Meningococcal Infections

Neisseria meningitidis invasive disease is a Class A Disease and must be reported to the state within 24 hours by phone.

Neisseria meningitidis is a major cause of bacterial meningitis and sepsis in the United States. Meningococcal invasive disease includes meningococcal meningitis, septicemia, bacteriologically confirmed pneumonia and any other disease with isolation of *N. meningitidis* in internal fluids or organs. *N. meningitides* (also called meningococcus) is also a common colonizer of the upper respiratory tract. The proportion of healthy carriers is 5% of the population. Carriage is not reportable. Meningococcal meningitis, the most common form of the disease, is characterized by sudden fever onset, with intense headache, nausea and often vomiting, stiff neck and sometimes a petechial rash.

The highest incidence of meningococcal disease occurred among infants younger than one-year old with a second peak occurring in adolescents and young adults. Among infants, disease incidence peaks within the first six months of life; the majority of cases in this age group are caused by serogroup B. Rates of meningococcal disease are at historic lows in the U.S., but meningococcal disease continues to cause substantial morbidity and mortality in persons of all ages.

Vaccine History

The first monovalent (serogroup C) polysaccharide vaccine was licensed in the U.S. in 1974. However, similar to the polysaccharide vaccine against pneumococcal disease, it is most effective in adults and does not consistently generate immunity in young children.

