



Public Health
England

Protecting and improving the nation's health

Laboratory reports of hepatitis A infections in England and Wales, 2018

Health Protection Report
Volume 13 Number 28
9 August 2019

Laboratory reports of hepatitis A infections: 2018

There were a total of 452 laboratory reports of new patients who tested positive for hepatitis A virus (HAV) in England and Wales in 2018, excluding the known false positive reports (Table 1). Laboratory reports were received via the Second Generation Surveillance System (SGSS) which is a voluntary electronic reporting system rolled out in 2014 to replace the existing CoSurv system. False positives were defined as 'patients' with a) samples that were received by the Virus Reference Department (VRD) where recent HAV infection was not confirmed by serology or where HAV RNA was not detected, b) samples for which the reporting laboratory notified the VRD of false positive results or reporting issues, for example through returning the letters received as part of the HAV enhanced surveillance system or c) samples which the VRD identified as laboratory quality controls. A total of 194 false positive reports were identified, including 187 where samples were sent to the VRD and recent infection was not confirmed.

The greatest number of reports were among those in the 25 to 34 year age group (87, 19.2%) closely followed by those in the 15-24 year age group (80, 17.7%) and those aged 65 years and over (64, 14.2%). One report of HAV in the under 1 year age group was received. More reports were received for males than females during every quarter of 2018 (Table 1).

Table 1: Laboratory reports of hepatitis A by age, sex, and quarter, England and Wales, 2018*

Age group (years)	Q1			Q2			Q3			Q4			Total
	Jan-Mar			Apr-Jun			Jul-Sep			Oct-Dec			
	Female	Male	NK	Female	Male	NK	Female	Male	NK	Female	Male	NK	
<1	0	0	0	0	0	1	0	0	0	0	0	0	1
1 to 4	1	2	0	0	2	0	4	4	0	2	5	0	20
5 to 9	8	7	0	9	6	0	6	6	0	5	10	0	57
10 to 14	5	4	0	6	2	0	6	6	0	5	3	0	37
15 to 24	15	10	0	5	7	0	11	17	0	8	7	0	80
25 to 34	15	17	0	10	17	0	10	7	0	7	4	0	87
35 to 44	4	7	0	3	5	0	5	7	0	1	4	0	36
45 to 54	3	2	0	3	9	0	2	7	0	0	6	0	32
55 to 64	5	5	0	8	7	0	3	2	0	1	4	0	35
≥65	6	10	0	11	11	0	9	4	0	11	2	0	64
NK	0	0	0	0	0	3	0	0	0	0	0	0	3
Total	62	64	0	55	66	4	56	60	0	40	45	0	452**

* Due to late reporting, numbers for each quarter may have changed slightly since their HPR quarterly reports. Reports from Wales for Q3 and Q4 have not yet been received due to reporting issues.

** Provisional numbers.

The number of laboratory reports by PHE Centre is presented below (Table 2). Reports were assigned to a PHE Centre according to either i) the patient's place of residence ii) the postcode of the patient's registered GP practice, or the iii) the postcode of the source laboratory. In 2018, the greatest number of hepatitis A reports were from the London region (150, 33.2%) followed by the South East, West Midlands and East of England with a similar number of reports (54-49, 11.9%-10.8%) (Table 2). The large number of reports from London compared to other regions is consistent with previous years. Due to reporting issues, laboratory reports from Wales for the latter half of 2018 have not yet been received.

Table 2: Laboratory reports of hepatitis A by PHE Centre (England) and Wales (2008-2018)

PHE Centre	Year										
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
East Midlands	19	14	9	6	7	8	10	11	30	29	22
East of England	34	38	36	24	25	23	15	24	47	86	49
London	54	53	72	69	71	91	118	79	180	414	150
North East	5	8	12	10	13	10	9	11	17	25	7
North West	48	64	56	24	28	34	22	43	22	50	41
South East	66	50	28	44	38	29	55	27	51	91	54
South West	30	24	48	11	18	29	14	15	22	71	34
West Midlands	67	59	61	41	44	29	32	47	46	99	50
Yorkshire and Humber	27	34	40	23	36	19	17	69	24	34	26
Wales*	10	12	9	5	8	11	8	4	5	43	19
Total	360	356	371	257	288	283	300	330	444	942	452

* Non-PHE Centre. Reports from Q3 and Q4 2018 currently outstanding

Overall, there was a 52% decrease in the number of reports in 2018 (n=452) compared to 2017 (n=942). The number of reports was lower in every quarter compared to the corresponding quarter in 2017, with the decrease ranging between 46-58%. The number of reports in 2018 followed a broadly decreasing trend, with the greatest number of reports in quarter 1 (126, 27.9%) and the smallest number in quarter 4 (85, 18.8%) (Table 1).

