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Umrah- and travel-associated meningococcal disease due to multiple serogroup W ST-11 sub-strains pre-Hajj 2024

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SUMMARY

Objectives: Collectively, the Hajj and Umrah pilgrimages draw > 30 million pilgrims to the Kingdom of Saudi Arabia (KSA) each year. Before Hajj 2024 (14 to 19 June), the meningococcal serogroup W ST-11 complex (W:cc11) Hajj-strain sublineage caused multiple international cases of invasive meningococcal disease (IMD) associated with travel to the Middle East and Asia. Here we identify and characterise the strains responsible.
Methods: All Hajj strain sublineage genomes on PubMLST.org underwent core genome MLST comparisons (PubMLST.org).
Results: Isolates from 30 cases, across seven countries, formed five phylogenetic clusters within two distinct strains. Travel histories included KSA, other Middle Eastern countries, India, Mauritius, Kenya via Turkey, and no known associated travel. The prevalent strain, representing four clusters, had no African, and limited Middle Eastern, representation. The geo-temporal distribution of available genomes indicated Eastern Europe as a possible source.
Conclusions: The rapid expansion of Umrah/travel-related W:cc11 IMD cases in early 2024 was due to multiple strains/sublineages. Despite the involvement of non-KSA travel-destinations, the coincidence of

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cases with the busy month of Ramadan, and the abrupt cessation during Hajj (when vaccine compliance is maximal), suggest that Umrah was a key driver and highlight the need to reinforce mandatory vaccination whilst maintaining global vigilance.

Introduction

Neisseria meningitidis (the meningococcus) is a commensal bacterium that occasionally causes severe invasive disease such as meningitis and septicaemia.[1,2] Cases of invasive meningococcal disease (IMD) may be sporadic or occur in outbreaks.[1,2] Even with antibiotic treatment, case fatality rates may exceed 10%, while up to a third of survivors suffer severe sequelae such as limb amputations and sensorineural hearing loss. Vaccines now exist against all of the main pathogenic serogroups - A, B, C, W, Y, and X.[3] Prevention of IMD, particularly among case contacts, also includes chemoprophylaxis with ciprofloxacin, rifampicin or ceftriaxone, which eliminates nasopharyngeal carriage, thereby protecting the individual and preventing onward spread of the bacteria.[4]

The annual Hajj pilgrimage to Mecca, the Kingdom of Saudi Arabia (KSA), takes place over several days and has an average attendance of ~3 million pilgrims. Hajj has been associated with large international IMD outbreaks, including a serogroup A outbreak in 1987 and serogroup W ST-11 complex (W:cc11) outbreaks in 2000 and 2001.[5] This led to the implementation of mandatory serogroup ACWY vaccination of all pilgrims, including those attending Umrah, another pilgrimage to Mecca, which takes place throughout the year with an annual attendance of ~30 million.[6] Pilgrims from the African meningitis belt have also been required to take antibiotic chemoprophylaxis to clear any carriage on entry.[7]

The W:cc11 strain that caused the Hajj outbreaks in 2000 and 2001 (the 'Hajj outbreak strain') belongs to the wider W:cc11 Hajj strain sublineage.[8] This also includes the 'endemic South African strain', a Hajj outbreak strain descendent that caused increased endemic W:cc11 disease in South Africa from 2003, and the ancestral 'Burkina Faso/North African' strains that caused several large epidemics in sub-Saharan Africa from 2001.[8] At its origin, the Hajj strain sublineage diverges from two further W:cc11 sublineages - the proposed Chinese strain sublineage,[9] and the South American strain sublineage that originated in South America in the late 1990s and spread globally to become endemic in countries within Europe, Australasia, and North America.[10,11]

In June 2024, the USA, France and UK collectively reported 12 cases of IMD in travellers, or household contacts thereof, that had visited KSA for Umrah during March-May 2024.[12] Of the nine patients with known vaccine history, none had been immunised. Characterisation of available isolates (n=11) revealed one serogroup C ST-4821 complex (C:cc4821) and ten W:cc11 isolates. Culture-free sequencing[31] of genomic material from the 12th case identified non-groupable ST-175 complex (NG:cc175) meningococci (PubMLST ID 150811). The C:cc4821 isolate, two of the W:cc11 isolates, and the NG:cc175 meningococci all had a mutation in *gyrA* resulting in a threonine at position 91 of the DNA gyrase protein being replaced by isoleucine, which imparts ciprofloxacin resistance. Accordingly, the ciprofloxacin MICs for the cultures ranged from 0.12 to 0.25 µg/mL. Subsequent W:cc11 cases associated with KSA travel were also reported in Norway, the Netherlands, and the Maldives.[13,14] Concerns of a larger outbreak were heightened by the then-imminent Hajj pilgrimage (14th to 19th June 2024).

The W:cc11 cases associated with travel to KSA were quickly established, using genome sequence analysis, to belong to the W:cc11 Hajj strain sublineage. The aims of the current study were (i) to provide an update on the population structure of the W:cc11 Hajj strain sublineage and (ii) to identify the strain(s) responsible for the recent cases.

