

THE LANCET

Infectious Diseases

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: MacLennan JM, Rodrigues CMC, Bratcher HB, et al. Meningococcal carriage in periods of high and low invasive meningococcal disease incidence in the UK: comparison of UKMenCar1–4 cross-sectional survey results. *Lancet Infect Dis* 2021; published online Jan 19. [https://doi.org/10.1016/S1473-3099\(20\)30842-2](https://doi.org/10.1016/S1473-3099(20)30842-2).

Supplementary data

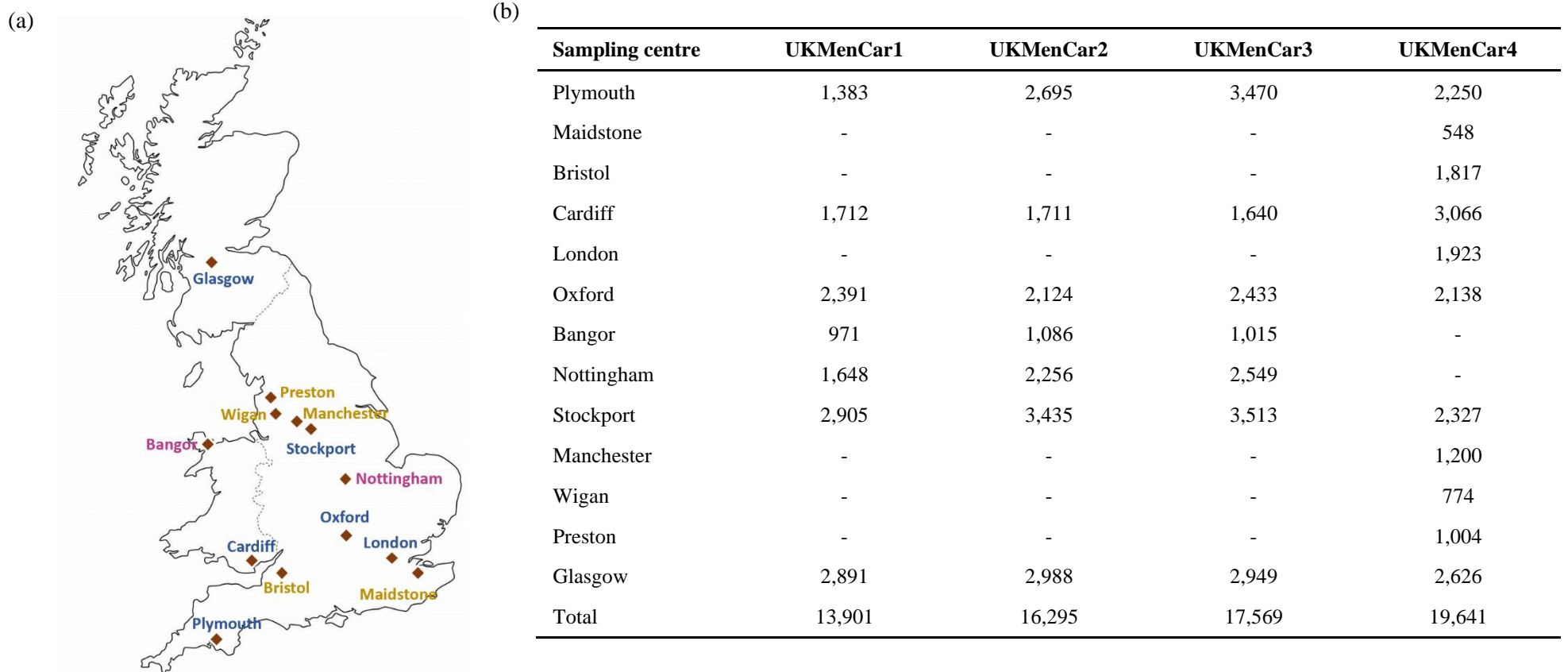


Figure 6 Geographical representation of the UKMenCar survey sampling centres (a) For UKMenCar1 (n=13,901), 2 (n=16,295) and 3 (n=17,569) eight centres participated, those coloured pink and blue. For UKMenCar4 (n=19,641) there were eleven sampling centres that took part, those coloured blue and gold. The six centres in blue took part in all four surveys. (b) The number of participants swabs included in the analysis from each sampling centre for the four carriage studies. Cultures from London were not available for analysis for UKMenCar1-3 due to technical issues^{9,12}.

