Early impact of an emergency teenage meningococcal ACWY vaccination programme in response to a national outbreak of group W meningococcal disease in England, 2015/16

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Abstract – 48 words
In the first 12 months of an emergency teenage meningococcal ACWY immunization programme in England, vaccine coverage among school-leavers, the first cohort to be

44 immunized, was 36.6%, with 69% fewer group W meningococcal cases (95% CI, 18-88%)
45 than predicted through trend analysis and no cases in immunized teenagers.

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Text – 1200 words

Introduction

A number of countries across Europe, South America and Australia are currently experiencing national outbreaks of group W meningococcal (MenW) disease caused by a hyper-virulent strain belonging to sequence type 11 (ST-11) clonal complex (cc), associated with severe disease and a high case fatality ratio [*1*]. In England, MenW cases predominantly due to ST-11 increased from 19 in the 2008/09 epidemiologic year to 176 in 2014/15, representing 2% and 24% of all invasive meningococcal disease (IMD) cases, respectively [2].

In response to the national increase in MenW cases, an emergency adolescent immunization programme with meningococcal ACWY conjugate vaccine (MenACWY) was commenced in August 2015 [3]. This replaced the adolescent MenC programme for 13/14 year-olds alongside a two-year, phased catch-up for those aged 15-18 years on August 31, 2015 as summarised in Table 1 [3]. The vaccine was also offered to new university entrants aged up to 25 years. Compared with those of the same age who do not attend university, new university entrants have a significantly higher risk of IMD, most likely because of social factors that increase meningococcal transmission [4]. This single dose immunisation programme aims to both directly protect vaccine-eligible cohorts and, in the longer-term, indirectly protect the wider population by reducing acquisition of meningococcal carriage [5].

Those in the age-group considered to be leaving high school in summer 2015 and aged 18 before September 2015 (referred to as 2015 school-leavers throughout), were the first cohort offered the vaccine through general practice from August 2015. Nearly a third of this cohort would be expected to start full-time university in September 2015 [6].

To help support decision-making in other countries affected by recent MenW outbreaks, we present impact and vaccine effectiveness (VE) data after the first 12 months of the MenACWY programme for school-leavers in England.

Methods

Public Health England conducts enhanced national IMD surveillance in England, where 84% of the UK population resides.

National Health Service (NHS) hospital laboratories routinely submit local invasive meningococcal isolates to the PHE Meningococcal Reference Unit (MRU) for confirmation and characterisation with national PCR-testing also offered by the MRU [7]. Confirmed cases are routinely followed-up for further details including vaccination history and outcome [8].

To assess whether MenACWY vaccine coverage might be higher among new university entrants, we compared vaccine coverage by June 2016 estimated from data automatically extracted from primary care databases in university-affiliated (n=79, located on a university campus or recommended by the university on their website) and non-university-affiliated (all others, n=7543) general practices for the 2015 school-leaver cohort.

To estimate vaccine impact, confirmed MenW, MenY and MenB cases in 2015 school-leavers were compared with projected cases for the first academic year (September 2015-August 2016) after programme introduction. To estimate projected 2015/16 case numbers in the absence of vaccination, a Poisson regression model with age and time-trend parameters was fitted to case numbers aged 19-24 from 2010/11-2015/16 who were not in vaccine-target cohorts. This was thus used to estimate case projections and incidence rate ratios (IRR) presented as percentage decline (1-IRR). MenC cases were excluded because of successful

pre-existing MenC vaccination programmes for 14-16 year olds and new university entrants from September 2013.

We assessed VE among 2015 school-leavers during the 2015/16 academic year. VE was estimated using the screening method [9], whereby vaccine coverage in cases was compared to population vaccination coverage in age-matched peers across England [10].