A quadrivalent polysaccharide vaccine was licensed in 1981. The first conjugate meningococcal vaccine in the United States, MCV4 (Menactra™), was licensed in 2005, with a second, MenACWY-CRM (Menveo®), licensed in 2010. These are the preferred vaccines for individuals between two years and 55 years of age; Menactra™ is approved for ages two years and 55 years of age, and Menveo® for ages 11 years to 55 years of age. The Advisory Committee on Immunization Practices (ACIP) recommends routine use of quadrivalent (A, C, Y, W-135) meningococcal conjugate vaccine in adolescents and others at increased risk for disease. In October 2010, a booster dose was recommended for adolescents at age 16 years. In 2016, coverage with one dose of meningococcal conjugate vaccine was approximately 80% among adolescents aged 13 to 17 years in the United States. This is an increase from approximately 70% in 2011.

A bivalent conjugate combination vaccine (with Hib) was licensed in the U.S. in 2012.

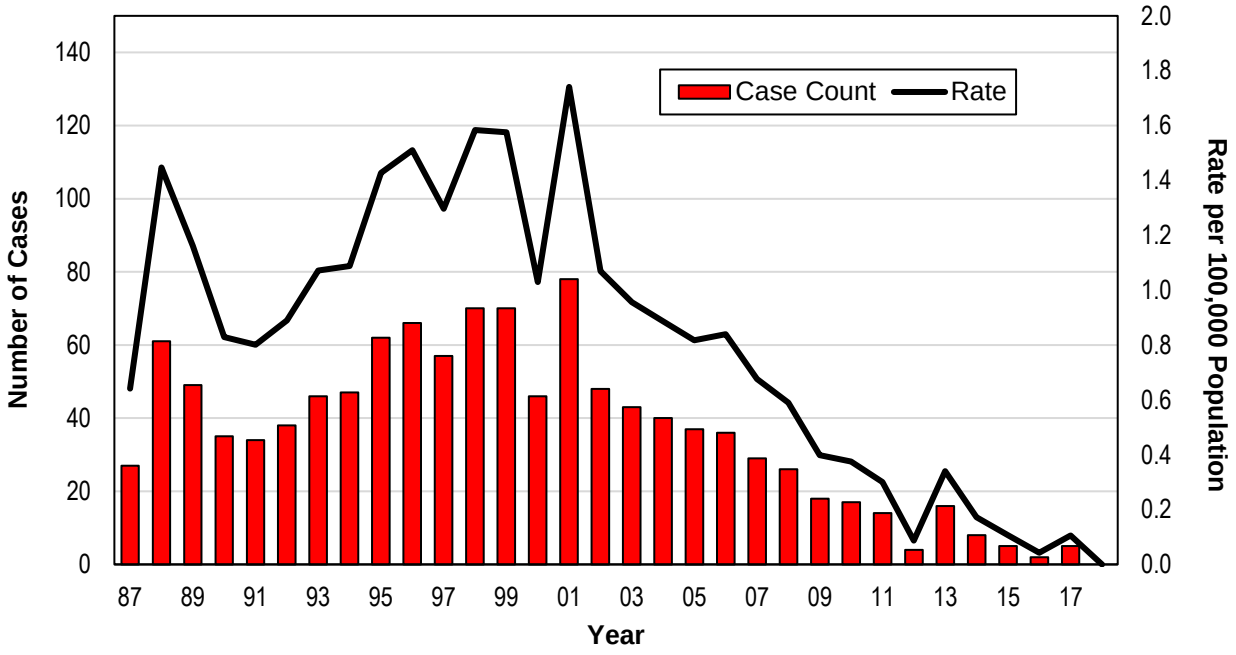
Vaccines for group B meningococcal disease were licensed in the U.S. in 2014 and 2015. MenB-FHbp (Trumenba®, Wyeth Pharmaceuticals, Inc.} is a three-dose vaccine, and MenB-4C (Bexsero®, Novartis Vaccines) is a two-dose vaccine. In October 2015, the Centers for Disease Control and Prevention adopted the position of the ACIP that group B meningococcal vaccine be recommended to individuals ages 16 years to 23 years of age who are at risk of disease during