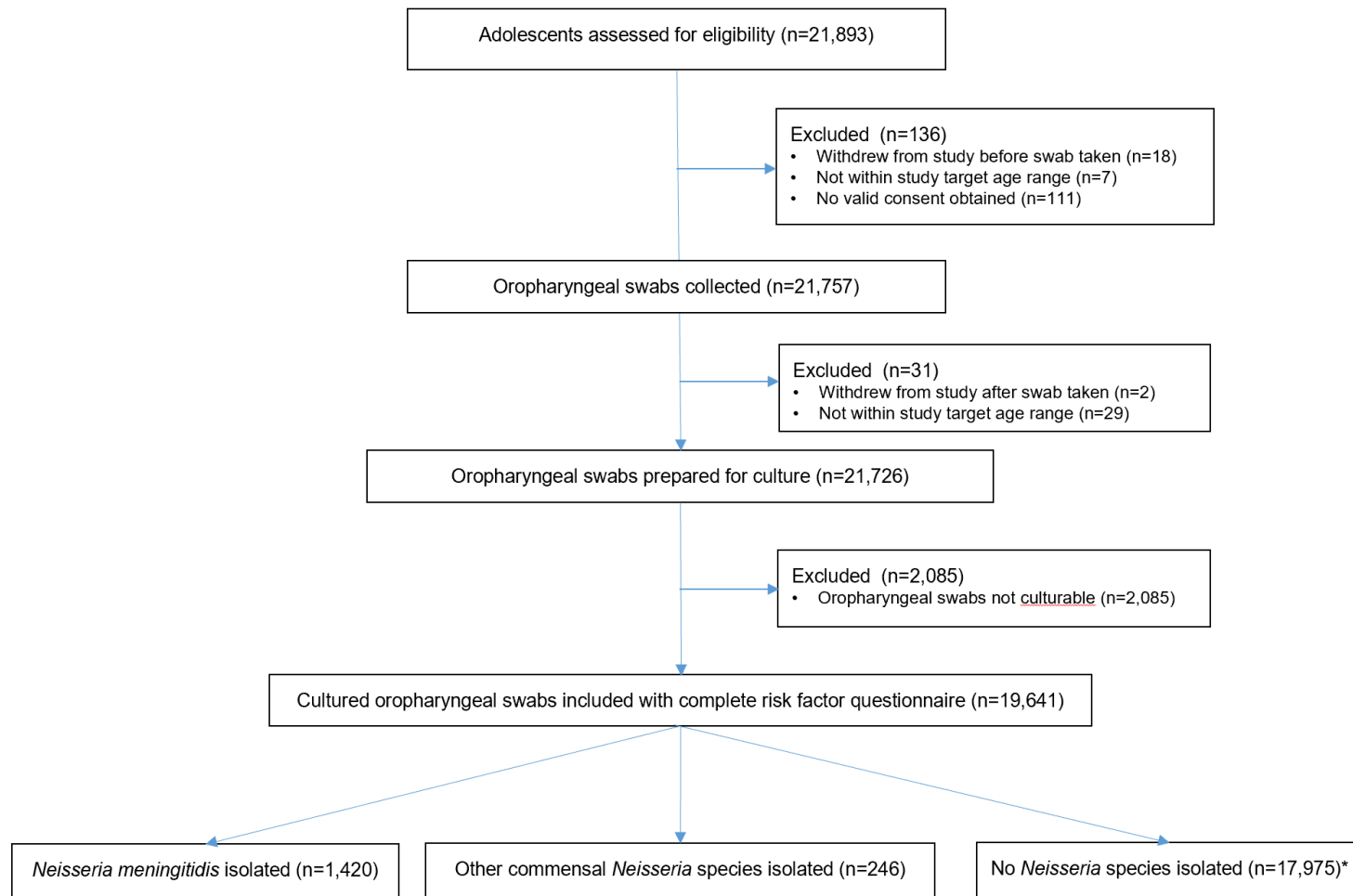
