Public Health England

Protecting and improving the nation's health

Hepatitis C in the East Midlands

2017 data

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The Field Service (FS) supports Public Health England (PHE) Centres and partner organisations through the application of epidemiological methods to inform public health action. FS does this in 2 main ways, firstly by providing a flexible expert resource, available, as and when needed, to undertake epidemiological investigations for key health protection work and secondly through the expert analysis, interpretation and dissemination of surveillance information to PHE Centres, local health partners, service providers and commissioners of services. Within the FS network, excellence and innovation is encouraged, we foster academic collaborations and take active part and lead in research, development and training.

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1. Executive summary

Hepatitis C is blood borne virus (BBV) that usually silently infects and damages the liver (most individuals are asymptomatic in the early stages of infection and can therefore remain undiagnosed for many years). It is estimated that around 113,000 individuals are chronically infected with Hepatitis C in England most of whom are from marginalised and underserved groups in society [1].

Since 2016, the UK has been signed up to the WHO Global Health Sector Strategy (GHSS) on Viral Hepatitis [2] which has meant the UK, along with other participating countries, are committed to eliminating Hepatitis C virus (HCV) in the UK by 2030.

Within the East Midlands there were 736 new reports of HCV through laboratory reporting in 2017; the trend has remained broadly similar for the East Midlands for the last 10 years. This is however thought to be an under-estimate of the true number of new HCV diagnoses for the East Midlands due to under-reporting by laboratories, however local efforts between PHE and the laboratories in the East Midlands has improved the quality and timeliness of reporting of hepatitis C and B over recent years.

The prevalence of HCV remains greatest amongst people who inject drugs (PWID). This poses a risk to the wider community where recreational drug taking with equipment sharing may lead to exposure in those who do not recognise themselves as problematic drug users and who may therefore not present themselves to drug services. Encouraging testing in more services may help identify these people and reduce further transmission.

Addressing the need to increase wider awareness of the risk factors associated with HCV PHE has been working with stakeholders to distribute various information resources to encourage those at risk to seek testing using social media and primary care to display some of the material. PHE both nationally and locally have been working with the NHS to identify previously diagnosed patients who may not have accessed care or cleared their infections, to offer them testing and treatment. As the tolerability and efficacy of treatments have improved it is important that detections and access to the care pathway are maximised to reduce onward transmission.

While we are seeing small increases in detections through laboratory reporting figures, the number of admissions to hospitals with HCV as the diagnosis, HCV related end stage liver disease and hepatocellular carcinoma has been broadly static since 2013 as seen in the Hospital Episode Statistics (HES). Transplant registry information shows a decline in the number of new liver transplant registrations associated with HCV from 2014-2017 compared to 2010-2013, although the overall number of liver transplants

undertaken in the East Midlands has increased, implying HCV may not be the cause of more recent episodes of liver disease which have led to transplantation.

In England we have seen a 16% fall in deaths between 2015 and 2017exceeding the WHO target of a 10% decrease in HCV-related mortality by 2020. The under 75 mortality rates indicator is measured in 3-yearly grouped figures; the pattern seen in the East Midlands compared to England is similar, showing an increase from the 2007-2009 rate to the 2013-2015 rate followed by a slow decline up to 2015-2017.

With improved treatments now available this report highlights the need for better detection of HCV to reach new and previously undiagnosed cases as well as the follow up of cases previously detected who did not receive treatment. But also to ensure as many of these cases as possible are promptly placed onto appropriate care pathways leading to earlier treatment of the infection, reducing morbidity and mortality along with reducing transmission will eventually get us closer to the WHO target of elimination of HCV.

2. Introduction and background

Hepatitis C is a blood borne virus that infects and damages the liver. Most individuals with an HCV infection remain asymptomatic in the early stages of infection and may therefore remain undiagnosed for many years [1].

After the initial infection, approximately 20% of individuals will clear the infection within 6 months, the remainder developing chronic HCV infection which usually remains asymptomatic until late stage disease and therefore usually remains undiagnosed. Consequently, these individuals do not access treatment at the earlier stages in the disease process. If untreated chronic infection may lead to liver disease in 75% of cases and of these 25% will progress to liver cirrhosis, of whom 1-4% will develop liver cancer each year [3]. Hepatocellular carcinoma and HCV-related end-stage liver disease (ESLD) require expensive and complicated treatments and have poor survival rates.

The global burden of deaths resulting from viral hepatitis was 1.34 million in 2015, comparable to deaths caused by TB and greater than those caused by HIV, however deaths caused by both TB and HIV are declining over time whereas those caused by viral hepatitis are increasing [3].

It is estimated that there were approximately 71 million people with chronic HCV infection worldwide. In England, modelled estimates indicate that 113,000 people are chronically infected with HCV, the majority of whom are from marginalised and underserved groups in society, such as people who inject drugs (PWID) with injecting drug use being cited in about 90% of all laboratory reports where a risk factor was recorded[1]. Other risk factors account for less than 10% of all positive diagnoses in England. These are:

- people who received a blood transfusion prior to 1991 or other blood products before 1986
- people born in countries where there is a prevalence of hepatitis C of 2% or more
- prisoners (due to injecting drug use and other lifestyle risks)
- children in care
- the homeless (also due to injecting drug use and other lifestyle risks)
- men who have sex with men, especially those with HIV (related to trauma and bleeding during intercourse, having sex under the use of drugs and frequent partner change
- close contacts of a person with chronic hepatitis C
- babies born to mothers who have hepatitis C

The aim of the surveillance of HCV is to monitor population health and provide information to help improve the planning and provision of prevention and control

activities. The latest report on HCV in England was recently published and summarises the current scale of the HCV problem. It sets out a Public Health England (PHE) vision and progress in tackling the infection and identifies where focused action is needed if we are to eliminate hepatitis C as a major public health threat by 2030 in line with World Health Organisation target [1].

2.1 Purpose of the report

This report presents data up to the end of 2017 for the population resident within the East Midlands. Data are shown for PHE East Midlands Centre which includes the counties of Derbyshire, Leicestershire, Rutland, Lincolnshire, Northamptonshire, and Nottinghamshire. A summary of the East Midlands population area is provided in Appendix 1.

Along with the geographies described in the appendix 2, it is important to understand the Operational Delivery Networks (ODNs) which were formed in 2016 to deliver hepatitis C treatment across England. In the East Midlands there are 2 ODNs; “Leicester”, whose lead organisation is University Hospitals of Leicester, partnered with Kettering General Hospital NHS Foundation Trust, Northampton General Hospital NHS Trust and Leicestershire Partnership NHS Trust and which covers Leicestershire. The second ODN is “Nottingham”, whose lead organisation is Nottingham University Hospitals NHS Trust, partnered with Sherwood forest Hospitals NHS Foundation Trust, United Lincolnshire Hospitals NHS Trust and Derby Hospitals and which covers Nottinghamshire, Derbyshire and Lincolnshire.

These ODNs have been working with PHE to undertake an exercise to approach previously diagnosed HCV cases who do not have a record of receiving treatment, to get these cases on care pathways.

2.2 Data quality

This report brings together data from different sources including reports of HCV testing from local NHS laboratories. Within the East Midlands there are 8 key hospital trusts / laboratories that report data to PHE (although Bassetlaw residents tests are reported from the Doncaster and Bassetlaw laboratory and so are also included). In 2016 automated routine reporting was not in place for all laboratories. Also, no data is received from some private laboratories used by a number of drug services within the region.

The lack of data from some laboratories is likely to lead to an underestimate in the population burden of HCV. PHE is continually working with individual laboratories to improve the quality of data reporting. Data in this report may not reflect all the recent improvements in data reporting due to when the data was extracted from SGSS for

analysis, however, both Chesterfield and Northampton's laboratory data shows improvements in both quality and volume of data being submitted during 2017, which will be more evident in 2018. Derby's laboratory data which has been steadily improving since 2017. Also, in light of the current re-engagement exercise, PHE are working with laboratories to try to get as much historic data into the SGSS system as possible, subsequent reports will show all these changes to both historic and recent data. The reporting of data has been a difficult problem to resolve, however significant improvements have been made in 2017 and so future reports should show a greater degree of data coverage from all laboratories in the East Midlands.

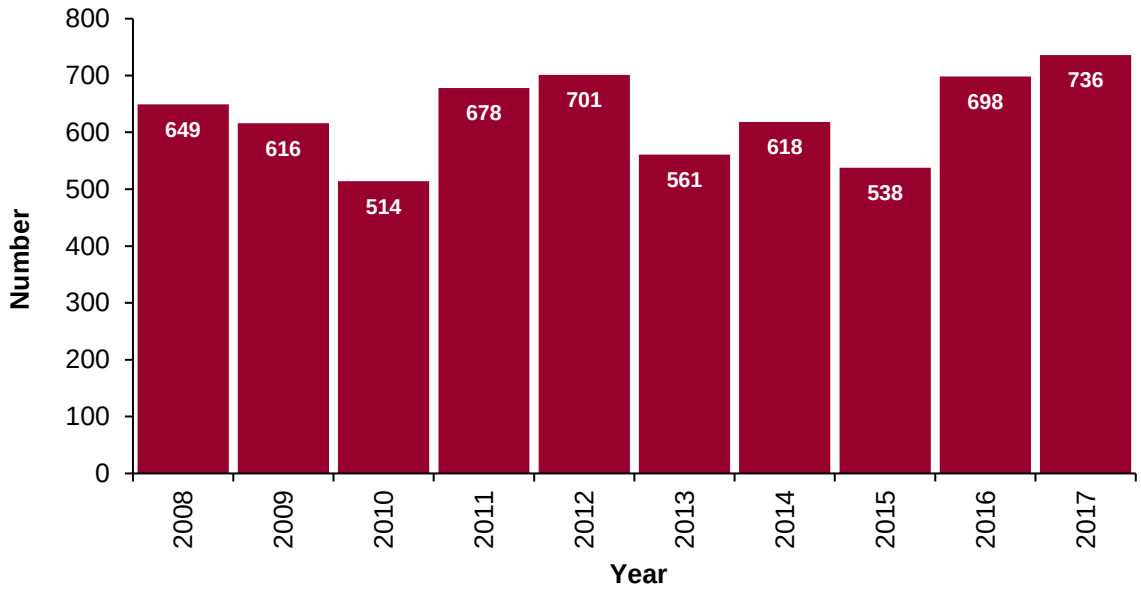
3. Burden of hepatitis C

3.1 Laboratory reports of hepatitis C

In the East Midlands there has been a broadly stable trend in the number of HCV infections reported by laboratories between 2008 and 2017, although the exact number of cases varies year on year (Figure 1). Currently, the number of HCV cases for the East-Midlands are at their highest since 2008, suggesting better case identification and data capture.

Laboratory data includes individuals with a positive test for hepatitis C antibody and/or detection of hepatitis C RNA. Due to the variability in the quality of laboratory reports and the inability of current serological assays to differentiate acute from persistent infections, data presented here represents all new cases, those with evidence of past infection and cases with a persistent hepatitis C infection.

Figure 1. Number of laboratory reports of hepatitis C, residents of East Midlands PHE Centre, 2008-2017

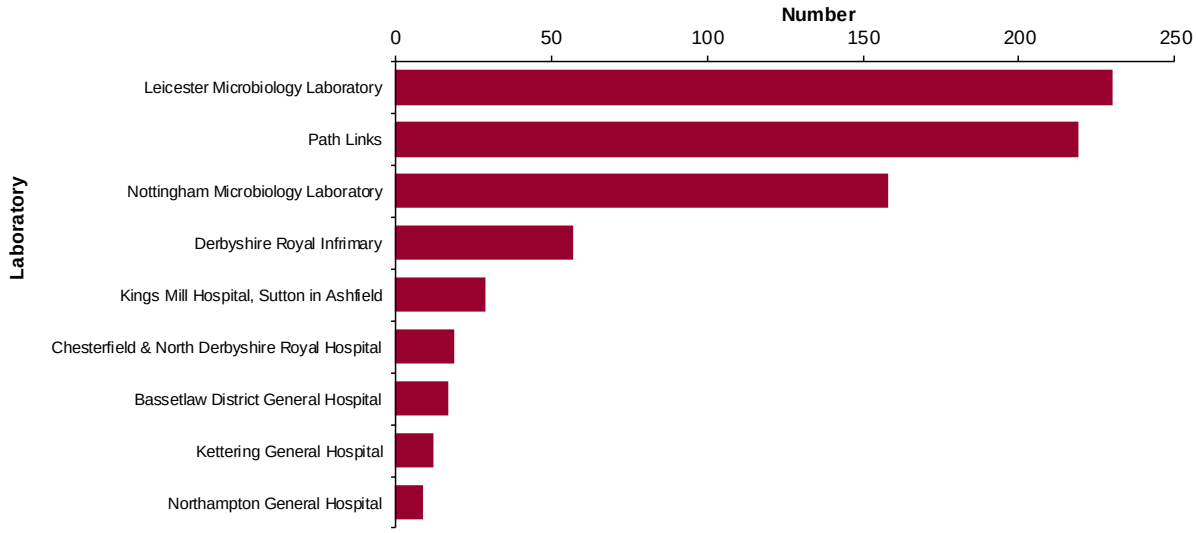


Note: Includes individuals with a positive test for hepatitis C antibody and/or detection of hepatitis C RNA.

The majority of residents of the East Midlands will have laboratory testing carried out within a local laboratory. However, Figure 2 demonstrates considerable variation by laboratory in the number of positive tests identified, where data is received. The reasons underlying this variation are unclear but may reflect sample referral patterns, the level of awareness by local clinicians and patients, siting of tertiary services, increased local prevalence, variation in testing approaches or coding issues. Compared to previous year's data, 2017 shows improvements in reporting from some of these laboratories,

and PHE is working with local laboratories to ensure reporting continues to improve in all laboratories across the region.

