

**LIVER CANCER**

**Map 20:** Variation in mortality rate in people aged under 75 years due to hepatocellular carcinoma per population by Sustainability Transformation Partnerships (STP) (2011-2015)

Directly standardised rate per 100,000

NHS Domain 1: Preventing people from dying prematurely

NHS Domain 4: Ensuring that people have a positive experience of care

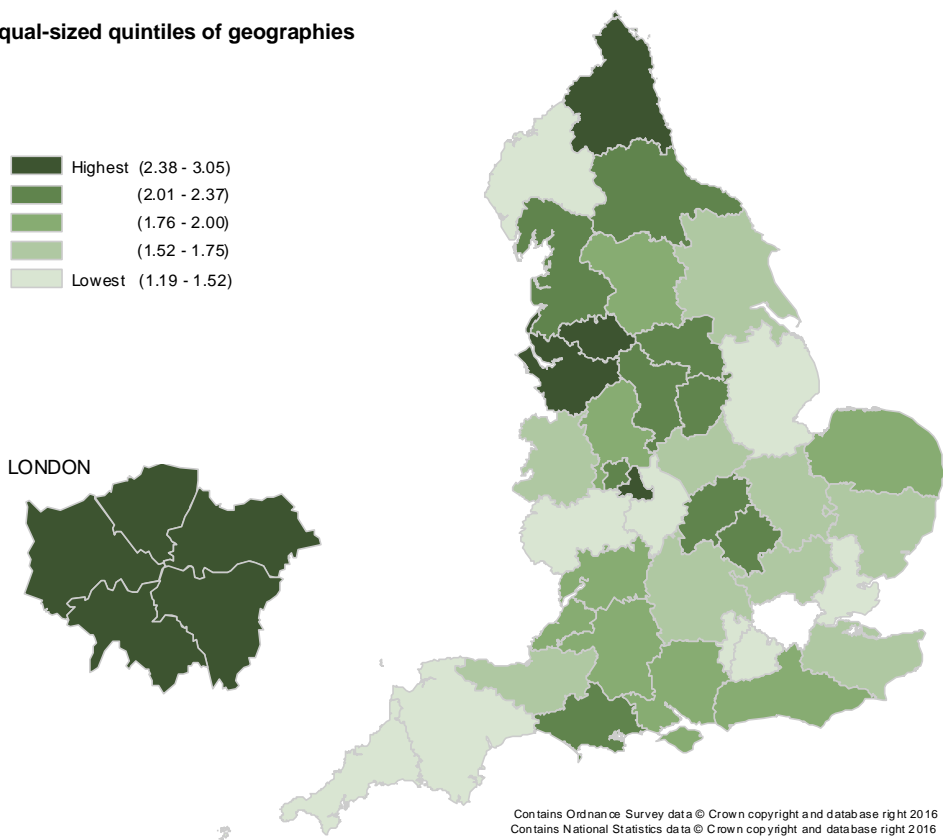
PHOF Domain 4: Healthcare public health and preventing premature mortality

**OPTIMUM VALUE: LOW**

Equal-sized quintiles of geographies

- Highest (2.38 - 3.05)
- (2.01 - 2.37)
- (1.76 - 2.00)
- (1.52 - 1.75)
- Lowest (1.19 - 1.52)