Methods

Identification of Hajj strain sublineage genomes

Sequence bin data for all serogroup W cc11 genomes (n=3685) on the PubMLST *Neisseria* database[15] (accessed 25/05/2024) were downloaded using the 'export' function. Poorly assembled genomes (> 350 contigs or > 2.5 Mb; n=142, collectively) were discarded. The remaining genomes (n=3543; 96%) were split into 13 manageable groups of up to 300 genomes. Each group underwent core genome MLST ('*N. meningitidis* cgMLST V2′; n=1422 loci) comparisons along with sublineage marker isolates for (i) the Hajj strain sublineage (PubMLST IDs 30089 and 30090), (ii) the Chinese strain sublineage (PubMLST IDs 53769 and 53772) and (iii) the South American strain sublineage (PubMLST IDs 20057 and 20158) using the PubMLST genome comparator tool.[16] The resulting distance matrices were visualised using SplitsTree4.[17] Hajj strain sublineage genomes were identified as those falling within the lineage containing the Hajj strain sublineage marker isolates. These were taken forward for further analyses.

Generation of a representative phylogeny for the Hajj strain sublineage

The Hajj strain sublineage genomes (n**=**980; Supplementary spreadsheet) were split into country-specific groups. Groups containing > 20 genomes underwent cgMLST comparison/visualisation (as previously). For each country, one to two representative genomes for each phylogenetic cluster (strain) were randomly selected from the phylogeny (with a preference for those with shorter edges), to take forward to a collective cgMLST comparison/visualisation including (i) all country representatives, (ii) all genomes for countries represented by ≤20 genomes in total, (iii) the 'sublineage marker isolates' and (iv) all 50 isolates identified as close relatives to Umrah 2024 outbreak isolate 24MN0165 (PubMLST ID:150006) using classification scheme 'Nm_cgc3_10′ ('*single linkage clustering with each group member having fewer than 10 allelic mismatches to at least one other member of the group*') on PubMLST.org. Prevalent strains, and their constituent genomes, were assigned to existing (i.e. endemic South African strain, Hajj strain, Burkina Faso/North African strains) or new (strains A, B and C) strains (table S1). The collective tree was then further sampled by cluster to give a 'minimal representative' tree (n=54 genomes).

Assigning corresponding strain IDs to all Hajj strain sublineage isolates

The remaining unassigned genomes, i.e. those not in the original collective tree, underwent cgMLST comparisons with the minimal representative tree genomes on a country-by-country basis to assign corresponding strains (Table S1).

All genomes are available on the PubMLST *Neisseria* database. PubMLST IDs are provided in table S1.

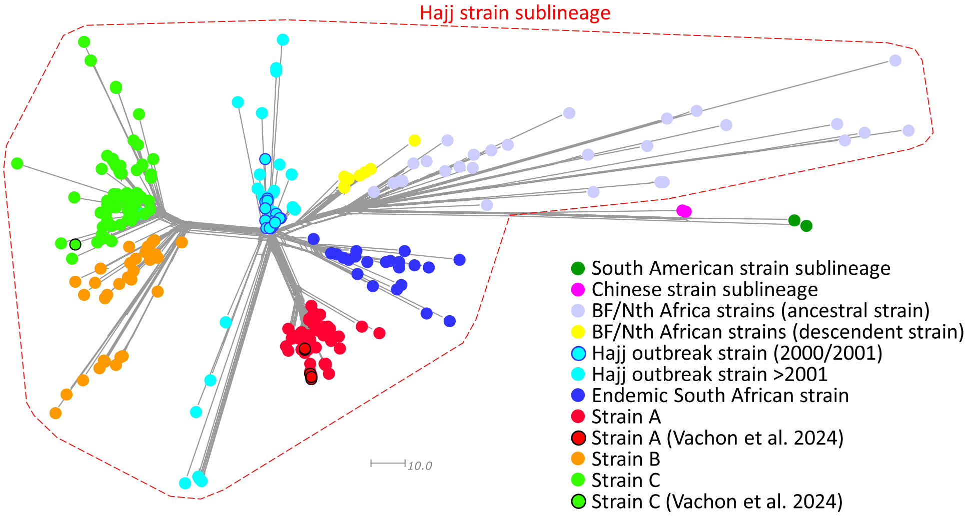

Fig. 1. Population structure of the MenW:cc11 Hajj strain sublineage. The phylogeny includes a representative panel of n=311 Hajj strain sublineage isolates (red dashed line) and two isolates each for the Chinese strain sublineage and South American strain sublineage. The Hajj strain sublineage comprised known strains including the Hajj outbreak strain, ancestral and descendent Burkina Faso/North African strains, and endemic South African strain, and three newly identified strains identified here as strains A, B and C. Hajj strain isolates with a blue border are from the outbreak years (2000/2001). Strain A and C isolates with a black border were the Umrah/KSA travel-related isolates reported by Vachon *et al.*, (2024) (n=10). The scale bar indicates distance in terms of the number of different loci (out of 1422 core genome loci compared). Among the Hajj strain isolates sitting between strains A and B on the phylogeny was a small cluster of three isolates from Sweden (2017).

