Public Health England

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Laboratory reports of hepatitis A infections in England and Wales, 2016

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Laboratory reports of hepatitis A infections: 2016

During 2016, there were 444 confirmed laboratory reports of hepatitis A virus (HAV) infection in England and Wales (Table 1). The greatest number of reports were among the 65 and over age group (n=79), followed by the 25 -34 age group (78); only one case of hepatitis A was reported in the under 1 year age group. More reports were received for females than males during the first and second quarter of 2016, with more reports among males during the remaining quarters (Table 1).

Table 1: Laboratory reports of hepatitis A by age, sex, and quarter, England and Wales, 2016*

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	1	0	0	0	0	0	0	0	1
1 to 4	2		0		4	0	4	3	0		4	0	17
5 to 9	2	2	0	2	1	0	5	4	0	6	6	0	28
10 to 14	3	3	0	3	3	0	2	7	0	3	4	0	28
15 to 24	11	3	0	1	3	0	5	13	0	3	12	0	51
25 to 34	14	6	0	13	11	0	6	12	0	2	14	0	78
35 to 44	9	12	0	8	9	0	8	8	0	4	13	0	71
45 to 54	9	9	0	11	7	0	3	2	0	6	5	0	52
55 to 64	3	5	0	4	2	0	1	2	0	10	8	0	35
≥65		7	0	18	10	0	10	2	0	9	11	0	79
NK	0	0	0	0	0	0	2	1	0	0	0	1	4
Total	**65**	**47**	**0**	**60**	**51**	**0**	**46**	**54**	**0**	**43**	**77**	**1**	444

* Due to late reporting, numbers for each quarter may have changed slightly since their HPR quarterly reports.

The number of laboratory reports by PHE Centre is presented below. Reports were assigned to a PHE Centre according to i) the patient's place of residence ii) the postcode of the patient's registered GP practice, iii) the postcode of the source laboratory. In 2016, the greatest number of hepatitis A reports were from the London (n=180) and South East (=51) regions (Table 2). The comparatively high number of reports from London was consistent with previous years.

Overall, there was 26% increase in the number of reports received during 2016 (n=444) compared to 2015 (n=330). The overall trend has been a decline in the number of reports since 2006. The increased number of reports during 2010 was due to unrelated outbreaks of hepatitis A in the London and the South West regions. A number of clusters were also identified in 2014 and 2015.

Between July and December 2016, clusters of HAV were being investigated by PHE. There had been a number of laboratory confirmed cases of genotype 1A with identical RNA sequences. The

cases were initially reported from geographically distinct clusters. As the outbreak progressed men who have sex with men were identified as the main risk group and a recent travel history to Spain was also noted in some cases [1]. These distinct strains reported as Event 1, 2 and 3 by ECDC are currently still being investigated in a number of European countries including the United Kingdom [2].

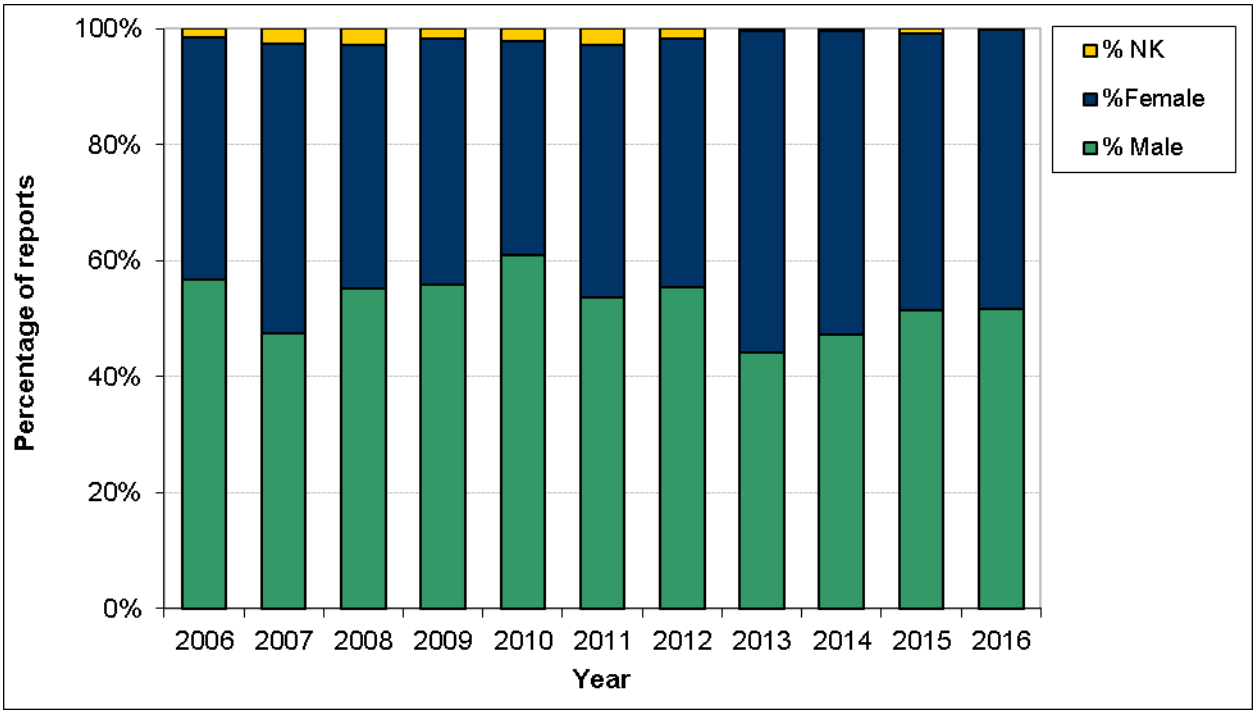
Due to the small number of laboratory reports per PHE Centre for all centres apart from London, trends in sub-national data over time should be interpreted with caution.

