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Original article

Impact of meningococcal ACWY conjugate vaccines on pharyngeal carriage in adolescents: evidence for herd protection from the UK MenACWY programme

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ABSTRACT

Objective: Serogroup W and Y invasive meningococcal disease increased globally from 2000 onwards. Responding to a rapid increase in serogroup W clonal complex 11 (W:cc11) invasive meningococcal disease, the UK replaced an adolescent booster dose of meningococcal C conjugate vaccine with

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quadrivalent MenACWY conjugate vaccine in 2015. By 2018, the vaccine coverage in the eligible school cohorts aged 14 to 19 years was 84%. We assessed the impact of the MenACWY vaccination programme on meningococcal carriage.

Methods: An observational study of culture-defined oropharyngeal meningococcal carriage prevalence before and after the start of the MenACWY vaccination programme in UK school students, aged 15 to 19 years, using two cross-sectional studies: 2014 to 2015 "UKMenCar4" and 2018 "Be on the TEAM" (ISRCTN75858406).

Results: A total of 10 625 participants preimplementation and 13 438 postimplementation were included. Carriage of genogroups C, W, and Y (combined) decreased from 2.03 to 0.71% (OR 0.34 [95% CI 0.27–0.44], p < 0.001). Carriage of genogroup B meningococci did not change (1.26% vs 1.23% [95% CI 0.77 −1.22], p = 0.80) and genogroup C remained rare (n = 7/10 625 vs 17/13 438, p = 0.135). The proportion of serogroup positive isolates (i.e. those expressing capsule) decreased for genogroup W by 53.8% (95% CI -5.0 − 79.8, p = 0.016) and for genogroup Y by 30.1% (95% CI 8.946·3, p = 0.0025).

Discussion: The UK MenACWY vaccination programme reduced carriage acquisition of genogroup and serogroup Y and W meningococci and sustained low levels of genogroup C carriage. These data support the use of quadrivalent MenACWY conjugate vaccine for indirect (herd) protection. **Jeremy P. Carr, Clin Microbiol Infect 2022;28:1649.e1–1649.e8**

Introduction

During the first two decades of the 21st century, serogroup W invasive meningococcal disease (IMD) increased globally. Previously confined to small local outbreaks, serogroup W expanded from 2 to 40% of IMD in the UK between 2008 and 2015 (Fig. 1) [1]. Serogroup Y IMD also increased, albeit with lower prevalence than serogroup W IMD and predominantly affecting the elderly [2]. These changes led to some countries introducing the quadrivalent protein-conjugate (MenACWY) vaccine [1,2]. The licensed MenACWY conjugate vaccines were anticipated, but not robustly demonstrated, to induce herd protection. Large-scale carriage studies accompanying the introduction of the monovalent Meningococcal C conjugate (MCC, 1999) and the serogroup A conjugate (MenAfriVac, 2011) vaccines demonstrated strong herd protective effect by reducing carriage acquisition of the targeted serogroup [3–5]. However, in early studies MenACWY immunogenicity against serogroup C was reduced when compared with the monovalent MCC [6]. A recent systematic review concluded that there was a lack of evidence supporting herd protective effects from multivalent MenACWY vaccines [7].