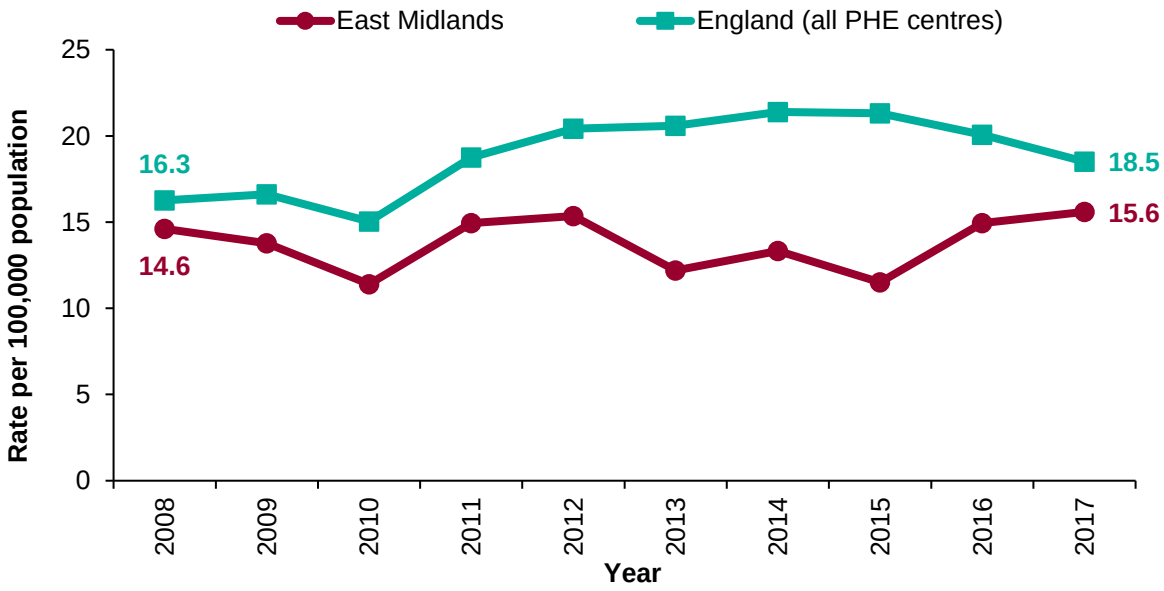
Figure 2. Number of reports of hepatitis C by reporting laboratory in East Midlands PHE centre, 2017



Note: Includes individuals with a positive test for hepatitis C antibody and/or detection of hepatitis C RNA.

The England rate for HCV infections from 2008 to 2017 shows a general increase until 2015, with a more recent decline. This differs from the East Midlands in which the rate has been broadly stable with a dip in 2015, followed by a sustained increase over 2016 and 2017. This increase has taken the East Midlands rates to its highest point over the 10-year period and opposes the decreasing England trend (Figure 3).

Figure 3. Laboratory reports of hepatitis C per 100,000 population, residents of East Midlands and England, 2008-2017

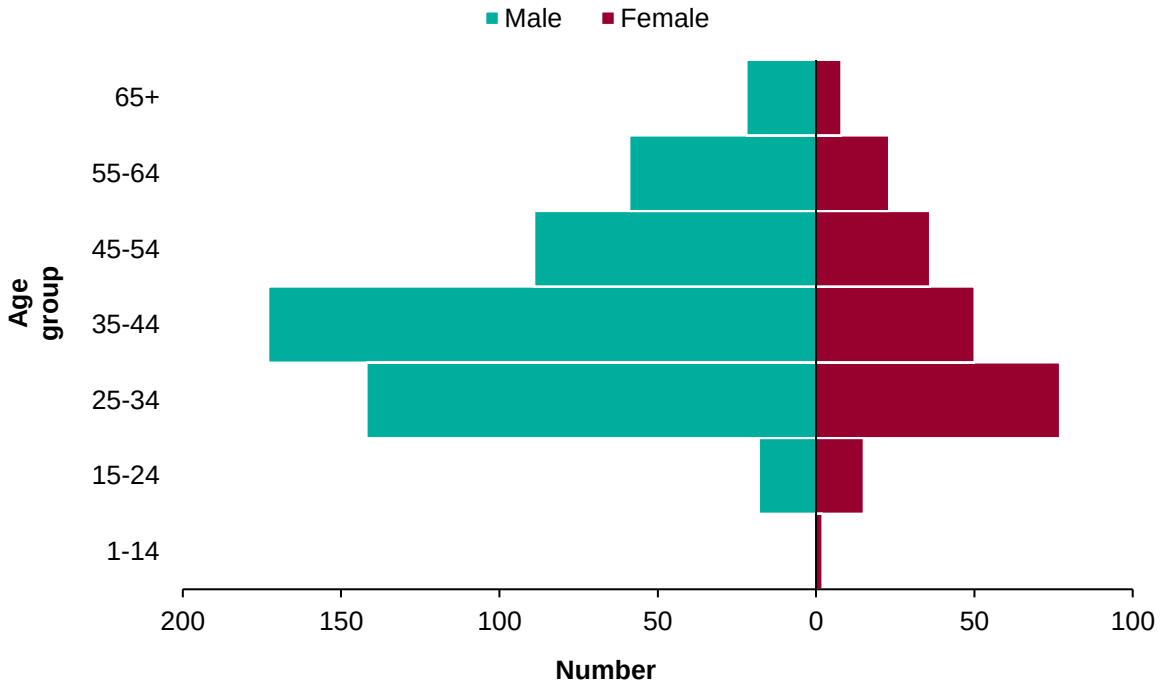


Note: Includes individuals with a positive test for hepatitis C antibody and/or detection of hepatitis C RNA.

Approximately 69% (509/736) HCV infections reported in 2017 were in men and most of these were between the ages of 25 and 64 years old (Figure 4). This could indicate a possible age-related risk factor which may relate to this demographic being more likely to undertake, or have previously undertaken, high risk behaviours such as the injection of drugs. The lowest number of cases in both sexes occurred in children under 14 years supporting the consensus that vertical transmission is rare.

The relative paucity of cases in older adults (65+) could be explained by non-exposure in earlier life to significant risk factors for acquisition (particularly intravenous drug taking). However, this cohort is formed of those who were young adults in the 60's and 70's – a period when injecting drug use first came to the fore – meaning they may have been exposed in earlier life. Due to this, clinicians should be encouraged to test in this group (where appropriate) to reduce case under ascertainment.

Figure 4. Age group and gender of reported cases of hepatitis C, residents of East Midlands, 2017



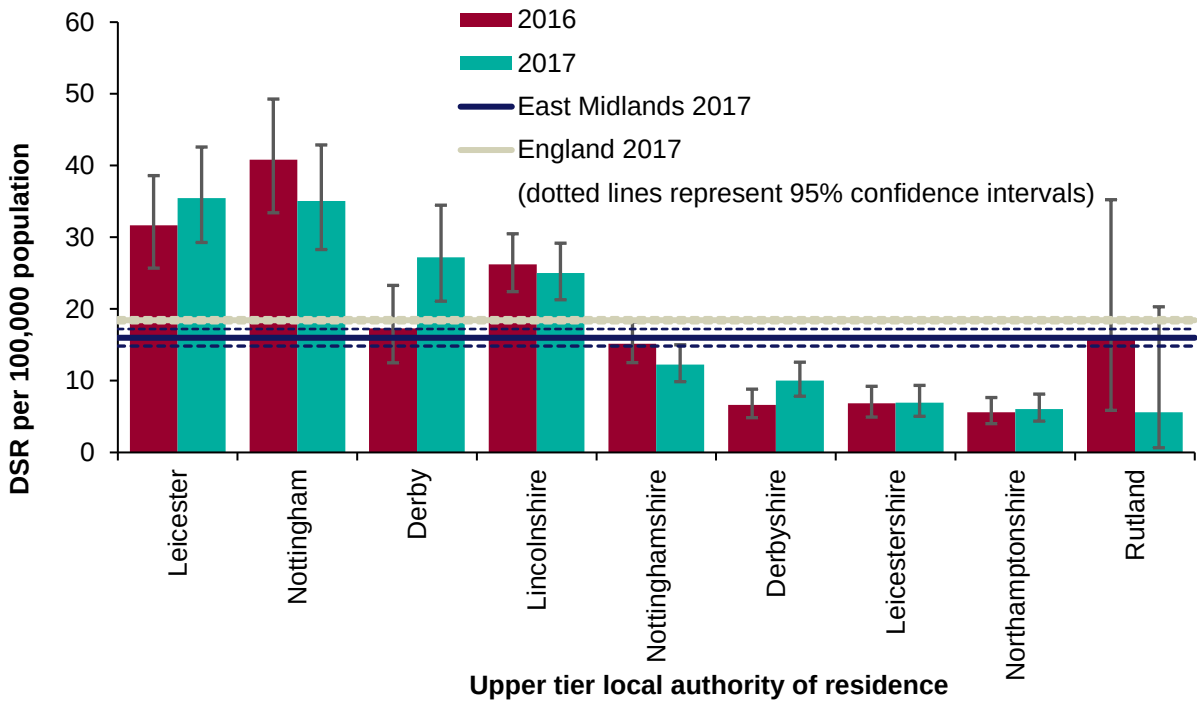
Note: Data are summarised by PHE centre of residence. Includes individuals with a positive test for hepatitis C antibody and/or detection of hepatitis C RNA. Chart excludes cases where gender or age unknown.

There was statistically significant variation in the rate of HCV reports per 100,000 population by upper tier local authority of residence, even after adjustment for age (Figure 5).

When compared to the rate per 100,000 for England, the 2017 rates by upper tier local authority of residence were significantly higher in Nottingham, Leicester, Derby and Lincolnshire, some of these areas are more urbanised so would be expected to have

higher rates, however, Lincolnshire is more rural, so to understand reasons for the high rates there needs to be a closer look at the data. Northamptonshire has low numbers of laboratory reports of hepatitis C which may reflect issues with laboratory reporting that are currently being addressed. Comparisons with the East Midlands rate should be interpreted with care in the light of the data quality issues. Some of the variation between upper tier local authorities may be due to differences in access to testing or health services between areas and therefore it may be appropriate to review the accessibility of services in these areas. However, much of the variation both over time and between upper tier local authorities is likely to be due to differences and changes in laboratory reporting of HCV.

Figure 5. Laboratory reports of hepatitis C, directly standardised rate (DSR) per 100,000 population by upper tier local authority of residence, East Midlands, 2016 and 2017



Note: Data are summarised by Local Authority of residence. Includes individuals with a positive test for hepatitis C antibody and/or detection of hepatitis C RNA

Table 1. Number of laboratory reports of hepatitis C, residents of the East Midlands by upper tier local authority, 2008-2017

Upper tier local authority of residence	Number of laboratory reports									
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Derby	55	50	53	65	46	32	16	22	44	69
Derbyshire	57	25	26	38	31	29	34	32	47	74
Leicester	111	130	105	111	118	77	83	85	112	130
Leicestershire & Rutland	8	13	37	82	67	46	49	51	49	46
Lincolnshire	112	115	95	117	132	122	151	117	173	178
Northamptonshire	59	38	*	*	31	18	38	31	40	43
Nottingham	200	172	152	132	138	109	108	98	117	103
Nottinghamshire	47	73	46	133	138	128	139	102	116	93
Total	649	616	514	678	701	561	618	538	698	736

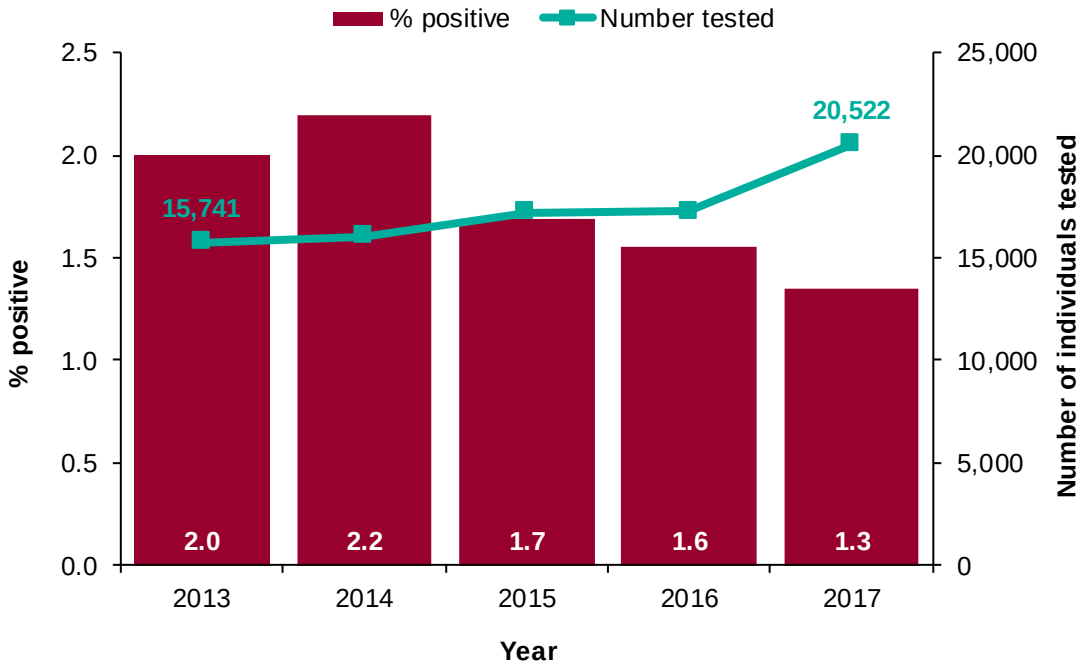
* has been used along with the grouping of Leicestershire and Rutland data to disguise any small cell values to avoid deductive disclosure. Note: Data are summarised by Local Authority of residence. Includes individuals with a positive test for hepatitis C antibody and/or detection of hepatitis C RNA.

4. Sentinel surveillance of hepatitis C testing

The national sentinel surveillance scheme was started in 2002 to improve the understanding of the epidemiology of HCV [6]. Risk factor data is collected from patients testing positive (and a proportion of negative testing samples). Within the East Midlands there is one sentinel laboratory based in Nottingham. Data provided by the laboratory have enhanced our knowledge and understanding of HCV testing, in terms of who is being tested and from which services individuals are accessing HCV testing. As the people tested at the Nottingham laboratory may differ from the East Midlands population as a whole, these data should be interpreted in that light before making inferences about the region.