LONDON

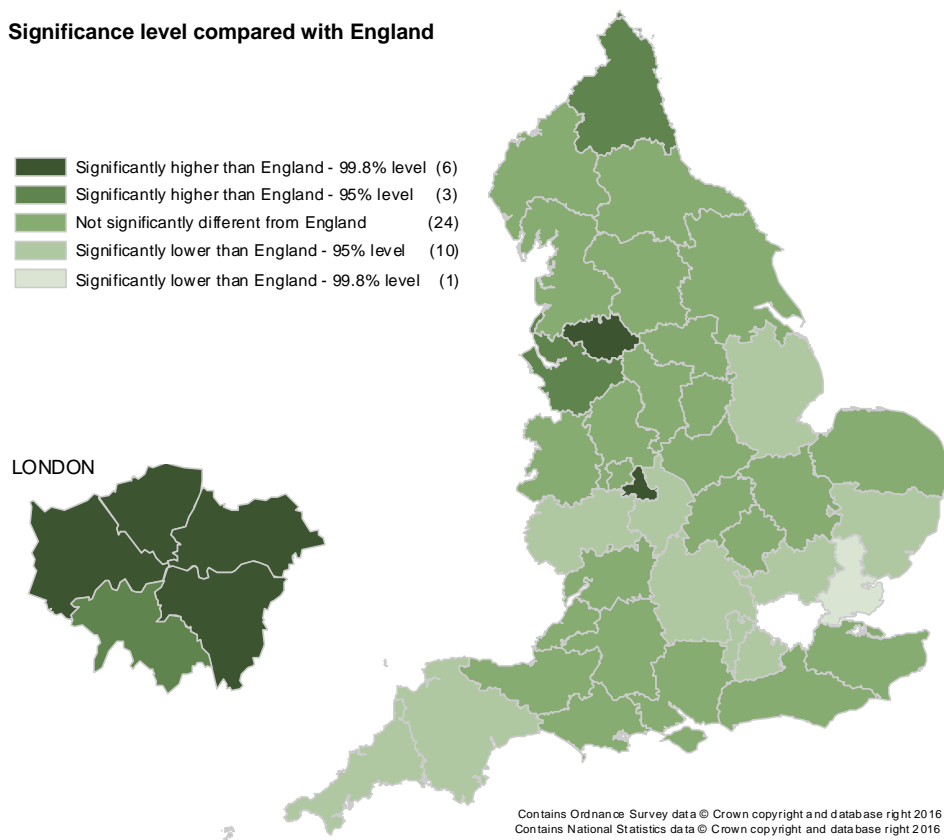


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Significance level compared with England

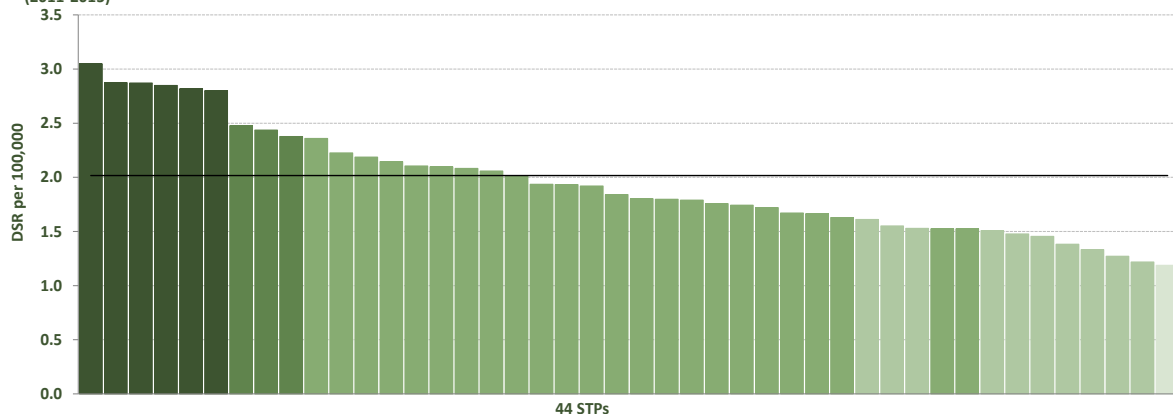
- Significantly higher than England - 99.8% level (6)
- Significantly higher than England - 95% level (3)
- Not significantly different from England (24)
- Significantly lower than England - 95% level (10)
- Significantly lower than England - 99.8% level (1)

