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Acute Hepatitis B (England): annual report for 2018

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Introduction

Hepatitis B is a blood borne infection of the liver caused by the hepatitis B virus (HBV). The virus can provoke an acute illness characterised by nausea, malaise, abdominal pain, and jaundice but can also produce a chronic persistent infection that is associated with an increased risk for chronic liver disease and hepatocellular carcinoma. Transmission is by parenteral exposure to infected blood and body fluids contaminated by blood, most often through sexual contact, blood to-blood contact and perinatal transmission from mother to child. HBV infection can be prevented by immunisation and in the UK immunisation is recommended for individuals at high risk of exposure to the virus e.g. people who inject drugs (PWID), healthcare workers and household contacts of people who are acutely and persistently infected with hepatitis B. Immediate post-exposure immunisation is used to prevent infection, especially in babies born to infected mothers or following needle-stick injuries [1]. In August 2017, the UK also introduced hepatitis B containing hexavalent vaccine into the routine infant immunisation programme [2].

Surveillance of acute hepatitis B is essential to target prevention and control activities such as the selective immunisation programme. Public Health England, formerly the Health Protection Agency (HPA) implemented national surveillance standards [3] for hepatitis B in 2007 which provided the framework for more consistent reporting of cases from PHE Centres. Available data on confirmed acute infections reported from NHS laboratories can then be used to augment the epidemiological data collected from the local PHE centres. The first report was published in 2008, and this current report provides an update and presents acute hepatitis B surveillance data for 2018.

For the first time, following the reporting of regional clusters of acute hepatitis B in 2015 to 2016, supplementary data from molecular surveillance of acute hepatitis B are included and these will continue to be published on a quarterly basis to provide more real-time monitoring of transmission events.

Methods

The surveillance definition for acute hepatitis B [4] is

"HBsAg positive *and* anti-HBc IgM positive *and* abnormal liver function tests with a pattern consistent with acute viral hepatitis."

As information on liver function is usually not available to PHE, for the purpose of this analysis:

- cases classified as acute viral hepatitis B by the local PHE Centre or the laboratory and/or with a documented positive anti-HBc IgM were classified as acute cases;

- cases classified as acute viral hepatitis B by the PHE Centre but without anti-HBc IgM test results, or not classified but with a positive anti-HBc IgM reported were assumed to be probable acute hepatitis B cases;

- cases classified as acute by the PHE Centre but with contradictory evidence e.g. positive hepatitis serology results dated before July 2012 were reclassified as chronic infections;
- cases classified as chronic persistent infections or those not classified where anti-HBc IgM was negative or equivocal were assumed to be chronic persistent infections;

PHE Centre cases with a date entered from 1 January 2018 to 31 December 2018 were extracted from HPZone (a national, web-based public health case management tool) and matched to a laboratory dataset using Microsoft Access and algorithms comparing combinations of the following variables: Surname, First name, date of birth, sex, clinic number and NHS number. The laboratory database contained all confirmed hepatitis B infections reported to PHE by laboratories in England and Wales (SGSS). A final reconciled dataset included cases classified as acute or probable acute and reported from the PHE Centre and/or from laboratories around the country to SGSS. After follow up with the clinician and/or the patient, PHE Centre staff assigned a probable route of exposure and collected information on other possible exposure routes. For the analysis, where the

probable route of exposure had not been assigned due to more than one exposure, the most likely route was assigned hierarchically (people who inject drugs, followed by sex between men, then heterosexual exposure, etc).

Two forms of 2018 supplementary HPZone data from the molecular surveillance of acute hepatitis B have been included and will continue to be published on a quarterly basis. HP Zone Context "Acute Hepatitis B" data includes personally identifiable information, which therefore allows for the rapid identification of cases and request of samples directly from laboratories for avidity and molecular characterisation at the Virus Reference Department (VRD), Colindale. HPZone data without personally identifiable information (HPZone Dashboard) on acute cases was matched to HPZone Context data using a unique identifier. The "Acute Hepatitis B" Context data was matched to laboratory testing data from the VRD using Microsoft Access algorithms comparing combinations of the following variables: Surname, First name, date of birth, sex, and NHS number.