Results

Hajj strain sublineage population structure

The Hajj strain sublineage originated at the intersection with the Chinese and South American strain sublineages and included several large clusters (referred to here as strains; Fig. 1). The ancestral so-called 'Burkina Faso/North African' strains preceded the Hajj outbreak strain. This, in turn, preceded three divergent strains - the 'endemic South African strain', and newly identified strains, 'strain A' and 'strain B'. 'Strain B' then evolved into 'strain C'. The ten previously reported 2024 W:cc11 outbreak isolates,[12] and closely related isolates from 2024, belonged to strain A and strain C (Fig. 1).

Strains not associated with travel-related 2024 cases

W:cc11 Hajj strain sublineage 'Burkina Faso/North African strains'

None of the 2024 cases were due to the Burkina Faso/North African strains. They comprised two distinct strains – a relatively diffuse ancestral strain (n=41; invasive disease n=31, throat swab n=4, unknown n=6) and a descendent strain (n=19; invasive disease n=17, unknown n=2). Isolates belonging to the ancestral strain were mainly from Africa in the early 2000s (Table 1; Fig. S1). A small number of subsequent cases were observed in Africa, Turkey, Australia, North America and Europe (France in particular). The African isolates formed several country-specific clusters. There were three clades exclusively containing non-African isolates including a French clade with two distinct clusters of three isolates from 2011/12 and 2014, respectively. The descendent strain included only 19 isolates (Table 2; Fig. S1). The majority were from Burkina Faso (n=5; 2001 to 2004) and Niger (n=12; 2001 to 2003). Only two other isolates were observed, from England (1998) and Italy (2005).[18]

W:cc11 Hajj strain sublineage 'Hajj outbreak strain'

None of the 2024 cases were due to the Hajj outbreak strain. Where known (155/172; 90%), these were all from invasive disease cases. The earliest representatives of the Hajj strain were from 2000 during the first W:cc11 Hajj outbreak. Indeed, most isolates 131/172 (76.2%) were from 2000 and 2001 when the two W:cc11 outbreaks occurred (Table 3). There was a predominance of UK isolates 118/172 (68.6%) within the Hajj outbreak strain due to a prior comprehensive genomic analysis of cc11.[8] The KSA isolates (n=7; 2000 to 2001), UK isolates from 2000 (n=50), 2001 (n=54) and the three years that followed (n=14), and all of the other isolates from 2000 to 2002 including isolates from Africa (n=16), Saudi Arabia (n=7), North America (n=3), France (n=1) and Italy (n=1)[18] sat close to the centre of the strain (Fig. 1) reflecting the rapid spread of a single strain during an acute outbreak. Three invasive disease cases from an outbreak among children in Sweden in 2017[19] formed a very divergent cluster of closely related isolates.

W:cc11 Hajj strain sublineage 'endemic South African strain'

None of the 2024 cases were due to the endemic South African strain (n=99). The isolates were collected between 2003 and 2021 (inclusive) and all were from invasive disease. The vast majority (n=94/99) of the isolates were from South Africa with a further five from the UK (n=4; 2007 to 2017) and Germany (n=1; 2016) (Table 4). One of the UK cases had recently travelled to southern Africa (not South Africa).

W:cc11 Hajj strain sublineage 'strain B'

Strain B (n=66; Fig. 2) corresponded to sub-clade 2.1 described by Topaz *et al.* (2019).[20] It did not include any cases from 2024. It included 64 invasive isolates, one carriage isolate, and one isolate with unknown origin. The strain B isolates were collected from six countries in Africa (n=55; 2005 to 2016) and six countries in Europe/North America (n=12; 2015 to 2018) (Table 5). Except for a single French isolate from 2016, the European/North American isolates uniquely occupied three clades distinct from those containing African isolates. The remaining French isolate shared a clade with an isolate from Togo (2015). The isolates from the USA and Canada clustered within one clade and isolates from Switzerland and Sweden in another. Notably, one clade in strain B included invasive isolates from Chad (n=8; 2012 to 2015) giving rise to a tight cluster of invasive isolates in neighbouring Central African Republic (n=28; 2015 to 2016) as previously described.[20]

Table 1

Geo-temporal distribution of the ‘ancestral’ Burkina Faso/North African strain isolates.