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Variation in mortality rate in people aged under 75 years due to hepatocellular carcinoma per population by Sustainability Transformation Partnerships (STP) (2011-2015)



|                      | Example | 2005-09 | 2006-10 | 2007-11 | 2008-12 | 2009-13 | 2010-14 | 2011-15 |                        |
|----------------------|---------|---------|---------|---------|---------|---------|---------|---------|------------------------|
| Max-Min (Range)      |         | 2.19    | 2.61    | 1.96    | 2.18    | 2.20    | 1.91    | 1.86    | No significant change  |
| 95th-5th percentile  |         | 1.61    | 1.76    | 1.74    | 1.65    | 1.69    | 1.70    | 1.59    | No significant change  |
| 75th-25th percentile |         | 0.54    | 0.64    | 0.61    | 0.66    | 0.67    | 0.69    | 0.65    | No significant change  |
| Median               |         | 1.37    | 1.39    | 1.50    | 1.68    | 1.76    | 1.75    | 1.82    | INCREASING Significant |

## Context

The liver controls much of the body's biochemistry, and performs many important functions, including:

- storing nutrients
- storing and redistribution of fat
- converting fats to energy when the body needs it
- producing bile and proteins
- helping the blood to clot
- breaking down harmful substances including alcohol
- helping the immune system to fight infection.

According to Cancer Research UK, around 5,550 people are diagnosed with primary liver cancer each year in the UK, which accounts for about 2% of all cancers in the UK.<sup>1</sup> Secondary liver cancer, spreading from elsewhere in the body, is far more common than primary liver cancer. Most people in the UK who are diagnosed with tumours in their liver will have secondary rather than primary liver cancer. The most common form of liver cancer is hepatocellular carcinoma.

Primary liver cancer is more prevalent among men than among women. Primary liver cancer is becoming more common at all ages. It is now the ninth commonest cause of cancer death and has the largest increase in mortality over the last 10 years compared to all other cancers.<sup>1</sup>

<sup>1</sup> Cancer Research UK: Cancer Statistics [www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer](http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer)

The main cause of primary liver cancer (hepatocellular carcinoma) is cirrhosis of the liver, in which the liver is scarred as a result of damage over a long period of time.<sup>2</sup>

Other risk factors for liver cancer include:

- chronic hepatitis B and hepatitis C
- excessive alcohol consumption
- haemochromatosis, an uncommon genetic condition resulting from an overload of iron in the body – the risk is high if the condition is not treated
- non-alcoholic fatty liver disease (NAFLD), specifically the advanced form known as non-alcoholic steatohepatitis (NASH), thought to be the cause of many cases of cirrhosis previously ascribed to an unknown cause.<sup>2</sup>

Primary liver cancer arises most commonly in people with cirrhosis and may be seen as an indicator of the failure of an integrated approach to healthcare for people with liver disease. Incidence of primary liver cancer is likely to correlate with and reflect all forms of liver disease; the variation in the incidence of cancer appears to be similar to that in overall mortality from liver disease (see Map 1c).

Liver cancer in adults has a poor prognosis because it tends to be diagnosed late. By the time a person has symptoms and consults a doctor, the disease is frequently at an advanced stage. Only a small proportion are diagnosed in the early stages of the disease,<sup>3</sup> and it is only in these early diagnosed cases that treatment can be curative.<sup>1</sup>

Surveillance scans can be offered to people with cirrhosis who are at risk of liver cancer and this has been shown to lead to earlier diagnosis. However, the provision of high quality surveillance is variable across England.<sup>4</sup>

Overall, after diagnosis, at least 36% of people live for one year and at least 12% live for five years.<sup>5</sup>

## Magnitude of variation

The maps and column chart display the data for 2011-15, during which STP values ranged from 1.2 to 3.0 per 100,000 population, which is a 2.6-fold difference between STPs. The England value for 2011-15 was 2.0 per 100,000 population.