Results

The PHE Centres reported 4,390 hepatitis B cases from 1 January to 31 December 2018 to the PHE Immunisation, Hepatitis and Blood Safety Department. The matching and classification exercise resulted in 291 of these being confirmed as acute and 22 re-classified as probable acute cases with the remainder classified as chronic or excluded.

A total of 7,255 confirmed hepatitis B infections were reported from laboratories to SGSS in the same period, 292 (4.0%) of which were classified as acute cases, 20 (0.3%) as probable acute cases. The remainder were classified as chronic or excluded.

After the two databases were linked and reconciled, a total of 381 acute or probable acute cases of hepatitis B were reported for England in 2018. This gives an annual incidence of 0.68 per 100,000 populations lower than the incidence of 0.80 per 100,000 population reported for 2017.

London is still the region with the highest incidence (1.23 per 100,000) and this has decreased from the previous year (1.43 per 100,000). The highest increase in incidence was reported from North East (from 0.49 to 0.75 per 100,000 in 2017 and 2018 respectively) and Yorkshire and Humber (from 0.72 to 0.88 per 100,000). The largest decrease was reported

from East Midlands (from 0.82 to 0.52 per 100,000 in 2017 and 2018 respectively) and South West (from 0.69 to 0.41 per 100,000 in 2017 and 2018 respectively). In the remaining regions incidence was similar or slightly decreased / increased from last year (table 1).

There continues to be regional variation in the contribution of the different data sources to the overall total, although the degree of overlap between sources has continued to improve suggesting that completeness of reporting by laboratories and local clinicians has shown a slight improvement (table 1).

As in previous years, where known the majority of cases were in men (64.7%) who had an overall incidence of 0.87 per 100,000 – a decrease from 1.14 per 100,000 in 2017 [4]. The corresponding incidence in women in 2018 was 0.47 per 100,000 continuing from the 0.47 per 100,000 in the previous year. Men aged 45-54 years had the highest incidence of acute hepatitis B in 2018 at 1.52 per 100,000.

Only 56 cases (14.7%) of the total acute or probable acute hepatitis B cases had their ethnicity recorded; a lower proportion than the previous year. Seventy one percent of the cases were white (an increase from 67% in 2017), followed by Black African or Black Caribbean (7.1%) and Indian (5.4%).

Of the total 381 acute and probable acute cases of hepatitis B, 110 (28.9%) had associated exposure information recorded (with the most probable route of acquisition assigned by the PHE Centre). A similar proportion (27.9% 124/445) had exposure information available in 2017. As in previous years where known the commonest reported risk attributed was heterosexual exposure, implicated as the probable route of exposure in 55 (50.0%), compared to 54.8% in this category in 2017 (n=68). Cases attributed to sex between men were reported in 19 (17.3%); a similar proportion to the 19 (15.3%) reported in 2017. There were four cases (3.6%) with known exposure attributed to PWID (an increase from none in the previous year).

Where known, 11 (10.0%) cases had health care related exposures (including surgery, dental treatment, and other hospital exposure) – an increase from the 9 (7.3%) cases assigned to medical risk factors last year. Skin piercing or tattooing was listed as probable exposures for seven cases (3.4%, 7/110).

Table 1: Acute or probable acute hepatitis B cases by region and source of report, 2018 (incidence 2008-2014 – mid 2013 population, incidence 2015 – mid 2015 population, incidence 2016 – mid-2016 population, incidence 2017 – mid-2017 and incidence 2018 – mid-2018 population ONS [5])