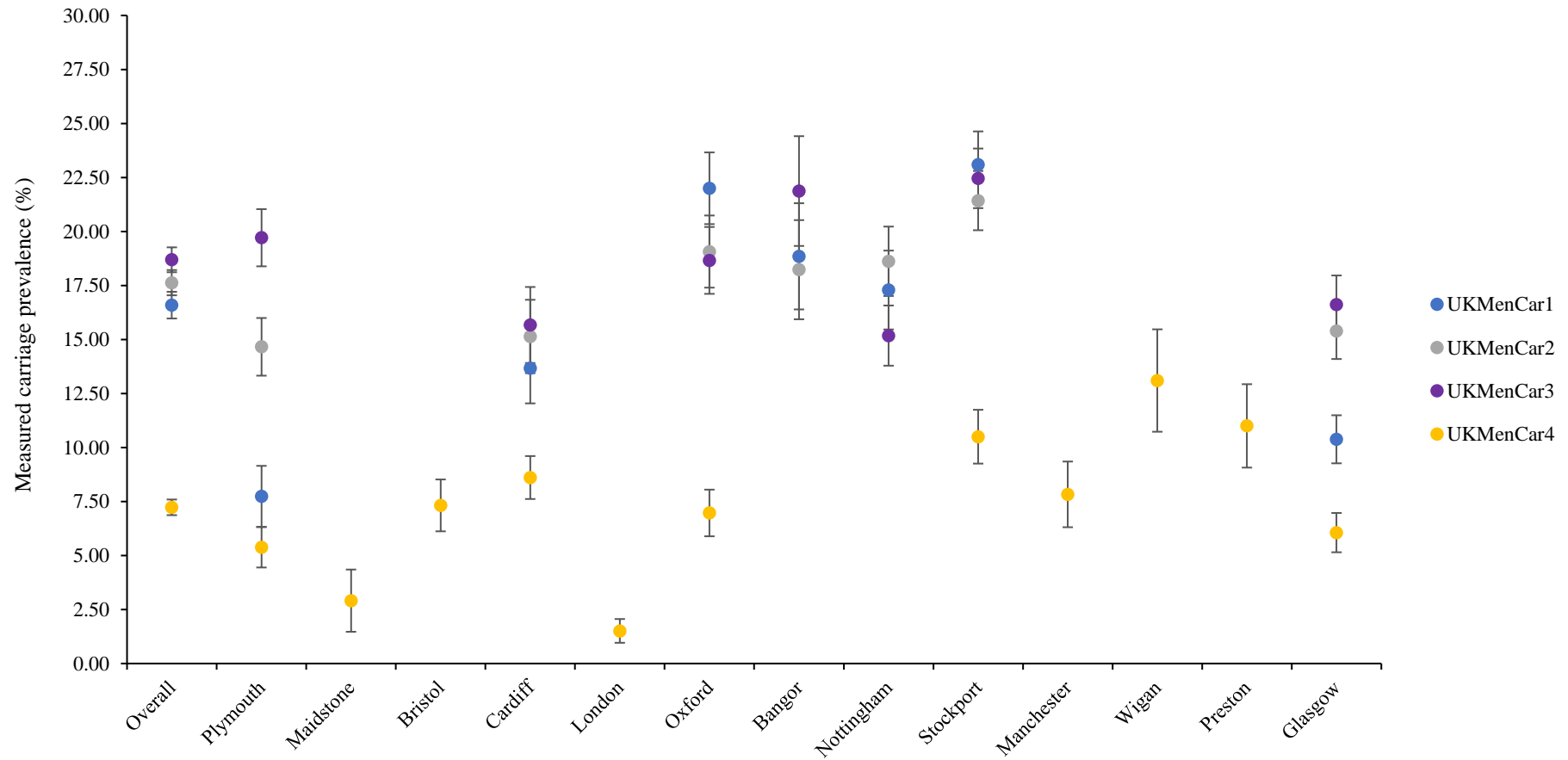