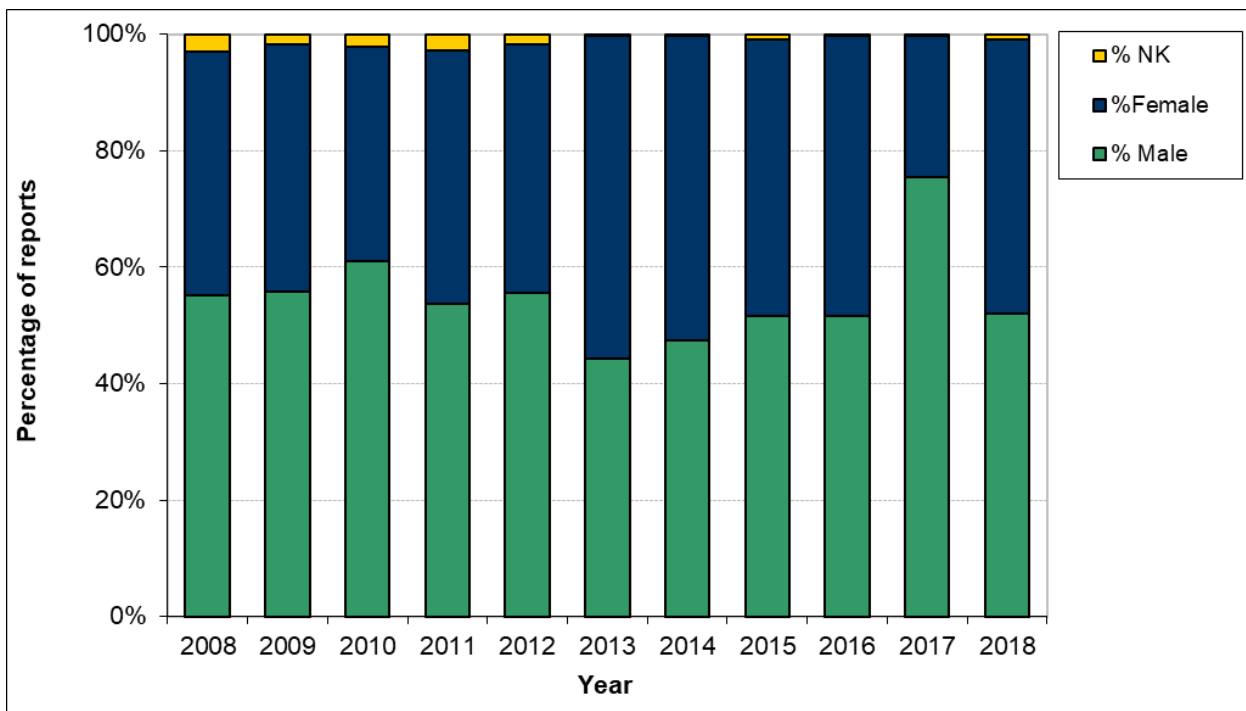
The trend observed in 2018 is consistent with the tail end of the national HAV outbreak largely associated with men who have sex with men (MSM) that began in 2016 [1].

Between July 2016 and December 2017, outbreak clusters of HAV were being investigated nationally by PHE and a PHE standard incident response was declared in December 2016. As the outbreak progressed the standard incident response was escalated to an enhanced incident response in April 2017. The outbreak cases were initially reported from geographically distinct clusters. However, as the outbreak progressed MSM were identified nationally as the main risk group and a recent travel history to Spain was also noted in some cases [2]. The enhanced surveillance of hepatitis A programme had confirmed these outbreak cases to be of genotype IA with identical RNA sequences. These three distinct outbreak strains reported as Event 1, 2 and 3 by the European Centre for Diseases Prevention and Control (ECDC) were investigated in a number of European countries including the United Kingdom [3]. The incident response was de-escalated to a standard incident in January 2018 and was declared over in June 2018. A total of 763 confirmed or probable cases associated with the outbreak strains were identified between July 2016 and January 2018, of which 92% were male [1]. A number of incidents of the outbreak spilling over into the community were also identified [1].

The annual number of HAV reports decreased from 2005 to 2013, followed by a slight increase from 2013 to 2015, and larger increases in 2016 and 2017 coinciding with the start and peak of the national outbreak. The reduction in the number of reports in 2018 coincides with the end of the national 2016-18 MSM outbreak.

Age and sex reported through the laboratory reporting systems have been well completed every year over the past decade (>97% complete) (Figure 1), including in 2018 (99.1% complete). Where known, males accounted for a slim majority of reports (52.5%, 235/448) during 2018, returning the proportion of males to the level seen before the 2016-18 MSM outbreak (Figure 1).

Figure 1: Percentages of hepatitis A laboratory reports by sex, England and Wales* (2008-2018)