Error! Reference source not found.6 shows an increase in the number of tests carried out by the sentinel laboratory between 2013 and 2017. Despite an increase in the number of tests, there were fewer positive results compared to the previous year, leading to a small decline in the positivity rate, from 1.6% in 2016 to 1.3% in 2017. It is possible that the sentinel scheme is testing a greater number of individuals at lower risk, therefore artificially deflating the positivity percentage.

Figure 6. Number of individuals tested and % testing positive for anti-HCV in sentinel laboratories in the East Midlands, 2013-2017

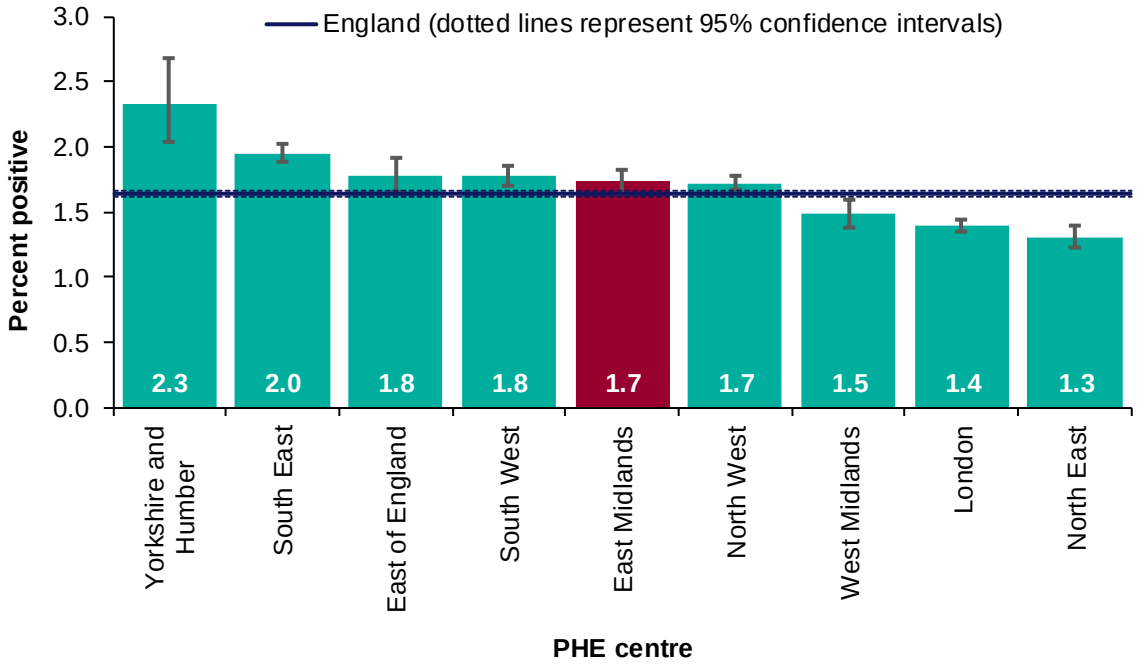


Notes:
Excludes dried blood spot, oral fluid, reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional. Trend data will not necessarily balance back to cumulative data because only locations that have been consistently reported in

each of the 5 years can be included in trend data.

There is also variation in positivity from sentinel testing by region across England. The East Midlands percentage positivity was slightly higher than the England average, this may indicate testing is possibly more targeted or a greater background prevalence of HCV in the East Midlands.

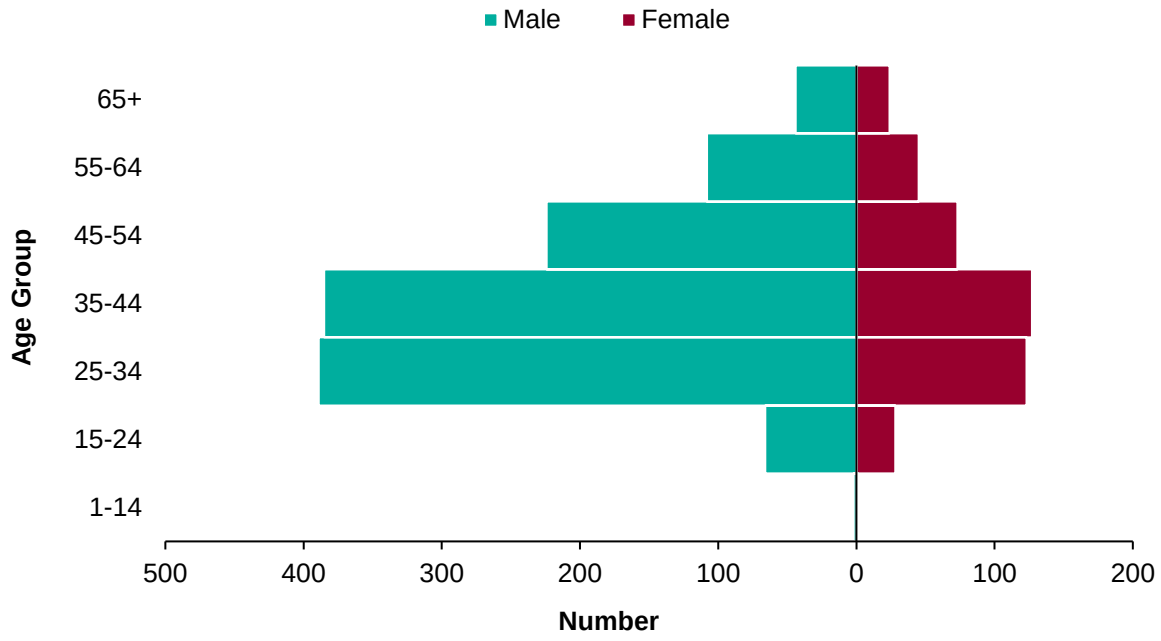
Figure 7. Percentage of individuals testing positive for anti-HCV in sentinel laboratories by PHE centre of laboratory, 2013-2017



Notes:
Excludes dried blood spot, oral fluid, reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional. Trend data will not necessarily balance back to cumulative data because only locations that have been consistently reported in each of the 5 years can be included in trend data.

The age profile for those tested in the sentinel scheme is similar to the age and sex profile of all laboratory results in the East Midlands overall tests (Figure 8), indicating that sentinel surveillance is closely representative of the overall East Midlands pattern for age and sex. In 2017, 74% of those tested positive for HCV were male and were mainly in the 25-34 and 35-44 age groups, females also had the highest number of HCV reports in the same age groups. This suggests men are at higher risk of infection. This is possibly due to a greater prevalence of high risk activities (currently or previously) amongst men, rather than differential presentation for and access to testing between the sexes or disease propensity per se.

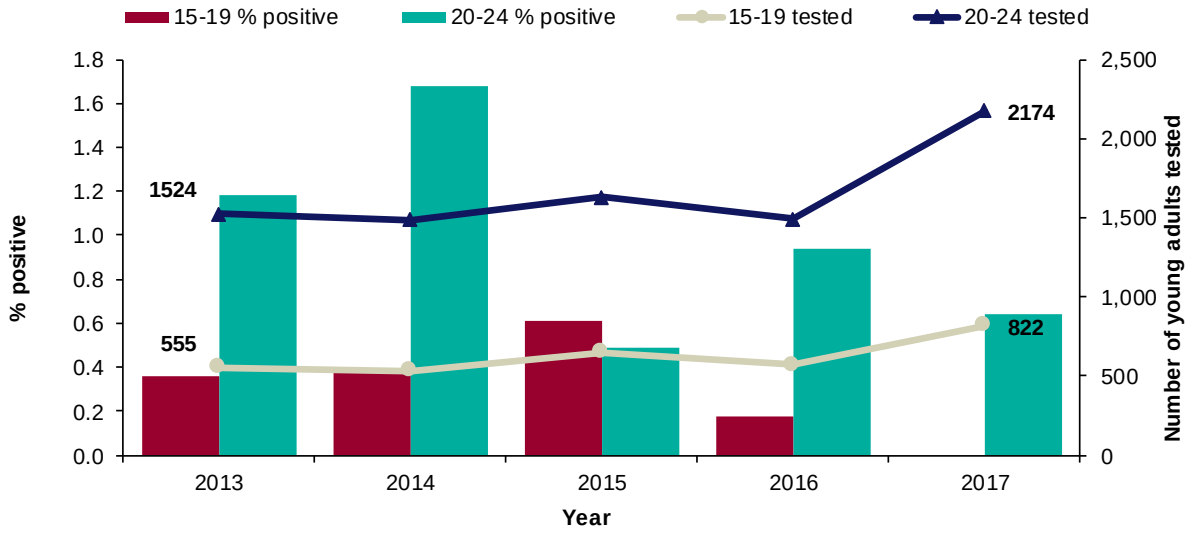
Figure 8. Age-group and gender of individuals testing positive for anti-HCV in the East Midlands sentinel laboratory, 2013-2017



Notes:
Excludes dried blood spot, oral fluid, reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional.
Chart excludes cases of unknown gender and/or age.
Cumulative data will not necessarily balance back to trend data because only locations that have been consistently reported in each of the 5 years can be included in trend data.

Risk taking behaviour is highest amongst adolescents and young adults. Historic data showing the positivity rates in young people by age group demonstrate that the HCV positivity rate amongst those tested increases between the 15-19 and 20-24 age groups (Figure 9). Testing in the 2 age groups has been at approximately the same level between 2013 to 2016 before increasing to their highest point over the past 5 years in 2017. Conversely the positivity rate has begun to fall after an increase in 2016. This increase in testing may suggest a change in targetting of testing by services towards this age group or availability of testing for this age group, it is encouraging to see the positivity fall particularly the level seen amongst the 15-19 for whom there are no cases recorded in 2017, if this is a sustained result then this is a positive outcome.

Figure 9. Number of young adults tested and testing positive for anti-HCV in sentinel laboratories in East Midlands PHE centre, 2013-2017



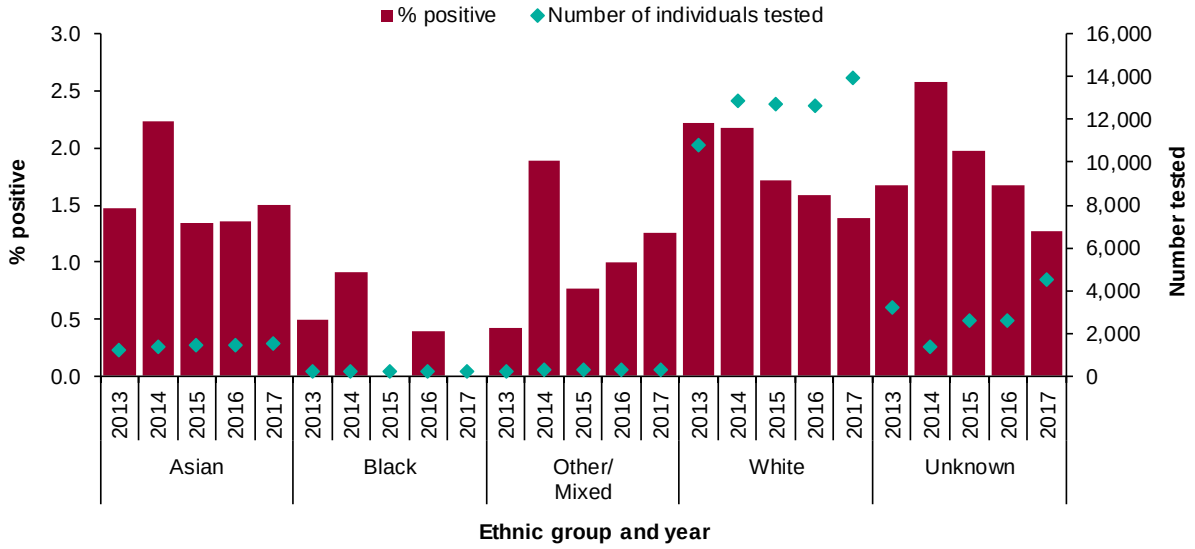
Notes:
Excludes dried blood spot, oral fluid, reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional.
Trend data will not necessarily balance back to cumulative data because only locations that have been consistently reported in each of the 5 years can be included in trend data.
The decline in testing observed in 2016 is likely attributed to testing drive at the start of each academic year being stopped.

Sentinel surveillance data provides additional information about ethnicity and HCV within the East Midlands. From 2013-2017, White and Asian ethnic groups had some of the highest HCV positivity rates (Figure 10). This may reflect different patterns of high risk exposures in the group and a lower prevalence as a result. However, it may also be partly due to issues with access to testing or an artefact of assumptions about allocation to a particular ethnic group.

The number of people tested with unknown ethnicity increased sharply between 2014 and 2015 (1,400 and 2,626 respectively) suggesting issues with data collection and completeness and has shown a similar increase again from 2,570 to 4,507 in 2016 to 2017 respectively.

There has been a decline in the proportion of HCV positive tests in the white group since 2013. This is despite a stable number of individuals tested and is therefore a positive development and hopefully will be a continued trend and may indicate that public health messaging / needle exchange schemes for PWID has helped to reduce the number of new cases.