The boxplot shows the distribution of STP values for the period 2005-09 to 2011-15. There was no significant change in any of the three variation measures between 2005-09 and 2011-15. The median increased significantly from 1.4 per 100,000 population in 2005-09 to 1.8 per 100,000 population in 2011-15.

Potential reasons for the degree of variation observed include differences in:

- the prevalence of hepatitis B and hepatitis C
- the prevalence of cirrhosis of the liver
- levels of alcohol consumption
- availability of surveillance tests to people with cirrhosis
- access to rapid diagnostic and treatment pathways
- level of patient compliance with prevention or treatment

<sup>2</sup> British Liver Trust. Fighting Liver Disease. Liver Cancer. [www.britishlivertrust.org.uk/wp-content/uploads/Liver-Cancer\\_lores1.pdf](http://www.britishlivertrust.org.uk/wp-content/uploads/Liver-Cancer_lores1.pdf)

<sup>3</sup> Tsuchiya N, Sawada Y, Endo I, Saito K, Uemura Y, Nakatsura T. Biomarkers for the early diagnosis of hepatocellular carcinoma. *World Journal of Gastroenterology* : WJG. 2015;21(37):10573-10583. [www.ncbi.nlm.nih.gov/pmc/articles/PMC4588079](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4588079)

<sup>4</sup> Cross TJS, Villaneuva A, Shetty S on behalf of the Hepatocellular Carcinoma UK (UK HCC) Study Group, et al A national survey of the provision of ultrasound surveillance for the detection of hepatocellular carcinoma *Frontline Gastroenterology* Published Online First: 07 December 2015. <http://dx.doi.org/10.1136/flgastro-2015-100675>

<sup>5</sup> Office for National Statistics. Cancer Survival in England: adults diagnosed between 2011 and 2015 and followed up to 2016

[www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed](http://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed)

## Options for action

When planning service improvement or development to reduce the mortality rate for primary liver cancer, commissioners, clinicians and providers need:

- to review the mortality rates and trends for primary liver cancer in the locality
- to identify whether there are opportunities for improving the early diagnosis of liver cancer
- to include liver cancer in the assessment of strategies for reducing alcohol consumption and improving outcomes for liver disease
- to consider developing registries and surveillance programmes at a local level given that the risk groups for primary liver cancer are known
- to review the clinical management of and configuration of services for primary liver cancer to ensure close collaboration among the different disciplines – hepatology, diagnostic pathology and radiology services, interventional radiology and liver surgery including transplantation.

## RESOURCES

- National Cancer Registration and Analysis Service. [www.ncin.org.uk/publications/data\\_briefings/trends\\_in\\_incidence\\_of\\_primary\\_liver\\_cancer\\_subtypes](http://www.ncin.org.uk/publications/data_briefings/trends_in_incidence_of_primary_liver_cancer_subtypes)
- Cancer Research UK. Liver Cancer Mortality Statistics. [www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer/mortality](http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer/mortality)
- British Liver Trust. Fighting Liver Disease. Liver Cancer. [www.britishlivertrust.org.uk/wp-content/uploads/Liver-Cancer\\_lores1.pdf](http://www.britishlivertrust.org.uk/wp-content/uploads/Liver-Cancer_lores1.pdf)
- NICE interactive flowchart. Liver cancers overview. <https://pathways.nice.org.uk/pathways/liver-cancers>
- NICE. Alcohol-use disorders – prevention. Public health guideline [PH24]. Published date: June 2010. <http://guidance.nice.org.uk/PH24>
- NICE. Alcohol-use disorders: diagnosis and management of physical complications. Clinical guideline [CG100]. Published date: June 2010. <http://guidance.nice.org.uk/CG100>
- NICE interactive flowchart. Alcohol-use disorders overview. <http://pathways.nice.org.uk/pathways/alcohol-use-disorders>
- PHE Alcohol Learning Resources. Improving Local Alcohol Interventions. [www.alcohollearningcentre.org.uk/](http://www.alcohollearningcentre.org.uk/)