	1994	2000	2001	2002	2004	2006	2007	2011	2012	2014	2015	2016	2017	Grand Total
Africa	**1**	**4**	**9**	**5**	**1**		**2**				**2**	**1**		**25**
Algeria											2			2
Burkina Faso			5	1	1									7
Cameroon		4	1											5
Central African			1											1
Madagascar			2	4								1		7
Mali	1						2							3
Asia											**1**		**1**	**2**
Turkey											1		1	2
Europe			**1**			**1**		**2**	**2**	**3**		**3**		**12**
France								2	2	3		1		8
Germany												1		1
Sweden												1		1
UK			1			1								2
North America												**1**		**1**
USA												1		1
Oceania												**1**		**1**
Australia												1		1
Grand Total	1	4	10	5	1	1	2	2	2	3	3	6	1	41

Table 2

Geo-temporal distribution of the ‘descendent’ Burkina Faso/North African strain isolates.

	1998	2001	2002	2003	2004	NK[a]	Grand Total
Africa		**4**	**4**	**5**	**4**		**17**
Burkina Faso		1			4		5
Niger		3	4	5			12
Europe	**1**					**1**	**2**
Italy						1	1
UK	1						1
Grand Total	**1**	**4**	**4**	**5**	**4**	**1**	**19**

[a] NK = not known

Strains associated with travel-related 2024 cases

W:cc11 Hajj strain sublineage ‘strain C’

Strain C (n=512; Table 6; Fig. 3) corresponded to the Clade 3 subclades described by Topaz *et al.* (2019).[20] It included four invasive isolates collected in 2024. Three of these, from Canada, France, and the USA (the latter two with known recent KSA travel), were identical on the phylogeny and shared a clade with eight distant isolates from Benin isolated in 2012. Within this clade, the isolates from 2024 were unique in possessing a T91I *gyrA* mutation imparting a genotype for ciprofloxacin resistance. This was phenotypically confirmed with a French isolate of the same genotype having a ciprofloxacin MIC of 0.190 mg/L. The other French isolate from 2024 shared a clade with four relatively distant isolates from Nigeria (2015).

Most of the remaining strain C isolates (90%; n=463/512) were African in origin with the majority (n=271), including all known carrier isolates (n=83; 2016/17), coming from Burkina Faso (2011 to 2016). The Burkina Faso isolates were distributed among at least six distinct clades as well as diffuse singletons. The carrier isolates were distributed among two of these clades and a further ‘carriage-only’ clade (n=64; Fig. 3 orange dashed line). Most of the invasive isolates from Burkina Faso were from 2012 (n=137; 51%) when a large epidemic occurred.[21] Six other African countries were also represented (since 2011; n=187) including three mainly Nigerian clusters (2015); three Benin clusters (2012), four Togo clusters (one of which, from 2014 to 2016, was directly descended from an earlier Benin cluster) and a largely Malian cluster that included isolates from Guinea, Burkina Faso, and France. The remaining Malian isolates belonged to a diffuse clade including isolates from Burkina Faso, Nigeria, and Guinea.

The remaining strain C isolates were from seven European countries (since 2012; n=49; for which 51 genomes), Canada (since 2023; n=2), and the USA (2024; n=1) (Table 6). Several French clusters of two or three isolates, from the same or adjacent years, were associated with recent travel to sub-Saharan Africa.[22] These were observed within several otherwise-African clades, including two clades dominated by Malian isolates (2011/12) and one dominated by Burkina Faso isolates (2011/12). Three further French clusters occupied their own sublineages. None of these earlier French isolates exhibited ciprofloxacin resistance. A relatively persistent sublineage included isolates from Italy (n=5; for which 6 genomes; 2015/16)[18] and Germany (n=2; 2015 and 2017), and another included isolates from Switzerland (n=12; 2014 to 2016), Austria (n=1; 2014); Italy (n=1, for which two genomes; 2014)[18]; France (n=1; 2015), and Germany (n=3; 2016). Branching off slightly earlier in this clade were three Burkina Faso isolates from 2015. Several isolates from 2014 from Switzerland, Austria, and Italy were identical or differed by one locus on the phylogeny suggesting a possible outbreak that may have seeded the subsequent European cases.

W:cc11 Hajj strain sublineage ‘strain A’

Strain A (Fig. 4) comprised 69 isolates collected from 15 countries across Eastern and Western Europe, Asia, North America, and the Middle East, dating back to 2013 (Table 7). Except for five carrier isolates from Russia (2016 to 2020) and one conjunctivitis isolate from the UK (2024), all isolates originated from invasive disease cases. Four ’strain A’ clusters comprised isolates from 2024 only:

Table 3
Geo-temporal distribution of the Hajj outbreak strain isolates.