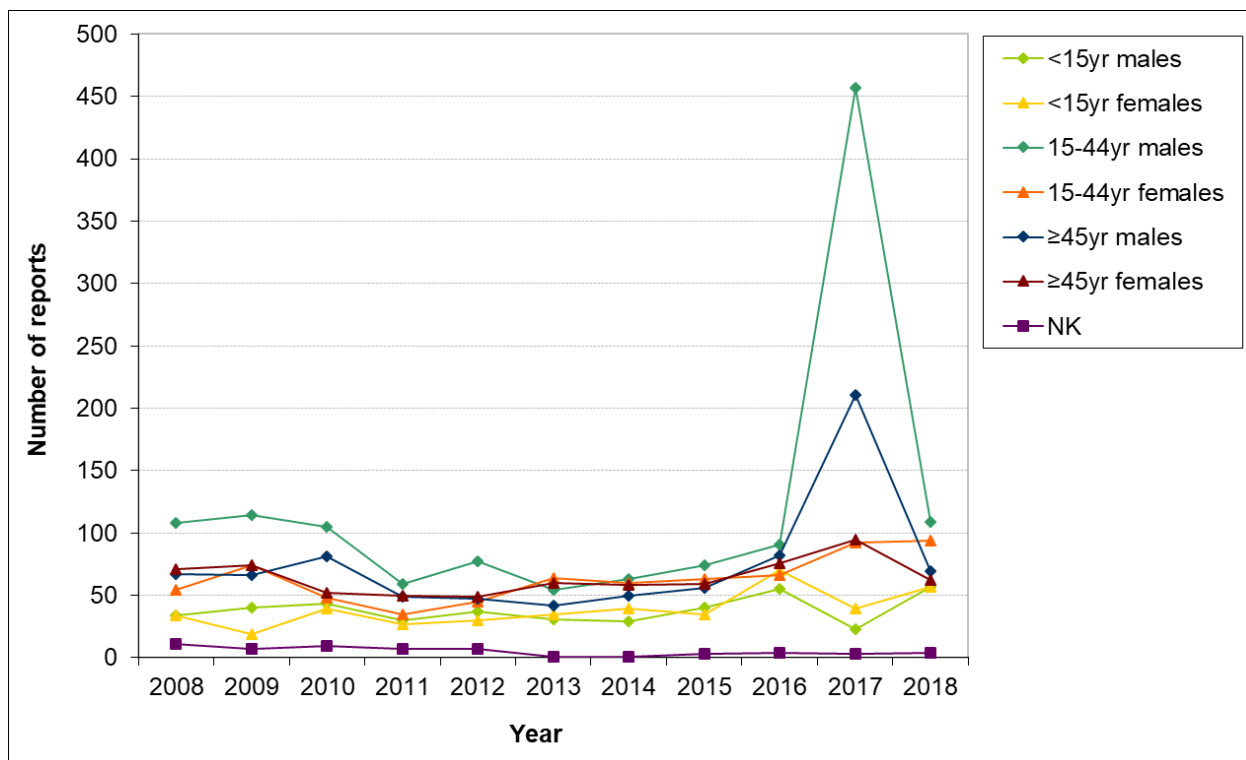


* Reports from Wales Q3 and Q4 2018 currently outstanding

In 2018, the number of reports in males aged 15 years and over and females aged 45 years and over decreased compared to 2017, whilst the number of reports in males and females under 15 years of age and females aged 15-44 years saw an increase (Figure 2). The largest decrease was seen for 15-44 year-old males where 109 reports were received compared to 457 in 2017 (difference=348, 76.1% decrease), followed by males aged 45 years and over, where 69 reports were received compared to 211 in 2017 (difference=142, 67.3% decrease) (Figure 2). This is consistent with the end of the 2016-18 MSM outbreak which was largely confined to males.

During 2018, females accounted for 49.6% of reports in the under 15 year old age group, males accounted for 53.7% of reports in the 15 to 44 age group, and 52.7% of reports among the 45 years and over age group. In comparison, in 2017 females accounted for 65.0% of reports in the under 15 years age group, males accounted for 80.6% of reports in the 15 to 44 age group, and 68.8% of reports among the 45 years and over age group.

Figure 2: Laboratory reports of hepatitis A by age and sex, England and Wales* (2008-2018)



* Reports from Wales Q3 and Q4 2018 currently outstanding

Risk factor information was poorly reported through the laboratory reporting system. Travel history was available for 14.6% (66/452) of reported cases; compared to an average of 17.4% (range 14.6%-22.7%) from 2008-2018 (Table 3). Of these, only 4.5% (3/66) were reported to have travelled abroad. Risk factor information reported through the laboratory reporting system including travel history remains rare, which limits the conclusions that can be drawn from these data.

Table 3: Trends in hepatitis A laboratory reports, England and Wales* (2008-2018)

Year	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Number of reports	360	356	371	257	288	283	300	330	444	942	452
Number (%) aged 15-44 years	167 (46.4%)	190 (53.4%)	157 (42.3%)	96 (37.4%)	122 (42.4%)	118 (41.7%)	123 (41.0%)	138 (41.8%)	157 (35.4%)	572 (60.7%)	203 (44.9%)
Number (%) male	209 (58.1%)	220 (61.8%)	230 (62.0%)	138 (53.7%)	162 (56.3%)	127 (44.9%)	142 (47.3%)	170 (51.5%)	229 (51.6%)	711 (75.5%)	235 (52.0%)
Number (%) with travel history	60 (16.7%)	64 (18.0%)	66 (17.8%)	43 (16.7%)	62 (21.5%)	43 (15.2%)	50 (16.7%)	61 (18.5%)	101 (22.7%)	147 (15.6%)	66 (14.6%)
Number (%) travelled abroad	18 (5.0%)	13 (3.7%)	29 (7.8%)	7 (2.7%)	20 (6.9%)	10 (3.5%)	4 (1.3%)	11 (3.3%)	11 (2.5%)	3 (0.3%)	3 (0.7%)

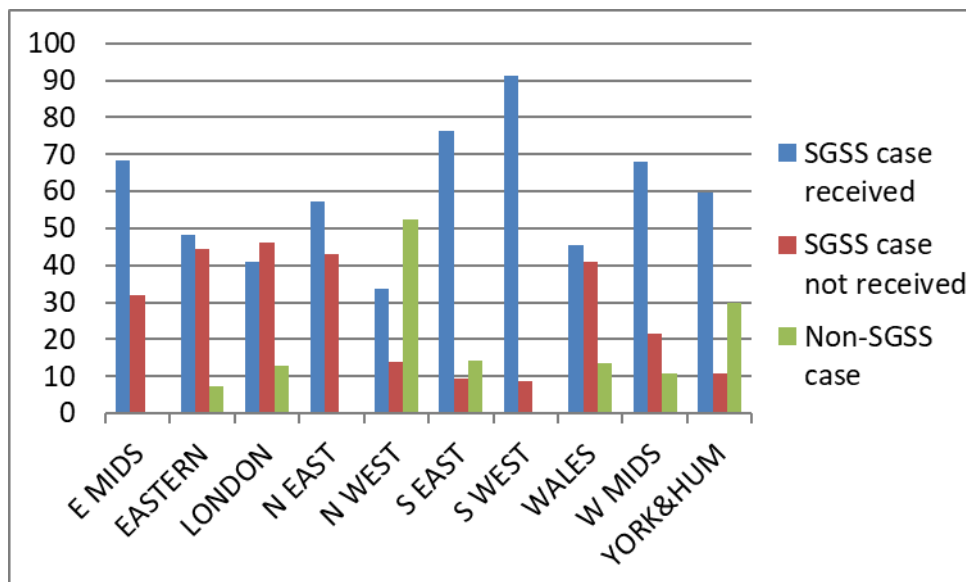
* Reports from Wales Q3 and Q4 2018 currently outstanding

Reference laboratory confirmation and phylogeny of hepatitis A infection: 2018

Of the 452 laboratory reports of acute HAV infection during 2018, 293 (64.8%) confirmed acute cases had samples forwarded to the Virus Reference Department (VRD) for genotyping. Of the 159 (35.2%) cases who did not have a sample forwarded to VRD for HAV confirmation, two cases had no sample remaining, eight cases had samples forwarded for HEV testing and one case had a sample forwarded for HDV testing.

In addition, 100 cases were confirmed to have acute HAV infection that had not been reported through the laboratory reporting system, however, all English cases were all recorded in HPZone. The breakdown of samples received per region can be seen in Figure 1.