REGION	HPT	Laboratory	BOTH	TOTAL	**Incidence of reported acute hepatitis B per 100,000 in 2018**	Incidence of reported acute hepatitis B per 100,000 in 2017	Incidence of reported acute hepatitis B per 100,000 in 2016	Incidence of reported acute hepatitis B per 100,000 in 2015	Incidence of reported acute hepatitis B per 100,000 in 2014	Incidence of reported acute hepatitis B per 100,000 in 2013	Incidence of reported acute hepatitis B per 100,000 in 2012	Incidence of reported acute hepatitis B per 100,000 in 2011
EAST MIDLANDS	2	3	20	25	**0.52**	0.82	0.70	1.07	0.41	0.35	0.77	0.76
EAST OF ENGLAND	5	0	26	31	**0.50**	0.68	0.62	0.76	0.89	0.81	0.89	1.08
LONDON	19	34	57	110	**1.23**	1.43	1.70	1.53	1.52	1.22	2.02	2.06
NORTH EAST	0	2	18	20	**0.75**	0.49	0.68	0.34	0.84	0.65	0.46	0.54
NORTH WEST	16	6	23	45	**0.62**	0.52	1.02	0.64	0.82	0.87	0.61	0.99
SOUTH EAST	9	5	27	41	**0.45**	0.68	0.49	0.69	0.71	0.67	0.84	0.96
SOUTH WEST	5	5	13	23	**0.41**	0.69	0.53	0.49	1.08	0.63	1.40	1.16
WEST MIDLANDS	4	8	26	38	**0.64**	0.82	0.50	0.85	0.78	0.55	0.98	0.90
YORKS AND HUMBER	9	5	34	48	**0.88**	0.72	0.72	0.65	0.82	0.82	0.83	1.06
NATIONAL	**69**	**68**	**244**	**381**	**0.68**	**0.80**	**0.82**	**0.83**	**0.91**	**0.77**	**1.04**	**1.13**

Table 2: Age and sex breakdown of acute or probable acute hepatitis B reports, 2018 incidence 2018 – mid-2018 population ONS [5]

	Female		Male		NK		TOTAL	
Age group	N	Incidence of reported acute hepatitis B per 100,000 population	N	Incidence of reported acute hepatitis B per 100,000 population	N	Incidence of reported acute hepatitis B per 100,000 population	N	Incidence of reported acute hepatitis B per 100,000 population
Under 15	1	0.02	4	0.77	1	0.01	6	0.06
15-24	27	0.84	30	0.88	3	0.05	60	0.91
25-34	24	0.64	54	1.41	2	0.03	80	1.05
35-44	23	0.64	36	1.02	1	0.01	60	0.84
45-54	24	0.61	58	1.52	0	–	82	1.06
55-64	20	0.60	38	1.17	0	–	58	0.88
65+	13	0.24	22	0.47	0	–	35	0.34
NK	0	–	0	–	0	–	0	0.00
Total	**132**	**0.47**	**242**	**0.87**	**7**	**0.01**	**381**	**0.68**

Supplementary data from acute hepatitis B molecular surveillance

In 2018, 297 cases of acute hepatitis B were reported onto HPZone Dashboard (without personally identifiable information) across England (confirmed, probable and possible)[1]. A graph of HPZone cases in England are shown in figure 1, a summary of HPZone Dashboard cases reported by PHE region is shown in **appendix 1**. In 2015 there was a slight increase in cases likely caused by the outbreak of acute hepatitis B in men who have sex with men but identify as heterosexual [9].