Results

MenW cases in England increased overall by 15% from 189 in the 2014/15 academic year to 218 in 2015/16. Isolates were available for 178 culture-confirmed cases in 2015/16; 155 (87%) belonged to the ST-11 cc. Case numbers and incidence increased in every age group except 15-19 year-olds (26 to 18 cases; 31% reduction) and infants <1 year (26 to 17 cases, 35% reduction) (Table 2). Six of the 18 teenage cases (33%) died whilst infant cases were not fatal.

By June 2016, vaccine coverage in school-leavers was 36.6%; 79% of these immunizations had been administered between August and September 2015. Vaccine coverage among school leavers was higher in university-affiliated practices compared with non-university affiliated practices (56.1% vs. 33.8%, p<0.0001) (Figure 1).

During the first 12 months of the teenage MenACWY immunization programme, there were six confirmed MenW cases in among ~650,000 school-leavers compared to a projected 19.4 cases (69% decrease; 95% CI, 18-88%), (Figure 2). Four cases were culture-confirmed including three that belonged to the ST11 cc; the remaining two were PCR-confirmed only. None of these six eligible cases had received MenACWY vaccination and only one (an unimmunized, overseas student) occurred in a university setting. Based on the population

117 coverage of 36.6% among school-leavers, the early estimated VE was 100% (95%CI, -47 to
118 100) but with wide confidence intervals due to small numbers.

119 One case each of MenY and MenC disease (both unimmunized) were diagnosed in school-
120 leavers during 2015/16 compared to three of each in 2014/15. MenB cases increased from 10
121 in 2014/15 to 17 in 2015/16. Of these 17 MenB cases, 6 (35%) had received MenACWY
122 vaccine, consistent with national vaccine coverage.

123

124 **Discussion**

125 We found a statistically significant 69% reduction in observed compared to predicted MenW
126 cases among the first cohort to be offered MenACWY conjugate vaccine following the
127 introduction of an emergency teenage immunisation programme, even with the small number
128 of cases. This occurred despite national vaccine coverage of only 36.6% in this cohort. All
129 confirmed MenW cases in the school leaver cohort were unimmunized and the only
130 university case was in an unimmunised overseas student. The higher vaccine coverage among
131 university-affiliated general practices suggests that school-leavers attending university were
132 more likely to be vaccinated than age-matched peers who did not enter higher education.
133 Some universities have actively vaccinated new entrants and achieved very high uptake [11].

134 Our early data on vaccine effectiveness and impact among the 2015 school-leavers are
135 encouraging although continued surveillance is vital. The decline in MenW cases among
136 infants is also interesting. The multicomponent group B meningococcal (MenB) vaccine
137 (4CMenB, Bexsero), was introduced into the national infant immunization programme in
138 September 2015 [12]. Unlike conjugated polysaccharide meningococcal vaccines, 4CMenB
139 vaccine is not capsule-specific and has the potential to offer broader protection against all

meningococcal strains. We have previously shown that antibodies from 4CMenB-immunised infants demonstrated potent serum bactericidal antibody (SBA) activity against the hypervirulent MenW ST-11 strain [13].

PHE will continue to monitor the impact of both programmes as more cohorts are vaccinated. Younger cohorts are now receiving the MenACWY conjugate vaccine through a school-based programme and achieving much higher vaccine uptake (72-84%) than school-leavers immunized through general practice [14]. Interestingly, although overall MenW cases increased in 2015/16 compared to 2014/15, the proportionate increase in cases was lower than the previous few years, when cases were nearly doubling year-on-year. Whether this represents early signs of indirect impact is speculative. Four months into the 2016/17 academic year, total MenW case numbers are only 8% higher than at the same time point in 2015/16.

By summer 2017, MenACWY vaccine will have been offered to all teenagers across the UK. Since this group also has the highest meningococcal carriage rates [15] it is hoped that, by preventing carriage through vaccination, the programme will reduce cases and deaths in unvaccinated cohorts across all age-groups in the coming years.