Figure 1: Percentage of SGSS-reported and non-SGSS-reported cases received for confirmation by region



Twenty eight saw the continuation of the nationwide outbreak which was originally seen in men who have sex with men (MSM) and for the purposes of this review these cases have been separated out.

Non-outbreak cases

Of the 299 non-outbreak cases, 190 (63.6%) reported a travel history, 99 (33.1%) had no travel history and 10 (3.3%) had no information. For the majority of regions travel cases predominated (Figure 2).

The age of the cases ranged from 1 to 91 years of age with travel being the main risk between the ages of 1 and 44 (Figure 3). There has been an increase in cases confirmed in all age groups compared to 2017; age groups 5-9, 10-14, 15-24, 25-34 and 55-64 have seen their highest number of cases since the start of the enhanced surveillance (Figure 4).

Figure 2: Confirmed HAV infections by region and travel history

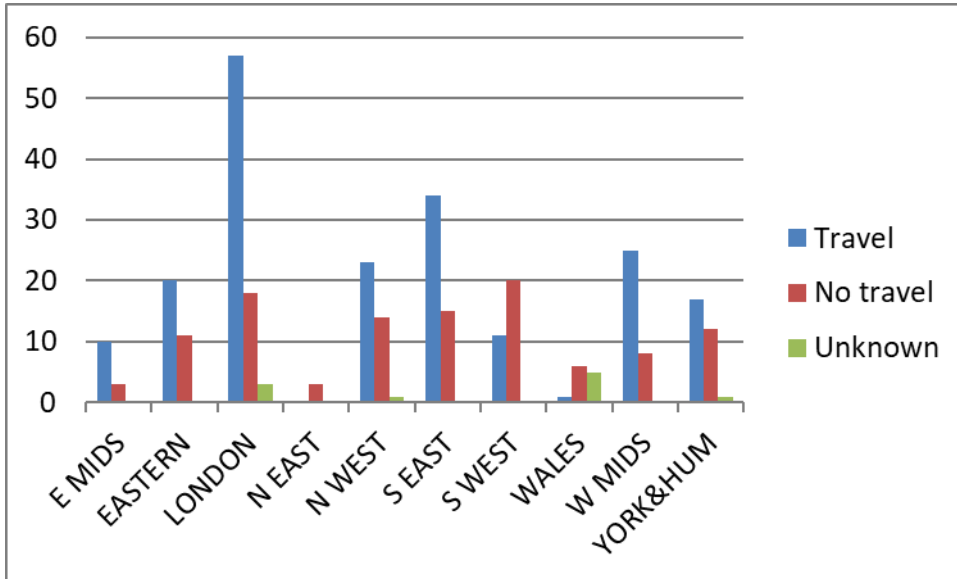


Figure 3: Confirmed HAV infections by age and travel history

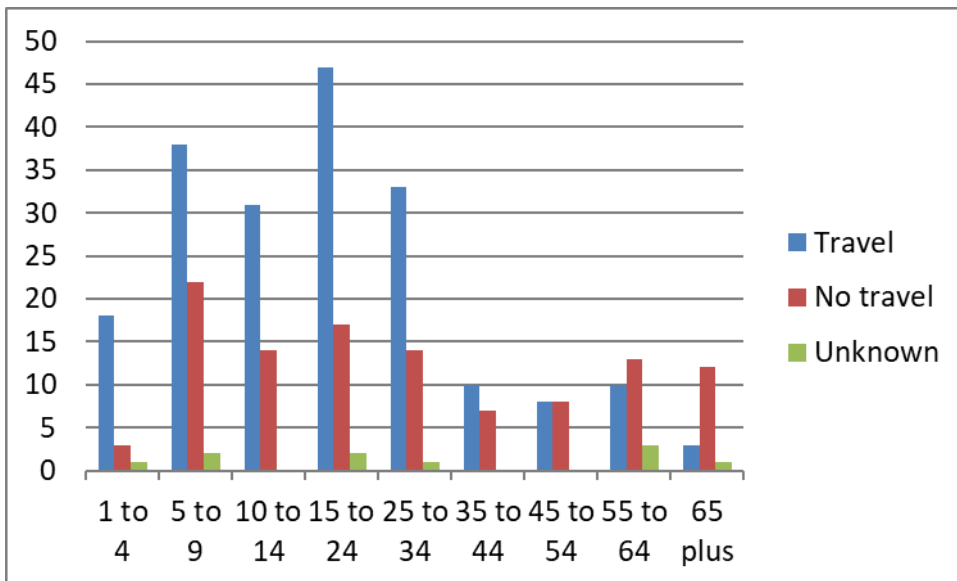
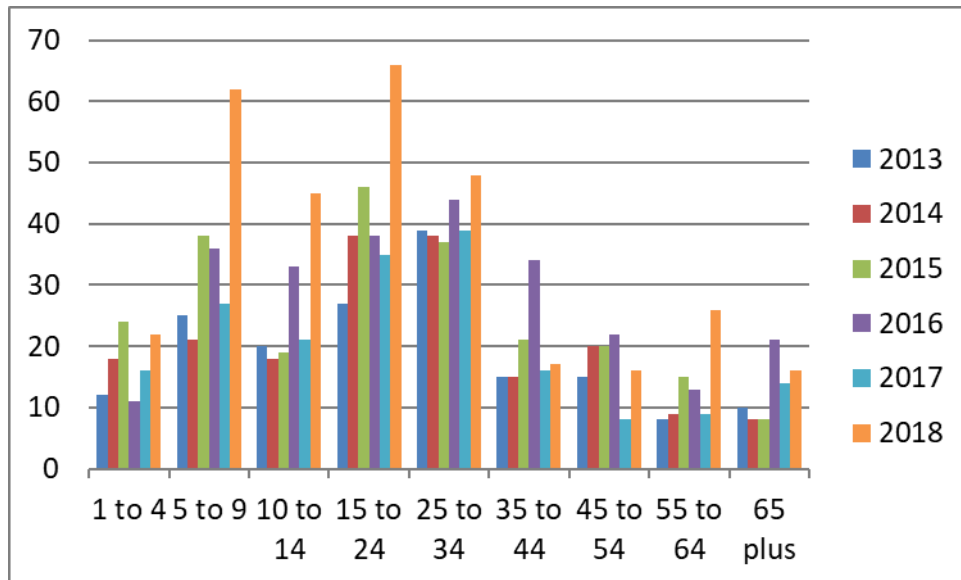