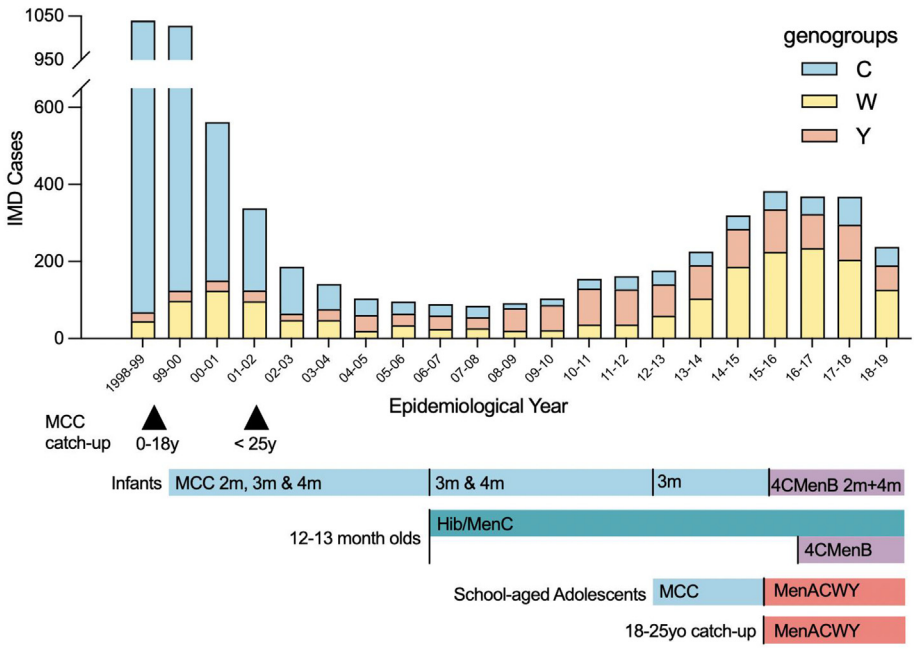

Fig. 1. Meningococcal vaccine schedule and invasive meningococcal disease due to genogroups C, W, or Y in England & Wales 1998–-2018 by epidemiological year. MCC single-dose catch-up given in 1999 aged 0 to 18 years and an expanded in 2002 to <25 years old who were unvaccinated. Infant MCC ceased in July 2016. Adolescent vaccines given in schools at 13–14 years old. MenACWY commenced in schools in 2015, with a staggered catch-up over 1 year (Scotland) and 3 years (England, Wales) to vaccinate all those aged 14 to 18 years. A community/general practitioner catch-up programme was implemented for school leavers aged ≤25, but uptake was low. IMD, invasive meningococcal disease (culture and/or PCR confirmed, data collected by Public Health England, Meningococcal Reference Unit); m, months; MCC, meningococcal C conjugate vaccine; MenACWY, quadrivalent meningococcal serogroup ACWY polysaccharide conjugate vaccine; Hib-MenC, Haemophilus influenzae type B & meningococcal C conjugate vaccine; 4CMenB, sub-capsular protein surrogate meningococcal B vaccine (Bexsero, GSK) introduced Sep 2015.

The absence of large-scale carriage studies represented an important evidence gap and this uncertainty affected the immunization programmes introduced. For example, Chile introduced an infant-only programme providing direct protection to the age group at highest risk of IMD [8], whereas the United Kingdom targeted adolescents as the age-group with both a 'peak' in IMD incidence and the highest asymptomatic pharyngeal carriage rates. This strategy aimed to interrupt transmission and provide protection to unvaccinated age groups [9].

The UK MenACWY programme was implemented in 2015 using MenACWY-TT (Nimenrix, Pfizer) and MenACWY-CRM_{197} (Menveo, GSK) vaccines (Fig. 1) to replace the MCC school booster given at 13 to 14 years of age [10]. In England, there was a phased rollout over 3 years, with a school-based catch-up programme and a general practitioner–based programme ≤25 years of age. In Scotland, vaccination was delivered in schools within 1 year. In Wales, the catch-up programme was delivered in school and primary care over 2 years. By mid-2018, MenACWY vaccine school-based coverage in England, Wales, and Scotland was 84%, ranging from 71 to 86% in each year cohort between 14 to 19 years of age [11,12]. Vaccination coverage in the cohort aged 20 to 25 years was significantly lower; for example, in England it was 35 to 39%. The MenACWY vaccine was not introduced for any other age group. An infant-only '2 + 1' schedule of 4CMenB (Bexsero, GSK) commenced in September 2015 [13], which was not anticipated to impact on meningococcal carriage [14].

The UK Meningococcal Carriage (UKMenCar1-4) surveys demonstrated the impact of herd protection from the MCC vaccine and highlighted behaviours that increase the risk of meningococcal carriage and transmission [4,15,16]. UKMenCar4 was conducted in 2014 and 2015 just prior to the introduction of the MenACWY vaccination programme. The subsequent 'Be on the TEAM (Teenagers Against Meningitis)' study (ISRCTN75858406) commenced in 2018 using compatible methods. Here we report the impact of the MenACWY campaign on meningococcal carriage in adolescents using these two studies.

Methods

Study design and sample population

We compared two cross-sectional oropharyngeal carriage surveys of adolescents, taken before (UKMenCar4, September 2014 to March 2015) [15] and after ('Be on the TEAM', March to November 2018) [17] MenACWY vaccine introduction. The participants were aged 15 to 19 years attending their penultimate year of school or college. Both studies were done by the same research network with participants recruited in schools across multiple sites in England, Wales, and Scotland. The characteristics of included schools reflected the diversity of educational settings across the community [15]. The 2018 cohort was eligible for MenACWY vaccination 2 to 3 years prior [18], whereas those sampled in 2014 and 2015 were eligible for the adolescent MCC vaccine. This study was approved by the NHS Research Ethics Committee (UKMenCar4 reference 14/SC/1163, Be on the TEAM reference 18/SC/0055). The study protocols have been previously published [17,19] and the 'Be on the TEAM' protocol is publicly available at beontheteam.web.ox.ac.uk.