Figure 7 UKMenCar4 survey profile Adolescents aged 15-19 years old were recruited from eleven UK sampling centres, with the aim of recruiting 18,000 participants to adequately power the study for the detection of rare variants. There were 21,893 adolescents assessed for eligibility and 19,641 participants were included in the final analysis of meningococcal carriage and risk factor participation.

Table 2 Carriage prevalence by sampling site for UKMenCar1-4 studies For each study centre (shown geographically south to north of the UK), the number of carriage isolates is shown (n/N) and the carriage point prevalence for each of the centres participating in all four UKMenCar surveys, compared to the overall carriage prevalence. Eight centres took part in the UKMenCar1-3 surveys and eleven centres in UKMenCar4, though isolates from London were not included in the UKMenCar1-3 analysis due to technical issues^{9,12}. The number of participants recruited at each sampling centre is in Figure 6 supplementary.

	UKMenCar1		UKMenCar2		UKMenCar3		UKMenCar4	
	n/N	%	n/N	%	n/N	%	n/N	%
Overall	2,306/13,901	16.59	2,873/16,295	17.63	3,283/17,569	18.69	1,420/19,641	7.23
Plymouth	107/1,383	7.74	395/2,695	14.66	684/3,470	19.71	121/2,250	5.38
Maidstone	-	-	-	-	-	-	16/548	2.91
Bristol	-	-	-	-	-	-	133/1,817	7.32
Cardiff	234/1,712	13.67	259/1,711	15.14	257/1,640	15.67	264/3,066	8.61
London	-	-	-	-	-	-	29/1,923	1.51
Oxford	526/2,391	22.00	405/2,124	19.07	454/2,433	18.66	149/2,138	6.97
Bangor	183/971	18.85	198/1,086	18.23	222/1,015	21.87		
Nottingham	285/1,648	17.29	420/2,256	18.62	387/2,549	15.18		
Stockport	671/2,905	23.10	736/3,435	21.43	789/3,513	22.46	244/2,327	10.5
Manchester	-	-	-	-	-	-	94/1,200	7.83
Wigan	-	-	-	-	-	-	101/774	13.1
Preston	-	-	-	-	-	-	110/1,004	11.0
Glasgow	300/2,891	10.38	460/2,988	15.39	490/2,949	16.62	159/2,626	6.06

Figure 8 Carriage prevalence by sampling site for UKMenCar1-4 studies For each study centre (shown geographically south to north of the UK), the carriage point prevalence is shown with 95% confidence intervals for each of the centres participating in all four UKMenCar surveys, compared to the overall carriage prevalence. Eight centres took part in the UKMenCar1-3 surveys and eleven centres in UKMenCar4, though isolates from London were not included in the UKMenCar1-3 analysis due to technical issues^{9,12}. The number of participants recruited at each sampling centre is in Figure 6 supplementary.