Figure 4: Comparison of confirmed HAV infections by age 2013 - 2018



Outbreak cases

The outbreak was associated with three distinct sequences: VRD_521_2016 (Event 1 – strain 1), RIVM-HAV16-090 (Event 2 – strain 2) and V16-25801 (Event 3 – strain 3). During 2018, the numbers of cases with outbreak strains continued to decline (Figure 5) and in July 2018 the outbreak was declared over with the majority of cases being seen in the North West (Figure 6) and the most affected age group remained the 25 to 34 year olds (Figure 7).

Figure 5: Chronology of Events 1, 2 & 3 during 2018

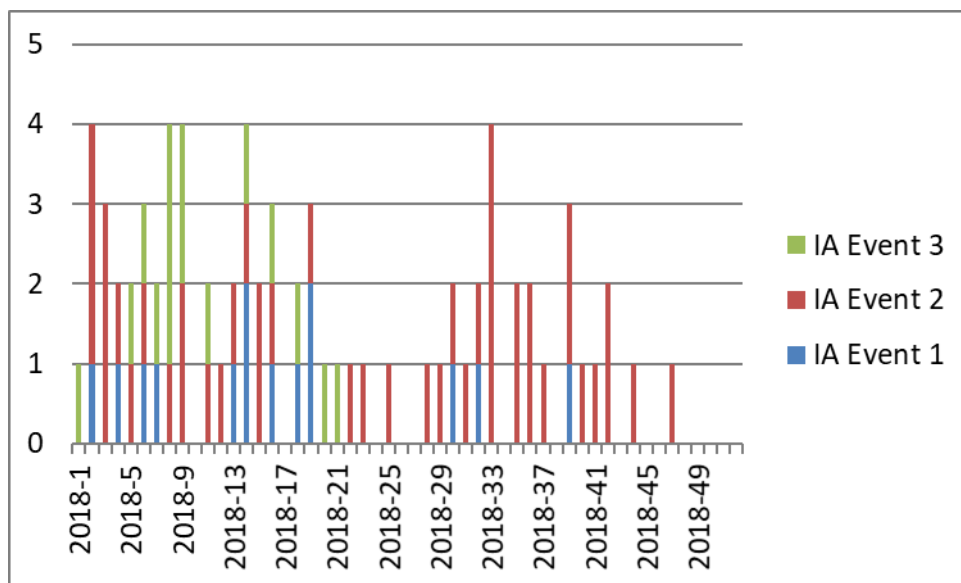


Figure 6: Regional breakdown of cases with Events 1, 2 and 3.

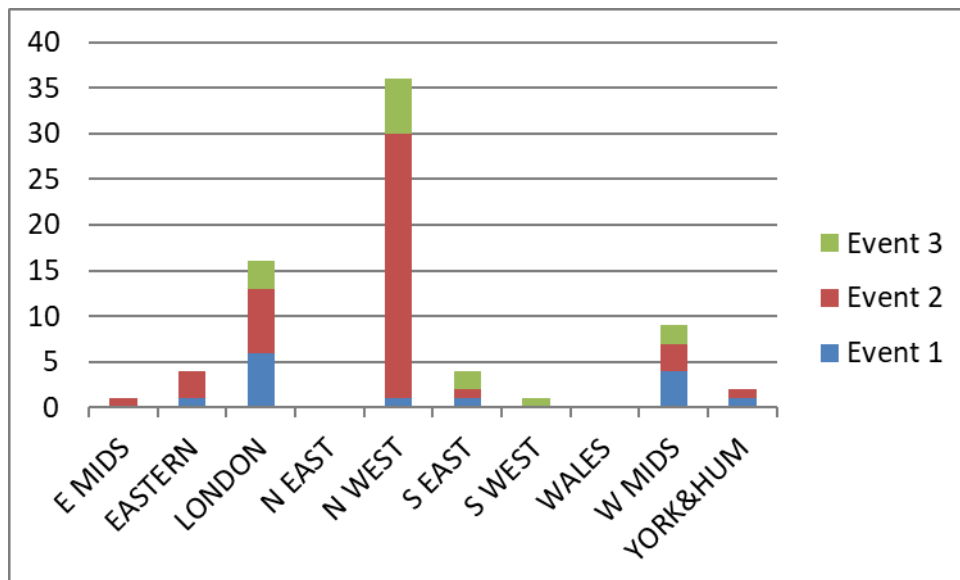
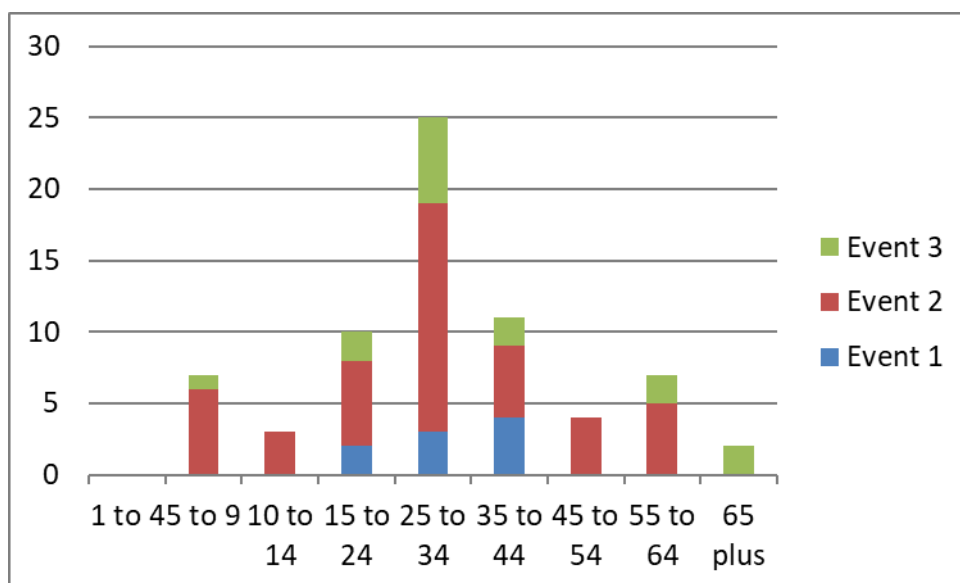


Figure 7: Age distribution of cases with Events 1, 2 and 3.