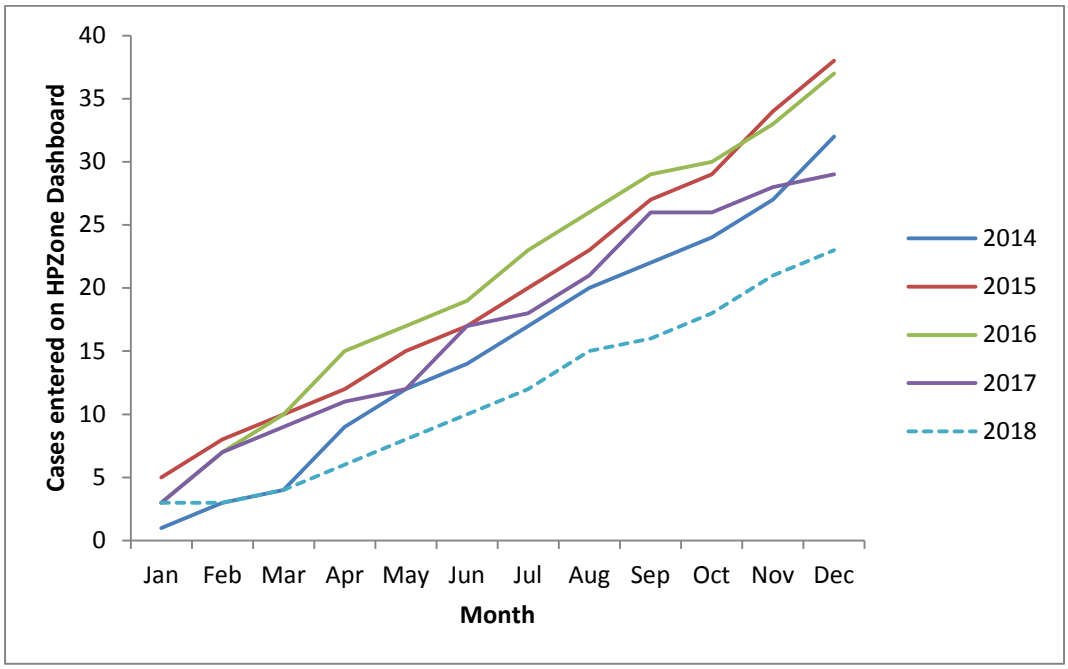

Figure 1: Cumulative cases of acute hepatitis B in England entered on HPZone Dashboard 2014 – 2018

Since 2016, acute hepatitis B cases entered on HPZone have been assigned to an acute hepatitis B Context (which includes personally identifiable information). On linking the 2018 HPZone Context dataset and 2018 HPZone Dashboard datasets, a total of 86.5 % (257/297) of the cases were found in both datasets (figure 2). Of the cases with HPZone Context, 28.5% of cases had a sample forwarded to the VRD.