- Public Health England. Alcohol Care in England's Hospitals: An opportunity not to be wasted. November 2014. [www.alcohollearningcentre.org.uk/\\_assets/Alcohol\\_Care\\_in\\_Englands\\_Hospitals\\_An\\_opportunity\\_not\\_to\\_be\\_wasted\\_PHE\\_Nov\\_14.pdf](http://www.alcohollearningcentre.org.uk/_assets/Alcohol_Care_in_Englands_Hospitals_An_opportunity_not_to_be_wasted_PHE_Nov_14.pdf)

## LIVER CANCER

## Map 21: Variation in percentage of people aged 15 years and over with hepatocellular carcinoma that have had treatment with curative intent (liver transplantation, major liver resection or ablation) by region (2010-2014)

NHS Domain 1: Preventing people from dying prematurely

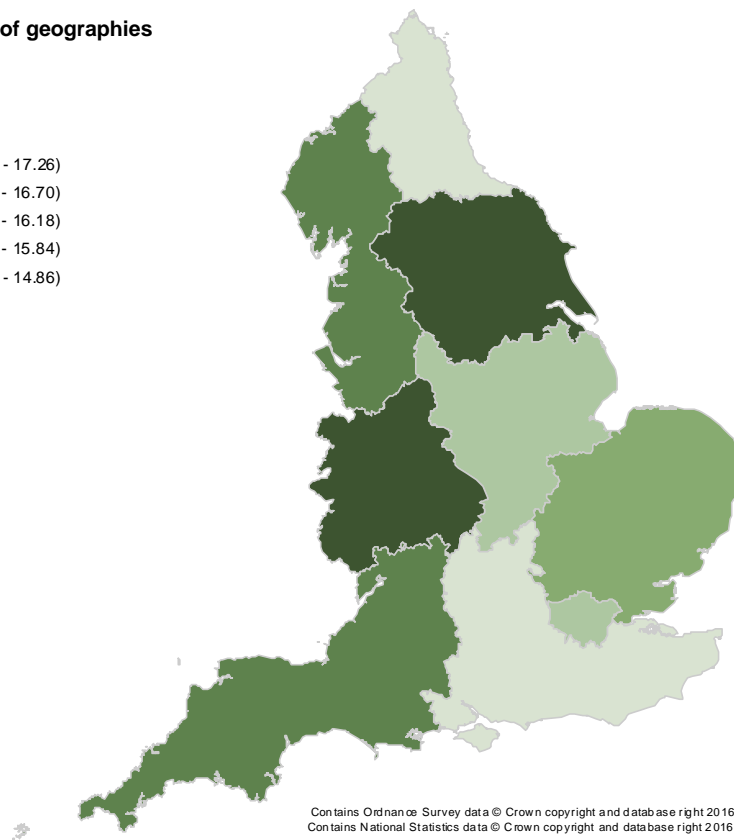
NHS Domain 3: Helping people to recover from episodes of ill health or following injury