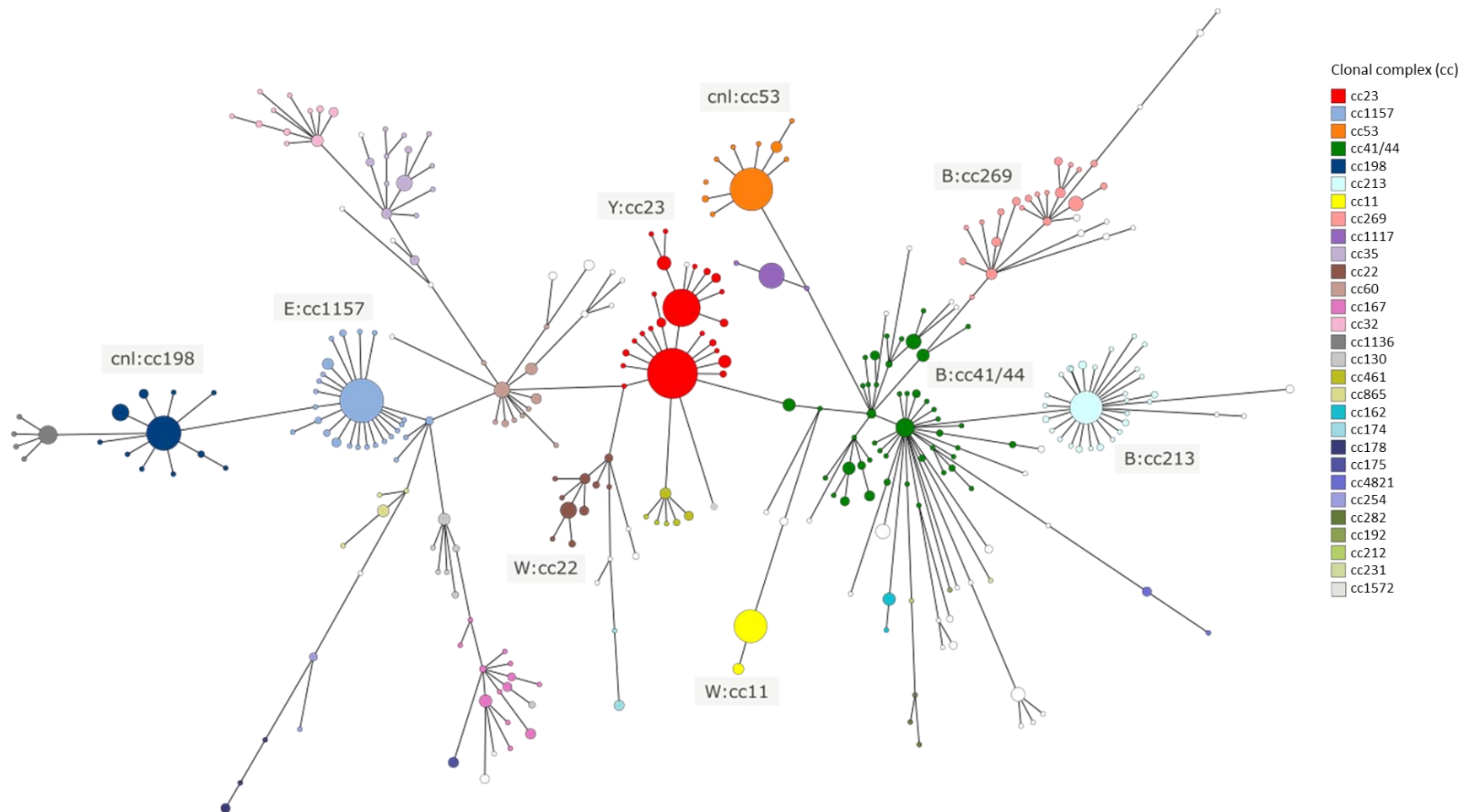


Figure 9 Minimum-spanning tree of carriage *Neisseria meningitidis* genomes from UK adolescents in 2014/15. All 1,420 meningococcal carriage isolates from 2014/15 were analysed using seven locus multilocus sequence typing (MLST) and the relationships among clonal complexes (ccs) are visualised using GrapeTree software. Different ccs are shown by colour, unfilled nodes represent incomplete MLST profiles, and the size of the circles is proportional to the number of isolates. Predominant genogroups are shown in grey boxes with their associated clonal complexes.

Table 3 Demographic information about UKMenCar4 survey participants. Detailed breakdown of participant demographics shown by number of oropharyngeal swabs cultured (n=19,641), those with meningococcal carriage (n=1,420) and those with other *Neisseria* species identified (n=246). Weighted proportion represents the carriage (%) by demographic stratum. UKMenCar4 surveyed 1.74% of the UK birth cohort for 2014 and 2015. The self-reported ethnicity of participants was broadly similar to UK population estimates for ethnic group for 2014-16: White British 78.7%; Asian/Asian British 8.0%; Black/African/Caribbean/Black British 3.5%; Mixed/Multiple ethnic groups 1.8%; Other ethnic group 1.9%.

(<https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/articles/researchreportonpopulationestimatesbyethnicgroupandreligion/2019-12-04#population-estimates-by-ethnic-group>)