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Biographical Sketch

Helen Campbell is a senior clinical scientist at Public Health England, London, UK and is the epidemiological lead for meningococcal ACWY disease and for pertussis. Her additional research interests include attitudinal aspects of immunization and communication with health professionals and parents.

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Table One: Summary of the scheduling of the MenACWY routine and three year catch-up vaccination programmes in England

Birth cohort	school year – age at the end of the 2014/15 academic year (on Aug 31, 2015)	Academic year in which MenACWY vaccination began and school year at time of vaccination			
		2014/15	2015/16	2016/17	2017/18
Sep 1, 2003-Aug 31, 2004	Y6 – 11years				Y9 ACWY
Sep 1, 2002-Aug 31, 2003	Y7 - 12 years			Y9 ACWY	
Sep 1, 2001-Aug 31, 2002	Y8 - 13 years		Y9 ACWY		
Sep 1, 2000-Aug 31, 2001	Y9 - 14 years	Y9 MenC		Y11 ACWY	
Sep 1, 1999-Aug 31, 2000	Y10 - 15 years		Y11 ACWY		
Sep 1, 1998-Aug 31, 1999	Y11 - 16 years			Y13 ACWY	
Sep 1, 1997-Aug 31, 1998	Y12 - 17 years		Y13 ACWY		
Sep 1, 1996-Aug 31, 1997	Y13 – 18 years (2015 school leavers)	Y13 ACWY			

Key

Routine schedule MenC vaccination
New routine schedule MenACWY vaccination
School based MenACWY catch-up cohorts
General practice based MenACWY catch-up cohorts
Completed MenACWY vaccination of cohort

222

223 Table Two: Age distribution of laboratory confirmed cases of MenW in England by academic year (Sep 1 to Aug 31), 2011/12 to 2015/16

academic year	2010/11		2011/12		2012/13		2013/14		2014/15		2015/16	
Age group	case number	incidence per 100,000	case number	incidence per 100,000	case number	incidence per 100,000	case number	incidence per 100,000	case number	incidence per 100,000	case number	incidence per 100,000
<1 year	3	0.45	4	0.59	3	0.43	12	1.77	26	3.91	17	2.56
1-4 years	8	0.31	6	0.23	5	0.19	5	0.18	22	0.80	26	0.94
5-14 years	1	0.02	1	0.02	3	0.05	1	0.02	4	0.06	7	0.11
15-19 years	4	0.12	1	0.03	13	0.40	13	0.40	26	0.80	18	0.56
20-24 years	3	0.09	1	0.03	3	0.08	7	0.19	6	0.17	18	0.50
25-44 years	1	0.01	3	0.02	6	0.04	6	0.04	7	0.05	10	0.07
45-64 years	7	0.05	6	0.04	13	0.10	12	0.09	29	0.21	43	0.31
65+ years	11	0.13	11	0.13	15	0.17	34	0.37	69	0.72	79	0.81
all ages	38	0.07	33	0.06	61	0.11	90	0.17	189	0.35	218	0.40

224

225 Figure One: Frequency distribution of MenACWY vaccine coverage among school-leavers in
226 university affiliated (n=79) and non-university affiliated (n=7543) general practice in
227 England, June 2016

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229 Figure Two: Observed cases and projected cases based on trend lines fitted to the pre-
230 vaccination period (2010/11 to 2014/15) and extrapolated to the 2015/16 academic year for
231 the school-leaver cohort with group W, Y and B invasive meningococcal disease.