PHOF Domain 4: Healthcare public health and preventing premature mortality

OPTIMUM VALUE: HIGH

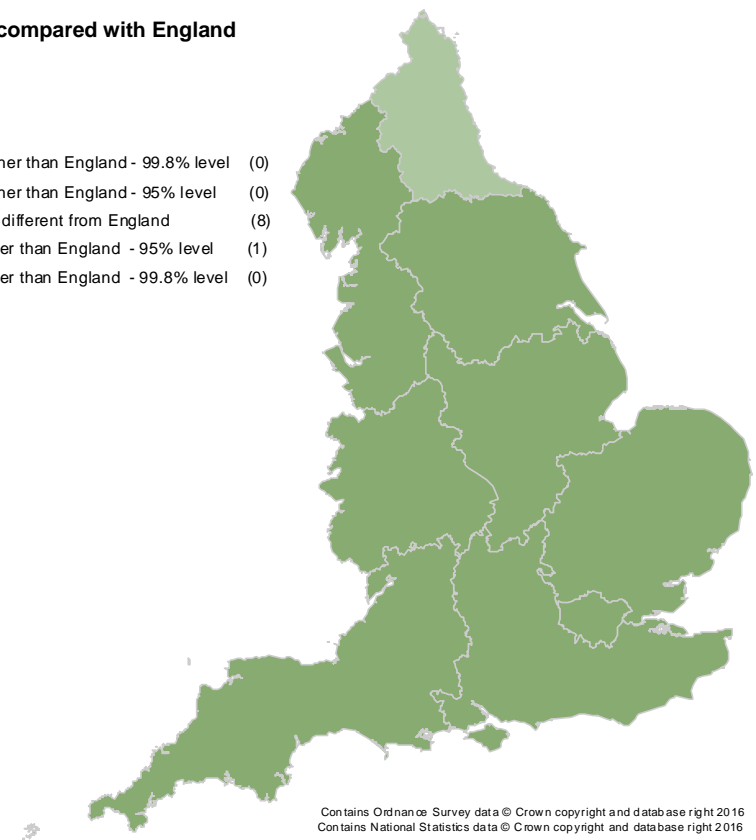
### Equal-sized quintiles of geographies

|           |                 |
|-----------|-----------------|
| ■ Highest | (16.71 - 17.26) |
| ■         | (16.19 - 16.70) |
| ■         | (15.85 - 16.18) |
| ■         | (14.87 - 15.84) |
| ■ Lowest  | (11.39 - 14.86) |



### Significance level compared with England

|   |     |
|---|-----|
| ■ Significantly higher than England - 99.8% level | (0) |
| ■ Significantly higher than England - 95% level   | (0) |
| ■ Not significantly different from England        | (8) |
| ■ Significantly lower than England - 95% level    | (1) |
| ■ Significantly lower than England - 99.8% level  | (0) |



Variation in percentage of people aged 15 years and over with hepatocellular carcinoma that have had treatment with curative intent (liver transplantation, major liver resection or ablation) by region (2010-2014)

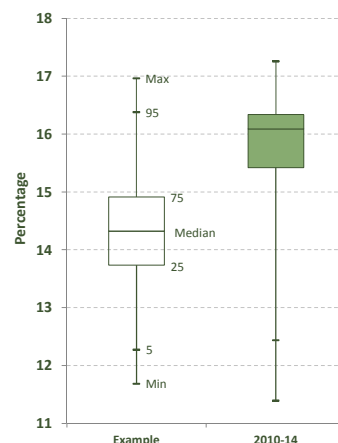


## Context

In 2014, there were 5,550 new cases of liver cancer in the UK, which accounted for 2% of all cancers; two-thirds (66%) of new cases of liver cancer occurred in men.<sup>1</sup>

There are two main types of liver cancer:

- primary liver cancer, which is uncommon but serious and more likely to affect people who are aged over 60 years
- secondary liver cancer, where cancer has developed in another part of the body and spread to the liver, eg from the bowel, and which is far more common than primary liver cancer



|                      |  |      |
|----------------------|--|------|
| Max-Min (Range)      |  | 5.9  |
| 95th-5th percentile  |  | 4.8  |
| 75th-25th percentile |  | 0.9  |
| Median               |  | 16.1 |

The most common form of primary liver cancer in men is hepatocellular carcinoma; it is the second most common in women.<sup>2</sup> Most cases of hepatocellular carcinoma are associated with cirrhosis of the liver, in which the liver is scarred as a result of damage over a long period of time. The causes of cirrhosis include:

- long-term hepatitis B and hepatitis C infection
- excessive alcohol consumption
- haemochromatosis, an uncommon genetic condition resulting from an overload of iron in the body – the risk is high, if the condition is not treated
- primary biliary cirrhosis, a long-term disease in which the bile ducts become damaged
- non-alcoholic fatty liver disease (NAFLD), specifically the advanced form known as non-alcoholic steatohepatitis (NASH), thought to be the cause of many cases of cirrhosis previously ascribed to an unknown cause – NAFLD is increasingly being associated with hepatocellular carcinoma

Treatment of liver cancer depends on the stage of the disease. Most clinicians use a combination staging system to categorise the stage of the disease encompassing:

- the features of the cancer
- the person's underlying liver function

In the Barcelona Clinic Liver Cancer (BCLC) staging system, there are five stages, starting at 0, through A, B and C to D.