Figure 10. Number of individuals tested and % positive for anti-HCV by ethnic group, sentinel laboratories in the East Midlands, 2013-2017

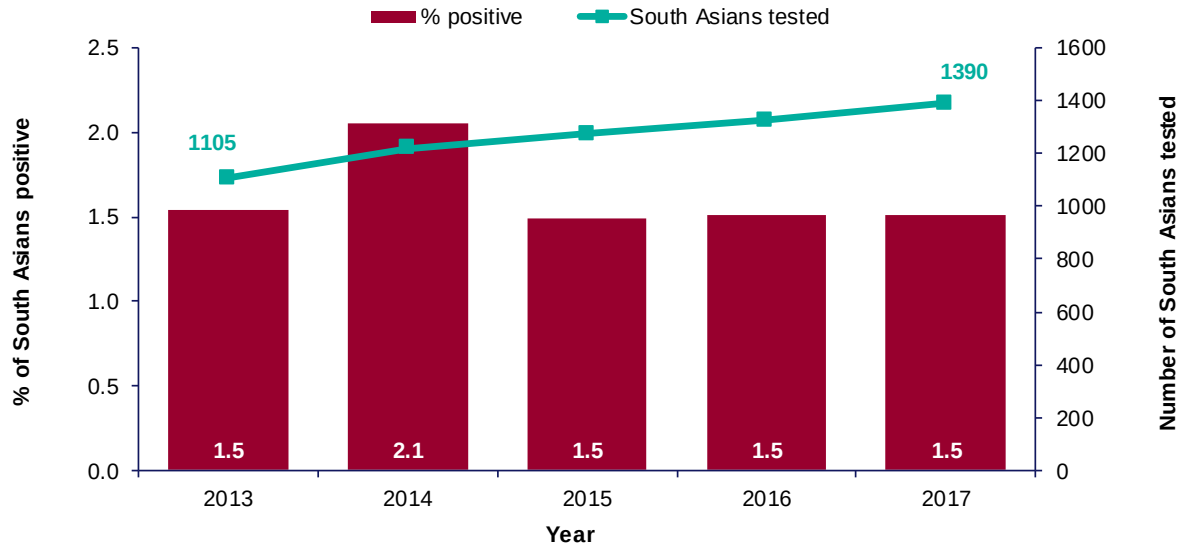


Notes:
These sentinel surveillance data exclude dried blood spot, oral fluid, reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional.
Trend data will not necessarily balance back to cumulative data because only locations that have been consistently reported in each of the 5 years can be included in trend data.
A combination of self-reported ethnicity, and OnoMap and NamPehchan name analyses software were used to classify individuals according to broad ethnic group.

Previous work has suggested that migration from a high prevalence country or living in a population with close links to countries with a high prevalence of HCV increases the risk of infection. The World Health Organisation has previously identified countries in South Asia as having a high prevalence, such as Pakistan (5%) [4] and India (0.5%) [3] compared with 0.02% for the UK. Although this work identified other high prevalence countries outside of South Asia also.

Within the East Midlands there are large populations of people of South Asian ethnicity. Surveillance using ethnic groupings assigned using NamPehchan analysis of names has identified that people in the South Asian ethnic group had a steady HCV positivity rate of 1.5% between 2015 to 2017 (Figure 11).

Figure 11. Number of South Asian individuals tested and testing positive for anti-HCV by ethnicity in sentinel laboratories in the East Midlands, 2013-2017

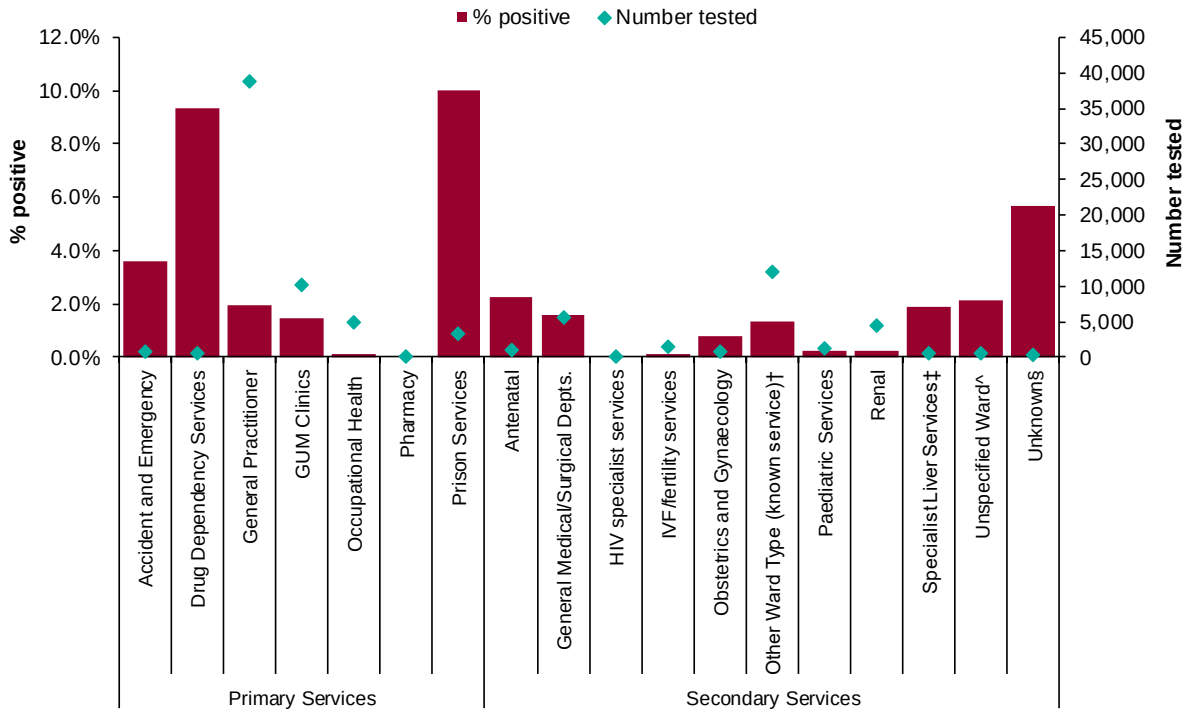


NamPehchan was used to identify individuals of South Asian origin as ethnicity is not routinely available from the participating laboratory information systems.
Excludes dried blood spot, oral fluid, reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional.
Trend data will not necessarily balance back to cumulative data because only locations that have been consistently reported in each of the 5 years can be included in trend data.

Most HCV testing is carried out by GPs in primary care, but the prevalence of positive results in those tested is low (1.9%). Prison services identify the highest percentage positivity amongst those tested (10%) and drug dependency services (9.3%) reflecting exposure to high risk behaviours in persons accessing drug dependency services / currently in prison (Figure 12).

As HCV is usually asymptomatic and treatments have improved in tolerability and efficacy, testing in all settings, such as primary care or GUM and HIV specialist services, should be encouraged. Changing risk-taking behaviour among different groups perhaps not typically associated with being at risk of HCV acquisition should be encouraged. This includes those engaging in recreational drug use linked to sex, particularly men who have sex with men (MSM) who may not present to drug services. The increase in this demographic highlights the importance of increased awareness across services of HCV risks and of encouraging all health professionals to consider testing for HCV in those previously not recognised as high risk.

Figure 12. Number of individuals tested for anti-HCV and % positive by service type in sentinel laboratories in the East Midlands, 2012-2016



† Other ward types include cardiology, dermatology, haematology, ultrasound, x-ray, ‡ Specialist liver services refer to infectious disease services, hepatology departments and gastroenterology departments, ^ Unspecified wards are hospital services may include any of the secondary care services listed, § These services are currently being investigated to identify specific service type.
Excludes dried blood spot, oral fluid, reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional. Cumulative data will not necessarily balance back to trend data because only locations that have been consistently reported in each of the 5 years can be included in trend data.

The place and service type where a test was carried out reflects the risk or reason for testing (Table 2). From those tested for HCV and recorded by the sentinel surveillance scheme, the risk group with the greatest positivity rate was PWID (24.8 %, Table 2). Where testing was for confirmation 18.4% were found to be positive, and 5.8% who were tested because of having liver disease symptoms were positive.

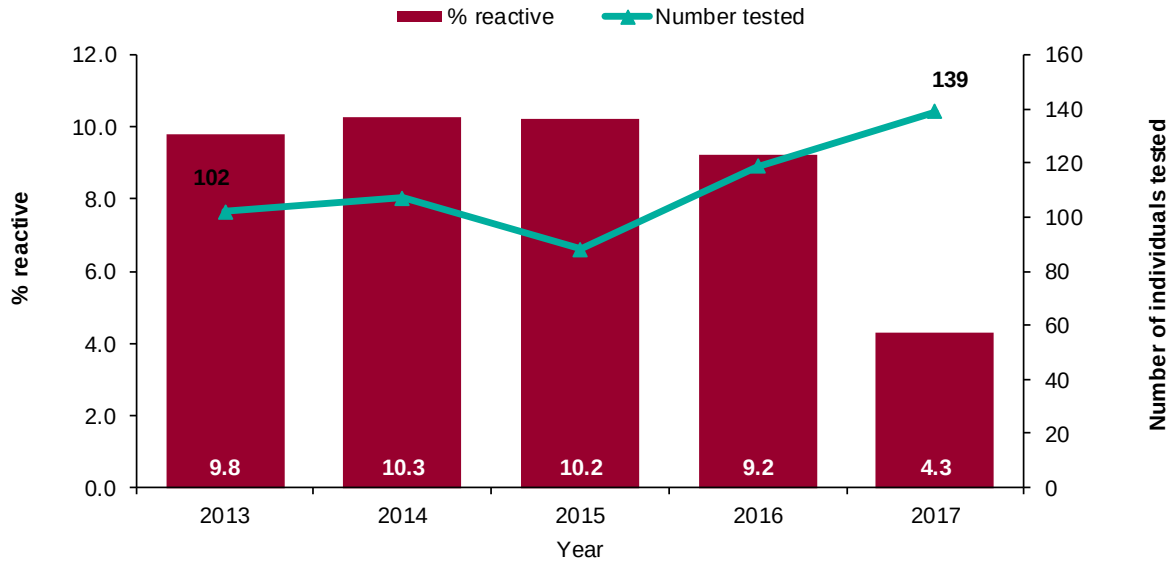
Where the reason for testing was known, the greatest number of tests (n=23,412 in 18245 people) were undertaken for screening, with a positivity rate of 3% (Table 2). Screening can include a number of differing reasons including testing through occupational health, pre-operative or pre-therapy, donor, on patient request, or any asymptomatic test with no risk factor mentioned. Over half of tests (n=58,536 in 47126 people) had an unknown reason for testing. The underlying reasons for this are unclear and may relate to data collection and quality issues. However, it is likely these data underestimate testing for some risk factors more than others and should be interpreted with caution.

Table 2. Numbers of individuals tested for HCV, and testing positive for anti-HCV by risk/reason for test in sentinel laboratories in the East Midlands, 2013-2017

Risk factor/reason for testing	Total number of tests	Number of individuals tested	Number positive	% positive
Antenatal screening	1625	1417	19	1.3
Confirmatory test	99	87	16	18.4
Contact testing	131	119	4	3.4
Fertility treatment screening	1224	1110	2	0.2
LFTs - abnormal result	7272	6545	61	0.9
Liver disease symptoms	1168	1007	58	5.8
Maternal/vertical exposure	20	18	0	0.0
Needlestick donor/recipient	2151	1715	4	0.2
Other medical condition	1728	1338	4	0.3
PWID	380	323	80	24.8
Renal patient	7088	2000	8	0.4
Risk of infection	418	361	16	4.4
Screening	23412	18245	541	3.0
Sexual exposure	5088	4362	60	1.4
Study participants	23	20	0	0.0
Symptoms (non-liver)	1364	1191	13	1.1
Travel or lived abroad	199	179	1	0.6
Unknown	58536	47126	754	1.6
Total	111926	87163	1641	1.9

Annual data reported by sentinel surveillance for PWID tests by drug dependency services indicates an overall increase in the number of tests from 2013 with a small decline in 2015 (Figure 13), the reasons for the 2015 decline is unclear. Positivity rates also declined between 2013-2017, with the exception of 2014 and 2015 (Figure 13), the increase in positivity in 2015 could be due to the decrease in testing, but those tests possibly being more targeted. Careful monitoring of this local trend data is essential to help inform the need for public health action and assess its impact. It is unclear whether the reduction in positivity seen in 2017 will be a sustained so should be monitored.

Figure 13. Number of persons who inject drugs (PWID) tested and testing positive for anti-HCV at specialist drug services in sentinel laboratories in East Midlands PHE centre, 2013-2017



These sentinel surveillance data exclude reference testing and testing from hospitals referring all samples. Data are de-duplicated subject to availability of date of birth, soundex and first initial. Excludes individuals aged less than one year, in whom positive tests may reflect the presence of passively-acquired maternal antibody rather than true infection. All data are provisional.
Only one laboratory offers dried blood spot testing of anti-HCV. These data are presented from 2010 and are shown by PHE centre of the requesting clinician.
Trend data will not necessarily balance back to cumulative data because only locations that have been consistently reported in each of the 5 years can be included in trend data.
Please note: Sentinel surveillance captures a small proportion of all dried blood spot testing in England, therefore these data should be interpreted with caution.

The analysis below is by ODN. Figure 14 shows that Leicester ODN has the second highest percentage positively nationally, however, the South Yorkshire is vastly greater than other ODN areas. Nottingham ODN, represents Derbyshire, Lincolnshire and Nottinghamshire, The pattern shown in the sentinel surveillance data shows that testing has increased steadily since 2013, whereas the positivity has decreased since 2013 apart from a peak in 2014. This could imply that the further testing that is being done may not be as targeted however, it is encouraging to see increases in the volume of testing.

Leicester ODN shows a greater positivity from 2013 to 2017 compared to Nottingham ODN however the level of testing is very much lower. Leicester has seen an overall increase in positivity with a peak in 2015, however the level of testing has approximately halved over since 2013. Please treat Leicester ODN figures form sentinel surveillance with caution as the sentinel surveillance is taken from Nottingham University Hospitals laboratory there is possibly little data for Leicester ODN cases in this surveillance system, which could be why there is high positivity and low testing figures as showing in figures 14 and 16.