	Oropharyngeal swabs cultured (n=19,641) No. (%)	Confirmed <i>Neisseria meningitidis</i> (n=1,420)			Confirmed other <i>Neisseria</i> species (n=246)		
		No. (%)	% weighted proportion	% carriage prevalence	No. (%)	% weighted proportion	% carriage prevalence
Age (years)							
15	380 (1.93)	15 (1.06)	3.95	0.08	5 (2.03)	1.32	0.03
16	6,287 (32.01)	379 (26.69)	6.03	1.93	82 (33.33)	1.30	0.42
17	8,667 (44.13)	618 (43.52)	7.13	3.15	107 (43.50)	1.23	0.54
18	3,628 (18.47)	345 (24.30)	9.51	1.76	46 (18.70)	1.27	0.23
19	679 (3.46)	63 (4.44)	9.28	0.32	6 (2.44)	0.88	0.03
Gender							
Male	8,242 (41.96)	689 (48.52)	8.36	3.51	85 (34.55)	1.03	0.43
Female	11,332 (57.70)	725 (51.06)	6.49	3.69	161 (65.45)	1.42	0.82
Not stated	67 (0.34)	6 (0.42)	8.96	0.03	0 (0.00)	0.00	0.00
School/College year							
12	10,624 (54.09)	615 (43.31)	5.79	3.13	130 (52.85)	1.22	0.66
13	7,424 (37.80)	668 (47.04)	9.00	3.40	97 (39.43)	1.31	0.49
Not in formal education	47 (0.24)	8 (0.56)	17.02	0.04	0 (0.00)	0.00	0.00
Other	1,431 (7.29)	118 (8.31)	8.25	0.60	19 (7.72)	1.33	0.10
Not stated	115 (0.59)	11 (0.77)	9.57	0.06	0 (0.00)	0.00	0.00
Ethnicity							
White	15,881 (80.86)	1,286 (90.56)	8.10	6.55	197 (80.08)	1.24	1.00
Asian descent	1,877 (9.56)	68 (4.79)	3.62	0.35	26 (10.57)	1.39	0.13
Black decent	875 (4.45)	20 (1.41)	2.29	0.10	9 (3.66)	1.03	0.05
Mixed ethnicity	634 (3.23)	36 (2.54)	5.68	0.18	11 (4.47)	1.74	0.06
Other ethnic group	336 (1.71)	9 (0.63)	2.68	0.05	3 (1.22)	0.89	0.02
Not stated	38 (0.19)	1 (0.07)	2.63	0.01	0 (0.00)	0.00	0.00

Table 4 Odds ratio for carriage by age for UKMenCar1 and UKMenCar4 The odds ratio is calculated with 95% confidence intervals (CI) for each age group in the survey with n=13,901 participants in UKMenCar1 (1999) and n=19,641 participants in UKMenCar4 (2014/15).

Age	OR for carriage 1999	95% CI 1999	OR for carriage 2014/15	95% CI 2014/15
15	1		1	
16	1.35	1.09-1.67	1.56	0.92-2.64
17	1.82	1.47-2.25	1.87	1.11-3.15
18/19	2.41	1.90-3.05	2.55	1.50-4.31

Table 5 Demographic information about UKMenCar1-3 survey participants. Detailed breakdown of participant demographics is shown for the UKMenCar1-3 studies performed in 1999, 2000 and 2001 respectively. The number of oropharyngeal swabs cultured (1999 n=13,901, 2000 n=16,295, 2001 n=17,569), those with meningococcal carriage (1999 n=2,306, 2000 n=2,873, 2001 n=3,283). Data regarding ethnicity was not collected for UKMenCar1-3.