<sup>1</sup> Cancer Research UK. Liver cancer statistics. [www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer/incidence#heading-Zero](http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer/incidence#heading-Zero)

<sup>2</sup> National Cancer Intelligence Network (February 2012) Trends in incidence of primary liver cancer subtypes. NCIN Data Briefing. February 2012. [www.ncin.org.uk/cancer\\_type\\_and\\_topic\\_specific\\_work/cancer\\_type\\_specific\\_work/upper\\_gi\\_cancers](http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/upper_gi_cancers)

At stage 0, the tumour is less than two centimetres in diameter and the person has normal liver function; in stage D, the liver has lost most of its function and the person has symptoms of end-stage liver disease, eg build-up of fluid in the abdomen. Only a small proportion of people are diagnosed in the early stages of the disease.<sup>3</sup>

If primary liver cancer is diagnosed at an early stage – stage 0 or stage A – it may be possible to treat the cancer using:

- resection, removing part of the liver surgically – the liver is the only organ in the body that has the capacity to regenerate (ie if part of a healthy liver is removed the remainder can increase in volume until it returns to the original volume)
- liver transplantation, replacing a person's original liver with a donor liver
- microwave or radiofrequency ablation to destroy the cancer cells
- There are two types of surgical resection:
- open surgical resection of the liver, which is the standard treatment for patients with hepatocellular carcinoma
- laparoscopic liver resection, a technique usually used to treat secondary liver cancer but which can be used to treat hepatocellular carcinoma

“Major” resection has been defined in National Cancer Registration and Analysis Service (NCRAS) documentation as an operation in which the surgeon “would attempt to remove the entire tumour”. In liver resection this usually involves the removal of 3-4 or more liver segments. The decision whether to undertake surgical resection will be based not only on the size and extent of the tumour but also on the degree of associated cirrhosis because that affects liver function and the liver's regenerative capacity.

For the time-period 2010-14, 15.7% of hepatocellular carcinoma patients underwent treatment of curative intent, either liver transplant, major liver resection or ablation, within 6 months of their cancer diagnosis.

The correlation of the incidence of primary liver cancer with surgical resection could be viewed not only as an indicator of early detection but also of whether measures are in place to identify

cases of primary liver cancer early. Primary liver cancer arises only in people with cirrhosis and may be seen as an indicator of the failure of an integrated approach to healthcare.

In 2017 a national collaboration has been established to develop a prospective detailed registry of all patients with HCC identified in England & Wales through liver cancer multidisciplinary team meetings and PHE. It is hoped that this will provide an accurate picture of the causes of any underlying liver disease in those with HCC, help identify changes in risk factors with time and the affected demographic data as well as a clear analysis of the treatments offered and the outcome.

In addition there will be a collaboration with Swansea University Health Economics Group to assess the costs of HCC and any interventions, data which will help future plans for therapy to be evaluated more readily.

Furthermore, clinical colleagues in both Scotland and Northern Ireland working with patients affected by HCC have agreed to collate data corresponding to that available in England & Wales to complete a UK wide picture.

### Magnitude of variation

The maps and column chart display the data for 2010-14, during which region values ranged from 11.4 to 17.3%, which is a 1.5-fold difference between regions. The England value for 2010-14 was 15.7%. The boxplot shows the distribution of region values for the period 2010-14.