Table 2: Laboratory reports of hepatitis A by PHE Centre (England) and Wales (2006-2016)

PHE Centre	Year										
	2006	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**
East Midlands	15	13	19	14	9	6	7	8	10	11	30
East of England	40	31	34	38	36	24	25	23	15	24	47
London	47	50	54	53	72	69	71	91	118	79	180
North East	12	14	5	8	12	10	13	10	9	11	17
North West	71	63	48	64	56	24	28	34	22	43	22
South East	28	32	66	50	28	44	38	29	55	27	51
South West	40	33	30	24	48	11	18	29	14	15	22
West Midlands	66	71	67	59	61	41	44	29	32	47	46
Yorkshire and Humber	54	36	27	34	40	23	36	19	17	69	24
Wales	25	20	10	12	9	5	8	11	8	4	5
Total	**398**	**363**	**360**	**356**	**371**	**257**	**288**	**283**	**300**	**330**	**444**

Age and sex were well completed each year (>98% complete) (Figure 1). Where known, males accounted for 52% (239/440) of reports during 2016 (Figure 1). As reported last year, since 2006 the majority of reports were among males for all years excluding 2007, and most recently also 2013 and 2014 (Figure 1). The proportion of reports among males has varied slightly each year; overall males have accounted for 53% of hepatitis A laboratory reports during this period (range 44-61%).

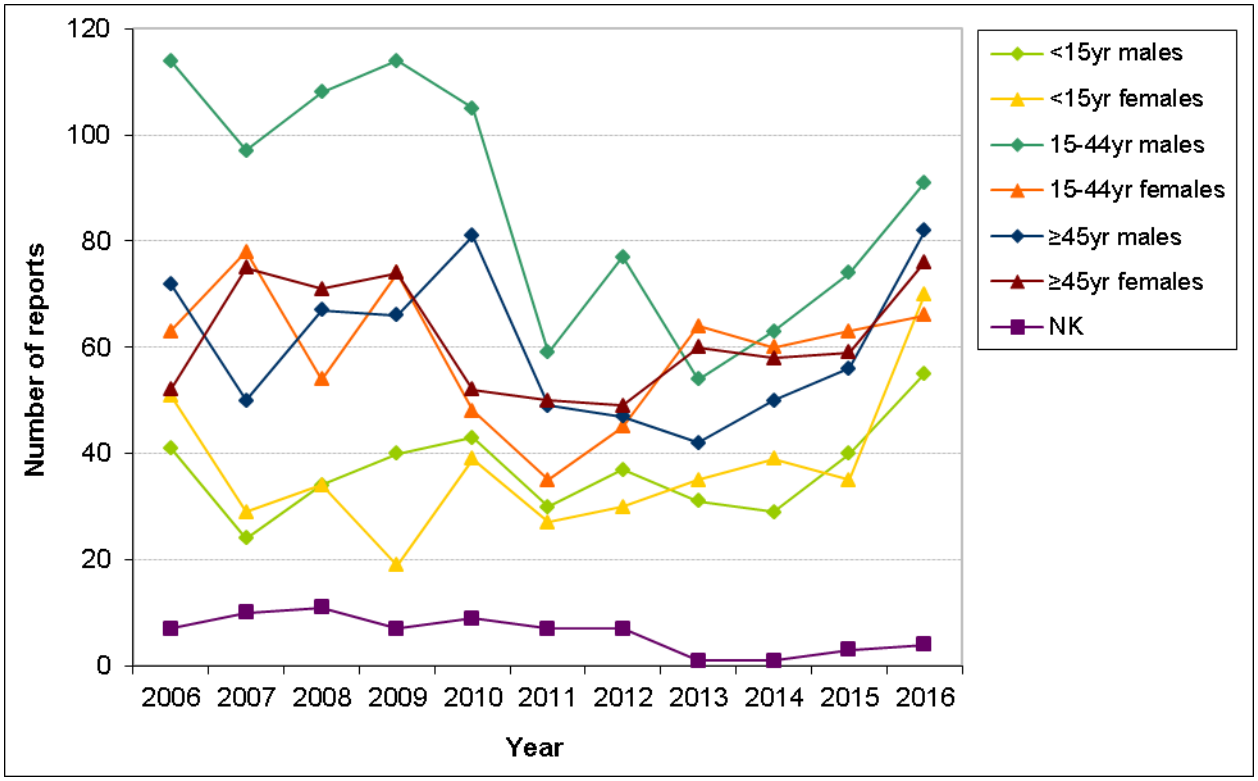
Figure 1: Percentages of hepatitis A laboratory reports by sex, England and Wales (2006-2016)



In 2015, the number of reports across all age groups from both males and females increased compared to 2015 (Figure 2).

