons were diagnosed with HCV in sexual health services, as these services anonymise their data. However, persons not available for linkage with HES were similar with regards to the proportion who were male and median age at HCV diagnosis. Furthermore, we are unable to account for the HCV infected, but undiagnosed period, and persons who may have been previously diagnosed with HCV before they were reported to PHE or had HCV reported with a HES admission. With regards to the undiagnosed period, case-finding efforts in the DAA-era will improve early diagnosis rates and it will be important to bear in mind when interpreting future trends, particularly for estimates where parameters are assumed to be constant. A prompt diagnosis, will result in a person being treated earlier in their infection, preventing disease progression to ESLD, and HCC. Continued monitoring, regardless of the shift in testing will highlight gaps in the care pathway, or additional risks from multi-morbidities. For persons who did not have their first diagnosis reported to PHE, this will have a greater impact on persons diagnosed pre-2010, as laboratories have been legally required to notify PHE of all positive HCV tests since 2010. However, if persons first diagnosed pre-legislation have subsequently been tested post-legislation we should have captured them, and enhancements with data from other surveillance systems have improved the accuracy of diagnosis date.

In conclusion, our findings suggest a reduction in the incidence of ESLD and HCC-associated admissions following the introduction of DAAs in 2014. However, we uncovered additional data quality issues within HES, which, unless addressed, will limit our ability to use HES to monitor ESLD and HCC admission incidence in persons with HCV as we move towards WHO elimination goals.

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Table 1: ICD-10 groupings.

| Disease grouping | IDC-10 Codes |
|---|---|
| Hepatitis C (HCV) | B171 , B182 |
| End stage liver disease (ESLD) | I850, I983, K704, K720, K721, K729, K767, R18 |
| Hepatocellular carcinoma (HCC) | C22 |
| Alcohol-associated diagnoses | F10, E244, G312, G621, G721, I426, K292, K70, K852, K860, Q860, R780, T51, X45, X65, Y15, Y90, Y91 |
| Opioid-associated diagnoses | F11, X42, X62, Y12 |

Table 2: Demographics of persons diagnosed with HCV between 1998 and 2016, and proportion who have had an admission for ESLD or HCC.

| | HCV | ESLD admission | | HCC admission | |
|---|---|---|---|---|---|
| | diagnosed | n | % | n | % |
| *Total* | 104,674 | 9,346 | 8.9 | 2,610 | 2.5 |
| *Sex* | | | | | |
| Male | 71,256 | 6,612 | 9.3 | 2,100 | 2.9 |
| Female | 33,402 | 2,734 | 8.2 | 510 | 1.5 |
| Not reported | 16 | 0 | 0.0 | 0 | 0.0 |
| *Age* | | | | | |
| 15-29 years | 20,759 | 683 | 3.3 | 12 | 0.1 |
| 30-39 years | 33,988 | 2,151 | 6.3 | 133 | 0.4 |
| 40-49 years | 26,754 | 3,070 | 11.5 | 695 | 2.6 |
| 50+ years | 22,916 | 3,440 | 15.0 | 1,770 | 7.7 |
| Not reported | 257 | 2 | 0.8 | 0 | 0.0 |
| *Ethnicity* | | | | | |
| White | 73,124 | 7,200 | 9.8 | 1,810 | 2.5 |
| Asian | 6,465 | 594 | 9.2 | 256 | 4.0 |
| Black | 1,721 | 114 | 6.6 | 79 | 4.6 |
| Other | 1,937 | 86 | 4.4 | 43 | 2.2 |
| Not reported | 21,427 | 1,352 | 6.3 | 422 | 2.0 |
| *Year Diagnosed* | | | | | |
| 1998-2002 | 14,312 | 1,898 | 13.3 | 535 | 3.7 |
| 2003-2007 | 29,806 | 3,273 | 11.0 | 873 | 2.9 |
| 2008-2012 | 33,483 | 2,989 | 8.9 | 818 | 2.4 |
| 2013-2016 | 27,073 | 1,186 | 4.4 | 384 | 1.4 |
| *Treated with DAAs* | | | | | |
| Yes | 7,467 | 582 | 7.8 | 243 | 3.3 |
| *Alcohol-mentioned in any inpatient record* | | | | | |
| Yes | 32,007 | 6,651 | 20.8 | 1,136 | 3.5 |
| *Opioid use mentioned in inpatient record* | | | | | |
| Yes | 40,369 | 4,014 | 9.9 | 328 | 0.8 |

Table 3: Factors associated with an ESLD and HCC admission among persons diagnosed with HCV between 1998 and 2016, adjusted for follow-up time.

| | ESLD admission | | | HCC admission | | |
|---|---|---|---|---|---|---|
| | IRR | 95% Confidence Interval | p-value | IRR | 95% Confidence Interval | p-value |
| *Sex* | | | | | | |
| Male | 1 | | <0.001 | 1 | | <0.001 |
| Female | 0.82 | 0.78-0.87 | | 0.40 | 0.36-0.44 | |
| *Age at diagnosis* | | | | | | |
| Per 10 year increase | 1.61 | 1.58-1.64 | <0.001 | 2.46 | 2.39-2.52 | <0.001 |
| *Ethnicity* | | | | | | |
| White | 1 | | | 1 | | |
| Asian | 0.90 | 0.81-0.99 | | 1.05 | 0.92-1.21 | |
| Black | 0.41 | 0.32-0.51 | <0.001 | 0.68 | 0.53-0.87 | <0.001 |
| Other | 0.48 | 0.37-0.62 | | 0.91 | 0.67-1.24 | |
| Not reported | 0.68 | 0.63-0.73 | | 0.69 | 0.62-0.78 | |
| *Year of follow-up* | | | | | | |
| 1998-2001 | 0.80 | 0.68-0.94 | | 0.54 | 0.39-0.76 | |
| 2002-2004 | 0.75 | 0.67-0.84 | | 0.68 | 0.56-0.83 | |
| 2005-2007 | 0.76 | 0.70-0.83 | <0.001 | 0.68 | 0.59-0.79 | <0.001 |
| 2008-2010 | 0.91 | 0.85-0.98 | | 0.83 | 0.74-0.94 | |
| 2011-2013 | 1 | | | 1 | | |
| 2014-2016 | 0.81 | 0.77-0.86 | | 0.90 | 0.82-1.00* | |

*p=0.045

Figure 1: Crude incidence for first ESLD- and HCC-related inpatient stay in persons diagnosed with HCV in England between 1998 and 2016.

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