<sup>3</sup> Tsuchiya N, Sawada Y, Endo I, Saito K, Uemura Y, Nakatsura T. Biomarkers for the early diagnosis of hepatocellular carcinoma. World Journal of Gastroenterology : WJG. 2015;21(37):10573-10583. [www.ncbi.nlm.nih.gov/pmc/articles/PMC4588079](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4588079)



Potential reasons for the degree of variation observed include differences in:

- the age-sex structure of the local population
- the ethnic composition of the local population – the incidence is higher in Chinese, Black African, Bangladeshi and Pakistani men than in White men, and higher in Bangladeshi and Pakistani women than in White women<sup>4</sup>
- the incidence of hepatitis B and hepatitis C
- the incidence of cirrhosis
- levels of alcohol consumption in the local population
- the configuration of local services
- the provision of surveillance programmes for people at risk of developing primary liver cancer (eg people with cirrhosis)
- the timing of diagnosis
- criteria for the selection of people undergoing major resection
- degree of adherence to guidance
- level of patient compliance with prevention or treatment

## Options for action

When planning service improvement or development to increase the early diagnosis rate for hepatocellular carcinoma, commissioners, clinicians and service providers need:

- to review the mortality rates and trends for primary liver cancer including hepatocellular carcinoma in the locality
- to identify whether there are opportunities for improving the early diagnosis of liver cancer
- to include liver cancer in the assessment of strategies for prevention and improving outcomes for liver disease
- to consider developing and reviewing local registries and surveillance programmes (eg ultrasound scanning and blood testing every 6-12 months) given that the risk groups for primary liver cancer are known

- to review the clinical management of and configuration of services for primary liver cancer to ensure close collaboration among the different disciplines – hepatology, diagnostic pathology and radiology services, interventional radiology and liver surgery including resection and transplantation.

## RESOURCES

- National Cancer Intelligence Network. (2010) Geographic variation in primary liver and gallbladder cancer. NCIN Data Briefing. [www.ncin.org.uk/publications/data\\_briefings/liver\\_and\\_gall\\_bladder](http://www.ncin.org.uk/publications/data_briefings/liver_and_gall_bladder)
- National Cancer Intelligence Network. (February 2012) Trends in incidence of primary liver cancer subtypes. NCIN Data Briefing. [www.ncin.org.uk/publications/data\\_briefings/trends\\_in\\_incidence\\_of\\_primary\\_liver\\_cancer\\_subtypes](http://www.ncin.org.uk/publications/data_briefings/trends_in_incidence_of_primary_liver_cancer_subtypes)
- NICE. NICE interactive flowchart. Liver cancers overview. <https://pathways.nice.org.uk/pathways/liver-cancers>
- NICE. Laparoscopic liver resection. Interventional procedures guidance [IPG135]. [www.nice.org.uk/guidance/ipg135](http://www.nice.org.uk/guidance/ipg135)
- NICE. Radiofrequency-assisted liver resection. Interventional procedures guidance [IPG211]. Published date: February 2007. [www.nice.org.uk/guidance/IPG211](http://www.nice.org.uk/guidance/IPG211)
- NICE. Living-donor liver transplantation. Interventional procedures guidance [IPG535]. Published date: November 2015. [www.nice.org.uk/guidance/IPG535](http://www.nice.org.uk/guidance/IPG535)
- British Liver Trust. Liver cancer. [www.britishlivertrust.org.uk/liver-information/liver-conditions/liver-cancer](http://www.britishlivertrust.org.uk/liver-information/liver-conditions/liver-cancer)

<sup>4</sup> National Cancer Intelligence Network (2012) Variation in incidence of primary liver cancer between ethnic groups, 2001-2007. NCIN Data Briefing. [www.ncin.org.uk/cancer\\_type\\_and\\_topic\\_specific\\_work/cancer\\_type\\_specific\\_work/upper\\_gi\\_cancers](http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/upper_gi_cancers)