outbreaks. The ACIP, however, did not recommend that the group B meningococcal vaccine join the quadrivalent meningococcal vaccine as a vaccine recommended universally for all adolescents.

Incidence and Trends

Incidence of meningococcal invasive disease in Louisiana decreased during the 80s, steadily increased during the 90s, from a low of 34 cases in 1991 to a high of 78 cases in 2001, and again decreased over the last 18 years (Figure 1).

Figure 1: Meningococcal Meningitis Trends - Louisiana, 1987-2018



Serogroups

Neisseria meningitidis is a Gram-negative diplococcus. A major virulence factor is the capsular polysaccharide, of which there are 13 types. Based on these capsular polysaccharides, there are five groups of meningococci which cause most human meningococcus infections. These groups are important to consider because of their epidemiologic, clinical and preventive implications. The three main groups observed in Louisiana are B, C and Y. Groups A and W135 are uncommon in Louisiana. This is important because the quadrivalent vaccine available in the U.S. is effective only against A, C, Y and W135. It is ineffective against B, which represents about one-third of the cases in Louisiana. *N. meningitidis* isolated by hospitals should be sent to the Office of Public Health (OPH) Laboratory for sero-grouping (Figures 2A and 2B).

Figure 2A: Distribution of Serogroups for Those Known - Louisiana, 1988-2018

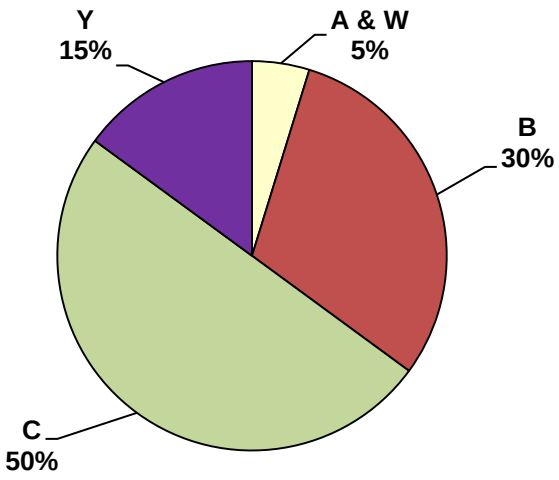
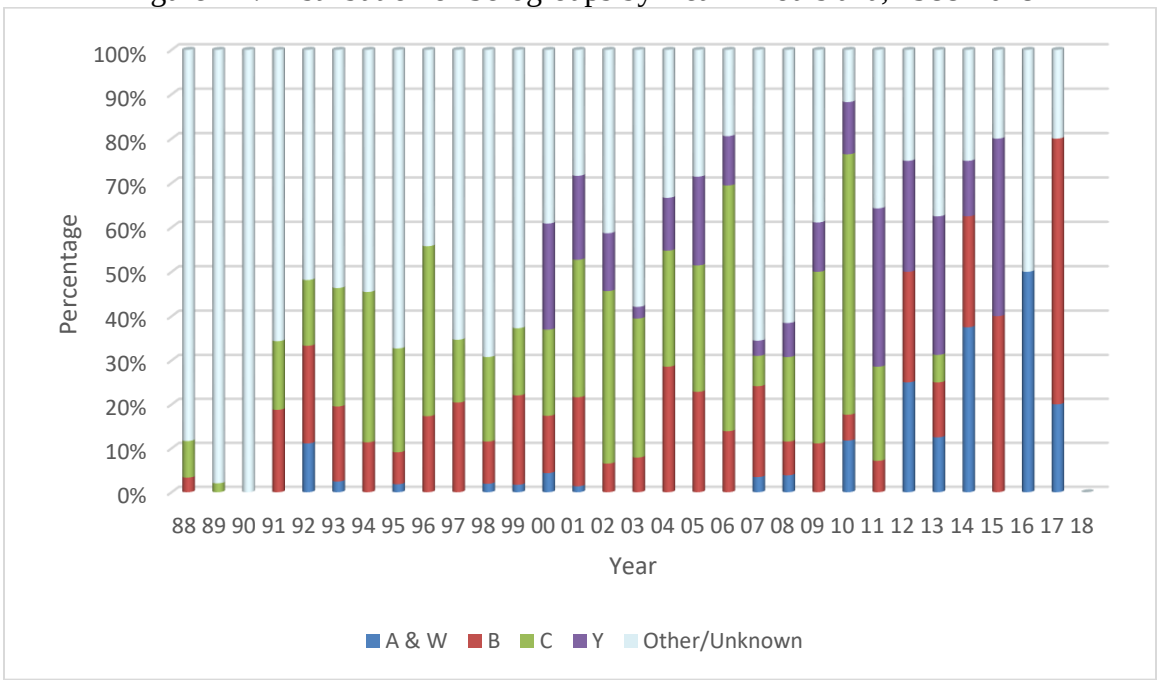