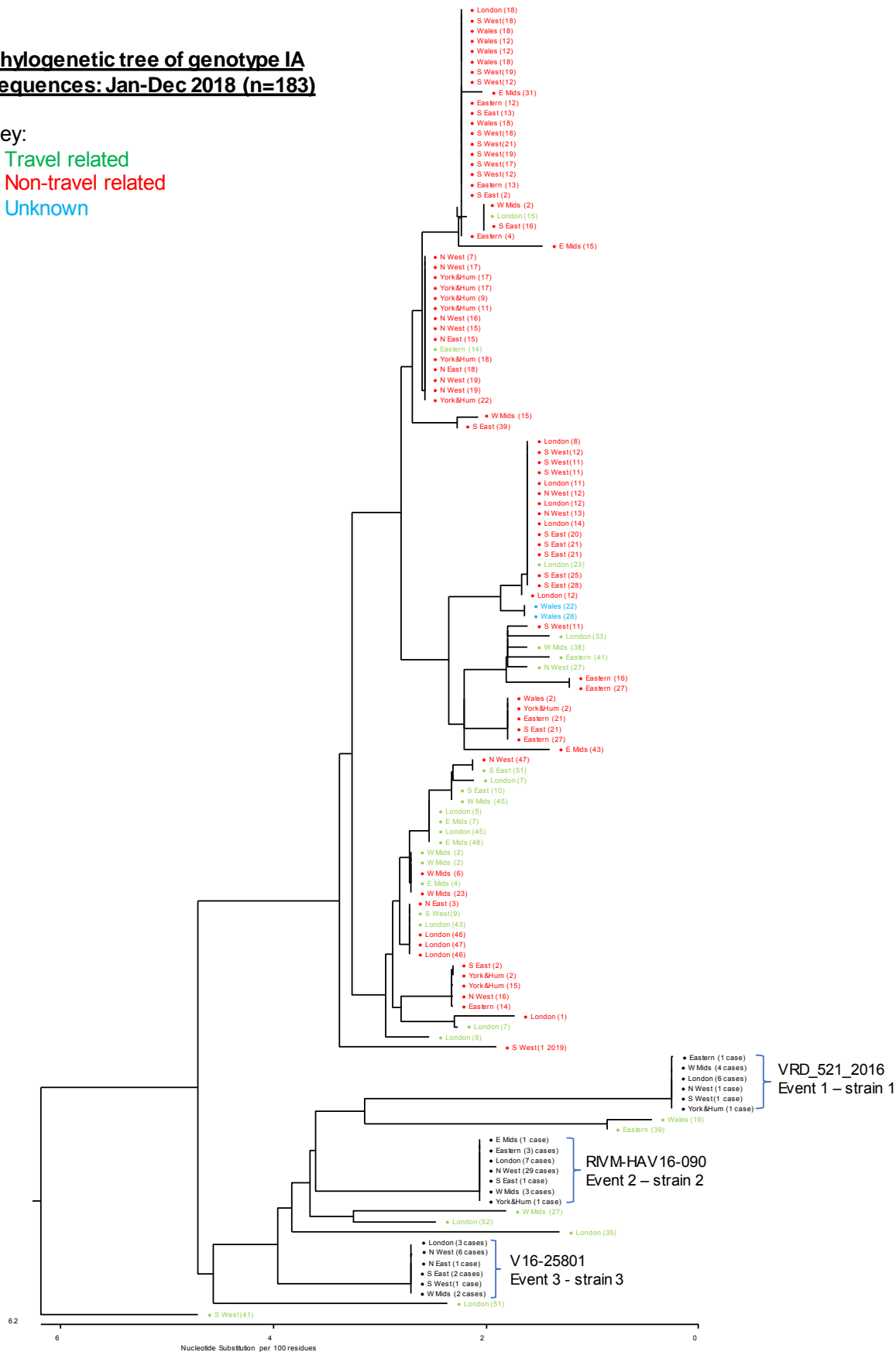


It was possible to genotype 386 confirmed cases (286 SGSS-reported cases and 100 non-SGSS cases); 183 (47.4%) were genotype IA, 101 (26.2%) were genotype IB, one (0.2%) were genotype IIA and 101 (26.2%) were genotype IIIA. This sequence information for each genotype is presented as phylogenetic trees with each sequence represented by a dot with the patient region and the week of sampling in brackets with the exception of sequences VRD_521_2016 (Event 1 – strain 1), RIVM-HAV16-090 (Event 2 – strain 2) and V16-25801 (Event 3 – strain 3) which have been represented in the tree by region and the number of cases observed due the large numbers of cases. No phylogenetic tree has been compiled for genotype IIA only one case being seen in 2018 which was associated with travel to Libya.