During 2016, females accounted for 56% of reports in the under 15 year old age group, males accounted for 58% of reports in the 15 to 44 age group, and 52% of reports among the 45 years and over age group. In comparison, males accounted for 53% of reports in the under 15 year's age group, 54% of reports in the 15 to 44 age group, and 49% of reports among the 45 years and over age group.

Figure 2: Laboratory reports of hepatitis A by age and sex, England and Wales (2006-2016)



As reported previously, there was no risk factor information reported for anything other than recent travel in 2016. Travel history was available for 23% of reported cases; compared to 2015 when 18.5% had a known travel history (Table 3). Overall, risk factor information including travel history remains rare, which limits the conclusions that can be drawn from these data. More complete risk factor information would enable a better understanding of the current epidemiology of hepatitis A virus infection in England and Wales.

Table 3: Trends in hepatitis A laboratory reports, England and Wales (2006-2016)

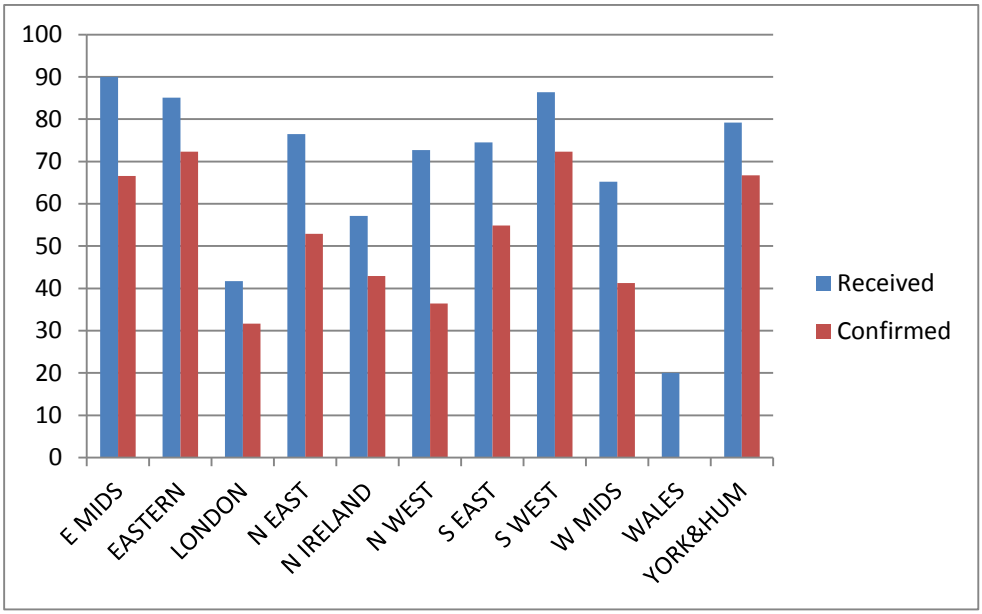
Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Number of reports	**398**	**363**	**360**	**356**	**371**	**257**	**288**	**283**	**300**	**330**	**444**
Number (%) aged 15-44 years	182 (46%)	178 (49%)	167 (46%)	190 (53%)	157 (42%)	96 (37%)	122 (42.4%)	118 (42%)	123 (41%)	138 (41%)	157 (35%)
Number (%) male	227 (57%)	172 (47%)	209 (55%)	220 (56%)	230 (61%)	138 (54%)	162 (55%)	127 (44%)	142 (47%)	170 (51.5%)	229 (52%)
Number (%) with travel history	35 (8.8)	53 (14.6)	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 (23%)
Number (%) travelled abroad	17 (4.3)	23 (6.3)	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%)

Reference laboratory confirmation and phylogeny of hepatitis A infection: 2016

Of the 451* laboratory reports of acute HAV infection during 2016, 282 (62.5%) had samples forwarded to the Virus Reference Department (VRD) for confirmation which is a decrease of 11.1% from 2015. Of the 169 (37.5%) cases who did not have a sample forwarded to VRD for HAV confirmation, three cases were notified as being false positives, nine cases had no sample remaining, eight reports were due to errors in SGSS reporting, 16 had samples forwarded for HEV testing, one sample was forwarded for HCV testing and one sample was forwarded for HDV testing.