Sampling collection & laboratory methods

The methods were compatible between the two surveys. After standard informed consent, participants completed a meningococcal carriage risk factor questionnaire [15,17]. Oropharyngeal swab samples were taken using a standardized collection technique. The swab samples were either directly plated (in some sites in 2014/15) or placed in STGG (skim milk, tryptone, glucose, glycerol) broth and frozen at −80°C within 4 hours of collection [15]. After rethawing, swab samples were incubated on GC-VCAT (vancomycin, colistin amphotericin B, trimethoprim; ThermoFisher Scientific, Basingstoke, UK) at 37°C with 5% CO_2 for ≤48 hours. Putative *Neisseria* isolates (oxidase-positive gram-negative colonies) were serogrouped by an in-house dot-blot ELISA method to identify serogroups B, C, W, and Y (UK Health Security Agency Meningococcal Reference Unit) [17]. Following short-read whole genome sequencing (Illumina HiSeq or NovaSeq6000 platform; Wellcome Trust Oxford Genomics Centre, Oxford, UK), the genomes were assembled, characterized, and uploaded on the *Neisseria* database (https://pubMLST.org/neisseria), as described in the study protocols [15,17,19].

Statistical methods

The survey sample sizes were predetermined by a subset of the two cross-sectional studies: all Year 12 students (or S5 in Scotland) from the 2014 to 2015 MenCar4 study ($n = 10625$) and all Year 12 (S5) students recruited in 2018 at the time of a planned interim analysis of the 'Be on the TEAM' study ($n = 13438$). In 2014 and 2015, the carriage prevalence of genogroup W was 0.34%, genogroup Y 1.60%, and genogroup C 0.07%. The sample size was estimated to provide a detectable effect size of a 24% reduction in the carriage prevalence of genogroups C, W, and Y combined at 80% power and alpha of 0.05. The primary analysis used logistic regression to compare the difference in carriage prevalence between the pre- and postimplementation surveys, adjusting for study site. Several secondary analyses were done to assess the robustness of our findings including: (1) clustering at the school level; (2) restricting analysis to sites that were included at both time points only; and (3) multivariable logistic regression to adjust for risk factors for any meningococcal carriage. The risk factors included on the questionnaire were chosen based on significance from prior carriage studies [15]. These included age; sex; self-reported ethnicity; smoking and vaping status; household smokers; current sore throat; current or recent use of antibiotics; attendances at clubs, pubs, or parties in the last week; number of people kissed in the last week; relationship status and regular partner smoking status. The risk factors with p values of <0.20 in the univariable models were included in the multivariable regression model and retained in the full model if the $p < 0.05$. Carriage prevalence was reported as odds ratios with 95% CIs (Clopper-Pearson). Carriage prevalence reduction was derived from the odds ratio using the formula $([1 - OR)] \times 100$). Missing data were not imputed and assumed to be missing at random. Statistical analyses were performed using Stata version 17.

Results

In total 24 062 oropharyngeal swab samples were included: 10 624 from the preimplementation survey (2014–15) and 13 438 from the postimplementation survey (2018). The cohorts were demographically similar, with minor reductions in carriage risk factors consistent with previously reported trends (Table 1) [15]. In 2014 and 2015, 5.80% of participants were carriers of any meningococcus compared with 4.49% in 2018 (Table 2). There was a significant decrease in combined genogroup C, W, and Y meningococcal carriage from 2.03 to 0.71% (OR 0.34 [95% CI 0.27 − 0.44], $p < 0.001$) (Table 2). Genogroup W carriage decreased from 0.34 to 0.09% (OR 0.27 [95% CI 0.14 − 0.51], $p < 0.001$) and genogroup Y carriage decreased from 1.60 to 0.50% (OR 0.31 [95% CI 0.23 − 0.41), $p < 0.001$). Genogroup C remained rare, with no evidence of a difference in carriage prevalence between the time points, 0.07

