Potential Public Health Impact of *Neisseria meningitidis* Serogroup B Vaccination

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OBJECTIVE

To explore the potential public health impact of implementing different meningococcal serogroup B (MnB) vaccination strategies into the US adolescent population

BACKGROUND

- **Invasive meningococcal disease (IMD) is a serious infection caused by *Neisseria meningitidis* and is associated with rapid onset of symptoms, substantial risks of serious long-term sequelae, and high rates of fatality, even with appropriate antibiotic treatment.**
- **Of the 12 meningococcal (Mn) serogroups, B, C, and Y each account for about one-third of cases in the United States (US) (Figure 1).[1]**
- **Adolescents are at increased risk of contracting IMD as a result of typical social behaviors.[2,3,4]**
- **Most IMD cases are sporadic, however outbreaks can occur; recent outbreaks on college campuses were mainly caused by MnB.[5]**
- **Since 2015, the US Advisory Committee on Immunization Practices (ACIP) has recommended MnB vaccination (Table 1).[6]**
- **As of 2016, 2 conjugate Mn vaccines targeting Mn serogroups A/C/W/Y (MnACWY), 1 targeting C/Y, and 2 recombinant protein vaccines targeting serogroup B (MnB) are available in the United States**

Table 1: Meningococcal recommendations in the United States

Recommendation Category*		Serogroup	Age	Dosing
Persons at increased risk†	A	A/C/W/Y	2 months -55 years	1 to 4‡
	A	B	≥ 10 years	Mn-FHbp: 3 MnB-4C: 2
Routine vaccination	A	A/C/W/Y	11 or 12 years + booster at 16	1+1
	B	B	16 -23 years, preferred at 16-18 years	2

*Category A-all persons in an age- or risk-factor-based group; Category B-individual clinical decision. †MnAWCY and MnB: persons with HIV, persistent complement component deficiency or functional or anatomical asplenia, at risk during a community outbreak; MnACWY only: those traveling to or living in areas of high Mn disease, 1st-year college students ≤21 years living in residential housing. ‡Varies by age and risk factor, see refs 7 and 8.

METHODS

Model Structure

- **Discrete dynamic model simulating transmission of meningococcal carriage among 10 mutually exclusive age groups (Figure 2)**
- **At each time point, the number of carriers in each age group is based on:**
  - **Carriage prevalence and age group distribution in the previous time period, and**
  - **Carriage transmission and mixing patterns within and among the age groups**
- **Model specifications:**
  - **Time horizon: 30 years**
  - **Time step: 1 year**
- **Outcomes: Total number of meningococcal disease cases and deaths**

Data Sources

- **Projected US population for the year 2016[9]**
- **Carriage prevalence (Figure 3) and interpersonal contacts among age groups were obtained from published literature and expert opinion [10,11]**
- **Disease incidence was obtained from the US Centers for Disease Control[12]**
- **Vaccine efficacy against invasive disease and carriage obtained from the published literature and expert opinion (Table 2)[13]**

Scenario Analyses (Table 3)

- **Routine vaccination at age 16, with uptake equal to MnACWY uptake at same age[14]**
- **Vaccination at 18, representing vaccination upon college entry**
- **Vaccination at age 11, concurrent with MnACWY**
- **Vaccination at the recommended age with higher uptake**

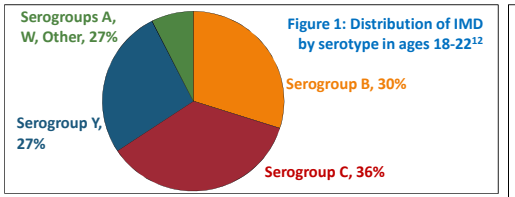

Figure 1: Distribution of IMD by serotype in ages 18-22[12]

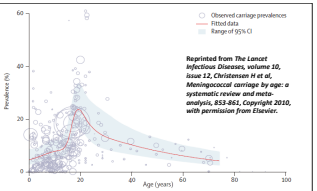

Figure 3: Meningococcal carriage prevalence by age. Isolates assembled from a global meta-analysis of Embase, Medline, Cochrane Library, and Web of Science databases.[17]

