

Original Research Article

Post-vaccination alteration in meningococcus disease rate in the US from 1980-2019

ABSTRACT

Aim: To study the impact of vaccination on Meningococcal infection in the United States from 1980 to 2019.

Study Design: The study used deidentified publicly available data.

Place and duration of Study: Department of Anatomical & Developmental Sciences, and Pathological Processes, Microbiology & Immunology, Department of Preventive Medicine & Epidemiology, Department of Nutritional, Biochemical & Molecular Sciences American University, School of Medicine, Aruba, Between July 2023 to September 2023.

Methodology: All analyses for this study were conducted using The Health, United States Data Finder, Center for Disease Control, which provides detailed trend tables and charts for recent editions of Health, United States. All the data was collected and compared year-wise, age-wise, and new cases of meningococcal infection per 100,000 population. The data was also compared concerning the year of initiation of the vaccine.

Results: With time, it was observed that the cases of meningococcal infection declined. The rate was found to be higher with the initiation of vaccination.

Conclusion: Stringent vaccination, surveillance, and timely use of antibiotics in the United States contributed to the drop in instances of meningococcal infection. However, the recent outbreak in Florida could be due to negligence among the people.

Keywords: *Meningococcal disease, Vaccination, Neisseria meningitides, United States*

1. INTRODUCTION

Neisseria meningitides is the source of meningococcal disease and a prominent contributor to bacterial meningitis in the United States. In addition to pneumonia and localized diseases such as septic arthritis, it can also result in meningitis and sepsis. Weichselbaum made the initial discovery of *Neisseria meningitides* in 1887 while evaluating the cerebrospinal fluid (CSF) of a patient with meningitis (Rouphael

Comment [w1]: The objective to study the impact of vaccination on meningococcal infection over a long time frame is clearly stated.
- The manuscript uses publicly available CDC data, which lends credibility to the analysis.

Comment [w2]: The introduction section gives a thorough background of *Neisseria meningitides* and the epidemiology of the disease.

and Stephens 2012). The gram-negative, aerobic diplococcus bacterium *Neisseria meningitidis* is encased in a polysaccharide capsule that enhances its pathogenicity. Based on the polysaccharide capsule's structure Meningococci has different serogroups. So far twelve different polysaccharide capsules with unique antigens and chemical compositions have been identified. One of the six serogroups—A, B, C, W, X, and Y—have reported invasive infections that affect the entire world (Brandtzaeg and Deuren 2012; Mishra, 2023).

Humans are the only source of *Neisseria meningitidis*; in around 25% of the population, it establishes as a commensal diplococcus in the nasopharynx (Pizza and Rappuoli 2015). Meningitis and bloodstream infection are the two most prevalent kinds of meningococcal infections, both of which can swiftly turn fatal. The infection through *Neisseria meningitidis* can spread from person to person by respiratory droplets or secretions with asymptomatic colonization.

Bacteria adhere to the nasopharynx's and oropharynx's mucosal cells, multiply there, then break through the host's mucosal cells and enter the bloodstream. After crossing the blood-brain barrier and entering the cerebrospinal fluid, it can cause systemic illness and, lately, fulminating meningitis.

The incubation phase can last anywhere from 1 to 10 days, but it usually lasts 3 to 4 days. Meningococcal invasive illness is the primary cause of 50% of reported cases of meningitis in the United States (<https://www.cdc.gov/vaccines/pubs/pinkbook/mening.html>). The patient displays the typical abrupt onset of fever, headache, and stiff neck. Additional symptoms, such as nausea, vomiting, photophobia (eye sensitivity to light), and altered mental status are frequently present as well.

Meningococcal septicemia without meningitis can occur in about 30% of invasive meningococcal infections (<https://www.cdc.gov/vaccines/pubs/pinkbook/mening.html>). Meningococcal septicemia is characterized by an abrupt onset of fever, chills, cold hands, and feet, intense aches or pains in the chest or abdomen, vomiting, diarrhea, and a petechial or purpuric rash that is frequently accompanied by hypotension, shock, an acute adrenal hemorrhage, and multiorgan failure (Tsheten et al., 2016). Additionally, among the senior population in the United States, *Neisseria meningitidis*-related bacteremia pneumonia accounts for 15% of cases.