Table 1
Participant demographics and risk factors for meningococcal carriage

	Preimplementation survey 2014–15	Postimplementation survey 2018	Difference between groups % (95% CI) unless stated
Sample size	10 624	13 438	
Sampling period	Sept 2014–March 2015	2018 Mar–May; 2018 Sept–Nov	
Vaccination schedule	MCC boost (aged 13–14 y)	MCC boost (aged 13–14 y) MenACWY (from Sept 2015)	
MenACWY vaccination coverage (England; age-year specific cohort)	n/a	80.95%	
Age in years, % of cohort, respectively			
15	3.4	0.01	
16	52.6	65.3	
17	40.3	31.9	
18	3.26	2.6	
19	0.45	0.01	
Mean	16.45 y	16.38 y	−0.07 y (−0.06 to −0.09 y) p < 0.001
Gender			Binary gender M:F −2.5% (−1.4 to −3.9%) p < 0.001
Male	41%	38%	
Female	59% n/a	61%	
Nonbinary		0.5 %	
Self-identified ethnicity			p < 0.001
White	80.3%	79.2%	
Asian/Asian British	10.0%	9.6%	
Black/African/Caribbean/Black British	4.7%	4.7%	
Mixed/multiple ethnic	3.2%	4.2%	
Other ethnic group	1.6%	1.9%	
Not reported	0.1%	0.4%	
Current sore throat	23.5%	19.5%	−4.0% (−3.0 to −5.0%) p < 0.001
Antibiotics currently or in the last month	13.5 %	10.1 %	−3.4% (−2.6 to −4.2%) p < 0.001
Cigarette smoking (any amount) in last week	9.2%	6.8%	−2.4% (−1.7 to −3.1%) p < 0.001
Vape/E-cigarette use (any amount)	3.5%	6.2%	2.7% (2.2 to 3.2%) p < 0.001
Household smokers (inside or outside)	27.1%	20.0%	−7.1% (−6.0 to −8.2%) p < 0.001
Any attendance at club/pub/parties in the last week	33.2%	29.4%	−3.8% (−2.6 to −5.0%) p < 0.001
Intimate kissing in last week	33.5%	28.5%	−5.0% (−3.8 to −6.2%) p < 0.001
Regular partner/girlfriend/boyfriend	26.6%	24.9%	−1.7% (−0.6 to −2.8%) p < 0.001

Survey completion rate: 2014 to 2015 (99.7%); 2018 (99.6%).

($n = 7/10625$) to 0.13% ($n = 17/13\,488$) (OR 1.96 [95% CI 0.81 − 4.73], p = 0.135). There was no evidence of a change in the carriage prevalence of genogroup B (1.26% vs 1.24%, OR 0.97 [95% CI 0.77 − 1.22], p = 0·81), other genogroups (OR 1.01 [95% CI 0.87 − 1.39], p = 0.45), or capsule null (*cnl*) meningococci (OR 0.90 [95% CI 0.72 − 1.12], p = 0.36).

For the secondary analysis including meningococcal carriage risk factors, the final multivariable logistic regression model included smoking status, party/club/pub attendances, sex, recent antibiotic use, self-reported ethnicity, vaping, regular partner, and partner smoking status. Although key carriage risk factors such as smoking decreased between 2014 and 2015 and 2018, the inclusion of carriage risk factors in the model did not substantially change the outcome measurements (Fig. S1). The outcome was also unaffected by adjustment of clustering in schools or inclusion of only sites in both pre- and postimplementation surveys (Fig. S1). Carriage

Table 2
Meningococcal carriage prevalence and odds ratio of carriage after the introduction of the MenACWY adolescent vaccination programme in August 2015

	Meningococcal carriage								
	2014/15 ($n = 10624$)		2018 ($n = 13438$)						
	n	%	*n*	%	Odds Ratio[a] (95% CIs)				p
any *N. meningitidis*	616	5.80%	603	4.49%	0.76	(0.68	—	0.86)	<0.001
genogroup C, W, Y[b]	216	2.03%	96	0.71%	0.35	(0.27	—	0.44)	<0.001
serogroup C, W, Y	147	1.38%	37	0.28%	0.20	(0.14	—	0.29)	<0.001
genogroup C	7	0.07%	17	0.13%	1.96	(0.81	—	4.73)	0.135
serogroup C	1	0.01%	0	0.00%	–	–	–	–	–
genogroup W	36	0.34%	12	0.09%	0.27	(0.14	—	0.51)	<0.001
serogroup W	26	0.24%	5	0.04%	0.16	(0.06	—	0.40)	<0.001
genogroup Y	170	1.60%	68	0.50%	0.31	(0.23	—	0.41)	<0.001
serogroup Y	118	1.11%	33	0.25%	0.22	(0.15	—	0.32)	<0.001
genogroup B	134	1.26%	165	1.23%	0.97	(0.77	—	1.22)	0.801
serogroup B	73	0.69%	75	0.56%	0.81	(0.59	—	1.12)	0.205
other genogroups[c]	122	1.15%	168	1.25%	1.01	(0.87	—	1.39)	0.446
capsule null (cnl)	152	1.43%	174	1.29%	0.90	(0.72	—	1.12)	0.355