	UKMenCar1 (1999)			UKMenCar2 (2000)			UKMenCar3 (2001)		
	Oropharyngeal swabs cultured (n=13,901) No. (%)	Confirmed <i>Neisseria meningitidis</i> (n=2,306) No. (%)	% carriage prevalence	Oropharyngeal swabs cultured (n=16,295) No. (%)	Confirmed <i>Neisseria meningitidis</i> (n=2,873) No. (%)	% carriage prevalence	Oropharyngeal swabs cultured (n=17,569) No. (%)	Confirmed <i>Neisseria meningitidis</i> (n=3,283) No. (%)	% carriage prevalence
Age (years)									
15	959 (6.90)	105 (4.55)	0.76	582 (3.57)	88 (3.06)	0.54	524 (2.99)	89 (2.71)	0.51
16	5,835 (41.98)	832 (36.08)	5.99	7,416 (45.51)	1,143 (39.78)	7.01	8,138 (46.32)	1,380 (42.03)	7.85
17	5,584 (40.17)	1,020 (44.23)	7.34	6,182 (37.94)	1,191 (41.45)	7.31	7,035 (40.04)	1,367 (41.64)	7.78
18	1,350 (9.71)	301 (13.05)	2.17	1,788 (10.97)	380 (13.23)	2.33	1,682 (9.57)	396 (12.06)	2.25
19	173 (1.24)	48 (2.08)	0.35	327 (2.01)	71 (2.47)	0.44	190 (1.08)	51 (1.55)	0.29
Gender									
Male	6,862 (49.36)	1,165 (50.52)	8.38	7,680 (47.13)	1,310 (45.60)	8.04	8,322 (47.37)	1,546 (47.09)	8.80
Female	7,039 (50.64)	1,141 (49.48)	8.21	8,614 (52.86)	1,563 (54.40)	9.59	9,247 (52.63)	1,737 (52.91)	9.89
Not stated	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.01)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
School/College year									
12	7,257 (52.20)	1,090 (47.27)	7.84	9,657 (59.26)	1,527 (53.15)	9.37	10,259 (58.39)	1,787 (54.43)	10.17
13	4,856 (34.93)	880 (38.16)	6.33	5,475 (33.60)	1,122 (39.05)	6.89	6,309 (35.91)	1,274 (38.81)	7.25
Other	1,680 (12.09)	308 (13.36)	2.22	1,064 (6.53)	203 (7.07)	1.25	894 (5.09)	204 (6.21)	1.16
Not stated	108 (0.78)	28 (1.21)	0.20	99 (0.61)	21 (0.73)	0.13	107 (0.61)	18 (0.55)	0.10
Ethnicity	Data not collected in UKMenCar1-3 survey questionnaires								

Table 6 Measured carriage prevalence for UKMenCar1-4 surveys. The measured carriage prevalence by genogroup and by year for all UKMenCar surveys, shown as proportion and 95% confidence interval (95% CI) of meningococcal carriage (1999 n=2,306, 2000 n=2,873, 2001 n=3,283, 2014/15 n=1,420) from oropharyngeal swabs cultured (1999 n=13,901, 2000 n=16,295, 2001 n=17,569, 2014/15 n=19,641).

	UKMenCar1 (n=13,901) No. (% , 95% CI)	UKMenCar2 (n=16,295) No. (% , 95% CI)	UKMenCar3 (n=17,569) No. (% , 95% CI)	UKMenCar4 (n=19,641) No. (% , 95% CI)
B	785 (5.65, 5.28-6.04)	994 (6.10, 5.74-6.48)	1,180 (6.72, 6.36-7.10)	346 (1.76, 1.58-1.96)
C	139 (1.00, 0.85-1.18)	92 (0.56, 0.46-0.69)	91 (0.52, 0.42-0.64)	11 (0.06, 0.03-0.10)
W	242 (1.74, 1.54-1.97)	379 (2.33, 2.11-2.57)	414 (2.36, 2.14-2.59)	99 (0.50, 0.41-0.61)
Y	239 (1.72, 1.52-1.95)	300 (1.84, 1.65-2.06)	328 (1.87, 1.68-2.08)	349 (1.78, 1.60-1.97)

Table 7 Relative carriage prevalence for UKMenCar1-4 surveys by clonal complex. The relative carriage prevalence is shown for the nine most frequently occurring clonal complexes of meningococci in UKMenCar4 (2014/15) as proportions of all meningococci isolated per survey. The total meningococci isolated in each carriage survey: 1999 n=2,306, 2000 n=2,873, 2001 n=3,283, 2014/15 n=1,420 from oropharyngeal swabs cultured (1999 n=13,901, 2000 n=16,295, 2001 n=17,569, 2014/15 n=19,641).