Acute HAV infection was not confirmed in 25.5% (72/282) of the forwarded samples. The remaining 210 (74.5%) cases were confirmed to have acute HAV infection. In addition 80 cases were confirmed to have acute HAV infection that had not been reported through the laboratory reporting system and with the exception of 26 cases they were all recorded in HPZone (19 from Wales, three from Northern Ireland and three from England). The breakdown of samples received per region can be seen in Figure 1.

Figure 1: Percentage of cases received for confirmation by region and the percentage confirmed



* Includes seven cases from Northern Ireland excluded from the laboratory reports of Hepatitis A infections England and Wales 2016 Section

Of the 290 confirmed cases, 156 (53.8%) reported a travel history, 121 (41.7%) had no travel history and 13 (4.5%) had no information. There were regional differences with regards to travel versus non-travel related with London having the largest number of travel associated cases (Figure 2). Where non-travel related cases were higher than those associated with travel these regions invariably had large community outbreaks of unknown cause. The age of the cases ranged from 1 to 86 years of age with travel being the main risk between the ages of 1 and 34, after this age non-travel associated cases becomes more common (Figure 3). There has been an increase in cases confirmed in all age brackets except 1-4, 5-9 and 15-24 compared to 2015 (Figure 4).

Figure 2: Confirmed HAV infections by region and travel history

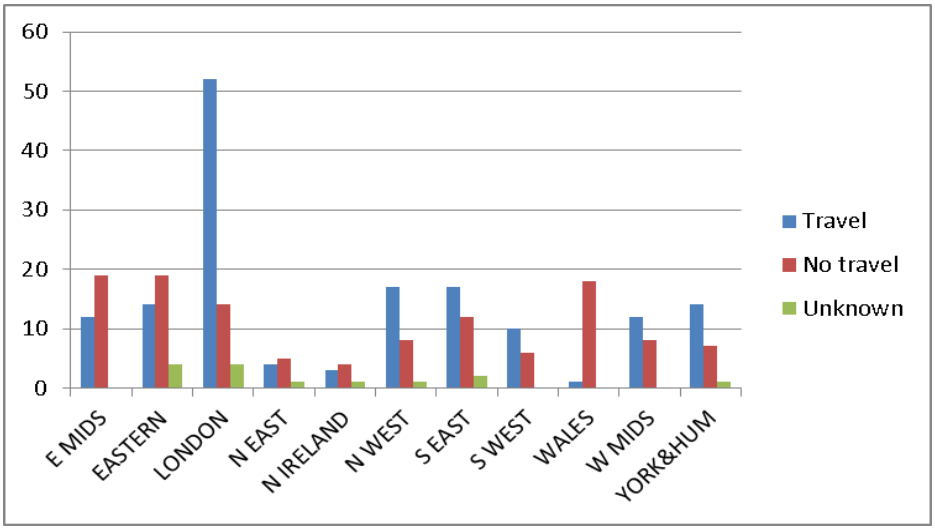


Figure 3: Confirmed HAV infections by age and travel history

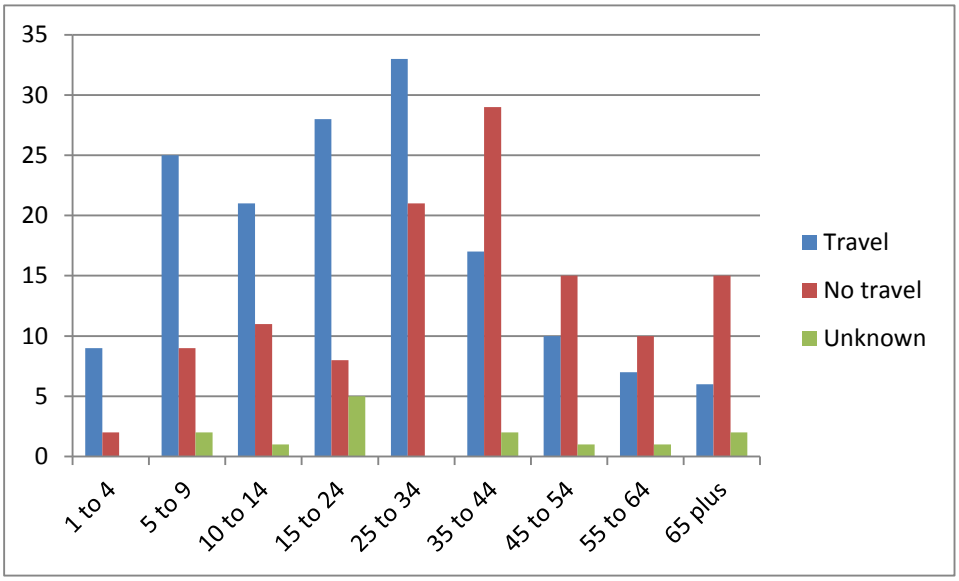
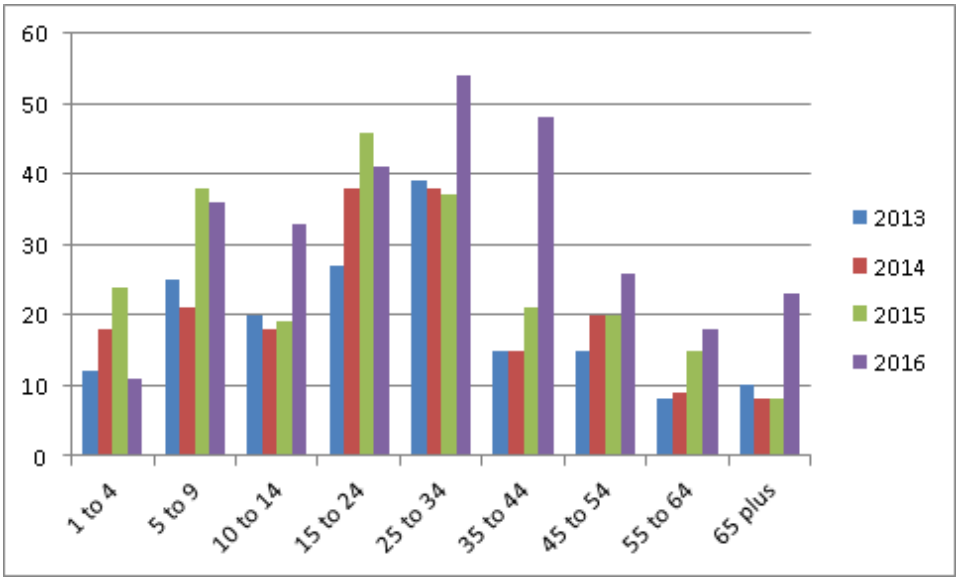