Figure 2B: Distribution of Serogroups by Year – Louisiana, 1988-2018

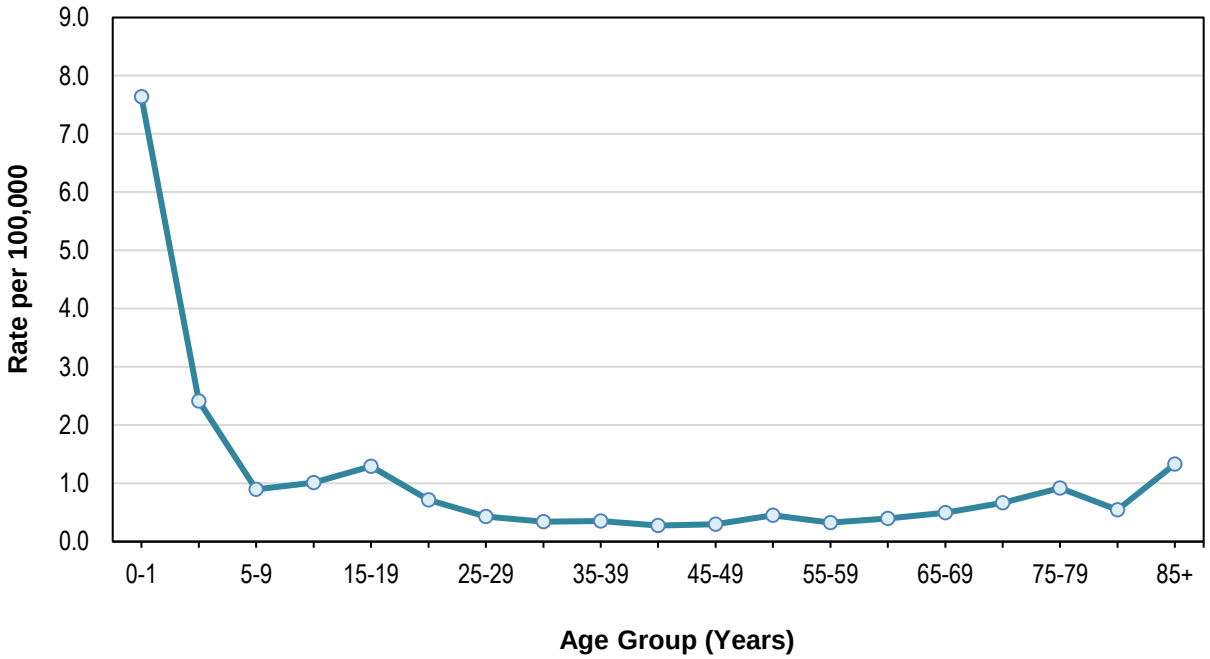


Gender and Age Group Distribution

There is no difference in rates by sex. The age group distribution shows the highest incidence in infancy and early childhood, rates then decrease until the age of 70 years, and slightly increase in those older. However the popular perception is that the adolescent and college age groups are at

highest risk. This perception results from the publicity given to fatal cases occurring among high school and college students (Figure 3).

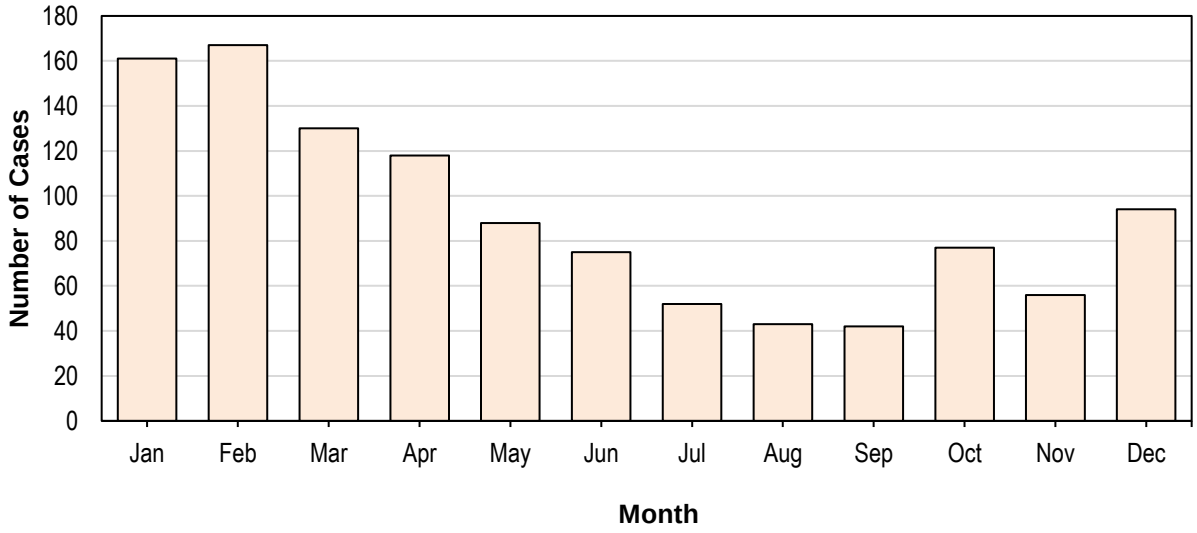
Figure 3: Rate by Age Group – Louisiana, 1990-2018



Seasonal Distribution

Most cases (52%) occur between January and April. This pattern has been consistent every year (Figure 4).