[a] Adjusted odds ratio with study site as a covariable.
[b] Genogroup C, W, Y, includes three genogroup ambiguous W/Y isolates of which two were serogroup W; other single genogroup classifications do not include these isolates.
[c] Other includes genogroups E, H, K, L, X, or Z or incomplete capsular group after manual capsular assignment.

showed between-site variation, as seen in previous studies (Table S1) [15,16].

The odds ratio for serogroup W carriage in 2018 was 0.16 (95% CI 0.06 − 0.40, p < 0.001) and 0.22 (95% CI 0.15 − 0.32, p < 0.001) for serogroup Y (Table 2). Capsule expression, defined by serogroup positive isolates, decreased as a proportion of all genogroup W isolates from 72.2 to 33.3% (relative difference in proportions 53.8% [95% CI −5·0 − 79.8], p = 0.016) and for genogroup Y, from 69.4 to 48.5% (relative difference in proportions 30.1% [95% CI 8.9 − 46.3], p = 0.0025) (Fig. 2). In 2014 and 2015, one of seven genogroup C isolates expressed capsule compared with none of the 17 genogroup C meningococci in 2018. There was no significant change in the proportion of genogroup B that were expressing capsules (relative difference in proportions 16.6% [95% CI −4.8 − 33.5], p = 0.120).

The change in the carriage of the major ccs reflected the serogroup-specific vaccine effects (Fig. 3): there were decreases in cc11 and cc22, associated with genogroups W, and cc23, cc167 and cc174, associated with genogroup Y. However, the proportion of clonal complexes associated with genogroups W, Y, and C remained similar (Table 3). The carriage of W:cc11 in 2014 and 2015 was 0.22%, despite its high disease burden, in contrast to Y:cc23 (1.34%), which has a lower IMD incidence but was carried more commonly.

Discussion

Three years after the introduction of the UK MenACWY vaccination programme, cross-sectional oropharyngeal carriage surveys showed: (1) a sustained low carriage of genogroup C meningococci; (2) a 73% reduction in carriage of genogroup W meningococci; and (3) a 69% reduction of genogroup Y meningococci. There was no change in genogroup B meningococcal carriage. Reductions of carriage were observed at both genogroup level (i.e. those meningococci with *cps* regions encoding these capsules) and to a greater extent the serogroup level (i.e. those meningococci expressing the capsule). These results were consistent with studies of monovalent meningococcal conjugate polysaccharide vaccines, notably in the UKMenCar1-3 and MenAfriCar Studies [3,4]. An impact of MenACWY on carriage was also seen in observational studies conducted in Polish soldiers and an individually randomized controlled trial in UK university students [5,20,21]. In this RCT, MenACWY-$_{CRM}$ vaccinated participants had relative genogroup B C, W, and Y carriage reduction of 27.1% (95% CI 6.9–42.9) at any timepoint between 2 and 12 months after vaccination compared with controls. In this present population-level study, the magnitude of the reduction in carriage was greater and was commensurate with the impact of both the monovalent MCC and serogroup A vaccines [3,4]. A 2020 systematic review reported an absence of evidence supporting carriage effects of MenACWY conjugate vaccines [7]. However, this review included only the primary outcome at 1 month after vaccination for the UK student RCT, which did not differ between control and vaccine groups [22]. The other negative studies reviewed were in university populations in the United States and the United Kingdom. In the USA MenACWY studies, meningococcal Y and W carriage rates were so low that any inference about the impact of vaccination on carriage could not be considered definitive with respect to these serogroups [23–25]. By contrast, in the UK student populations analysed, carriage prevalence of genogroup W increased during the surveillance period after MenACWY vaccination. This was likely due to an inadequate time interval between vaccination and the commencement of the university year, when the maximum frequency of transmission occurs [5,26]. An observational carriage study in Norwegian teenagers did not demonstrate any impact of individual MenACWY vaccination status on serogroup-specific carriage, although vaccination coverage in the cohort was less than 30% [27].