Figure 4: Comparison of confirmed HAV infections by age 2013 – 2016



It was possible to genotype 285 of the confirmed cases; 131 (46%) were genotype IA, 74 (26%) were genotype IB, three (1%) were genotype IIA and 77 (27%) were genotype IIIA. This sequence information is presented (on the following pages) as a phylogenetic tree for each genotype, with each sequence represented by a dot, with the patient region and the week of sampling in brackets.

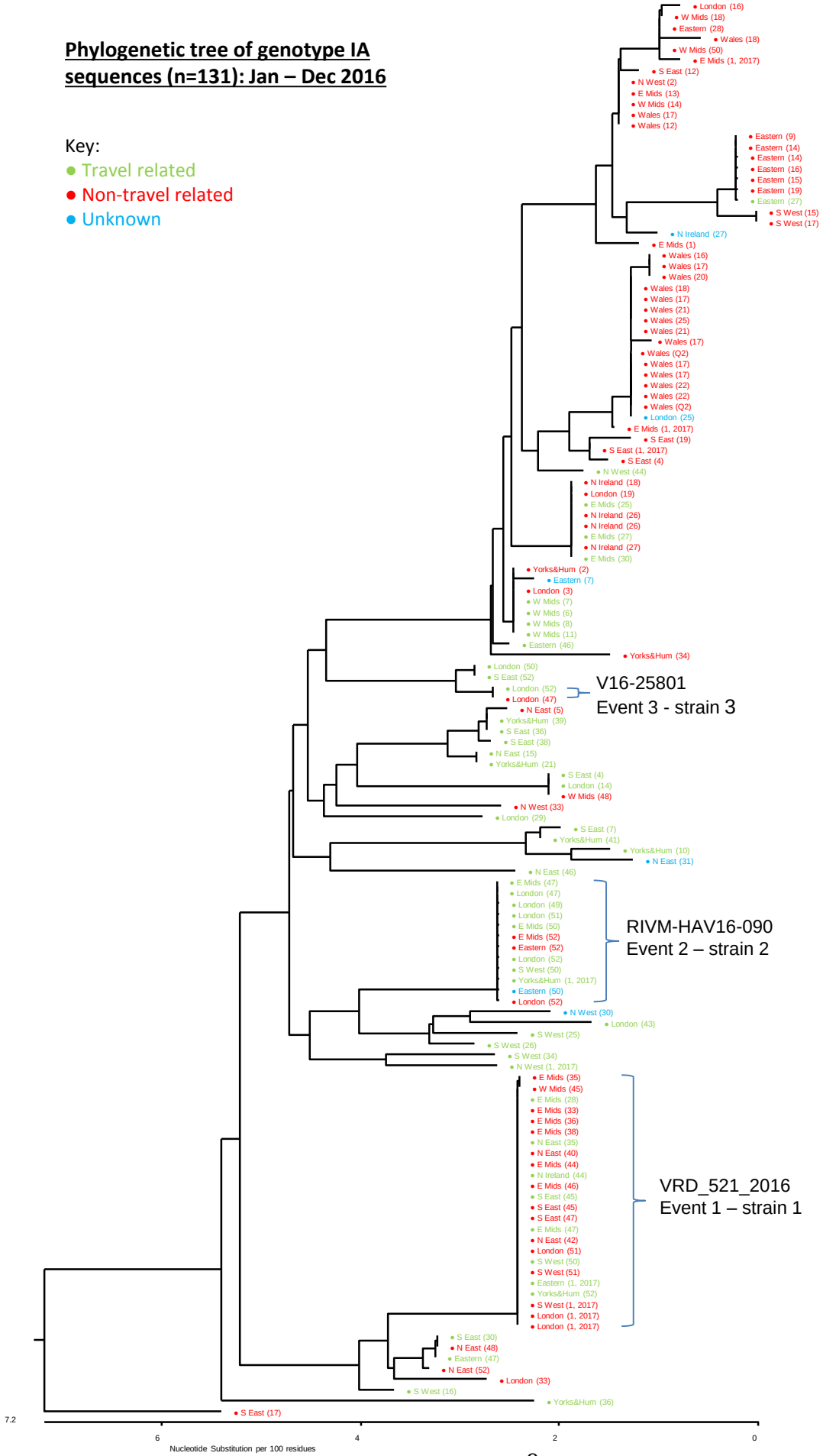
The majority of cases with **genotype IA** had no travel history 75/131 (57.2%) which can in part be attributed to a number of community outbreaks of known cause. In addition to these community outbreaks 2016 saw the emergence of three distinct genotype IA strains affecting the MSM community, VRD_521_2016 (Event 1 – strain 1), RIVM-HAV16-090 (Event 2 – strain 2) and V16-25801 (Event 3 – strain 3) [1,2,3,4]. For 2016 samples tested at the molecular level and found to have either the Event 1, 2 or 3 strain totalled 24, 12 and 2 cases, respectively