Figure 14. Percentage of individuals testing positive for anti-HCV in sentinel laboratories by ODN, 2013-2017

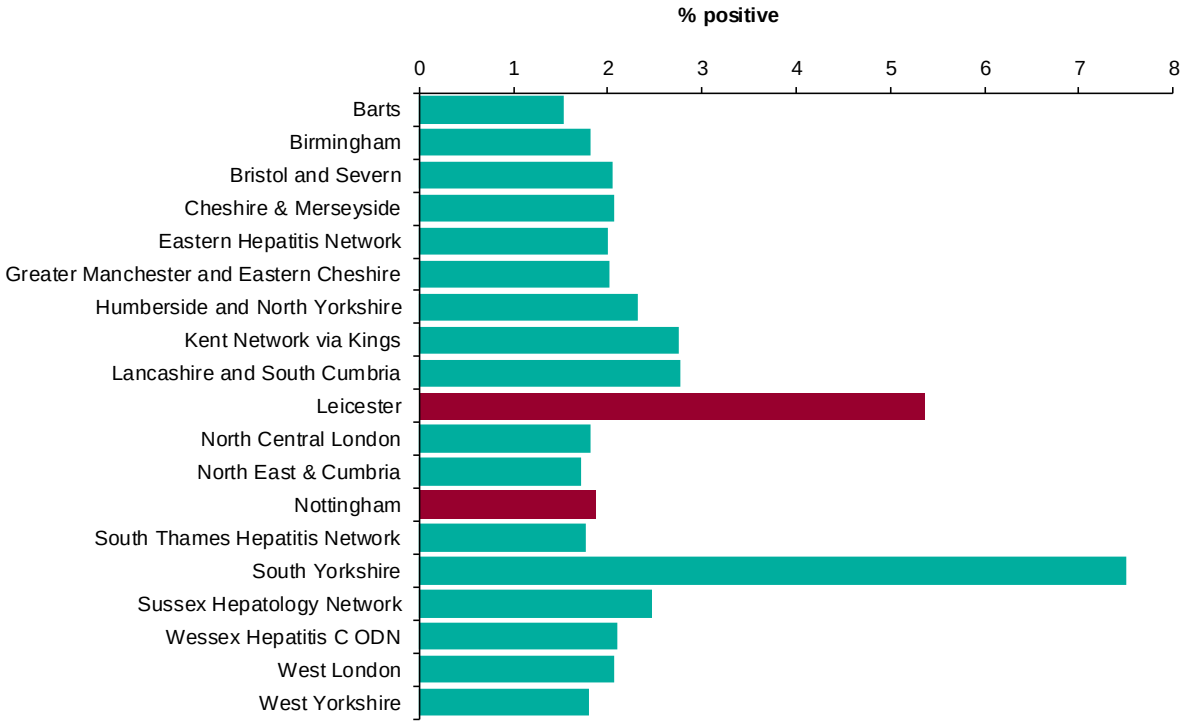


Figure 15. Number of individuals tested and % testing positive for anti-HCV in sentinel laboratories, Nottingham ODN, 2013-2017

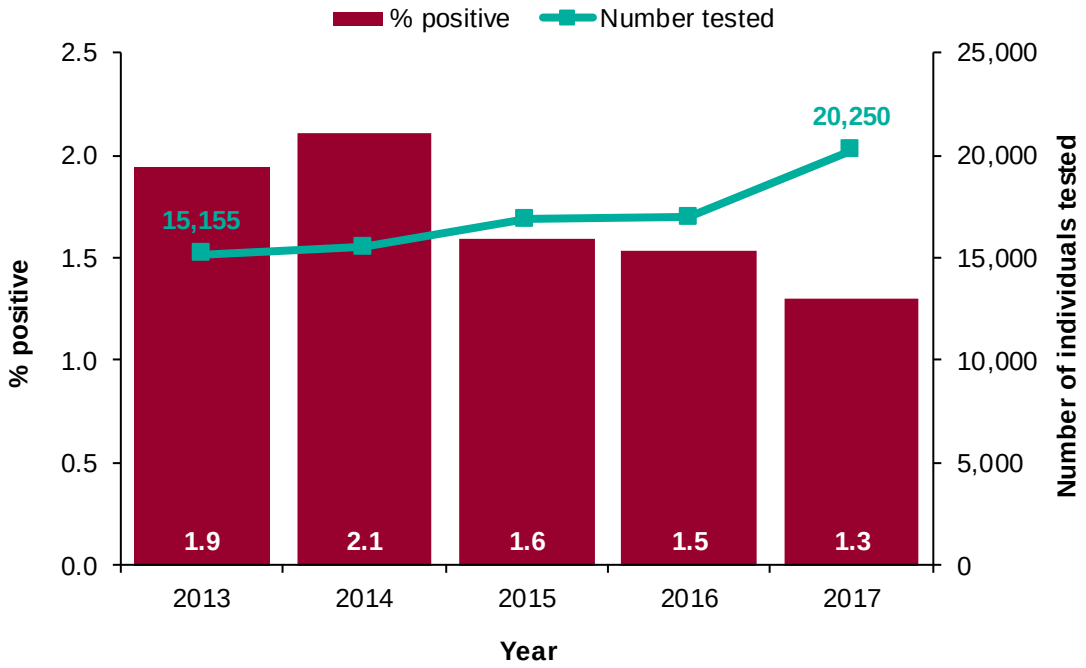
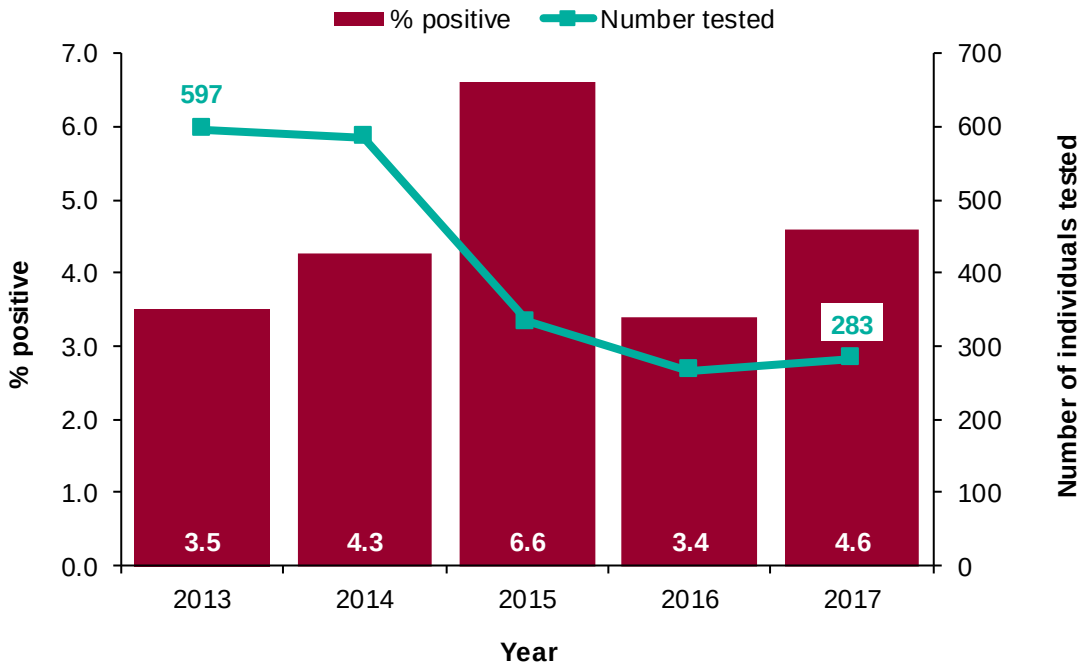


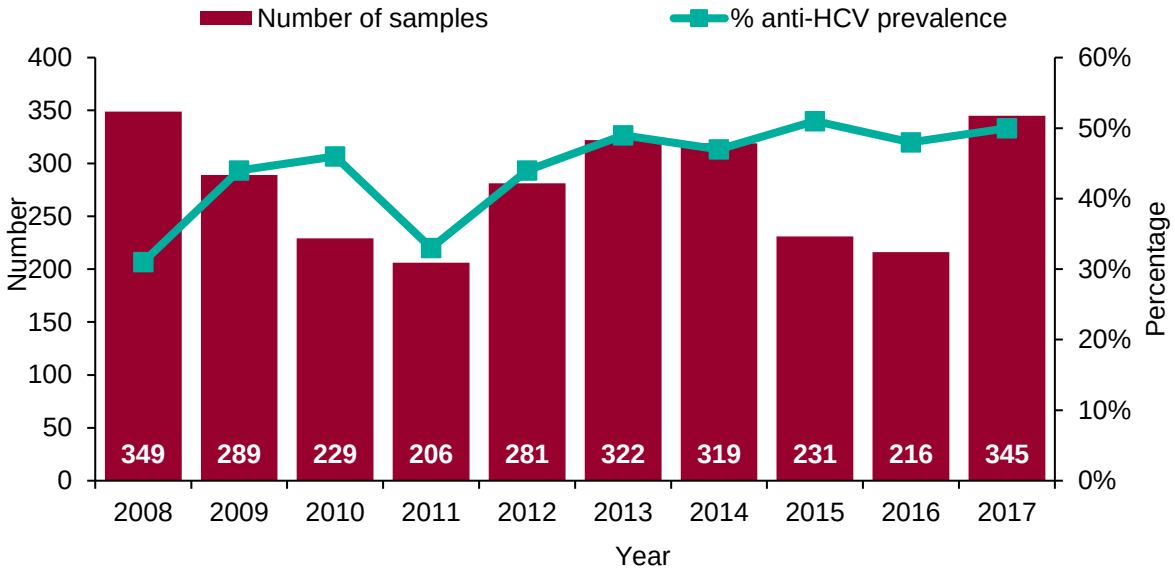
Figure 16. Number of individuals tested and % testing positive for anti-HCV in sentinel laboratories, Leicester ODN, 2013-2017



5. Unlinked Anonymous Monitoring Survey

Further data from the Unlinked Anonymous Monitoring Survey of HIV and Hepatitis allows surveillance of HCV prevalence in PWID. Testing amongst this group has varied since 2008 but stayed relatively stable; more recently, between 2016 and 2017 there has been an increase. This also indicates an annual increase in the HCV prevalence, with a rising trend from 2011 to 2013, has levelled off from 2013 onwards to approximately 50% (Figure 17).

Figure 17. Number of samples and percentage anti-HCV prevalence, PWID, East Midlands, 2008-2017



Source: Public Health England, Unlinked Anonymous Monitoring Survey of HIV and Hepatitis in People Who Inject Drugs

The anonymous nature of this survey also allows collection of data about sharing of needles and injecting equipment with a degree of veracity, as well as an understanding of the level of undiagnosed HCV there is in amongst this risk group. The proportion of recent sharing of needles (in the 4 weeks prior to testing) for both direct and indirect sharing (including the sharing of other injecting equipment) decreased between 2008 and 2016 (Figure 18) with a recent increase in 2017. The increase in direct needle sharing observed between 2012 and 2015 began to reverse in 2016, however unfortunately has begun to increase moderately in 2017. The level of testing and awareness of infection status has remained relatively level over the 10 years shown in figure 17 and it is encouraging that the number of PWID who are aware of their infection status has increased in 2017 compared to the previous year.

Whilst there is still a proportion of PWID who are unaware of the infection status, it is necessary for further work to reinforce the reduction in the sharing of needles. The delivery of effective harm reduction messages remains an important element during the delivery of drug services along with suitably accessible needle exchanges.

Figure 18. Level of direct and indirect sharing of injecting equipment amongst people who inject drugs, East Midlands, 2008-2017

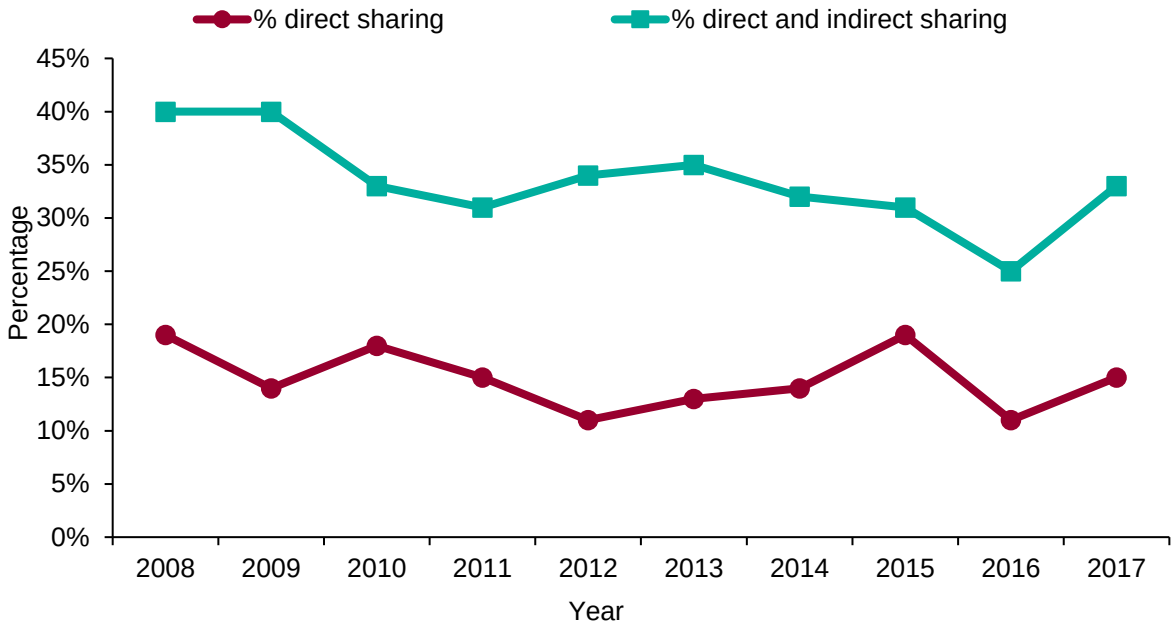
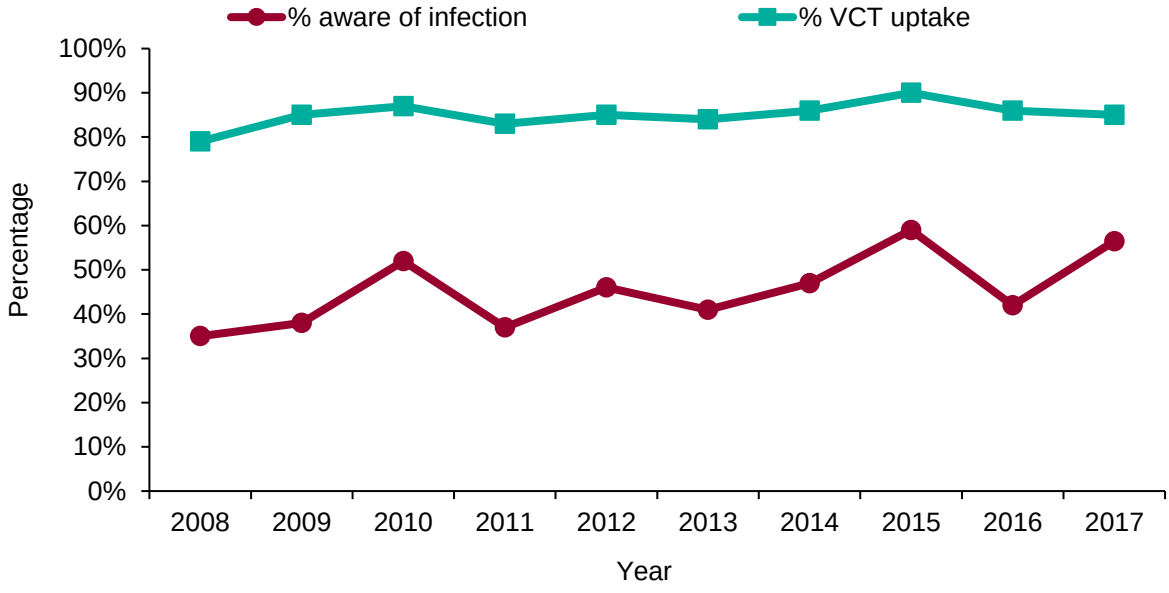


Figure 19. Hepatitis C test uptake (Voluntary Confidential Test (VCT)) among people who inject drugs and their awareness of infection, East Midlands region, 2008-2017



Source: Public Health England, Unlinked Anonymous Monitoring Survey of HIV and Hepatitis in People Who Inject Drugs

Further detail from the survey is shown in Table 3 which highlights that in 2017 85% of PWID reported having undertaken HCV testing at some point, however there may be a need to increase awareness of HCV as only 56% of the 101 people who responded were aware of their HCV infection status. This was an increase on the previous year.