	2000	2001	2002	2003	2004	2005	2006	2007	2009	2011	2012	2014	2015	2016	2017	NK	Total
Africa	**3**	**11**	**2**		**1**			**1**		**2**			**1**	**1**		**1**	**23**
Algeria		2															2
Burkina										1							1
Cameroon		5															5
Chad		1															1
Djibouti					1												1
Madagascar		1															1
Mali								1								1	2
Mauritius		1															1
Morocco										1				1			2
Niger			1										1				2
Senegal	3	1	1														5
Asia															**1**		**1**
Kazakhstan															1		1
Middle	**5**	**2**				**1**	**2**					**3**					**13**
Saudi	5	2															7
Turkey						1	2					3					6
Europe	**51**	**55**	**10**	**2**	**3**		**1**		**2**		**1**				**3**		**128**
France	1																1
Germany											1						1
Italy		1			1				1								3
Spain							1		1								2
Sweden															3		4
UK	50	54	10	2	2												118
North	**2**	**1**											**1**	**1**			**5**
Canada	1	1															2
USA	1												1	1			3
NK	**2**	**2**															**4**
Total	**62**	**70**	**12**	**2**	**4**	**1**	**3**	**1**	**2**	**2**	**1**	**3**	**2**	**2**	**4**	**1**	**172**

- Cluster A1 (n=9) comprised invasive isolates from Canada (n=7), France (n=1) and England (n=1). The English case had recent Middle Eastern travel (Egypt and Abu Dhabi), and the French case was a Canadian national. The Canadian cases reported no associated travel. The closest related isolates on the phylogeny were an invasive isolate from England in 2023 and an invasive isolate from Russia (2020) (respective travel histories not known).
- Cluster A2 (n=8) comprised invasive isolates from France (n=4), the USA (n=2), England (n=1) and the Netherlands (n=1). Three cases had recent travel to KSA (France, n=1; USA, n=1, Netherlands (n=1), while a further three had contacts with recent KSA travel (France, n=2; USA, n=1). The English case had travelled from Kenya via Turkey, and a further French case had contact with a recent returnee from Mauritius. The latter isolate was slightly more distant from the main cluster. The nearest historical isolate was a Russian carrier isolate from 2020.
- Cluster A3 (n=8) included seven invasive isolates from England (n=4), France (n=1), the USA (n=1) and KSA (n=1); and one conjunctivitis isolate from the UK. Five of the invasive cases had recent travel to KSA (England, n=3; France, n=1; USA, n=1) and one (from England) had recent travel to India. The conjunctivitis case (from England) was from the Muslim community with no

Table 4
Geo-temporal distribution of the endemic South African strain isolates.

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2016	2017	2018	2021	Grand Total
Africa	**1**	**3**	**9**	**10**	**10**	**9**	**8**	**9**	**6**	**7**	**6**	**6**	**6**	**3**	**1**	**94**
South Africa	1	3	9	10	10	9	8	9	6	7	6	6	6	3	1	94
Europe					**1**				**1**			**2**	**1**			**5**
Germany												1				1
UK					1				1			1	1			4
Total	**1**	**3**	**9**	**10**	**11**	**9**	**8**	**9**	**7**	**7**	**6**	**8**	**7**	**3**	**1**	**99**

Fig. 2. Population structure of 'strain B′ of the MenW:cc11 Hajj strain sublineage highlighting year of isolation (top) and country of origin within Africa (middle) or Europe/North America (bottom). Scale bars indicate distance in terms of the number of different loci (out of 1422 core genome loci compared). The three USA isolates are from two patients – the two isolates from a single patient were identical on the phylogeny.

known travel. The node at which these diverged from the clade containing cluster A2 included two singletons that were invasive isolates from Germany (2017; travel history not known) and Russia (2019; travel history not known).

- Cluster A4 (n=2) comprised an invasive case each for England and Sweden, both of whom had recent travel to the United Arab Emirates (UAE). These diverged from an invasive isolate from the USA from 2019 (internal travel within USA reported).

In addition to clusters A1 to A4, travel histories were also known for seven of the earlier invasive isolates within strain A including Eastern Europe (Ukraine; Russia, Estonia, Latvia, Lithuania) for isolates from Sweden (2015), Germany (2018), and Japan (2019); Pakistan for an English isolate (2023); an isolate from an American tourist in Greece (2023), and an isolate from a Russian tourist in Madeira (2020) (Fig. S2a). A phylogeny including year of isolation for strain A isolates is provided (Fig. S2b). The two isolates from 2023 with a history of travel belonged to a distinct cluster from 2023 that included invasive isolates from Sweden (n=2); Italy (n=2); England (n=1), and Greece (n=1). This cluster may, therefore, represent an earlier travel-related outbreak. It was, however, distinct from clusters A1 to A4.

Given the context of the outbreak, and the largely Africa/Middle East-centric geo-temporal distribution of the other major Hajj strain

Table 5

Geo-temporal distribution of W:cc11 Hajj strain sublineage 'strain B' isolates.

Continent/country	2005	2011	2012	2013	2014	2015	2016	2017	2018	Total
Africa	**1**	**7**	**9**	**4**	**1**	**10**	**23**			**55**
Burkina Faso		2								2
Central African Republic						7	23			30
Chad	1	1	7	4	1	1				15
Mali			2							2
Niger		4				1				5
Togo						1				1
Europe						**2**	**3**	**1**	**1**	**7**
France							1		1	2
Germany							2	1		3
Sweden						1				1
Switzerland						1				1
North America							**2**	**2**		**4**
Canada							1			1
USA							1	2[a]		3
Total	**1**	**7**	**9**	**4**	**1**	**12**	**28**	**4**	**1**	**66**

[a] Two isolates from a single patient.

sublineage strains, it is interesting that there was no African representation and just two recent (2020 and 2024) Middle Eastern isolates within strain A. This, and the lack of KSA/Middle East travel among earlier genomes from the strain, suggest the strain was not endemic to either Africa or the Middle East. It should, however, be noted that the Middle East in general is poorly represented among available meningococcal genomes.

