Dynamic Model to Optimize Meningococcal Disease Prevention

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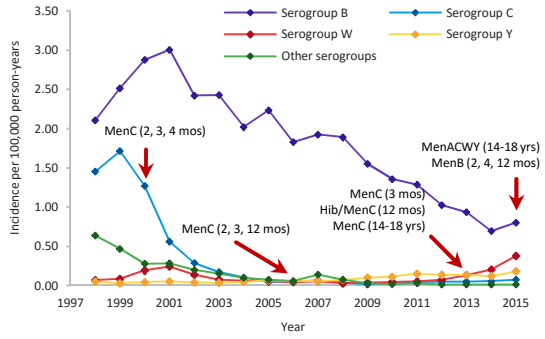
OBJECTIVE

To identify a vaccination schedule to maximize invasive meningococcal disease (IMD) prevention, considering current disease epidemiology and population dynamics in the UK

BACKGROUND

- IMD caused by *Neisseria meningitidis*, is unpredictable and life-threatening, and primarily caused by 5 distinct serogroups A, B, C, W, and Y
- Prior to the UK's introduction of routine MenC vaccination in children in 2000, serogroups B and C were the predominant cases of IMD (**Figure 1**)

Figure 1. Evolution of UK meningococcal vaccination strategy with changing epidemiology of disease by serogroup[1]



- Subsequent additions and modifications to the meningococcal vaccination programmes in the UK have been made in response to evolving knowledge of vaccine effectiveness and disease epidemiology such that vaccines against all 5 meningococcal serogroups are now recommended by JCVI for specific age groups (**Table 1**)

Table 1. Evolution of UK meningococcal vaccination program

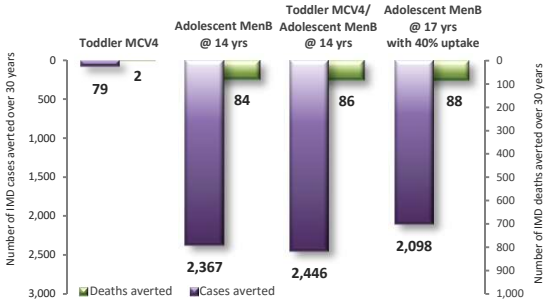
Age group	1999/2000	2006	2013	2015/16
Infants	MenC (2, 3, 4 months)	MenC (2, 3, 12 months)	MenC (3 months)	MenB (2, 4, 12 months)
Toddlers	MenC (Catch-up)	-	Hib/MenC (12 months)	Hib/MenC (12 months)
Adolescents	MenC (Catch-up)	-	MenC (14-18 years)	MenACWY (14-18 years)

RESULTS

Base Case Results

- Based on current UK disease epidemiology and vaccination program, the model estimated that 16,498 IMD cases and 1,135 deaths would occur over 30 years
- Adding MenB routine adolescent vaccination program with 80% uptake alongside the existing MenACWY at age 14 could prevent an additional 2,367 cases and 84 deaths (**Figure 3**)
- 2,098 cases and 88 deaths could be prevented if move MenB routine vaccination at age 14 with 80% uptake to age 17 with only 40% uptake

Figure 3. Number of direct and indirect meningococcal cases and deaths averted versus current UK vaccination program



Alternative Epidemiology Scenario Analysis Results

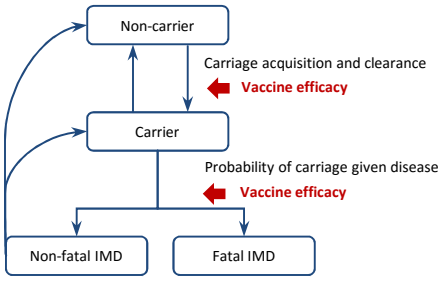
- Scenario ordering in terms of cases or deaths avoided did not change with use of either historical high or historical average incidence rates

METHODS

Model Structure

- Discrete dynamic model simulated transmission of meningococcal carriage (**Figure 2**)
- Number of carriers in each year and age group is based on:
  - carriage prevalence and age group distribution in the previous period, and
  - carriage transmission and mixing patterns within and among the age groups
- Model specifications
  - Time horizon: 30 years
  - Routine vaccination of infants, toddlers, and adolescents against MenB, MenC, and/or MenACWY
- Model outcomes
  - Additional meningococcal cases and deaths averted due to direct and indirect vaccination protection compared to current UK meningococcal vaccination programs

Figure 2. Meningococcal infection and vaccine pathway



Data Sources

- Total IMD cases in England and Wales (1998-2015)[2,3]
- Averaged similar incidence rates from recent years was used as the base case IMD incidence (**Table 2**)
- Model results using prior years' epidemiology were considered in sensitivity analysis
  - *Historical high incidence* (2002-2009 for serogroup B, 2005-2015 for serogroup C, 2004-2012 for serogroup W, and 2002-2008 for serogroup Y)
  - *Historical average incidence* (1998-2001 for serogroup B, 2005-2015 for serogroup C, 1999-2003 for serogroup W, and 1998-2001 for serogroup Y)