Table 3. Hepatitis C prevalence, injecting equipment sharing, hepatitis B vaccination uptake, and uptake of testing for hepatitis C 2008-2017

Year	2008	2009		2010	2011	2012	2013	2014	2015	2016	2017
Sample type	Oral	Oral	DBS	DBS	DBS	DBS	DBS	DBS	DBS	DBS	DBS
Anti-HCV Prevalence †††	**31%**	**44%**		**46%**	**33%**	**44%**	**49%**	**47%**	**51%**	**48%**	**50%**
Proportion of samples anti-HCV	29%	33%	52%	46%	33%	44%	49%	47%	51%	48%	50%
Number of samples anti-HCV positive	100	47	76	105	68	125	159	151	117	104	172
Total number of samples collected	349	144	145	229	206	281	322	319	231	216	345
HCV VCT uptake	**79%**	**85%**		**87%**	**83%**	**85%**	**84%**	**86%**	**90%**	**86%**	**85%**
Number reporting a VCT for HCV	261	235		186	153	214	251	265	203	179	238
Total number answering question	332	276		213	184	251	298	308	225	207	280
Proportion aware of HCV infection¥	**35%**	**38%**		**52%**	**37%**	**46%**	**41%**	**47%**	**59%**	**42%**	**56%**
Number aware of their HCV infection	30	43		48	21	47	55	63	62	37	57
Total number answering question	85	112		92	57	102	134	135	105	88	101
Among those who had injected in preceding 4 weeks											
Level of direct sharing ‡	**19%**	**14%**		**18%**	**15%**	**11%**	**13%**	**14%**	**19%**	**11%**	**15%**
Number reporting direct sharing	48	29		29	20	19	30	33	27	11	23
Total number answering question	258	207		162	134	173	225	230	143	99	151
Level of sharing (direct & indirect)	**40%**	**40%**		**33%**	**31%**	**34%**	**35%**	**32%**	**31%**	**25%**	**33%**
Number reporting sharing	88	83		53	42	58	79	73	44	25	50
Total number answering question	221	207		162	134	173	227	231	144	100	151
Proportion injecting crack	**23%**	**18%**		**36%**	**27%**	**34%**	**28%**	**37%**	**49%**	**57%**	**55%**
Number reporting crack injection	62	38		59	37	61	64	85	73	57	84
Total number answering question	268	206		166	136	177	228	230	148	100	154
Proportion injecting into their groin	**36%**	**40%**		**37%**	**31%**	**43%**	**39%**	**44%**	**29%**	**44%**	**30%**
Number reporting groin injection	95	81		60	43	77	89	104	42	44	47
Total number answering question	261	201		164	138	178	229	235	147	101	159
Among those with two or more (anal or vaginal) sexual partners in preceding year											
Proportion always using a condom	**15%**	**10%**		**8%**	**9%**	**9%**	**18%**	**23%**	**22%**	**29%**	**16%**
Number always using a condom	16	7		5	5	7	13	19	11	10	9
Total number answering question	109	70		63	56	80	73	81	49	34	57

Source: Public Health England, Unlinked Anonymous Monitoring Survey of HIV and Hepatitis in People Who Inject Drugs

* The sensitivity of the oral fluid test for anti-HCV is approximately 92%, and that for anti-HBc is approximately 75%.

††† Anti-HCV Prevalence = (number of oral fluids anti-HCV positive/0.92) + number of DBS anti-HCV positive / (number of oral fluids + number of DBS)x100.

§§ Self reports of a swelling containing pus (abscess), sore, or open wound at an injection site in preceding year.

‡ Sharing of needles and syringes in preceding 4 weeks.

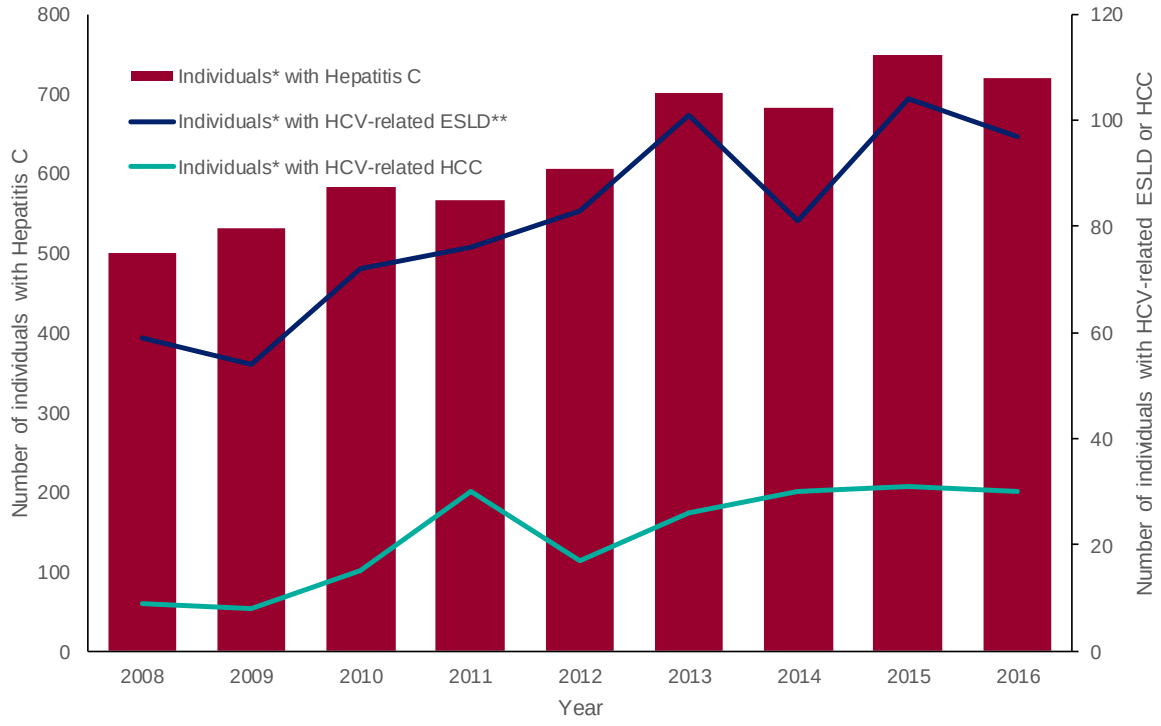
‡‡ Sharing of needles and syringes, mixing containers, or filters among those who had last injected during the 4 weeks preceding participation in the survey.

6. Clinical activity in secondary care and outcomes

6.1 Hospital admissions

Since 2008, there has been an increase in cases admitted to hospital with a diagnosis of HCV infection, which has also been reflected in the number of diagnoses made of HCV-related end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC, Figure 20), however, since 2013 all these figures have remained fairly stable.

Figure 20. Hospital admissions for individuals* with a diagnosis code for HCV, end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC), residents of the East Midlands, 2008-2016



*Patient counts are based on the unique patient identifier, HESID.
** Defined by codes for ascites, bleeding oesophageal varices; hepato-renal syndrome, hepatic encephalopathy or hepatic failure.

6.2 Liver transplants

The NHS Blood and Transplant service maintains a registry of all people who require a liver transplant and whether a transplant was carried out; this information shows a decline in the number of new liver transplant registrations associated with HCV from 2014-2017 compared to 2010-2013

(Table 4). The proportion of liver transplants which have been associated with an HCV infection has also fallen for the East Midlands, although the overall number of liver transplants undertaken has increased, this would imply that there has been an increase in other infections or risk behaviour which also attribute to liver disease in the East Midlands.

Table 4. Number of registrations and liver transplants in England where post-hepatitis C cirrhosis was the primary, secondary or tertiary indication for transplant, residents of the East Midlands, 2010-2017

Indicator	2010-2013	2014-2017	Total
Number* of first registrations for a liver transplant in England where post-hepatitis C cirrhosis was given as either the primary, secondary or tertiary indication for transplant	32	20	52
Number* of liver transplants in East Midlands	162	203	365
First liver transplants* for patients with post-hepatitis C cirrhosis as either primary, secondary or tertiary indication for transplant at registration or patients who were HCV positive at registration or transplant	25	19	44
% of all liver transplants with post-hepatitis C cirrhosis as primary, secondary or tertiary indication for transplant at registration who were HCV positive at registration or transplant	15%	9%	12%

* These figures are based on registry data as at 5 August 2018 and include both elective and super urgent registrations.

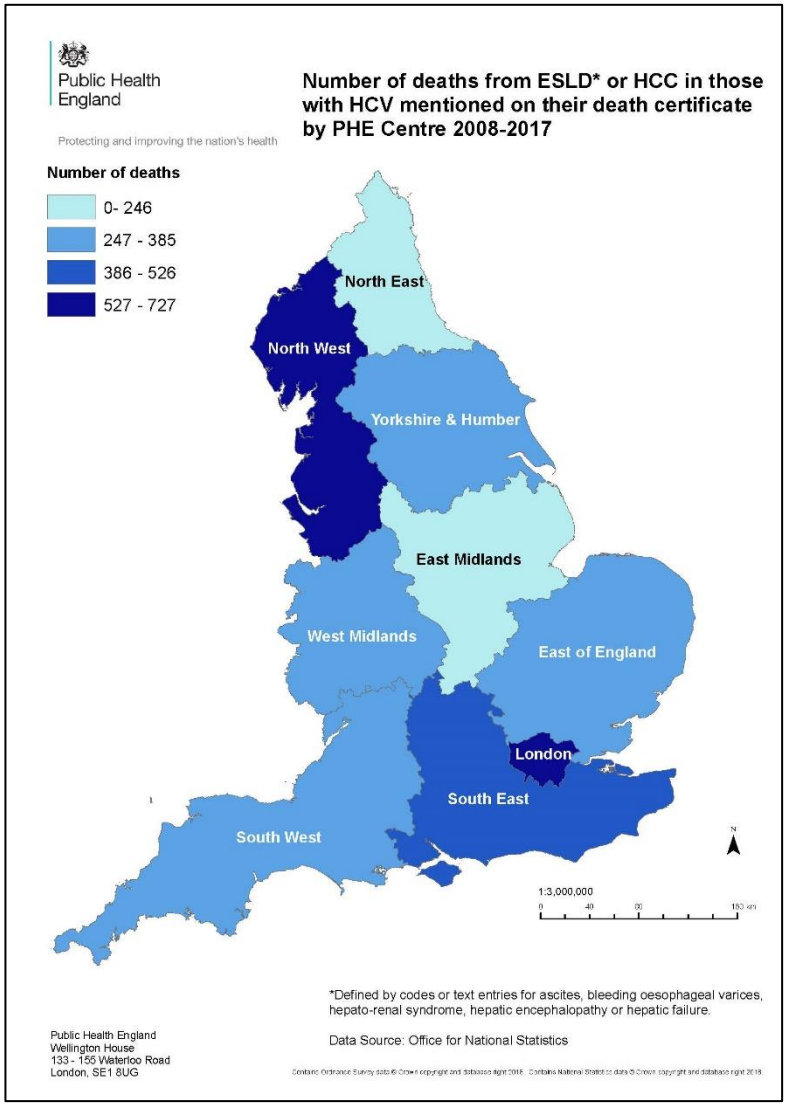
6.3 Mortality related to hepatitis C

The East Midlands falls into the second lowest quartile of regions suggesting the East Midlands mortality rates are higher than the absolute counts would imply.

The public health indicator for the mortality rate from hepatitis C related ESLD or HCC in persons less than 75 years of age per 100,000 population are presented as 3-yearly aggregated figures and are updated annually (Figures 22 and 23). The trend for the East Midlands compared to England, figure 20, is similar, showing an increase from the 2007-2009 to the 2013-2015 rate followed by a slow decline.

Looking closer at the current year's indicators for East Midlands' upper tier local authorities, Northampton remains to have the highest mortality rate being the only local authority with a significantly greater rate than the East Midlands and England rates, however please note that the numbers of these deaths are very small and therefore should be interpreted with caution.