Discussion

This study aimed to (i) update the known population structure of the W:cc11 Hajj strain sublineage and (ii) to identify the strain(s) responsible for the recent outbreak associated with travel to KSA for Umrah in early 2024.

The genomic analysis showed that the apparent outbreak actually comprised five distinct clusters and included non-KSA travel destinations. Three of the clusters (one strain C and two strain A clusters) were mainly or completely associated with travel to KSA, but also included travel to India, Mauritius, and Kenya via Turkey. The two remaining clusters were associated with travel to Egypt/Abu Dhabi and UAE. Despite the alternative travel histories, the link with Umrah is still likely legitimate, given that Ramadan was a particularly busy Umrah period[6] and the inevitable mixing of pilgrims and non-pilgrims on flights and at airports.

Table 6

Geo-temporal distribution of W:cc11 Hajj strain sublineage 'strain C' isolates.

Continent/country	2011	2012	2013	2014	2015	2016	2017	2018	2023	2024	NK	Total
Africa	**38**	**211**	**22**	**19**	**41**	**112**	**14**				**1**	**458**
Benin		38										**38**
Burkina Faso	19	138	14	3	10	72	14				1	**271**
Guinea			8									**8**
Ivory Coast		7										**7**
Mali	6	28			1							**35**
Niger	13				19							**32**
Togo				16	11	40						**67**
Europe		**9**	**7**	**8**	**13**	**9**	**2**	**1**		**2**	**1**	**49**
Austria				1								**1**
France		8	5	2	2		1			2		**20**
Germany					1	3	1					**5**
Italy			1	1[a]	1	4[b]		1			1	**9**
Spain			1									**1**
Switzerland		1		3	8	1						**13**
UK [England]					1							**1**
North America									**1**	**2**		**3**
Canada									1	1		**2**
USA										1		**1**
NK		**1**										**2**
Total	**38**	**221**	**29**	**27**	**54**	**121**	**16**	**1**	**1**	**4**	**2**	**512**

[a] Two genomes for a single isolate.

[b] Five genomes for four isolates/patients.

Fig. 3. Population structure of 'strain C′ of the MenW:cc11 Hajj strain sublineage highlighting year of isolation (top) and country of origin within Africa (middle) or Europe/North America (bottom). Scale bars indicate distance in terms of the number of different loci (out of 1422 core genome loci compared). One sublineage (orange dashes) comprised only carrier isolates from Burkina Faso. The inlay with the green border is a zoomed-in view of the 2024 outbreak clade in which the individual spots, initially superimposed indicating identical isolates in terms of cgMLST analysis, have been moved apart to aid viewing.

Although the single 'strain C' cluster from 2024 was associated with travel to KSA for Umrah, the lack of Middle Eastern strain C isolates and the overall geographical distribution of strain C isolates suggest Africa as the ultimate origin, as has been the case for other occasional W:cc11 Hajj strain sublineage cases in Western countries since the early 2000s.[23] The remaining four clusters were caused by strain A, which had no definitive geographic origin. Eastern Europe was a strong candidate, however, considering the geo-temporal distribution of available genomes and previous Eastern European travel-associated cases. Given the other two Hajj outbreak strain-derived strains, the endemic South African strain and strain B, emerged soon after the 2001/2 Hajj outbreaks (being first represented in 2003 and 2005, respectively), it is possible that strain A (first represented in 2013) emerged and remained endemic in a country with little or no representation on PubMLST.org before spreading more widely several years later.

The Hajj outbreak of 2001/2 was a focal outbreak involving a single novel strain.[5] The 2024 'outbreak', in contrast, was a coincidence of five small outbreaks/clusters, four of which involved related but distinct strain A sub-strains. Given that strain A had caused sporadic travel-related cases for over a decade, it is unclear why this period in 2024 saw so many cases/clusters. Several possible reasons