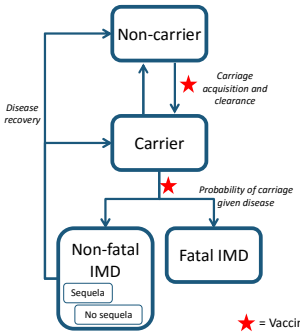

Figure 2: Schematic of meningococcal carriage and disease transmission

Table 2: Vaccine efficacy characteristics

Efficacy Attribute	Estimate	Sensitivity Analysis, range
Routine vaccine uptake, %[14]	29.6	22.2 – 37.0
Protection against invasive MnB disease, %[15]	85	70 – 100
Protection against MnB carriage, %[13]	26.6	10.5 - 39.9
Duration of protection against disease, yr[16]	5	2 - 10
Duration of protection against carriage, yr[16]	5	2 - 10
Annual decrease in MnB disease protection, %	10	0 - 20
Annual decrease in MnB carriage protection, %	20	0 - 40

Table 3: Base case and alternate scenario analyses

	Vaccination Scenario	Targeted Population, N	Vaccine Uptake, %	Comment
Base case	Age 16	4,061,497	29.6	Recommended age; same uptake as MnACWY vaccine at age 16[14]
Alternate analyses	Age 18	4,030,058	22.2	Recommended age; assume 75% uptake of base case
	Age 18	4,030,058	14.8	Recommended age; assume 50% uptake of base case
	Age 11 + booster at 16	4,241,000 + 4,061,497	77.8 + 29.6 revaccination	Recommended conjugate MnACWY vaccination schedule
	Age 11 + booster at 16	4,241,000 + 4,061,497	77.8 + 77.8 revaccination	
	Age 16	4,061,497	77.8	Recommended age; uptake equal to that of conjugate MnACWY vaccination at 11 years

RESULTS

- **Without vaccination, the model predicts 8,721 cases and 818 deaths due to serogroup B to occur across the entire population over the next 30 years**

Base Case Scenario Analysis

- **With current disease incidence, 823 cases and 78 deaths are estimated to be prevented over 30 years with adolescent MnB vaccination (Figure 3)**

Alternate Scenario Analyses

- **Of the scenarios tested, the greatest number of cases and deaths are prevented with MnB vaccination at age 16 years with 77.8% uptake**
- **Sensitivity analyses altering other parameters to assess their impact on model outcomes are shown**
- **Results from the sensitivity analysis shows the model is most sensitive to the assumptions surrounding vaccine efficacy against nasopharyngeal carriage (Figure 4)**

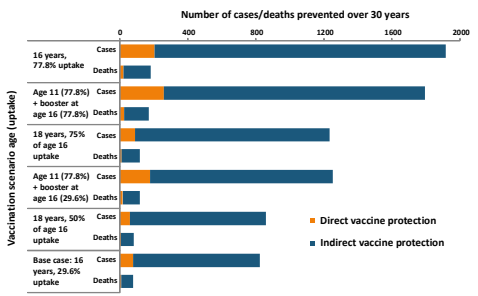

Figure 3: Number of cases and deaths prevented over 30 years with and without indirect protection under different potential vaccination scenarios

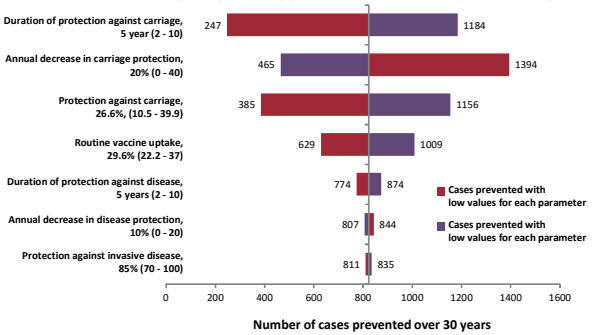

Figure 4: Univariate sensitivity analysis of key parameters (base case values and range tested)

DISCUSSION

- **The incidence of IMD caused by *N. meningitidis* serogroup B has declined during the past decade, but the disease is unpredictable, costly, and associated with high risks of long-term sequelae and death.**
- **Adolescents are at increased risk of transmitting *N. meningitidis* and IMD.**
- **Routine adolescent MnB vaccination is an effective strategy to prevent the clinical, humanistic, and economic impact of IMD caused by *N. meningitidis* serogroup B.**
- **Comparing vaccine uptake of MnACWY and MnB programs suggests Category B recommendations in 16-18 year-olds result in suboptimal vaccine uptake leading to vaccine preventable IMD in adolescents.**
- **Routine adolescent MnB vaccination achieving coverage levels equivalent to the MnACWY program is the most impactful strategy to prevent IMD.**
- **If MnB vaccine is shown to disrupt carriage acquisition, higher levels of vaccine uptake can reduce disease in other age groups.**
- **Shifting MnB recommendations from Category B to Category A would increase MnB vaccine uptake thereby providing additional protection to adolescents at risk for IMD.**

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DISCLOSURE

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