Phylogenetic tree of genotype IA sequences: Jan-Dec 2018 (n=183)

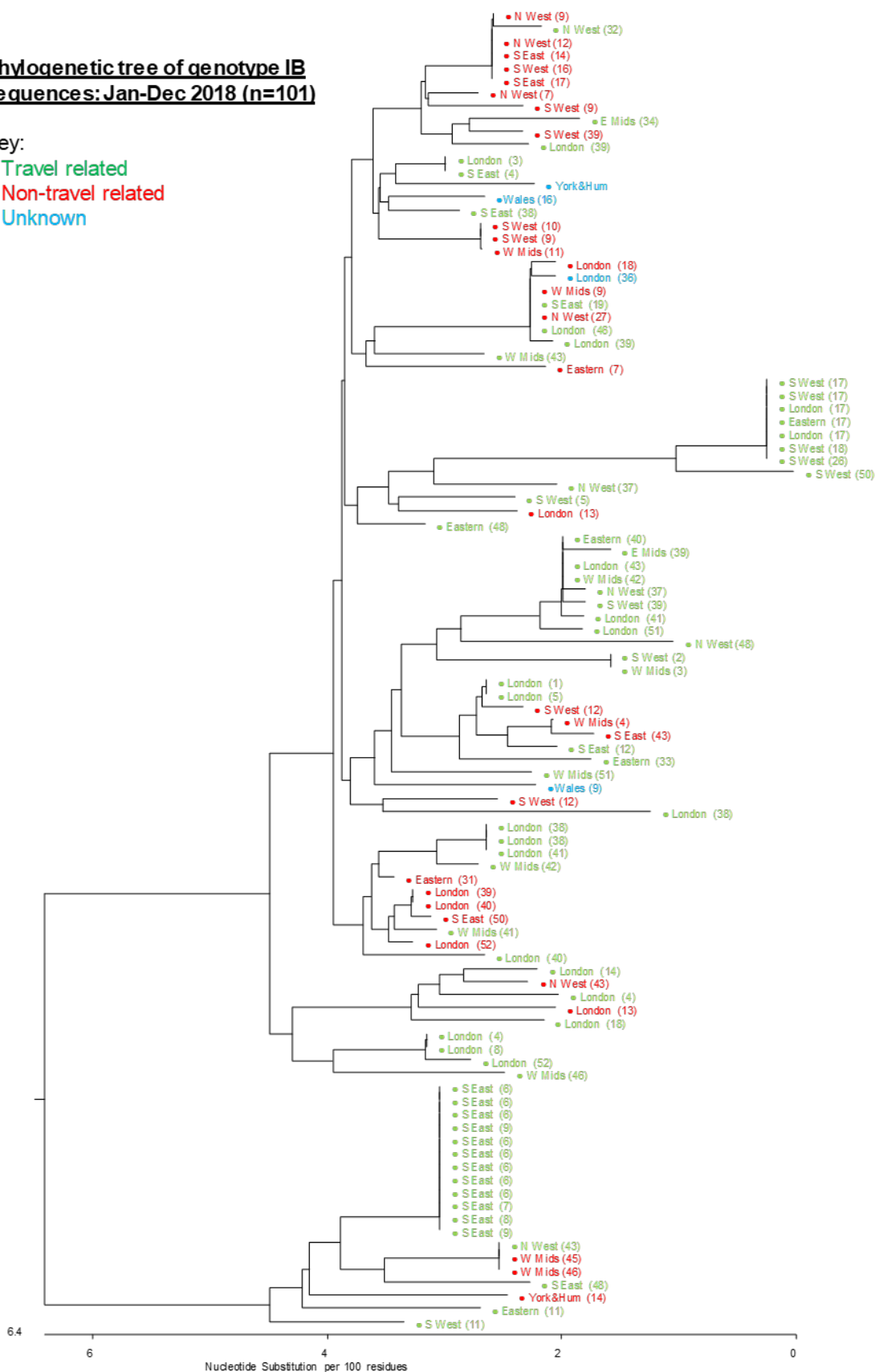
Key:

- Travel related
- Non-travel related
- Unknown



Phylogenetic tree of genotype IB sequences: Jan-Dec 2018 (n=101)