[1] Classified according to HPZone case definitions

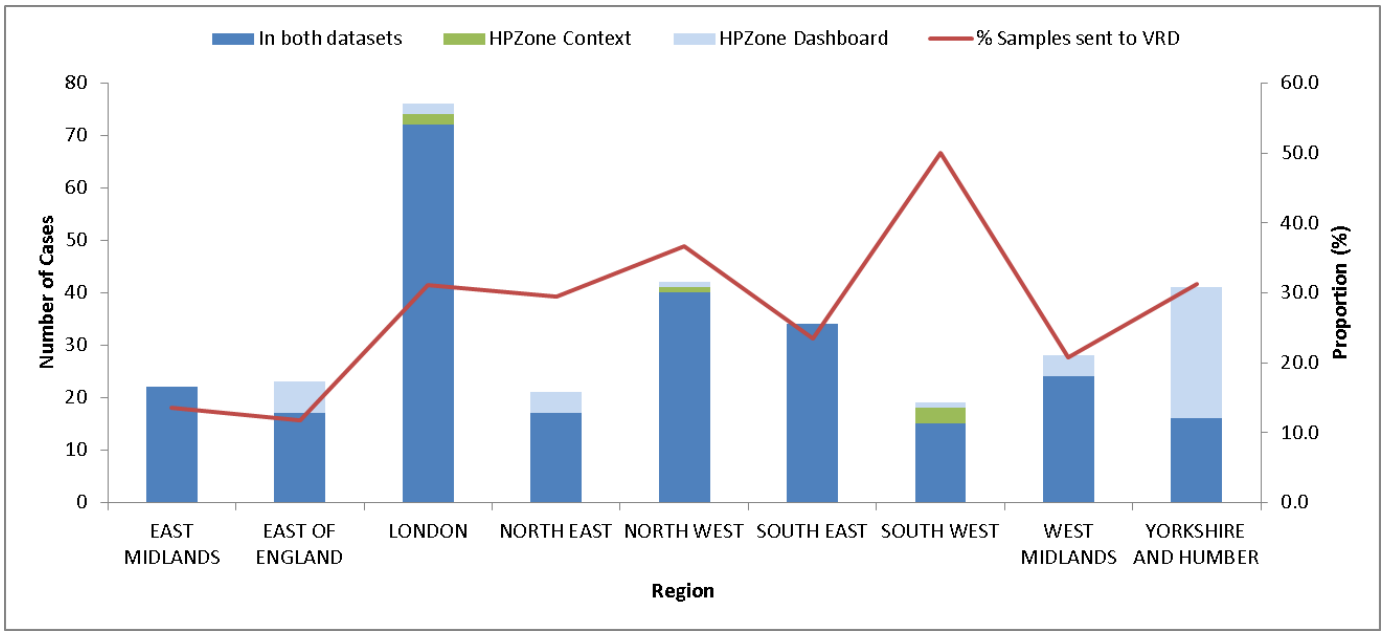

Figure 2: 2018 cases entered onto HPZone Context and / or HPZone Dashboard by HPTs. The line graph (right axis) shows the proportion of HP Zone Context cases that had a sample forwarded to the VRD.

From 2016 to 2018, a total of 88.0% (857/974) of acute hepatitis B cases were found in both the HPZone Context and HPZone Dashboard datasets (table 3). For the last two years, the highest proportion of reported cases have been from London, 72 (24.8%) in 2017 and 71 (27.6%) in 2018.

Table 3: Matched HPZone Context and HPZone Dashboard cases reported cases by PHE region, 2016 to 2018*

PHE region	Year		
	2016 (%)	2017 (%)	2018 (%)
East Midlands	29 (9.4)	6 (2.1)	22 (8.6)
East of England	34 (11.0)	29 (10.0)	22 (8.6)
London	57 (18.4)	72 (24.8)	71 (27.6)
North East	16(5.2)	15 (5.2)	18 (7.0)
North West	60 (19.4)	31 (10.7)	40 (15.6)
South East	25 (8.1)	33 (11.4)	28 (10.9)
South West	32 (10.3)	30 (10.3)	15 (5.8)
West Midlands	31 (10.0)	40 (13.8)	25 (9.7)
Yorkshire and Humber	26 (8.4)	34 (11.7)	16 (6.2)
England Total	**310**	**290**	**257**

*HPZone acute hepatitis B Context was introduced in 2016, therefore matching of HPZone Context and HPZone Dashboard datasets is only available after this period.

For the 2018 matched HPZone Context dataset and HPZone Dashboard dataset, age and sex was well reported (>98%). Where sex was known males accounted for 66.9% of cases (170/254). The median age of persons with acute HBV was 45 years old (IQR: 30-55), 47 (IQR: 30-55) for males and 42 (IQR: 29.5-54.5) for females. The age distribution by sex is presented in table 4; a majority of cases were in the 45-54 age group. The highest proportion of cases in males were in the 45-54 age group, whilst in females the highest proportion was in the 35-44 age group.

Table 4: Number and proportion of matched HPZone Context and HPZone Dashboard cases by sex and age group during 2018

Age group (years)	Sex		Total (%)
	Female (%)	Male (%)	
Under 15	0 (0.0)	2 (1.2)	2 (0.8)
15-24	17 (20.2)	19 (11.2)	29 (11.7)
25-34	11 (13.1)	35 (21.5)	46 (18.6)
35-44	18 (21.4)	21 (12.9)	39 (15.8)
45-54	17 (20.2)	46 (28.2)	63 (25.5)
55-64	13 (15.5)	30 (18.4)	43 (17.4)
65+	8 (9.5)	17 (10.4)	25 (10.1)
Total	**84**	**163**	**254**

Avidity testing and molecular characterisation investigations were undertaken on samples linked to HPZone Context cases to confirm the acute hepatitis B diagnosis with additional genotyping and phylogenetic analysis to inform on the diversity of the circulating viruses.

Of the 118 samples submitted to the VRD as part of enhanced molecular surveillance, 13 (11%) were confirmed as to be from individuals with chronic hepatitis B and 93 (79%) were confirmed to be from individuals with acute hepatitis B infection. The avidity testing in the remaining 12 samples were classified as inconclusive where it was not possible to confidently assign an HBV infection status.