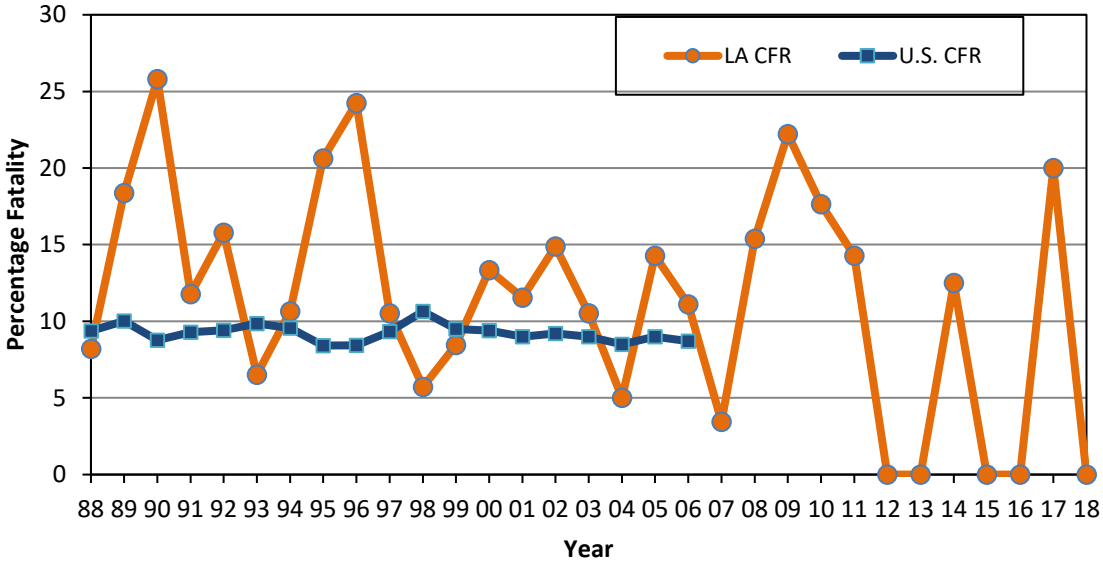
Figure 4: Meningococcal Meningitis Cases by Month – Louisiana, 1987-2018



Mortality

In spite of the availability of effective antibiotics, the case fatality rate remains high, both in the United States and in Louisiana. The case fatality rate in Louisiana varies widely from 5% to 25% (Figure 5). There was one death reported in 2017.

Figure 5: Meningococcal Meningitis Case Fatality Rates-Louisiana versus U.S., 1988-2018



Genetic Typing

The OPH laboratories began pulse field gel electrophoresis (PFGE) testing of all strains of *N. meningitidis* received since May 2001. PFGE is the equivalent of genetic "finger-printing" of strains of *N. meningitidis.* This gives OPH the ability to identify the presence of specific strains in particular areas, to track the progress of these strains and to issue warnings to medical providers and the public in these areas.

The 2001 Lethal Strains

In 2001, one particular strain that persisted throughout the year proved to be particularly lethal (four deaths out of eight cases) and "resistant" to vaccine (two vaccine failures out of eight cases). Strains seemed to be limited to some areas of the state. This particular strain was seen in both the Greater New Orleans area and the Rapides (Alexandria) area (Table).

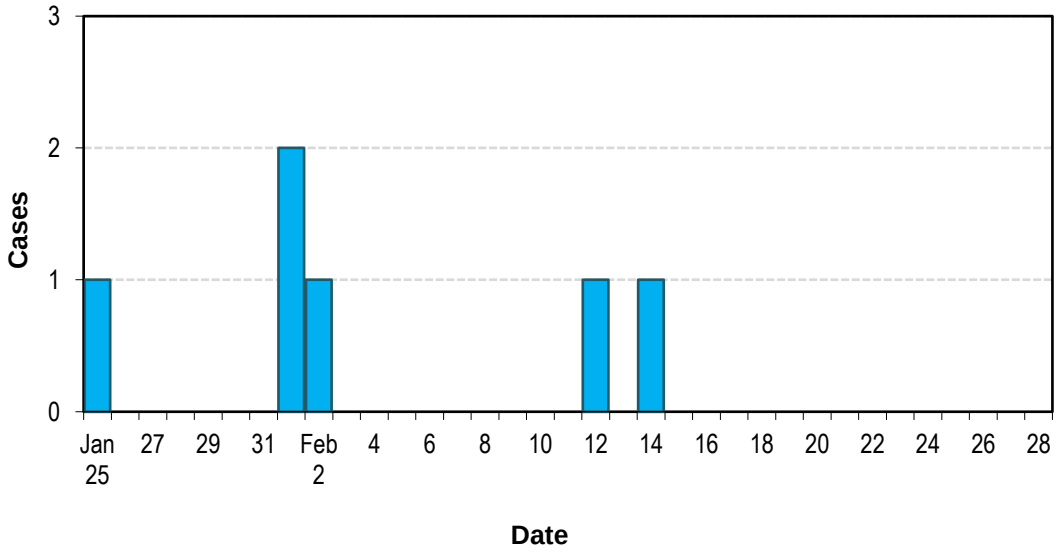
Table: *N. meningitidis* Cases of Lethal Strain - Louisiana, 2001