For **genotype IB** there was little difference in the number of travel versus non-travel related cases (34 and 36 respectively). During 2016 a large community outbreak was caused by a genotype IB strain the source of which was never identified.

Genotype IIA is rare worldwide and has only been seen once before in England in 2014. Most reports of genotype IIA are importations from West Africa but in these three cases no travel risk was identified although a common source is likely.

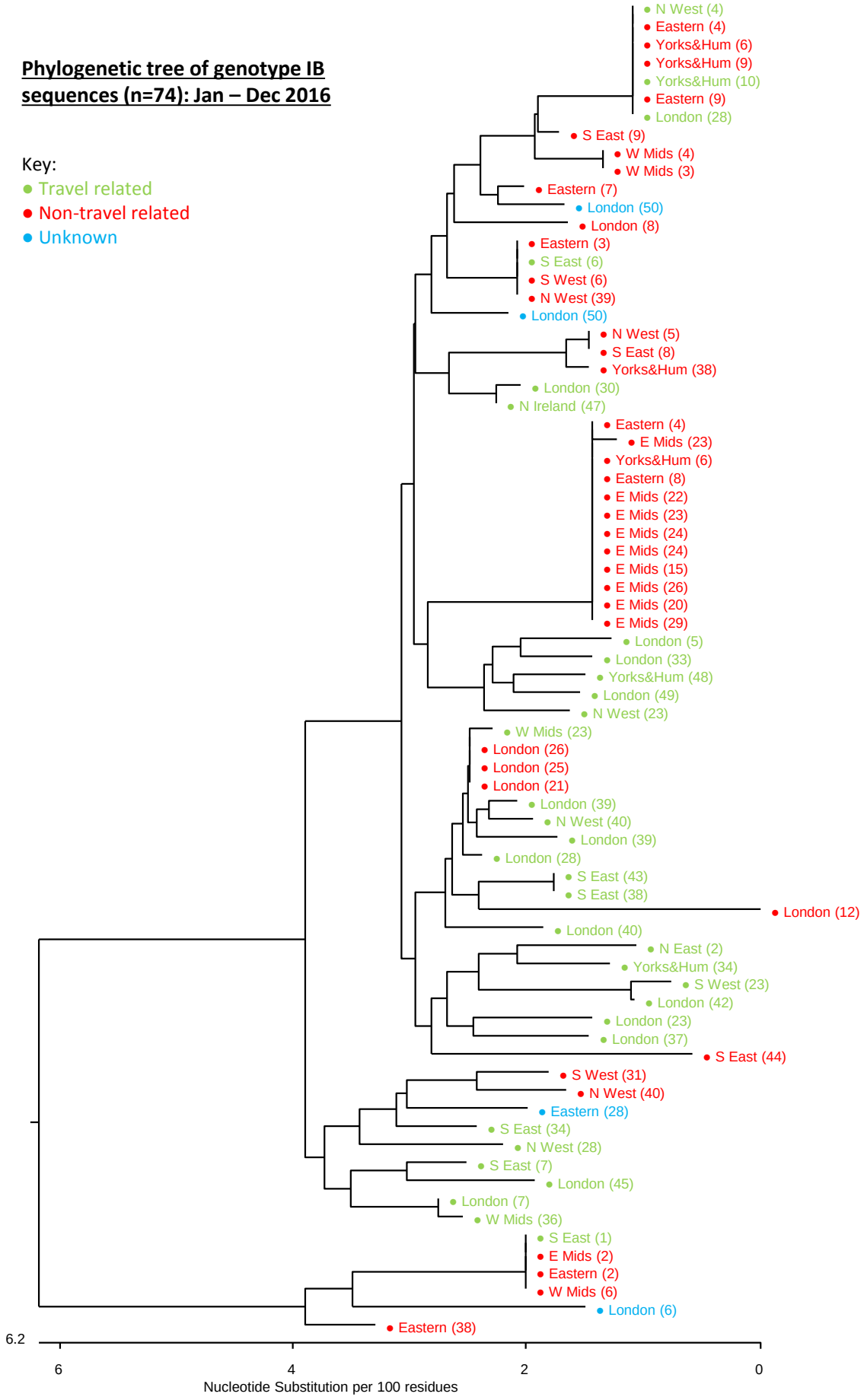
As in previous years, the majority of cases with **genotype IIIA** had a travel history (70/77, 90.1%). Genotype IIIA is geographically associated with South Asia and travellers may not perceive themselves or their family to be at risk if they grew up in an endemic area and are travelling “home” to visit friends and relatives [5].