A total of 86 confirmed acute cases could be genotyped over this period. The distribution of genotypes is shown in table 5. As with the previous year genotype A was the most commonly reported genotype with 55.8% of cases, this was an increase in the proportion of all tests compared to 2017. Additional sub genotype analysis of the A viruses indicated 87.5% to be A2 and 12.5% to be A1. The distribution of genotypes seen in PHE regions is shown in figure 3. No large clusters or outbreaks were identified by HP Zone or sequencing.

Table 5: Genotype distribution and proportions of acute hepatitis B cases tested at VRD in 2017 – 2018

Genotype	Cases 2017	Proportion of cases 2017	Cases 2018	Proportion of cases 2018
A	30	39.0%	48	55.8%
B	4	5.2%	2	2.3%
C	15	19.5%	11	12.8%
D	20	26.0%	15	17.4%
E	8	10.4%	9	10.5%
F	0	0.0%	1	1.2%
Total	**77**		**86**	

Figure 3: Genotypes of acute samples sent to VRD by PHE region

Discussion

In 2018, reporting of acute cases of hepatitis B from PHE Centres has continued to exceed the number reported from laboratories but the proportion of cases reported by both PHE Centres and laboratory systems is high at 64.0% (244/381), compared to 63.6% (283/445), of cases reported in 2017. Prior to 2018, there had been a slight decrease in overlap which may have been due to the introduction of a new database to process the SGSS laboratory reporting system data.

There was nonetheless an overall improved matching over the years that could be explained given the introduction of statutory laboratory reporting in October 2010 and the continued decline in the proportion of cases of unknown status reported from laboratories. Combining data from both sources does minimise under ascertainment and improves the completeness of associated data for analysis. Interpretation of trends should be made with caution, but based on this combined data, the incidence of acute hepatitis B remains low. Given the improved quality and completeness of data provided in 2017/2018, it is likely that there has been a continued gradual decline in incidence since 2008 which has become more apparent in the more recent years.

It is known that anti-HBc IgM, normally a marker of acute infection, may be detected during flares in chronic infections. To minimise misclassification, matching to historical laboratory reports can identify those chronic infections detected previously. However, there is still likely to be some misclassification of chronic cases as acute infections in both datasets. Given the large number of chronic cases diagnosed each year, even a small proportion of cases misclassified as acute can substantially increase the estimated incidence of acute hepatitis B, and confuse the attribution of exposures. Further testing using anti-HBc avidity is now being offered at PHE Colindale to enable better distinction between acute and chronic infection. Local laboratories can send samples from IgM positive cases to the Virus Reference Department at Colindale where both genotyping and avidity testing will be undertaken free of charge [6].

Risk factor data were available in 28.9% of cases. In addition to the poor completeness of risk factor information, the interpretation of these data is difficult because in many instances, more than one possible exposure is listed and a probable exposure had not been assigned by the local HPT. Despite this, the data suggests that the number of cases in PWID has remained low in 2018. The overall low incidence in this group is supported by the 2018

Unlinked Anonymous Monitoring Survey of people who Inject Drugs in contact with drug services which showed that anti-HBc prevalence and HBsAg prevalence among anti-HBc positives has remained low since 2009 [7]. However, while self-reported uptake of at least one dose of hepatitis B vaccine plateaued at around 72% between 2008 and 2018, in 2018, there has been a considerable drop in vaccine uptake in the under-35 year olds (most notable in under 25 year olds) and among recent initiates. This decline in vaccine uptake in a high risk population is of concern, particularly if associated with disinvestment in drug service delivery [8].

Improved reporting of risk factors associated with HBV acquisition will enable a more comprehensive interpretation of surveillance trends and appropriate response to clusters. HPTs should ensure that risk factor information determining most probable acquisition route is documented to enable effective surveillance.

The incidence of acute hepatitis B continues to remain higher in males than females. This excess of male cases is partly explained by cases in men who have sex with men (MSM); the number of cases with this exposure reported has remained high again this year, following a large increase in 2010. Such cases are more likely to attend GUM clinics, reinforcing the important role of GUM clinics in providing opportunistic hepatitis B immunisation to MSM and individuals with multiple sexual partners. The joint PHE and British Association of Sexual Health and HIV (BASHH) standard form for GUM clinics to report acute hepatitis to their local health protection team continues to improve the reporting of cases diagnosed in this setting [9].