Even with effective antibiotic therapy, the overall case-fatality ratio for meningococcal disease is 10% to 15%, and it may be higher in people with meningococcemia (<https://www.cdc.gov/vaccines/pubs/pinkbook/mening.html>.)

Meningococcal disease has a 10,000-fold greater risk in people with persistent deficiencies (e.g., genetic deficiencies) in the complement system (e.g., C3, properdin, Factor D, Factor H, or C5-C9), and these people can also have recurrent disease (Cohn et al., 2016). People with anatomic or functional asplenia, atypical hemolytic uremic syndrome, or paroxysmal nocturnal hemoglobinuria undergoing treatment with eculizumab are also at greater risk of meningococcal disease because the drug binds to C5 and suppresses the terminal complement pathway. The attack rate of laboratory-acquired meningococcal infection has been estimated at 13 per 100,000 people among microbiologists who frequently work with *Neisseria meningitidis* isolates, which is significantly higher than the rate for adults in the general population (Sejvar et al., 2005).

To fight back against Meningococcal disease two types of vaccines are available in the United States: MenACWY (conjugate) vaccines and MenB (recombinant protein) vaccines. MenACWY is against serogroups A, C, W, and Y and was introduced in 2005 while MenB is against serogroup B and was introduced in 2015. Meningococcal illness is sporadic, but outbreaks continue to occur. Despite of meningococcal vaccination schedule recently CDC observed an outbreak of meningococcal disease in Florida (<https://www.cdc.gov/meningococcal/outbreaks/FL2022-sp.html>). In the present study, we studied the impact of vaccination on meningococcal diseases from 1980 to 2019.

2. MATERIALS AND METHODS

All analyses for this study were conducted using The Health, United States Data Finder, Center for Disease Control, which provides detailed trend tables and charts for recent editions of Health, United States. These trend tables and charts cover a number of subjects and population groups. The data summarize the new cases per 100,000 population and the Number of new cases of Meningococcal diseases all through the years. The collective data is from 1980 to 2019. The study used deidentified publicly available data.

3. RESULTS AND DISCUSSION

Comment [w3]: The methodology section is relatively sparse. There is no detailed explanation of how data was cleaned, analyzed, or any statistical methods used to assess trends. A more structured description of the analytical approach, such as trend analysis or statistical significance testing, should be added. It mentions the use of CDC's Health Data Finder but does not explain how the trend figures were derived from the raw data.

The study includes cases of Meningococcal infection from the year 1980 to 2019. The data was collected for all age groups.

The data was assessed as new cases of meningococcal infection per 100,000 population. It was observed that if we compare the cases from 1980 to 2000, under the gap of 10 years each the highest number of cases was found in 1980 (Figure 1). Later while comparing the cases from 2001 to 2019, initially the cases were high but they slowed down with every passing year. After the introduction of the vaccine in 2005, the decline was faster but in 2008 again there was an increase in the rate of infection (Figure 2). The data also shows that after introducing Men B there was more reduction in the number of cases. The data expressed in Figure 3 and Figure 4 that after the introduction of the vaccine,, even there was a decline in new cases also.

The active bacterial core surveillance (ABC's) network, a population-based surveillance system for bacterial pathogens, has consistently supplied a wealth of information about the different infectious diseases, their rate of rise and decline, and their distribution across the population. (<https://www.cdc.gov/abcs/bact-facts-interactivedashboard.html>).

Other parts of the world, including China, Russia, Niger, Togo, and Western Kenya, as well as the United States, are affected by meningococcal illness.

In many countries, including the United States, serogroup B strains are the main culprits behind endemic meningococcal illness and protracted outbreaks [Diermayer et al., 1999; Baker et al 2001]. In the US and other countries in the Americas, serogroup Y strains account for a significant fraction of infections (Rosenstein et al., 1999; Harrison et al., 2006). Although the causes of the diverse serogroup distribution around the world are unknown, probable processes include population immunity variations and environmental influences.