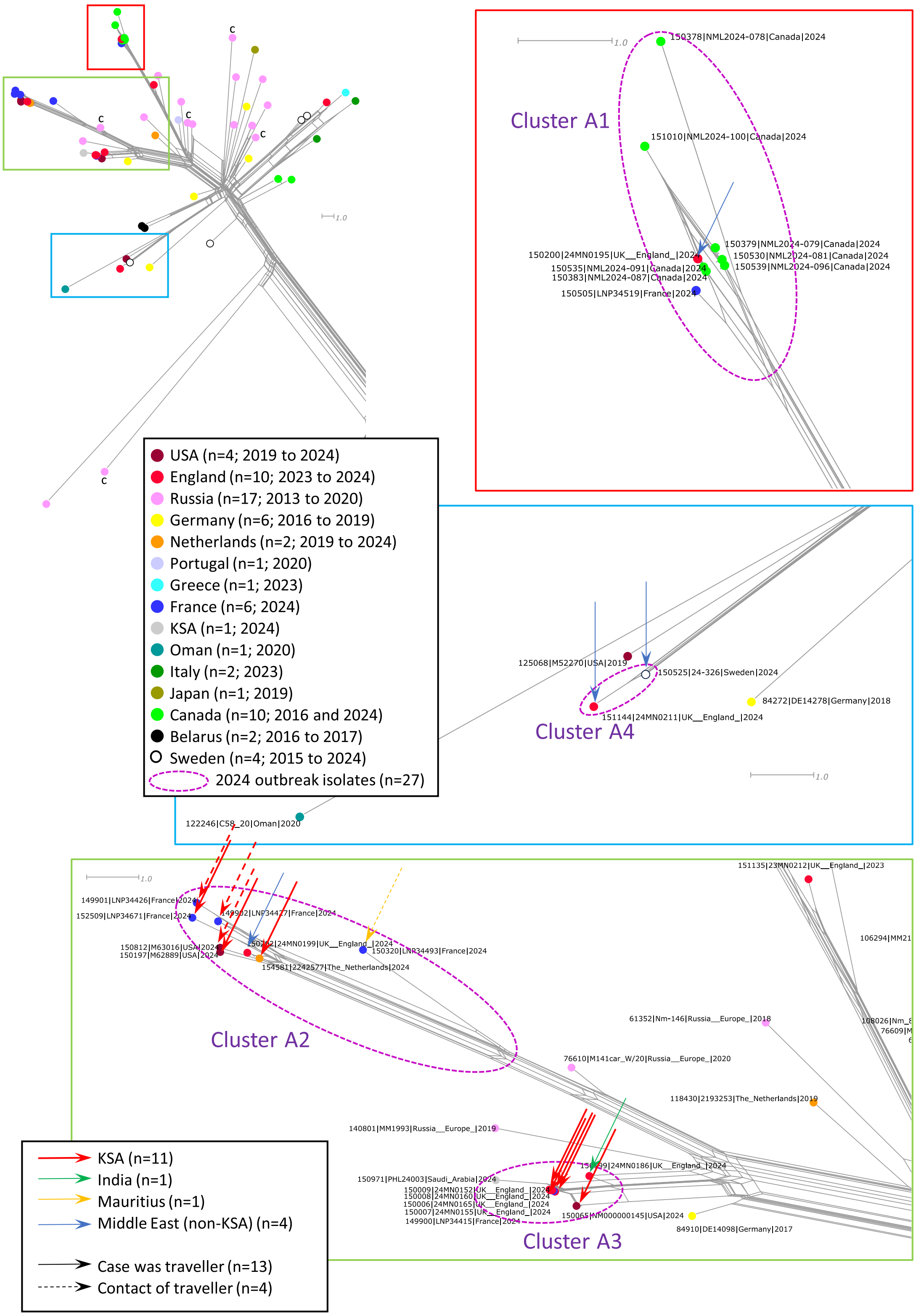

Fig. 4. Population structure of MenW:cc11 Hajj strain sublineage 'strain A′ highlighting clusters of isolates from 2024 and associated travel. Scale bars indicate distance in terms of the number of different loci (out of 1422 core genome loci compared). All but five isolates were from invasive disease. Carrier isolates are denoted by 'c′.

are proposed: i) reduced exposure to carried meningococci due to COVID 19-related social restrictions may have led to a reduction in natural immunity and a population immune deficit[24]; (ii) reduced travel and MenACWY vaccination among would-be pilgrims during the pandemic may have led to a reduction in herd protection and, subsequently, increased transmission in local countries and during pilgrimage,[24] (iii) Cases in individual's that had previously postponed their pilgrimage due to the pandemic may have 'caught up', en masse, having been delayed until the pilgrimage was taken (i.e. cases that might have occurred during the pandemic years were all occurring once the pilgrimage restarted); (iv) The increased pilgrim numbers during Ramadan likely facilitated increased transmission

Table 7
Geo-temporal distribution of W:cc11 Hajj strain sublineage ‘strain A′ isolates.