The reduction in IMD incidence in the UK in both immunized and unimmunized cohorts after the introduction of the MenACWY programme [28] was consistent with the maintenance of direct and herd protection against serogroup C IMD and the introduction of direct and herd protection against serogroup W and serogroup Y IMD. The number of lives <5 years saved by herd protection against serogroup W in England and Wales was estimated to be between 114 to 899 > 4 years [28]. Infant 4CMenB immunization may have provided some direct protection against serogroup W:cc11 IMD [28]. Serogroup W IMD, which had been rising rapidly until 2015, plateaued and fell (Fig. 1). Although there are natural fluctuations in the meningococcal carriage, in our study the interval between pre- and postintervention was short, and the carriage impact was shown to be specific to the dominant vaccine capsular targets genogroups Y and W and was demonstrated across multiple clonal complexes associated with these genogroups. In contrast, genogroup B carriage was unchanged.

The strengths of the present study included large-scale, consistent methodology and the use of age and school year-level matched cohorts. The culture-defined endpoint of meningococcal carriage permitted high-resolution phenotypic and genotypic isolate characterization, strengthening the evidence that the trends in UK IMD are owing to a capsule-specific vaccine impact, rather than secular changes in meningococcal epidemiology. The existence of a national immunization program precluded a cluster-randomized approach, and the study remains observational. The timing of sampling of each survey differed for pragmatic reasons, with more sampling during winter months in the preimplementation study. The meningococcal carriage, unlike IMD, has not been shown to exhibit seasonal variation and, even if present, it would not disproportionally affect specific carriage of genogroup W and Y. The absence of sampling from Northern Ireland was unlikely to have biased the results, given the similarity between the populations in these countries. Although vaccine roll-out was more rapid in Scotland than in England or

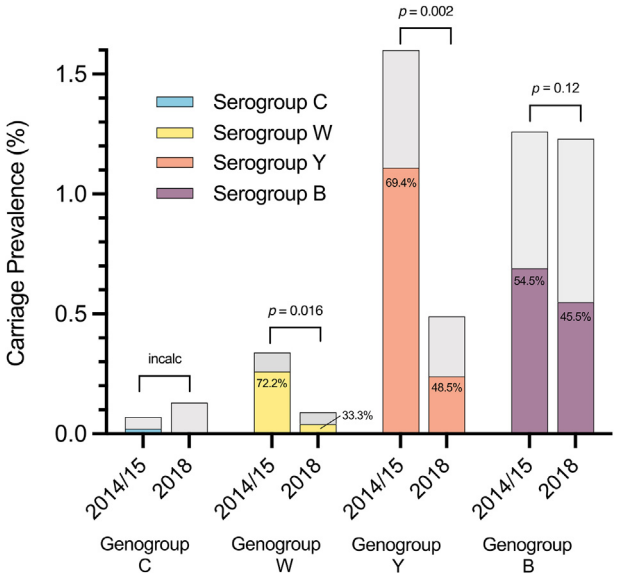

Fig. 2. Carriage of meningococcal genogroups and serogroups before and after the introduction of the MenACWY adolescent vaccination programme in August 2015. Coloured shading: serogroup positive isolates. Grey shading: serogroup negative isolates. Percentages in each column denote the proportion of genogroups that were serogroup positive with p values shown for the difference in proportions of serogroup-positive isolats at each time point. incalc, incalculable.

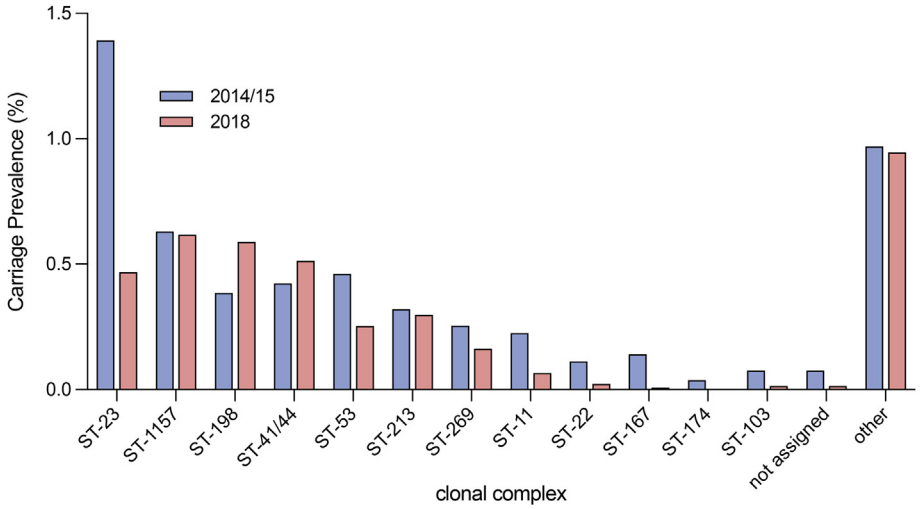

Fig. 3. Carriage prevalence by clonal complex in adolescents aged 15 to 19 years before and after the introduction of the adolescent MenACWY vaccination programme in August 2015.