Figure 21. Deaths from ESLD* or HCC in those with HCV mentioned on their death certificate by PHE Centre 2008-2017



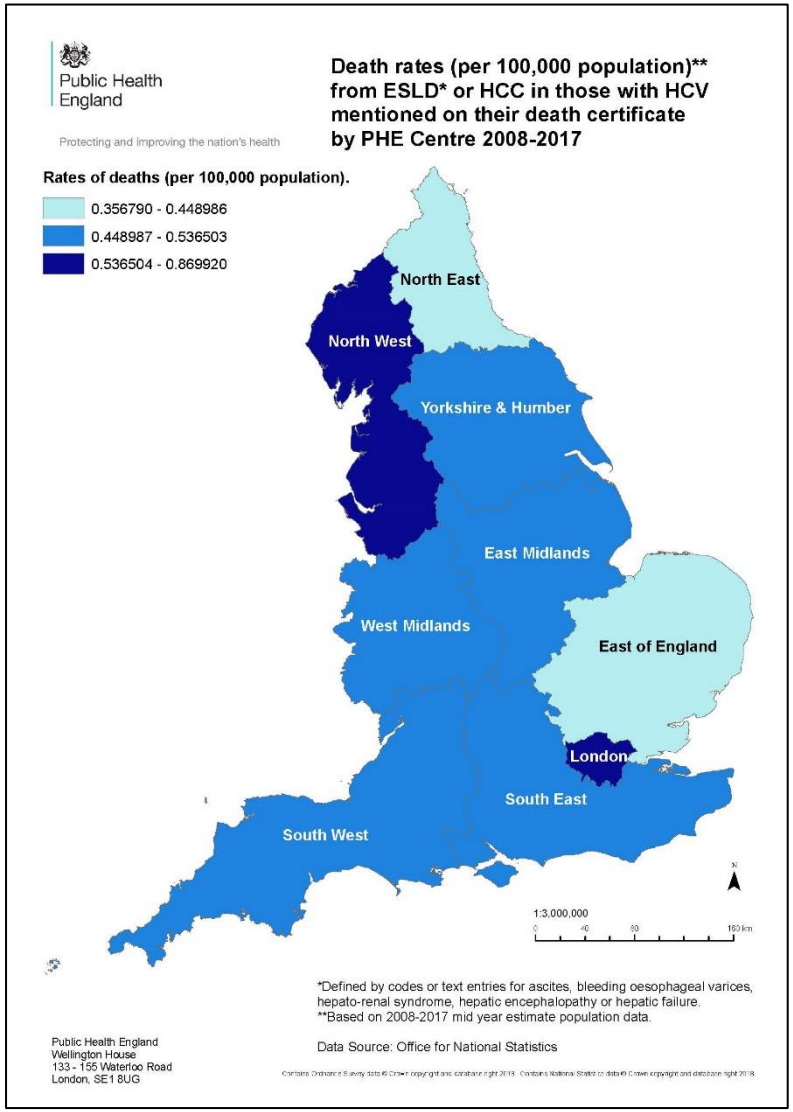


Figure 22. Trend of crude rate of mortality from hepatitis C related end-stage liver disease/hepatocellular carcinoma in persons less than 75 years of age for the East Midlands and England per 100,000 population, from 2007-09 to 2015-17

Source: Public Health Profiles, Public Health England (based on ONS source data)

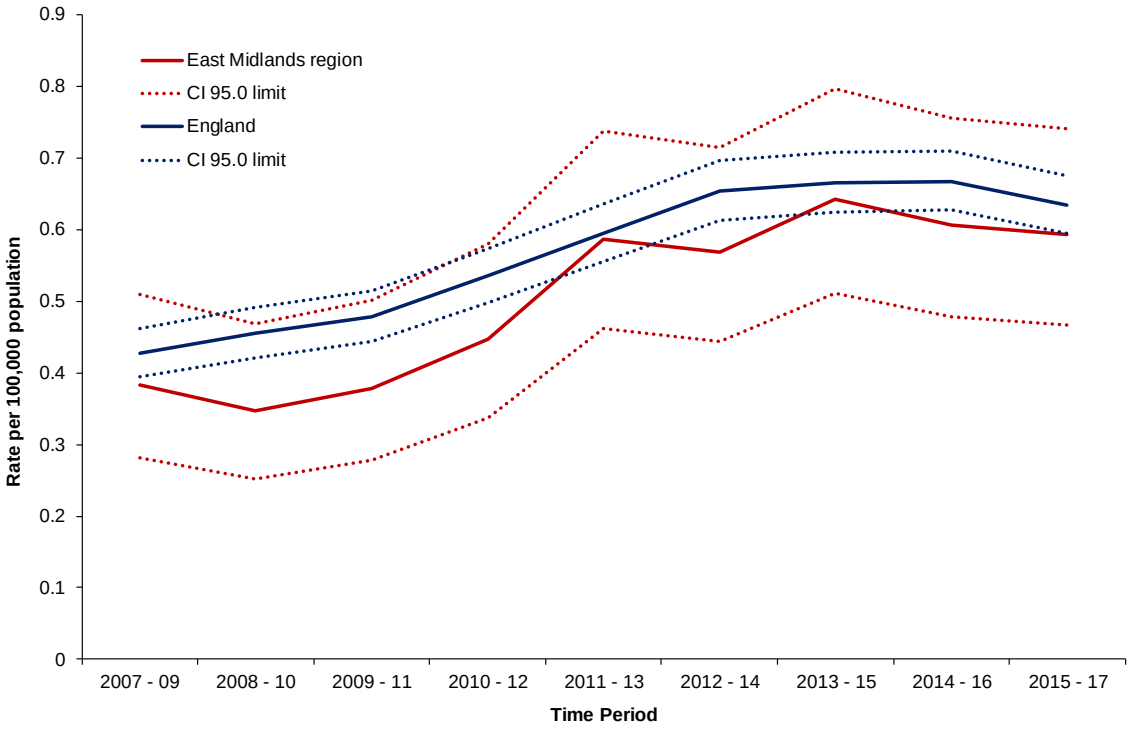
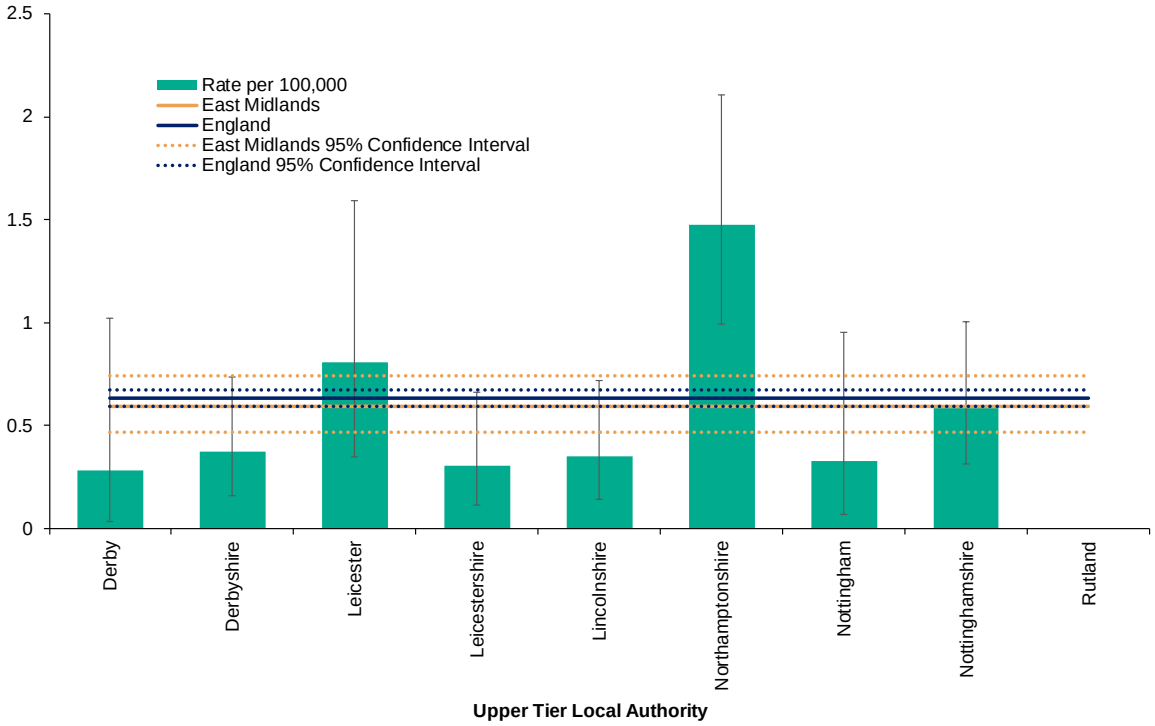


Figure 23. Crude rate of mortality from hepatitis C related end-stage liver disease/hepatocellular carcinoma in persons less than 75 years of age by upper tier local authority in the East Midlands per 100,000 population, 2015-17

Source: Public Health Profiles, Public Health England (based on ONS source data)



Note: data for Rutland has been suppressed

7. Conclusions

Laboratory figures for HCV indicate that there has been an increase in reports from 2016 to 2017 (698 and 736 respectively), however, due to issues with the laboratory reporting systems this is not likely to be indicative of the true pattern of diagnoses of HCV within the East Midlands. It should be noted that over recent years local laboratories have been working with PHE to improve reporting of hepatitis B and C and this is slowly filtering through into East Midlands' data and therefore having a positive impact on data quality and reporting of HCV.

The data that was reported through the laboratory reporting system indicated most new cases occur in males particularly between the ages of 25 to 44; this is similar to the sentinel surveillance data and the national picture. This might suggest the need to consider whether this is an indicator for risk taking behaviours in terms of HCV.

The sentinel surveillance scheme shows that across the East Midlands the volume of testing has increased since 2013, due to improvements in the system to allow a greater number of front line clinical tests to be included in the analysis. At the same time the number of positive tests has remained steady with a small decrease year-on-year beginning in 2014. This has led to a continued decline in proportion of positive tests to 1.2% in 2017 and may represent a new baseline rather than a true decrease in HCV infections identified through sentinel surveillance.

In line with previous understanding, the group at greatest risk of HCV infection remains PWID. Sentinel surveillance data shows tests undertaken by drug dependency services has been increasing since 2013, with positivity decreasing.

Unlinked Anonymous Monitoring Survey shows an overall increase since 2011 in the prevalence of HCV amongst PWID however, this has stabilised since 2013. This also highlights there is a continued level of HCV positive PWID who remain undiagnosed. This poses a risk to the wider community where recreational drug taking may lead to those being at risk who may not present themselves to drug services.

Worryingly this survey has shown that between 2016 and 2017, there was an increase in direct needle sharing as well as direct and indirect needle sharing amongst PWID, putting more people at risk of being infected. As numbers are small in this survey this may not be a continued trend. This does highlight the need to maintain good needle exchange services and continued messaging about the risks of infections through equipment sharing.

Hospital admissions due to HCV and HCV related ESLD and HCC diagnoses have increased over time since 2008, these figures are currently only available up to 2016 so would not show the impact of the work of ODNs so far. Data from the transplant registry has shown that although there seems to be an increase in liver transplants those associated with post-hepatitis C cirrhosis or an HCV diagnosis has declined, work may need to be done to understand the other causes for the increase in liver transplants within the East Midlands.

Mortality rates within the East Midlands with possible HCV association are not amongst the highest nationally, the pattern seen since the 2007 to 2009 indicator rate is similar to the England rate. Nationally it was noted that the England are 3 years ahead of the GHSS goal of reducing mortality by 10% by 2020, so it is positive to see that the East Midlands mortality rate pattern is following that of England, but closer work may be need to be done to understand why some upper tier authorities are showing much higher rates than others.

With direct acting antiviral (DAA) drugs becoming more available, and the asymptomatic nature of HCV, detection is increasingly important and should be encouraged in a wider number of settings and that there should be a high level of uptake of treatment by newly diagnosed cases. But also the success of the work of the ODNs and PHE to actively pursue previously diagnosed individuals and offer them the opportunity to be placed on suitable treatment pathways will be significant in reducing the background prevalence and transmission of HCV moving closer to the goals set out by WHO GHSS.

7.1 Recommendations

The PHE National Infection Service of Public Health England should ensure routine automated reporting of HCV data from all laboratories reporting to Public Health England in the East Midlands to improve surveillance of the burden of HCV infection. This should include improving data quality and include the retrieval of back data and coverage of PCR status, in light of the new re-engagement exercise with ODNs.

The National Infection Service of Public Health England should also continue to work with laboratories to build on improvements in data quality and to standardise the reporting of HCV.

To address the continued apparent differential between case identification and mortality rates in Northamptonshire, it is important for the Local Authority and their partners to encourage better case identification and uptake of treatment in the area.

Clinicians should be encouraged to appropriately target testing and recognise where it may not be obvious, possible individuals who may have previously put themselves at risk, e.g. those above 65 years who may have previously injected drugs.

Ensure treatment services are reflective of the burden of infection particularly ensuring the specific areas with highest rates within ruralised counties have good access to treatment services therefore encourage better uptake of treatments.

For preventive work directed towards adolescents and young adults who are undertaking risky behaviours to continue, so the low positivity seen in this group year on year will be sustained.

To improve data quality in sentinel laboratory surveillance to capture greater detail about HCV cases reported through their systems.

Looking at evidence from the Unlinked Anonymised Survey it is clear that there is still a need to maintain good needle exchange services and continued messaging about the risks of infections through equipment sharing, and continued promotion of voluntary testing amongst PWID to ensure people are aware of their HCV status and can be treated.

For PHE to prospectively and retrospectively share data with ODNs to support appropriate treatment and care.

Directors of Public Health and local Health and Wellbeing Boards should consider hepatitis C prevention, testing, treatment and elimination as areas for prioritisation within health strategies, ensuring appropriate intelligence to support this is published in JSNAs.

National recommendations for local stakeholders

For ODNs to continue to improve case identification. This could be achieved if all stakeholders help improve awareness among professionals, for example by encouraging participation in e-learning [5][6].

Further enhance evidence-based health promotion activity to encourage targeted case finding in varying locations, all stakeholders should improve the offer and uptake of HCV testing to those at risk of HCV infection by implementing NICE guidelines [7].

BBV prevention services should ensure that testing is sustained or enhanced as appropriate [8], among those attending drug, and other, services; the use of newer approaches to testing, including use of capillary blood sampling and point of care testing, that may facilitate testing in non-clinical setting s or alleviate delays in onset of treatment, should be further explored.