Age has a significant impact on the incidence of meningococcal infection, with infants being at the greatest risk [Hedari et al., 2013]. One of the most significant host factors influencing the likelihood of infection is low blood bactericidal antibody (SBA) levels. Minority ethnicity and low socioeconomic level have also been linked to higher risk. Meningococcal illness has been linked to immune system-compromising conditions like functional or anatomic asplenia, HIV infection, genetic polymorphisms, and deficits in innate immune system components. The risk of meningococcal illness has long been linked to

population crowding. Behavioral risk factors have also been linked to the likelihood of meningococcal carriage and disease. Other risk factors include passive and active smoking, drinking in pubs and bars, kissing, and living in a university dorm (Harrison, 2010).

Our data analysis revealed that with the passage of time, the number of cases varied. The annual incidence of meningococcal illness has fluctuated between 0.5 and 1.5 cases per 100,000 people since World War II. The incidence has fluctuated over the last few decades in multiyear cycles (<https://www.cdc.gov/meningococcal/surveillance/index.html>). Data shows a rise in infection in the period of 2008 despite of introduction of MCV4 vaccine. Because MCV4 lacks a serogroup B component, it may have an impact on the increased prevalence of infection in 2008. According to ABCs statistics, serogroup B accounted for 25% of cases in the US in 2007, followed by serogroup C for 30%, serogroup Y for 37%, and serogroup W-135 for 9% of cases (www.cdc.gov/ncidod/DBMD/abcs/survreports/mening07.pdf). In 2008 the percentage rate of infection by Sero group B was increased as there was no vaccine available for serogroup B at that time. Despite this widespread advice, the National Immunization Survey found that just 33% of 13-year-olds had gotten MCV4 in 2007 (Vaccination coverage 2008), Which could also be one of the reasons for the rise in infection in 2008.

After introducing the MenB vaccine against serotype B in 2015, there has been a continuous fall in meningococcal infection, our study is also supported by Mbaeyi et al.,2020.

Additionally, prompt antibiotic use for postexposure prophylaxis and treatment aids in limiting the spread of illness (Bröker, et al 2011). The vaccination strategies used by Italy (Neri et al, 2008); Canada (Siu et al 2008), and Germany (Hellenbrand, et al 2013) demonstrated that vaccination in children decreased the rate of Paediatric meningococcal infection, which is consistent with our observation. The tight and effective monitoring system of the Enhanced Meningococcal Diseases Monitoring (EMDS), centers for Diseases Control & Prevention, is another significant element contributing to the decrease in meningococcal cases. The EMDS gathers, isolates from the health departments of all the states and major jurisdictions, evaluates them, and maintains track of the infection rate. 98–99% of the population of the United States is still being monitored, and quick action is being taken to halt the spread of illness.

4. CONCLUSION

Comment [w4]: The conclusion is concise but too general. Expanding it to include implications for public health policy, future vaccine strategies, and how this data can influence current vaccination approaches would make the study more impactful.

The present study concludes that stringent vaccination, surveillance, and timely use of antibiotics in the United States contributed to the drop in instances of meningococcal infection.

ETHICAL STATEMENT

This study does not involve any ethical issues as data was collected from the Centers for Disease Control & Prevention.

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Comment [w5]: The introduction is overly reliant on references for basic information. While referencing is essential, certain common knowledge aspects (e.g., basic facts about *Neisseria meningitidis* or common symptoms of meningitis) do not need extensive citation. This could be streamlined for clarity.