Table 3
Carriage of clonal complexes listed by of genogroups C, Y, and W before and after implementation of the MenACWY immunization programme

		2014/15		2018	
Genogroup	Clonal complex	*n*	% Of genogroup	*n*	% Of genogroup
C					
	cc269	3	50.0%	9	52.9%
	cc41/44	0		4	23.5%
	cc11	0		1	5.9%
	cc1157	0		1	5.9%
	cc162	1	16.7%	0	
	cc231	1	16.7%	0	
	cc35	0		1	5.9%
	not assigned	1	16.7%	1	5.9%
	Total	6		17	
W					
	cc11	24	66.7%	7	58.3%
	cc22	12	33.3%	3	25.0%
	cc865	0		1	8.3%
	not assigned	0		1	8.3%
	Total	36		12	
Y					
	cc23	143	84.1%	63	94.0%
	cc167	14	8.2%	0	
	cc174	4	2.4%	0	
	cc1157	0		3	4.5%
	cc103	1	0.6%	0	
	cc41/44	0	0.0%	1	1.5%
	not defined	1	0.6%	0	
	not assigned	7	4.1%	1	1.5%
	Total	170		68	

Wales, Scotland was only in the preimplementation survey, hence these differences in roll-out did not impact on the post-implementation carriage results. Finally, although small changes in risk factors for meningococcal carriage reach statistical significance, this is a factor of the study sample size and the magnitude of differences is clinically small. The inclusion of risk factors in the secondary analysis did not change vaccine impact on carriage. It was unlikely that these differences between groups would affect the carriage of genogroups W and Y and not B.

We demonstrated that the UK meningococcal ACWY conjugate vaccine programme maintained low carriage of genogroup C meningococci and reduced carriage of serogroup and genogroup W and Y meningococci. This herd protection effect reduced IMD in all age groups, affirming the UK Joint Committee on Vaccines and Immunization strategy of deploying meningococcal conjugate vaccines in age groups with high meningococcal transmission [13]. As with monovalent meningococcal serogroup C and A conjugate vaccines, public health interventions that leverage herd protection from MenACWY vaccines will result in greater reductions in IMD across all age cohorts, more rapid impact, and favourable cost effectiveness. By contrast, there remains no evidence of indirect protection from outer membrane protein vaccines designed for group B meningococci, thus carriage studies are essential to complement IMD surveillance and inform meningococcal vaccine policy.

Transparency declaration

JPC GlaxoSmithKline grant to institution, Monash Health, for meningococcal vaccine study, no individual payment or inducements. JEB receives financial support from a Wellcome Trust Biomedical Resources Grant (218205/Z/19/Z). SNF NIHR payments only to institution; Pfizer, Sanofi, GlaxoSmithKline, J&J, Merck, AstraZeneca, Valneva, Moderna, Clinical trial investigator on behalf of institution, no personal payments of any kind; Novavax, Moderna, Pfizer – fees for symposium session participation paid to institution, not a personal fee; AstraZeneca, MedImmune, Sanofi, Pfizer, Seqirus, Sandoz, Merck, J&J, fees for advisory board participation paid to institution, not a personal fee; Chair of UK NICE Sepsis (2014–16) and Lyme Disease (2016–18) Guidelines (adults and children) expenses paid in line with NICE financial regulations. MR payments to the R&D University Hospitals Plymouth NHS Trust. CW Oxford Vaccine Group and Health & Care Research Wales, funding to institution for study conduct as part of the research grant. AL, SAC, and RB: Be on the Team & UKMenCar4 Projects funding for carriage study, work performed as part of UK Health Security Agency; GSK, Pfizer, Sanofi Pasteur, perform contract research on behalf of UK Health Security Agency. AJP institutional support from NIHR Oxford Biomedical Research Centre; Funding from the Meningitis Research Foundation to Institution, University of Oxford; Patent for a meningococcal B vaccine (all rights waived); Chair, Joint Committee of Vaccines and Immunization reporting to the Department of Health and Social Care; Member, WHO SAGE;