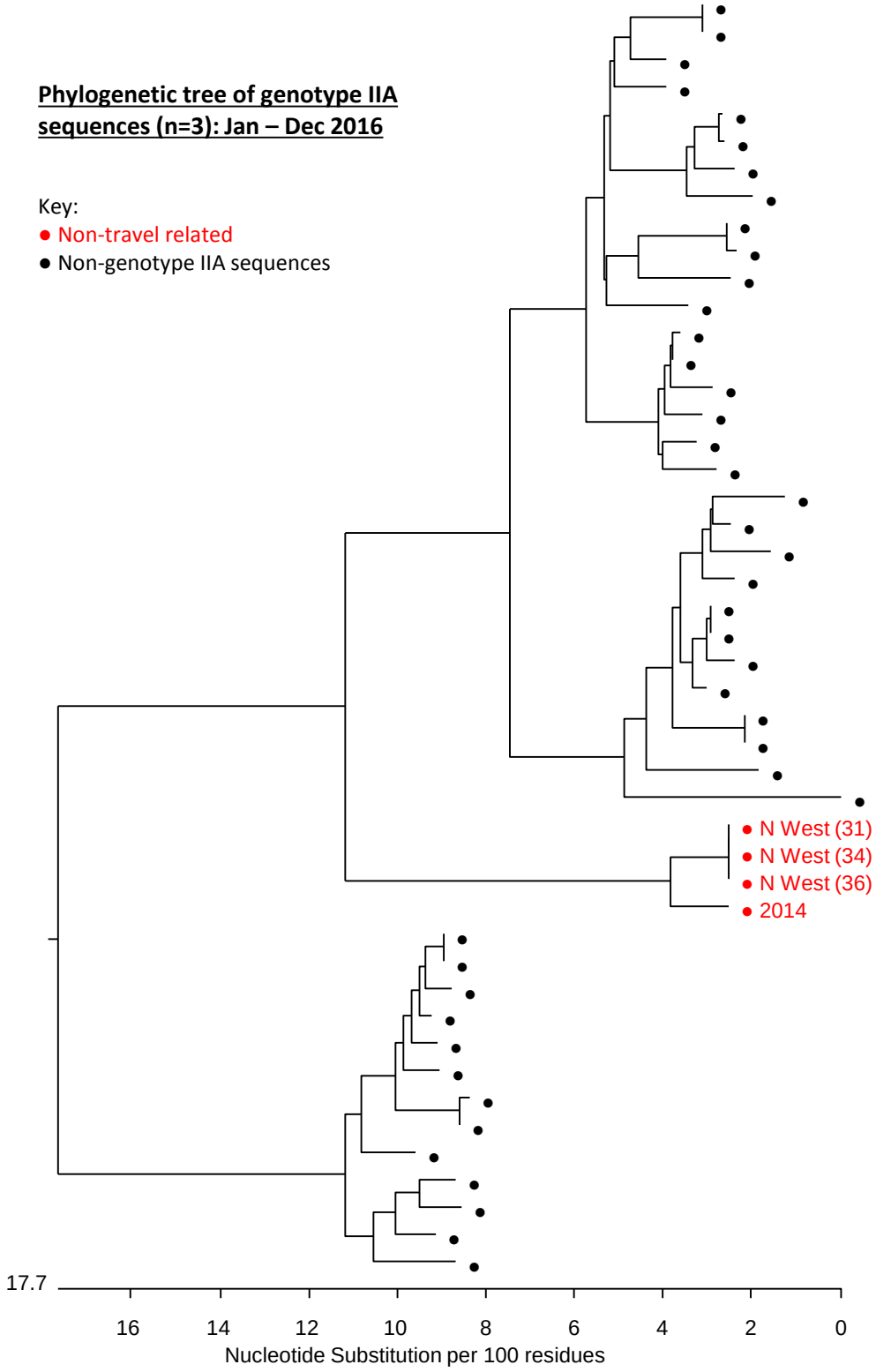
Phylogenetic tree of genotype IA sequences (n=131): Jan – Dec 2016