Key:
 ● Travel related
 ● Non-travel related
 ● Unknown

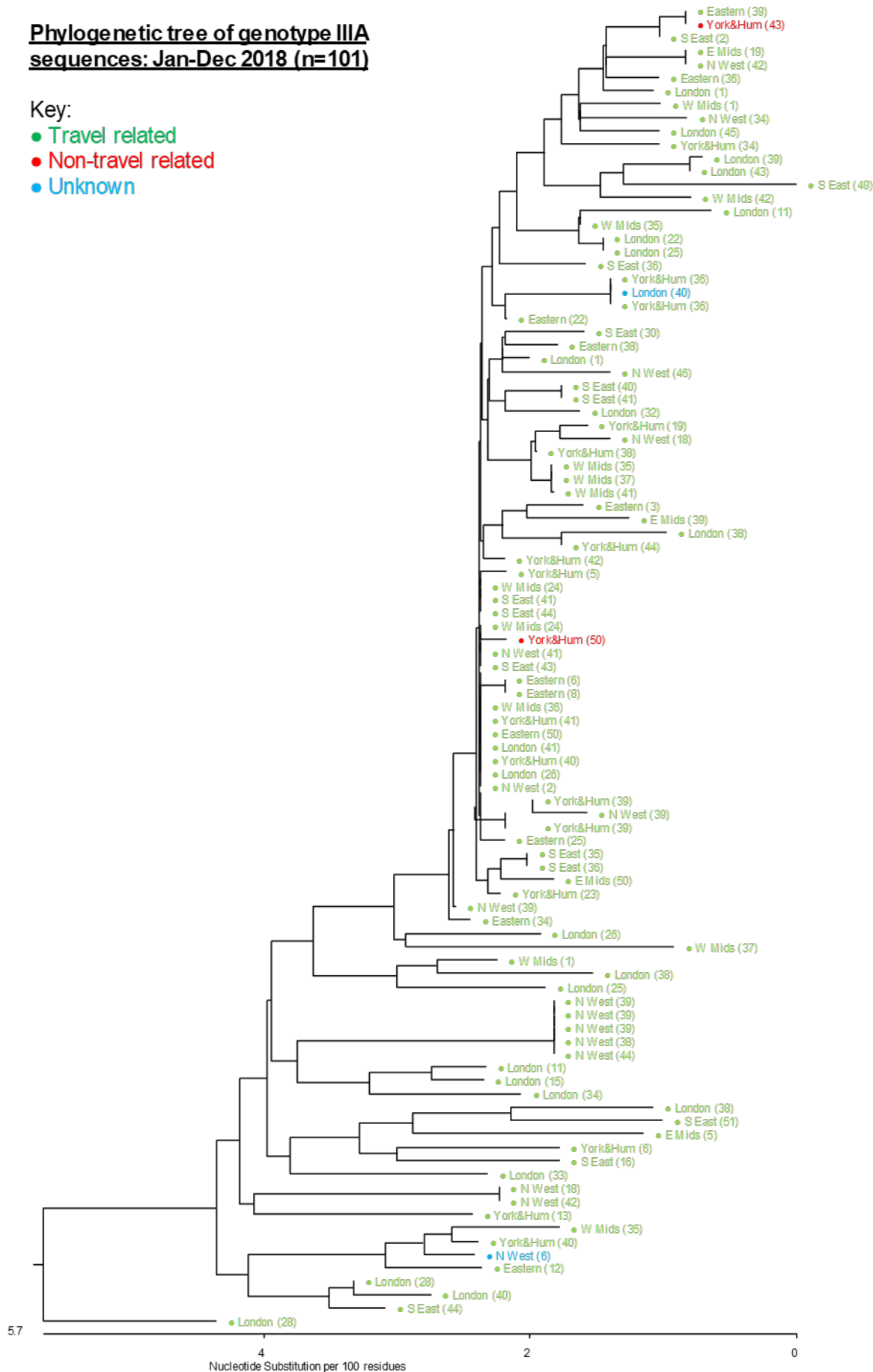


For genotype IB the majority of cases were travel related 67/101 (66.3%), the most common area of travel being Africa.

Phylogenetic tree of genotype IIIA sequences: Jan-Dec 2018 (n=101)

Key:

- Travel related
- Non-travel related
- Unknown



Seventy four cases with genotype IA were associated with three distinct outbreak strains VRD_521_2016 (Event 1 – strain 1), RIVM-HAV16-090 (Event 2 – strain 2) and V16-25801 (Event 3 – strain 3) and while the MSM population were still affected [1,2,3,4] most of the cases were imported from Europe or were in the general population suggesting limited spread into the community. Outside of the outbreak the majority of cases with genotype IA had no travel history 75/109 (68.8%) and were largely associated with Moroccan like strains [5].

As in previous years the majority of cases with genotype IIIA had a travel history (95/101, 94%) with Pakistan being the most commonly visited country (67 cases). Genotype IIIA is geographically associated with South Asia and travellers may not perceive themselves or their family to be at risk if they grew up in an endemic area and are travelling “home” to visit friends and relatives [6].

Summary

In 2018, nearly 65% of samples associated with laboratory reports of acute HAV infection were forwarded to VRD for genotyping. In addition, significant numbers of cases genotyped within VRD have not been reported through the laboratory reporting system –SGSS (100 cases) although the majority were notified to their local Health Protection Teams.

Typing of hepatitis A virus remains an invaluable tool in tracking community outbreaks and our increased understanding of the molecular epidemiology of the virus has enabled us to pin-point the likely country of origin of some outbreaks even when a source cannot be identified. Phylogenetic analysis has been invaluable in identifying the monitoring of the national outbreak of hepatitis A amongst MSM that was first identified in 2016. Identification of such community and national outbreaks is only possible by the continued submission of samples by laboratories from both travel associated and non-travel associated cases.

References

1. Plunkett J, Mandal S, Balogun K, Beebeejaun K, Ngui SL, Ramsay M, Edelstein M (2019). Hepatitis A outbreak among men who have sex with men (MSM) in England, 2016–2018: The contribution of past and current vaccination policy and practice. *Vaccine: X* 1: 100014.
2. Beebeejaun K, Degala S, Balogun K, Simms I, Woodhall SC, Heinsbroek E, et al (2017). Outbreak of hepatitis A associated with men who have sex with men (MSM), England, July 2016 to January 2017. *Euro Surveill.* 22(5), (2 Feb).
3. Werber D, Michaelis K, Hausner M, Sissolak D, Wenzel J, Bitzegeio J, Belting A, et al (2017). Ongoing outbreaks of hepatitis A among men who have sex with men (MSM), Berlin, November 2016 to January 2017 - linked to other German cities and European countries. *Euro Surveill.* 22(5), (2 Feb).
4. Freidl GS, Sonder GJ, Bovée LP, Friesema IH, van Rijckevorsel GG, Ruijs WL, et al (2017). Hepatitis A outbreak among men who have sex with men (MSM) predominantly linked with the EuroPride, the Netherlands, July 2016 to February 2017. *Euro Surveill.* 22(8), (23 Feb).
5. Gassowski M, Michaelis K, Wenzel JJ, Faber M, Figoni J, Mouna L, et al (2018). Two concurrent outbreaks of hepatitis A highlight the risk of infection for non-immune travellers to Morocco, January to June 2018. *Euro Surveill.* 23(27), (July).
6. Health Protection Agency (HPA). [Foreign travel-associated illness – a focus on those visiting friends and relatives: 2008 report.](#)

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 Social Care, 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.

Public Health England, Wellington House, 133-155 Waterloo Road, London SE1 8UG

Tel: 020 7654 8000 www.gov.uk/phe

Twitter: [@PHE_uk](https://twitter.com/PHE_uk) Facebook: www.facebook.com/PublicHealthEngland

Queries relating to this document should be directed to: the Immunisation, Hepatitis and Blood Safety Department, National Infection Service, 61 Colindale Avenue, London NW9 5EQ.

immunisation@phe.gov.uk



© Crown copyright 2019

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit [OGL](https://www.ogilive.gov.uk). Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

Published: **August 2019**

PHE publications

gateway number: **2019037**

PHE supports the UN

Sustainable Development Goals