Institution, Oxford University, has entered a partnership with AstraZeneca for development of a Covid-19 vaccine. HC Department of Health and Social Care, 2017, grant, "Evaluating the effect of immunization with group B meningococcal vaccines on meningococcal carriage," co-applicant; NIHR HPRU in Behavioural Science and Evaluation, (1) 2021, grant "Hold the door open: involving older adults from diverse backgrounds in health research," co-principal investigator (2) 2019, grant, co-investigator; NIHR Career Development Fellowship, 2018, grant, principal investigator, Career Development Fellowship; UK Research and Innovation, 2020, grant, "Joint UNIversities Pandemic and Epidemiological Research, co-investigator; Elizabeth Blackwell Institute University of Bristol, 2020, grant "Social contacts and mixing patterns under COVID19 social distancing measures, principal investigator; European Centre for Disease Control, 2020, grant "Estimating national prevalence of chronic hepatitis B Virus Infection in EU/EEA countries, co-investigator; GSK, 2019, grant "Investigating the potential impact of Bexsero vaccination against Neisseria gonorrhoeae, co-principal investigator; Department of Health and Social Care, 2017, grant "Evaluation of patient access to medical test results services in General Practice," principal investigator; Meningitis Research Foundation, Member of the Scientific Advisory Panel. AF UK government Department of Health via University of Oxford, funding to employers to support conduct of study; Sanofi, funding to employers for my time and for costs of conducting a clinical trial of a Meningococcal vaccine in young children; Member, Joint Committee on Vaccination and Immunization (Independent UK government advisory committee); Chair, WHO Euro Technical Advisory Group of Experts on Immunization. MCJM Wellcome Trust & NIHR, grant funding to the University of Oxford; Pfizer, preparation and remote delivery of a presentation in conjunction with the ESPID 2021 Meningococcal Vaccines Symposium project. The sole purpose of such project was to provide up-to-date information related to the current epidemiology of Meningococcal disease worldwide; consultancy via Oxford University Innovation. MDS NIHR payments to institution; Pfizer donation of vaccine; GlaxoSmithKline, grants to University of Oxford for RSV and meningococcal vaccines; Pfizer, grants and vaccines supplied to University of Oxford for research on pneumococcal and meningococcal disease; Janssen, grants to University of Oxford for RSV vaccine study; MCM Vaccines, grants to University of Oxford for clinical research on multivalent infant vaccine; MedImmune, grants to Oxford University Hospitals NHS trust for study of RSV monoclonal antibodies; AstraZeneca, grants paid to University of Oxford for COVID-19 vaccine studies; Novavax, vaccine supply for COMCOV2 and COMCOV3 COVID-19 vaccine studies; Meningitis Research Foundation, member of medical advisory board. JM EP, HBB, PTH, OBH, PA, SC, CMCR, KD, AB, DB, JCC, RC, KF, RG, SH, SK, DO, AS, DT, EW, CZ, BMA, and CT declare no conflicts.

Author contributions

'UKMenCar4' conceptual design by JMM, CT, AJP, RB, SNL, and MCJM. 'Be on the TEAM' study conceptual design and management committee: MDS, AF, MCJM, CT, HC, RB, SG, JMM, PH, SF, KD, SC, PA, EP, JPC. Study site investigators, local management, recruitment, microbiology processing and data handling, MDS, JC, SC, EP, AL, RB, AF, JO, BMA, SNF, PH, DPJT, EW, MR, SH, AS, JPC, MW, SR, CC, ASm, DO, DB, CW, RG, CSZ, PTH, AB, AV, MDS, RS, RC, KP, DS, NP, JMM, HBB, KF, and OBH. Bioinformatics and genomic analysis by HBB, JMM, CMCR, OH, KAJ, and JEB. Data reviewed by JC HC, CT, and MCJM with primary statistical analysis by JPC, JMM, HC, CT, MCJM, and MDS. Preparation of original draft manuscript, figures, and literature search by JPC, with conceptual design, original input, and initial revisions by MCJM, MDS, JMM, CT, and HC. All listed authors have reviewed, revised, and approved the manuscript.

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The Data Availability statement

UKMenCar4: All genomes and metadata for the UKMenCar4 study are available open access through PubMLST, with short-read sequence data available from the European Nucleotide Archive (reference PRJEB14319) with European Nucleotide Archive accession run identifiers accessible on Pub MLST. Corresponding data from the Be on the TEAM study will be added after publication of the final results.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.07.004.

Appendix B. Collaborators

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