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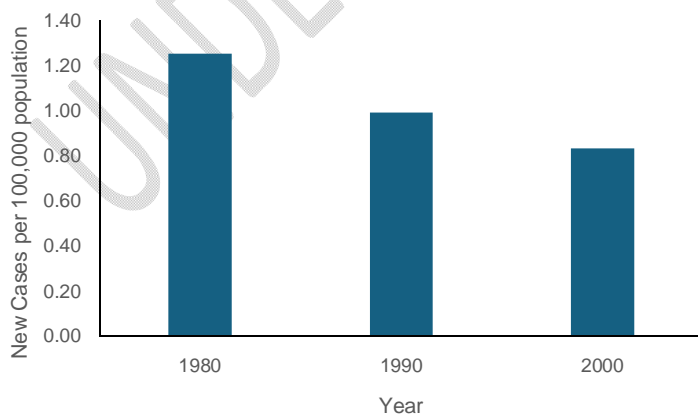
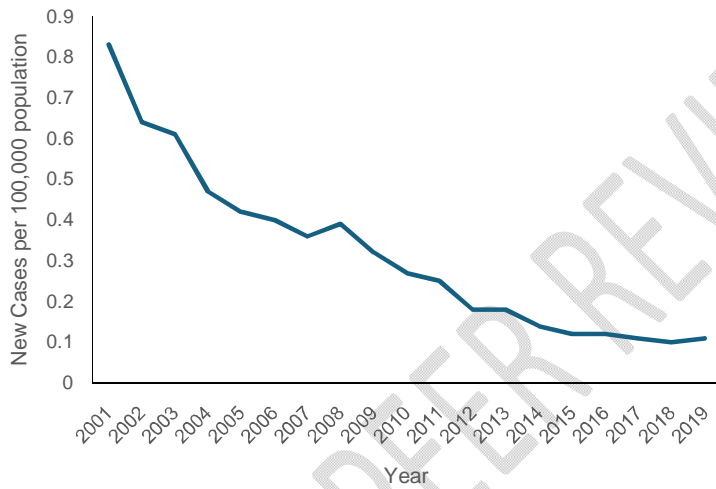


Figure 1: New cases of Meningococcal infection per 100,000 population from 1980 to 2000 in the United States



Comment [w6]: Figures and tables referenced (Figure 1, Figure 2, etc.) are not included in the document. These should be properly inserted or cited, as they are essential for understanding the trends discussed. Without these figures, it is hard to evaluate the conclusions drawn. - The comparison between different periods (e.g., 1980-2000 and 2001-2019) could benefit from more precise numeric data to substantiate the claims.

Figure 2: New cases of Meningococcal infection per 100,000 population from 2001 to 2019 in The United States

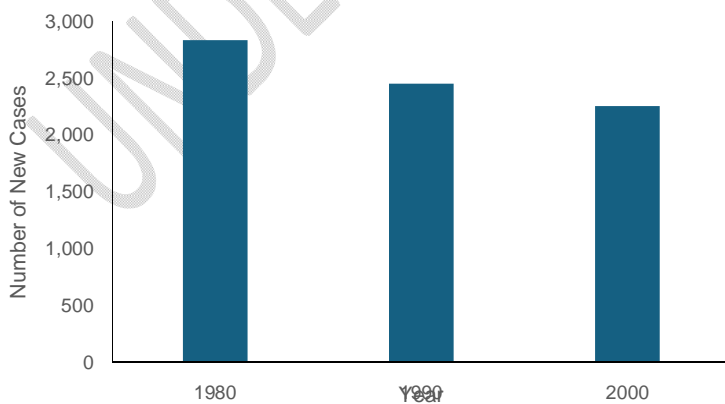
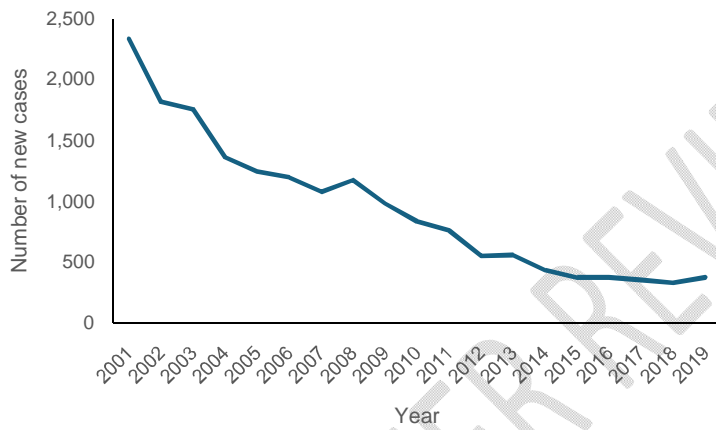


Figure 3: Overall new cases of Meningococcal infection from 1980 to 2000 in the United States



Comment [w7]: The manuscript acknowledges an increase in cases around 2008 but doesn't delve deep into potential reasons beyond the missing vaccine component (serogroup B). This section could explore other factors, such as public health policies or changes in reporting standards.

Figure 4: Overall new cases of Meningococcal infection from 2001 to 2019 in the United States