	1999 (n=13,901) No. (%)	2000 (n=16,295) No. (%)	2001 (n=17,569) No. (%)	2014/15 (n=19,641) No. (%)	Rate ratio 2014/15:1999 (95% CI)	Rate ratio 2014/15:2001 (95% CI)	p value for 2014/15:2001
Total meningococci	2,306 (16.6)	2,873 (17.6)	3,283 (18.7)	1,420 (7.2)	0.44 (0.41-0.46)	0.39 (0.36-0.41)	<2.2x10⁻¹⁶
Clonal complexes							
cc23	91 (3.95)	106 (3.69)	154 (4.69)	301 (21.20)	5.37 (4.29-6.73)	4.52 (3.76-5.43)	<2.2x10 ⁻¹⁶
cc1157	106 (4.60)	152 (5.29)	191 (5.82)	156 (10.99)	2.39 (1.88-3.03)	1.89 (1.54-2.31)	1.4x10 ⁻⁸
cc53	191 (8.28)	264 (9.19)	342 (10.42)	128 (9.01)	1.09 (0.88-1.35)	0.87 (0.71-1.05)	0.200
cc41/44	349 (15.13)	389 (13.54)	425 (12.95)	116 (8.17)	0.54 (0.44-0.66)	0.63 (0.52-0.77)	2.8x10 ⁻⁵
cc213	153 (6.63)	305 (10.62)	348 (10.60)	101 (7.11)	1.07 (0.84-1.37)	0.67 (0.54-0.83)	0.00077
cc198	87 (3.77)	109 (3.79)	148 (4.51)	100 (7.04)	1.87 (1.41-2.47)	1.56 (1.22-2.00)	0.0010
cc11	43 (1.86)	26 (0.90)	12 (0.37)	73 (5.14)	2.76 (1.90-4.00)	14.06 (7.66-25.82)	<2.2x10 ⁻¹⁶
cc269	88 (3.82)	114 (3.97)	165 (5.03)	52 (3.66)	0.96 (0.69-1.34)	0.73 (0.54-0.99)	0.060
cc22	272 (11.80)	407 (14.17)	430 (13.10)	33 (2.32)	0.20 (0.14-0.28)	0.18 (0.13-0.25)	2.2x10 ⁻¹⁶

Q9 How many people usually sleep in the same bedroom as yourself

1 (myself only) 2 3 or more

Q 10 Have you ever been given a vaccination against meningococcal meningitis in the last 5 years?

Yes No

Q 11 Are you **currently** taking or recently stopped taking antibiotics?

Yes stopped in stopped in not taken
currently taking last week last month in past month

Q 12 How many cigarettes do you smoke in a typical day?

None 1-5 6-10 11-20 21 or more

Q 13 Does any **other** person in your house smoke cigarettes?

Do not include yourself yes no

Q 14 How many days in the last week have you visited a pub or night club?

never 1 2 3 4 5 6 7

Q 15 How many people have you kissed in the last week (*snogged* tongues, wet, **only**)? Not just on lips or cheeks.

none 1 2 3 4 5 or more

Thank you for completing the questionnaire.

(b)

UK Meningococcal Carriage Study

LABEL

Today's Date 20 Name of School

Day month year

**** This information is completely confidential. It will not be seen by school staff or other students. ****

Q1 What is your current age in years? 15 16 17 18 19

Q2 I am: male female

Q3 What is your home postcode?

Q4 Which school year are you in? Year 12 Year 13 Other **Not in full time**
Lower Sixth Upper Sixth e.g. part time education college

Q5 Do you currently have a cold or sore throat? NO YES

Q6 Are you currently taking or have you recently stopped taking antibiotics?
not taken in the past month stopped in the last month stopped in the last week yes, currently taking

Q7 How many cigarettes do you smoke in a typical day?
0 1-5 6-10 11-20 more than 20

Q8 How many times have you smoked an e-cigarette in the last week?
0 1-2 3-6 7 or more

Q9 How many times have you smoked a waterpipe (shisha, hookah, hubbly bubbly) in the last month?
0 1 2 3-4 5 or more

Q10 Does any other person at home smoke cigarettes? NO YES, outside the house
YES, inside the house

Q11 How many days in the last week have you been to a party, pub, bar or night club?
0 1 2-3 4-5 6-7

Q12 How many people have you kissed (kissing with tongues, not just lips or cheeks) in the last week?
0 1 2-3 4 or more

Q13a Do you have a regular girlfriend or boyfriend? NO YES

Q13b If YES: do they smoke cigarettes? NO YES
do they smoke shisha? NO YES

Q14 What is your ethnic group?
White Asian/Asian British Black/African/Caribbean/Black British
Mixed/multiple ethnic Other ethnic group

Thank you for completing this questionnaire

UKMENCAR4 Questionnaire v1.2 11/08/14; REC REF 14/SC/1163

Figure 10 Risk factor questionnaires. The questionnaires were completed by participants of: (a) UKMenCar1-3 studies (1999, 2000, 2001) and (b) UKMenCar4 (2014/15) carriage surveys.