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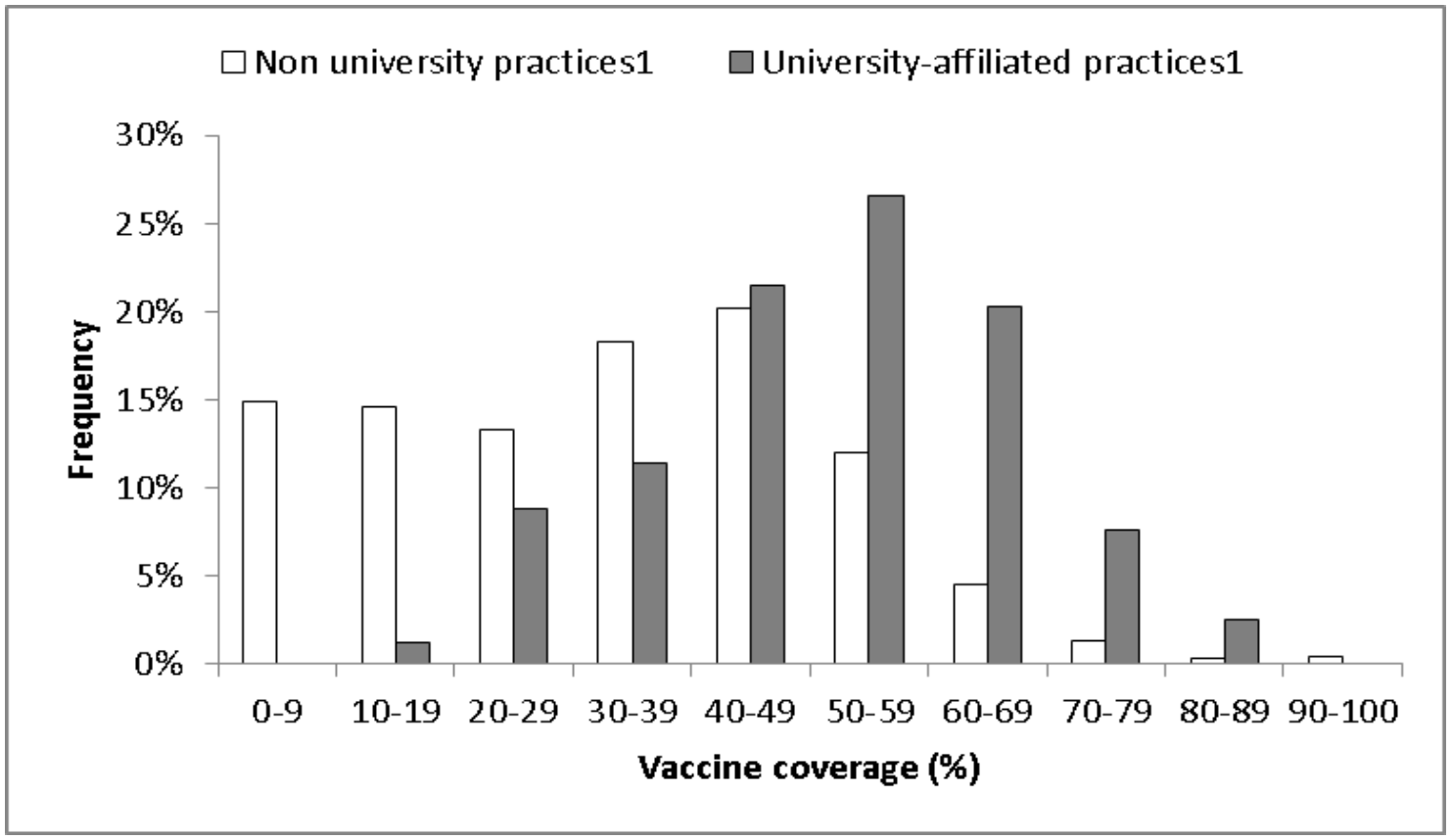
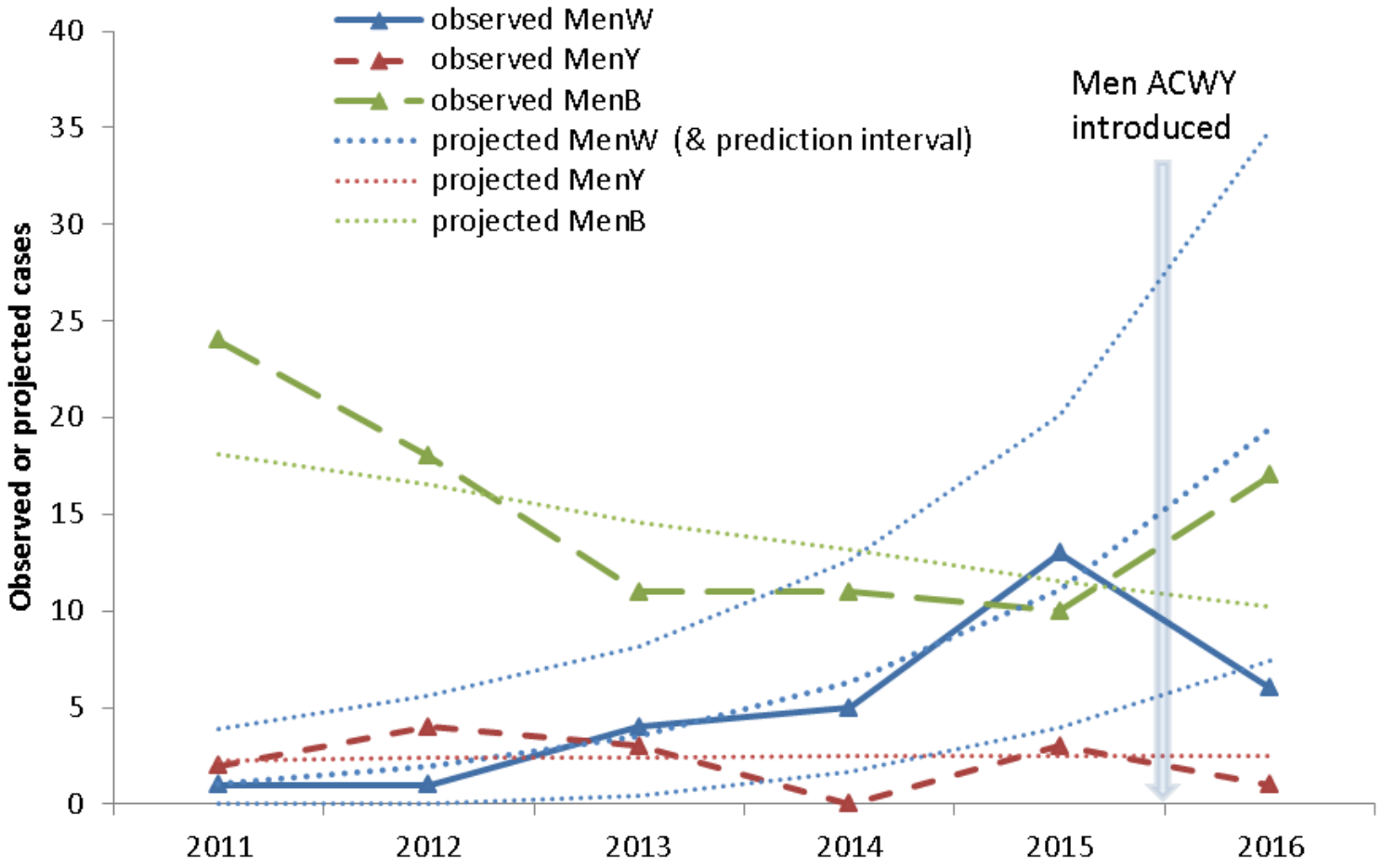


1University-affiliated practices are either on campus or recommended by universities. The list may not be comprehensive and non-university practices will still register students.


observed MenW
observed MenY
observed MenB
projected MenW (& prediction interval)
projected MenY
projected MenB
Men ACWY introduced
Observed or projected cases
40
35
30
25
20
15
10
5
0
2011
2012
2013
2014
2015
2016