In addition, following recent clusters of acute hepatitis B in men who did not disclose MSM activity initially [10], an enhanced surveillance questionnaire for acute hepatitis B cases was developed in 2016 to support HPTs in obtaining detailed risk factor information on cases with undisclosed risk factors, particularly during outbreaks, to inform and target control measures. More complete risk factor information and full hepatitis B virus serological markers will assist with the interpretation of surveillance data.

The supplementary data from enhanced molecular surveillance using matched HPZone and reference laboratory confirmatory and typing data, will allow real-time monitoring of acute hepatitis B transmission, when provided quarterly with a regional breakdown. Publication of molecular analyses provides insight into the current hepatitis B genotypes circulating in

England, although interpretation is limited by the small proportion of samples submitted to VRD. The A2 “prisoner variant” is the most common strain and is known to be well-established in the UK MSM population; other genotypes can indicate a geographical origin which can help provide an understanding of sources of infection and transmission routes, e.g. genotype D is associated with South Asia.

Timely assignment of cases to the HPZone Context and improved submission of samples for molecular characterisation will allow for more comprehensive monitoring of acute hepatitis B infection in England.

References

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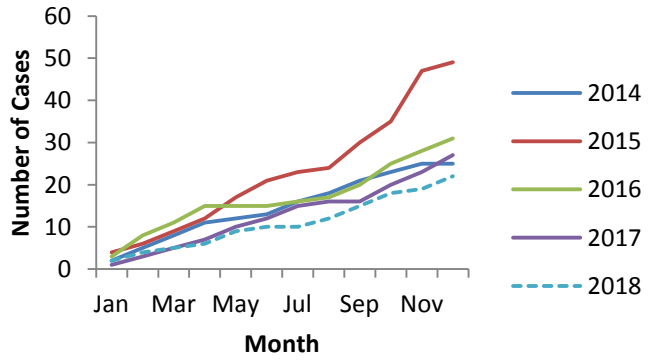
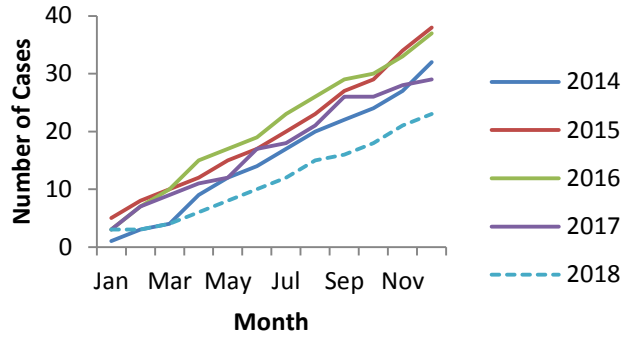
Appendix 1: Cumulative cases of acute Hepatitis B in regions in England entered on HPZone Dashboard 2014 – 2018