Table 2. Current average incidence (per 100,000 person-years) of meningococcal serogroups by age

Serogroup / Age, years	B	C	W	Y
<1	21.681	0.194	1.947	0.651
1-4	6.095	0.074	0.415	0.062
5-9	1.177	0.059	0.061	0.052
10-14	0.563	0.041	0.041	0.065
15-19	1.444	0.050	0.450	0.261
20-24	0.731	0.041	0.222	0.098
25-44	0.224	0.047	0.122	0.058
45-64	0.297	0.041	0.153	0.100
≥65	0.309	0.043	0.300	0.280

Note: Incidence of serogroup A was estimated to be 0
Average incidence rates were calculated: 2010-2015 for serogroup B, 2005-2015 for serogroup C, 2013-2015 for serogroup W, and 2009-2015, for serogroup Y

- Age-specific carriage prevalence for serogroups B and C was derived from Trotter et al, 2002 and 2006[4,5]
  - Carriage-to-incidence ratio from these studies was applied to UK-specific incidence data to obtain carriage prevalence for serogroups B and C
  - Carriage for other serogroups was assumed to be same as for serogroup C.
- 98% of the transmission was assumed to occur within age groups and the remaining 2% was distributed among other age groups, according to their relative population sizes (modified Trotter mixing matrix)[6]
- Vaccines' direct effect against invasive disease and indirect effect against carriage was obtained from the literature and expert opinion. (**Table 3**)

Table 3. Vaccine characteristics

Vaccine attribute		Estimate
Direct effect against invasive disease	MenB	83.0% (infants) 85.0% (adolescents)[8]
	MenC	95.0%[9,10]
	MenACWY	
Indirect effect against carriage	MenB	26.6%[8]
	MenC	30.0%[9,10]
	MenACWY	
Waning	Annual waning rate (direct and indirect effects)	10% (assumption)
Duration	Duration of protection (direct and indirect effects)	5 years (assumption)

Vaccination Scenarios

- Current UK recommended vaccination schedule and four alternative hypothetical scenarios were evaluated by varying vaccine administered and administration age (**Table 4**)
- Alternative meningococcal epidemiology was considered for scenario analysis with the same vaccine inputs
- School-based immunization uptake in 14-year-olds for the MenACWY vaccine was 77.2%-84.1% through August 2016;[7] at age 17, it is assumed that vaccine uptake would be somewhat lower[8]
- A published cost-effectiveness analysis assumed uptake of approximately 95% for infant MenB vaccination[9]
- Base case inputs for vaccine administration were used for scenario analysis of alternate epidemiology

Table 4. Vaccine administration age and uptake rates for the current UK meningitis vaccination schedule and four hypothetical scenarios evaluated in the model

Vaccine administration	Age *(Uptake Rate)*	Current UK vaccination schedule	Toddler MenACWY*	Adolescent MenB @ 14 years	Toddler MenACWY/ Adolescent MenB @ 14 years*	Adolescent MenB @ 17 years
Infants	<1 year *(95% uptake[9])*	MenB | 3 doses	MenB | 3 doses	MenB | 3 doses	MenB | 3 doses	MenB | 3 doses
Toddlers	1 year *(95% uptake)*	MenC | 1 dose	**MenACWY | 1 dose**	MenC | 1 dose	**MenACWY | 1 dose**	MenC | 1 dose
Adolescents	*14 years (80% uptake[7])*	MenACWY | 1 dose	MenACWY | 1 dose	MenACWY | 1 dose **MenB | 2 doses**	MenACWY | 1 dose **MenB | 2 doses**	MenACWY | 1 dose
	17 years *(40% uptake[8])*					**MenB | 2 doses**

Vaccines in **bold** represent differences from the UK vaccination scenario.
*Scenarios replacing MenC with MenACWY are unlikely since the existing MenC vaccine is combined with the Hib vaccine. These scenarios are hypothetical and are for illustrative purposes only to understand the impact of alternative vaccine policies.

DISCUSSION

- Dynamic transmission modeling can be used to inform optimal vaccination strategies to maximize meningococcal disease prevention and subsequent morbidity and mortality
- Determining vaccination policies and recommendations for meningococcal disease prevention can be a dynamic and complex decision process
- In the UK setting, implementation of a routine adolescent MenB vaccination program in either younger or older adolescents could improve disease prevention and have a substantial public health impact

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DISCLOSURE

ASC and SJS are employees of Pharmerit, which was paid by Pfizer Inc for study design, implementation, and poster development. LH, RF, and PB are employees and/or stakeholders at Pfizer Inc. DJ is an employee of Pfizer Ltd.