Phylogenetic tree of genotype IB sequences (n=74): Jan – Dec 2016

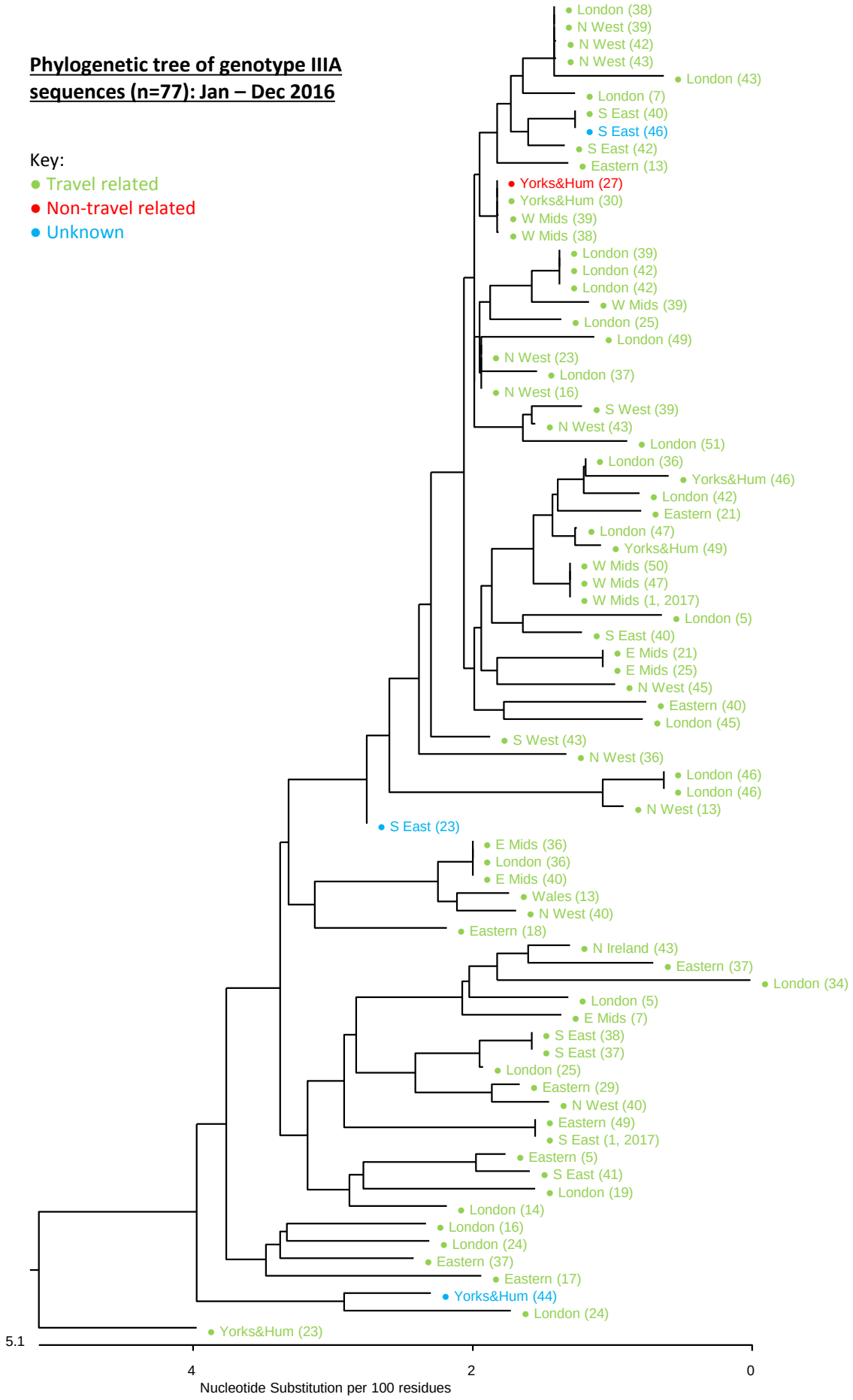
Key:
- Travel related
- Non-travel related
- Unknown




Phylogenetic tree of genotype IIA sequences (n=3): Jan – Dec 2016
Key:
Non-travel related
Non-genotype IIA sequences
N West (31)
N West (34)
N West (36)
2014
17.7
16
14
12
10
8
6
4
2
0
Nucleotide Substitution per 100 residues

Phylogenetic tree of genotype IIIA sequences (n=77): Jan – Dec 2016

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



Summary

In 2016, just over 60% of samples associated with laboratory reports of acute HAV infection were forwarded to VRD for confirmation. Comparisons of SGSS reports with data from VRD have shown that nearly a quarter of the reports (25.5%) were not true cases of acute HAV. In addition significant numbers of cases genotyped within VRD have not been reported through the laboratory reporting system (SGSS, 80 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 our 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 extent and spread of the national outbreak of hepatitis A amongst MSM identified in 2016 [1]. 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.

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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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