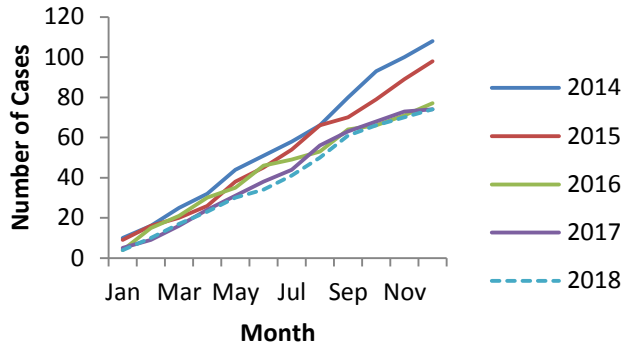
East Midlands



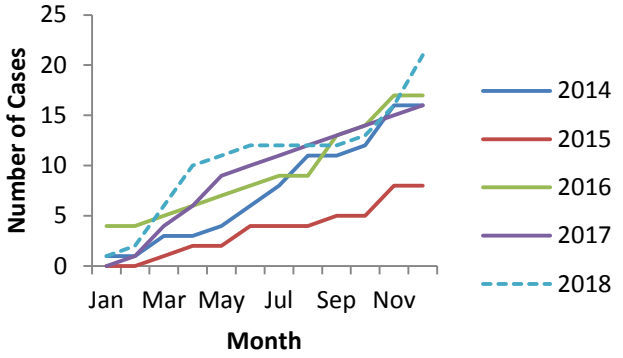
East of England



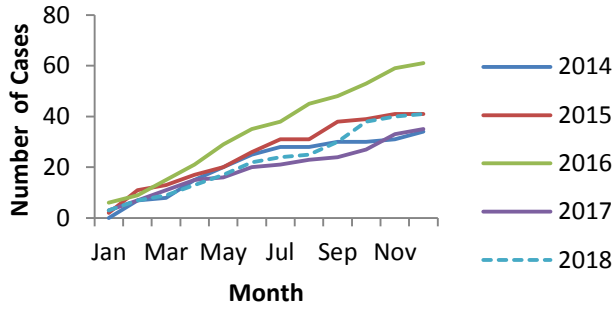
London



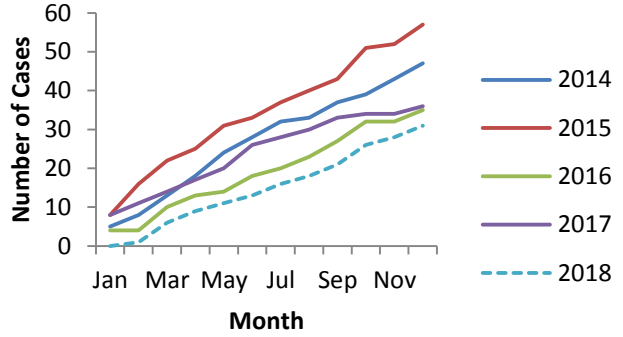
North East



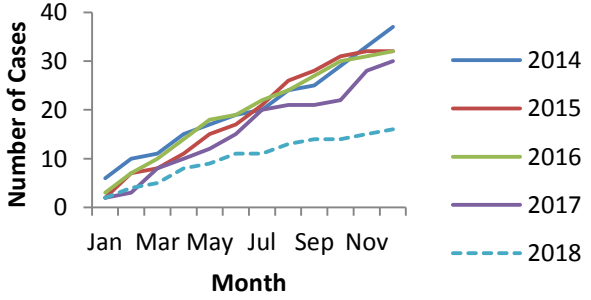
North West



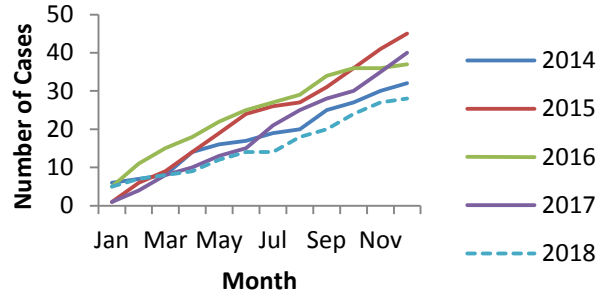
South East



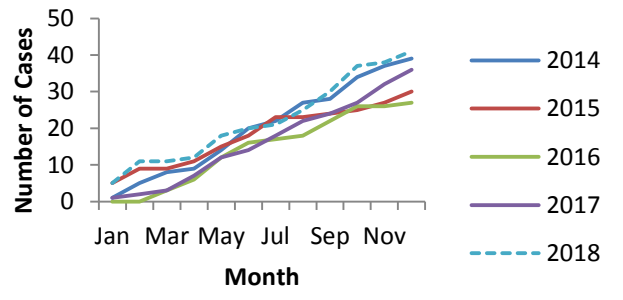
South West



West Midlands



Yorkshire and Humber



About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-class science, research, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health, and are a distinct delivery organisation with operational autonomy to advise and support government, local authorities and the NHS in a professionally independent manner.

About *Health Protection Report*

Health Protection Report is a national public health bulletin for England and Wales, published by Public Health England. It is PHE's principal channel for the dissemination of laboratory data relating to pathogens and infections/communicable diseases of public health significance and of reports on outbreaks, incidents and ongoing investigations.

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