Country	2013	2015	2016	2017	2018	2019	2020	2023	2024	Total
Asia			**1**			**1**	**2**			**4**
Japan						1				1
Russia			1				2			3
Middle East							**1**		**1**	**2**
Oman							1			1
Saudi Arabia									1	1
Europe		**1**	**2**	**2**	**3**	**2**	**1**	**7**	**17**	**35**
Belarus			1	1						2
France									6	6
Germany			1	1	3	1				6
Greece								1		1
Italy								2		2
Portugal							1			1
Sweden		1						2	2	5
The Netherlands						1			1	2
England								2	8	10
Russia	1	1			3	3	6			14
North America			**3**			**1**			**10**	**14**
Canada			3						7	10
USA						1			3	4
Total	**1**	**2**	**6**	**2**	**6**	**7**	**10**	**7**	**28**	**69**

Twenty-eight strain A isolates (41%), from 27 patients, were collected in 2024. These were collected in England (n=8), Canada (n=7), France (n=6), the USA (n=3), Sweden (n=2; both from the same patient), the Netherlands (n=1), and Saudi Arabia (n=1). The strain A isolates from 2024 exclusively grouped into four distinct clusters (clusters A1 to A4) (Fig. 4). Clusters A2 and A3 shared a common clade but were separated by isolates from previous years.

and disease[6]; and (v) The global military situation, with ongoing conflicts in Eastern Europe, Africa and the Middle East, for example, may have helped mobilise an endemic strain e.g. by propagation on the front lines or movement of refugees. A 2016 carriage study among Russian military recruits, for example, found an increase in MenW carriage from 9% to 58% in the first 60 days following arrival at military academy.[25] Unfortunately, genomes were not available for those meningococci to allow comparison.

A major concern from early in the ‘outbreak’ was the forthcoming Hajj pilgrimage in early June and the potential for a much larger outbreak, given the average attendance of ~2 million over a period of just six days. MenACWY vaccination is a condition for pilgrims to travel to KSA for both Hajj and Umrah. However, enforcement tends to be weaker for Umrah as pilgrims may travel on tourist visas, for example, that do not have the same MenACWY vaccine requirements.[6] This is reflected by the lack of vaccination among the existing cases. Nonetheless, no further clusters or outbreaks materialised during or immediately following Hajj, suggesting that vaccine compliance was high, perhaps in part due to the alerts and communications between local, regional, and national health authorities. In early 2025, a requirement for airlines to ensure that pilgrims attending Umrah were vaccinated was briefly implemented, but then withdrawn owing to limited availability of vaccines in some countries.[6] Cases observed among non-pilgrims raise the prospect of recommending vaccination for all travellers and not just pilgrims.

It is unclear why the predominantly African Burkina Faso/North Africa strains and strains B and C contained several ‘Western-specific’ clades with small country-specific clusters. The corresponding cases were sometimes too temporally distinct to constitute outbreaks and yet there was no evidence of these strains having become endemic in the respective countries.

It is also unclear why strains of the Hajj strain sublineage have been unable to gain a foothold to become endemic in Europe/North America, either during the original Hajj outbreaks of 2000/2001, or the multiple other introductions that have since occurred.[23] The closely-related South American strain, meanwhile, spread from South America to the UK and quickly became endemic throughout much of Western Europe, Australasia and Canada. The serogroup A strains that caused massive epidemics in sub-Saharan Africa prior to the introduction of MenAfriVac, like strain A, caused very few sporadic imported cases in Western countries.[26]

A key limitation of the study is the variable availability of country-specific meningococcal genomes, ranging from highly curated country-specific genome libraries with a single genome each for all culture-confirmed cases, to no genomes at all. There can be confidence that e.g. strain A is non-endemic to any of the well-sampled countries, several of which also have large collections of genomes from carriage studies, but not the other countries. Thus, many countries may be the unknown source of the strain A. Although several Middle Eastern countries are not well sampled, the timing and extent of the outbreak suggest the strain is unlikely to be endemic in the region.

In addition to identifying the various strains/sub-strains related to 2024 cases, the current study provides a benchmark against which to compare strains in future outbreaks. It emphasises the need for strong enforcement of vaccination for all pilgrims and continued vigilance for possible outbreaks relating to travel and mass gathering events such as Umrah and Hajj.[27] It also highlights the gaps in the global genomic surveillance of IMD that will hopefully be closed with initiatives like the WHO roadmap for defeating meningitis by 2030[28] and the Global Meningococcal Genome Partnership.[29]

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The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the CDC.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JL, AL, SAC, LW, LlW, XB, and RB perform contract work on behalf of UKHSA for GSK, PATH, Pfizer and Sanofi. SNL performs contract work on behalf of St. George's University of London for vaccine manufacturers. The Immunisation and Vaccine Preventable Diseases Division at UKHSA (authors EJH, HC, SR and SNL) has provided vaccine manufacturers with post-marketing surveillance reports on meningococcal, *Haemophilus influenzae*, and pneumococcal infections, which the companies are required to submit to the UK Licensing Authority in compliance with their risk management strategy. A cost recovery charge is made for these reports. M-K. Taha performs contract work for the Institut Pasteur funded by GSK, Pfizer and Sanofi and has a patent NZ630133A Patent with GSK "Vaccines for serogroup X meningococcus" issued. AD, SS, CM, LE, PM, HCl, NMvS, CB, PBL, RSWT, DAC, PS, AN, GT, TTL, BRW, VW, RLH, JN, AR, MV, LAM, declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2025.106558.

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