Health and Justice to ensure that bloodborne virus opt-out testing for new receptions to prisons in England continues to be monitored to inform strategies to improve the offer and uptake of testing.

Commissioners and providers of drug services to consider implementing bloodborne virus opt-out testing.

Commissioners and providers of laboratory services to ensure, wherever possible, that RNA amplification tests are performed on the same sample as the original antibody assay (reflex testing) to decrease the turnaround time for referral, benefit patient care and increase cost effectiveness.

Commissioners of HCV treatment and care services should continue to work with public health agencies, primary and secondary care clinicians, and other stakeholders to simplify referral pathways; improve the availability, access and uptake of approved HCV treatments in primary and secondary care, drug treatment services, prisons and other settings; and to drive innovative approaches to outreach and patient support under the supervision of operational delivery networks.

PHE to evaluate the impact of the national re-engagement exercise (the controlled release of PHE held laboratory data on previously diagnosed patients to support case-finding and treatment within the NHS).

Treatment and BBV prevention services should ensure that appropriate information and support are provided to help guard against re-infection among those achieving a SVR following treatment.

8. References

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9. Acknowledgements

Data Source	People and Department
Laboratory reports of hepatitis C	Dr Koye Balogun and Reisha Simmonds - Immunisation, Hepatitis and Blood Safety Department, Centre for Infectious Disease Surveillance and Control
Sentinel surveillance	Georgina Ireland, Celia Penman, Reisha Simmonds and Ruth Simmons - Immunisation, Hepatitis and Blood Safety Department, National Infection Service
Unlinked Anonymous Monitoring Survey of HIV and Hepatitis in People Who Inject Drugs	Stephanie Migchelsen and Claire Edmundson - HIV & STI Department, National Infection Service (data from Unlinked Anonymous Monitoring Survey of HIV and Hepatitis in People Who Inject Drugs)
Hospital admissions	Annastella Costella, National Infection Service. Data from Hospital Episode Statistics (HES), NHS Digital (NHS Digital is the trading name of the Health and Social Care Information Centre. Copyright © 2019, Re-used with the permission of NHS Digital. All rights reserved). Produced by Public Health England.
Deaths	Office for National Statistics (ONS) and Annastella Costella (mortality maps). ONS carried out the original collection and collation of the data but bear no responsibility for their future analysis or interpretation.
Transplants	Annastella Costella, National Infection Service and Rhiannon Taylor, NHS Blood and Transplant. Data source: NHS Blood and Transplant UK Transplant Registry
Transplant & Blood Donor	Callum Pearson, Bhavita Vishram and Claire Reynolds, NHS Blood and Transplant / PHE Epidemiology Unit (Blood donors)

10. Appendices

Appendix 1: East Midlands Region

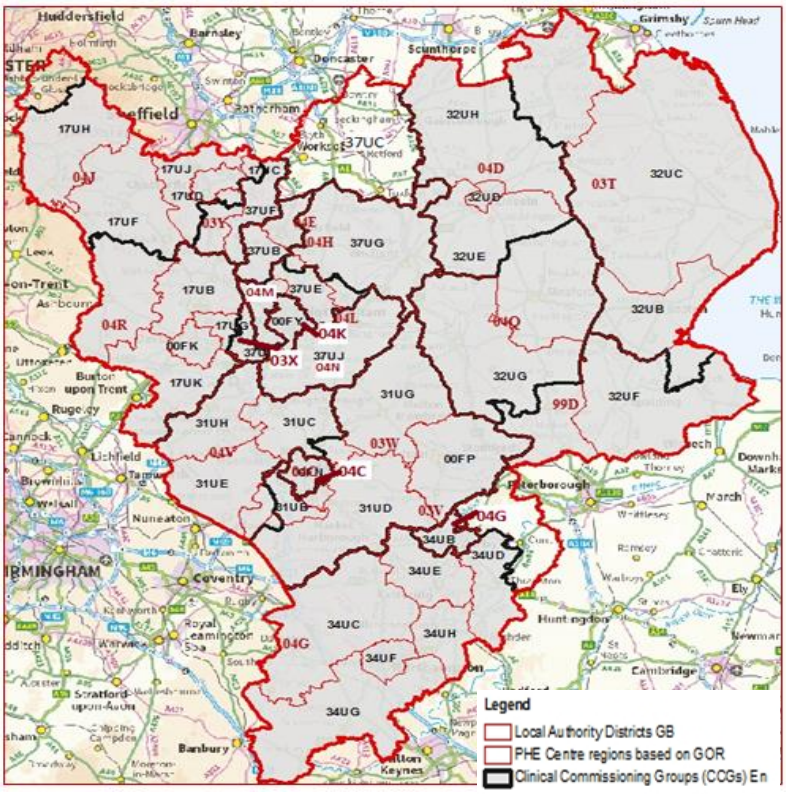
The East Midlands borders 5 other regions: Yorkshire and The Humber, the North West, the West Midlands, the South East and East of England and by the North Sea coastline to the east.

In area, it is **15,600** square km making it the fourth largest English region, smaller than the South West, East of England and the South East.

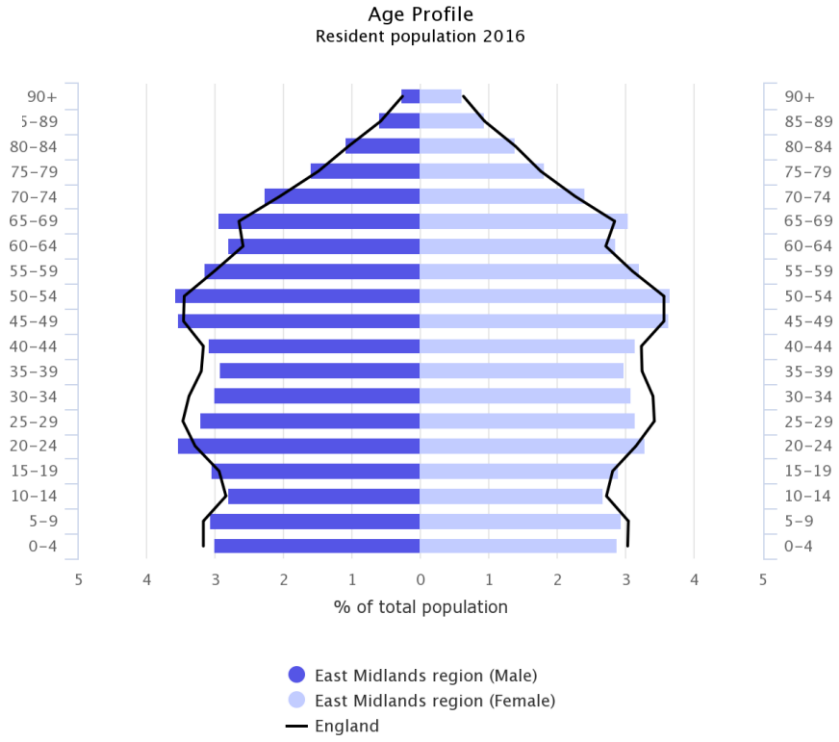
The region covers **12%** of the total area of England. It contains 5 counties, Derbyshire, Leicestershire, Lincolnshire, Northamptonshire and Nottinghamshire, and 4 unitary authorities, Derby, Leicester, Rutland and Nottingham.

There are **36** districts contained within the counties in the region, plus **4** unitary authorities.

Population (2015): The population of the East Midlands is **4.7 million** people one of the smallest regions, in terms of population, in England.



Map showing CCGs and LAs in the East Midlands, created by LKIS East Midlands

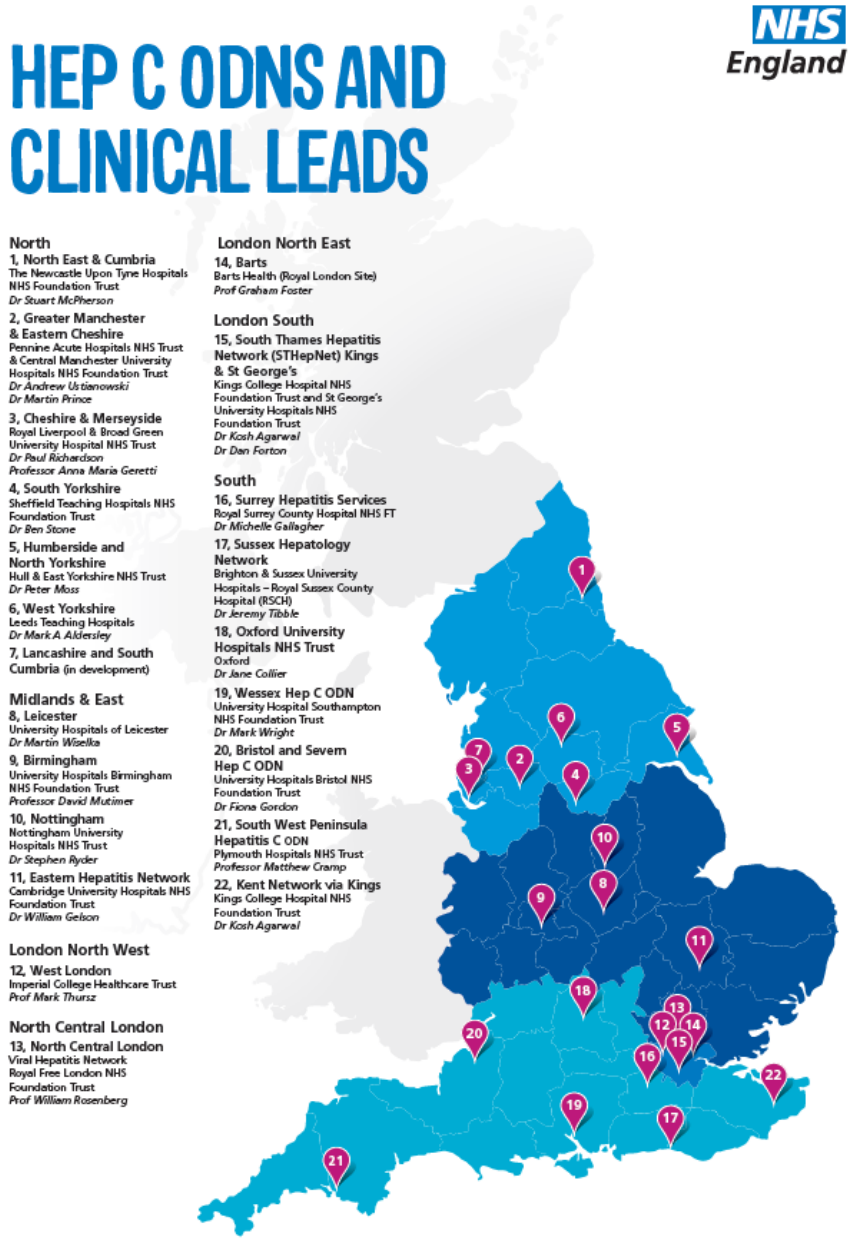


Appendix 2: Hepatitis C Operational Delivery Networks (ODNs)

East Midlands ODNs:

NETWORK NAME	LEAD PROVIDER	PARTNER ORGANISATONS	GEOGRAPHY COVERED
8. Leicester	University Hospitals of Leicester	• Kettering General Hospital NHS Foundation Trust • Northampton General Hospital NHS Trust • Leicestershire Partnership NHS Trust	Leicestershire
10. Nottingham	Nottingham University Hospitals NHS Trust	• Sherwood Forest Hospitals NHS Foundation Trust • United Lincolnshire Hospitals NHS Trust • Derby Hospitals	Nottinghamshire, Derbyshire & Lincolnshire

Source: www.england.nhs.uk/wp-content/uploads/2016/12/hep-c-odns-271016.pdf



Source: www.hcvaction.org.uk/resource/hepatitis-c-odns-and-clinical-leads

Appendix 3: Glossary of abbreviations

Anti-HBc	Antibodies to Hepatitis B virus
Anti-HCV	Antibodies to Hepatitis C virus
Anti-HIV	Antibodies to Human Immunodeficiency Virus
DAT	Drug Action Team
DBS	Dried Blood Spot
DSR	Directly Standardised Rate
ESLD	End Stage Liver Disease
ESP	European Standard Population
GUM	Genitourinary Medicine
HBc	Hepatitis B virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
MSM	Men who have Sex with Men
PCT	Primary Care Trust
PHE	Public Health England
PWID	Persons who inject drugs
RNA	Ribonucleic Acid
UTLA	Upper Tier Local Authority
VCT	Voluntary confidential test

Appendix 4: Data sources

Data source(s)	Short description of use(s)	Potential Limitation(s)
Morbidity (burden of disease plus risk factor data)		
Laboratory surveillance (LabBase/SGSS)	Quantifying burden of laboratory confirmed disease – overall and in specific groups/locations	Reporting variation makes it difficult to identify acute and chronic HCV
Sentinel Surveillance of BBV (hepatitis B and C)	Describe trends in testing and distribution of risk factors/exposures	Incomplete coverage of population; may be unrepresentative
Unlinked Anonymous Monitoring of Persons Who Inject Drugs (PWID)	Current burden of disease in a key at-risk population, secular trends, levels of protective and risky behaviours	
National Antenatal Infections Screening Monitoring Programme (NAISM)	Trends in testing of potentially low-risk population – secular trends can provide an early indication of any changes in the burden of disease	
Hospital Episode Statistics	Burden of disease (more severe end of the spectrum) and complications	
HPZone	Case management system used by health protection teams in PHE	
Hepatitis C commissioning template for estimated disease prevalence and treatment	Estimates to support health service commissioning, projections and prioritisation of resources.	The template draws heavily on methods produced for estimating HCV prevalence at a national level, with limited data available at a local level. The estimates less accurate than national estimates, as assumptions must be made about the distribution of HCV prevalence at the local level that do not fully reflect local variation and differences in populations. Similarly, projections of current and future morbidity, and rates of diagnosis and treatment are based on national or regional estimates.
Clinic activity, treatment, vaccination and other data on health service provision		
NHS Blood & Transplant	Measure of clinical activity to address an important complication/end-point of HCV infection	
Mortality data		
ONS mortality data	Outcome information used to quantify the impact of disease including premature death and inequities	