Date	Age	Sex	City	Parish	Comment	Fatality?
02/27/01	17	F	Laplace	St. John		Died
03/21/01	19	F	New Orleans	Orleans	University T	Died
03/26/01	12	M	Boyce	Rapides		Died
04/20/01	19	F	New Orleans	Orleans	University T Vacc	N
05/06/01	7	F	New Orleans	Orleans		N
10/29/2001	12	F	Pineville	Rapides		N
11/9/2001	19	F	New Orleans	Orleans	University T Vacc	Died
11/10/2001	19	F	Pineville	Rapides		N

The University of Louisiana at Lafayette (ULL) Outbreak

Between January 26, 2006 and February 14, 2006 a total of six cases of meningococcal disease, caused by *Neisseria meningitidis* serogroup C, were reported to OPH (Figure 6).

Figure 6: Epidemic Curve – ULL Outbreak – Louisiana, 2006



The case investigation identified an organizational outbreak linked to the local university. The population at risk was approximately 17,000 people. Additionally, the attack rate was 29.4 cases per 100,000 population at risk [(5 cases/17,000 population at risk)*100,000 = 29.4/100,000]. Only five of the six cases were directly linked to the university. Close personal contacts to the

infected individuals were identified as persons who may have been in close prolonged contact such as house-hold members. Antibiotic prophylaxis was recommended only for this high-risk group.

In an effort to prevent the continuation of the outbreak, recommendations were issued for three groups of individuals to get vaccinated with a meningococcal vaccine. The groups identified were members of social organizations including fraternities and sororities, all persons who lived on campus at the university, students, faculty and staff at the university through 20 years of age. As vaccine became available, groups deemed at lower risk were offered vaccinations. Upon completion of the vaccination campaign, 5,000 students received vaccinations through the OPH vaccination clinics. Private providers also provided vaccine for their patients.

This outbreak linked cases through the local university; however, the spread of disease can occur only when individuals are in close personal contact with each other. In some instances this includes sharing items that will facilitate droplet transmission from person-to-person. Casual contact, such as being in the same classroom, does not put a person at elevated risk or warrant prophylaxis. The recommendation for mass vaccination is not generally considered necessary, but the specifics of the outbreak at this university, required it.

Gibsland Meningococcal Meningitis Outbreak, February 2009

Between the dates of February 8 and February 19, five confirmed cases of meningococcal meningitis in Gibsland, LA. were reported to the OPH. Gibsland is a town of approximately 1,100 people in Bienville Parish. The ages of patients ranged from two years to 21 years-old and with the exception of the two year-old, who was not confirmed to be related, all cases were relatives or friends who spend time together and all were linked to a local school and a church sleep-over event. PFGE tests done on the four confirmed cases showed the exact same pattern. Common symptoms included high fever, headache, back pain, rash, lethargy and unresponsive-ness. One 18-year-old male died within three days of onset of the disease; the other three recovered. Following the outbreak, 38 contacts of the patients were prophylaxed, as well as 49 people from the church sleep-over event. At the school, 158 people were vaccinated on February 20th (118 students and 40 staff members).

Reporting Discrepancies

From 1999 to 2010, reporting of meningococcal meningitis (Meningococcal Invasive Disease or MID) has been captured in both the Infectious Disease Reportable Information System (IDRIS) as well as in the Louisiana hospital discharge database (LaHIDD).

When comparing the records however, there are some discrepancies with the reported numbers. Using last name, first name and date of birth, both data sets were matched. There were 218 cases found in both systems. IDRIS had a total of 517 cases and LaHIDD has a total of 418 cases.

In IDRIS only	289	507	
In both	218		418
In LaHIDD only	200		

Categorizing Concordance and Discrepancy

To understand these discrepancies a database of 707 patients was constructed with the following categories:

- Category A: Patient found in both IDRIS and LaHIDD with Meningococcal Invasive Disease (MID)=218
- Category B: Patients found in both IDRIS and LaHIDD=54, in IDRIS they are listed as having MID, in LaHIDD they are listed with a condition compatible with MID (for example their condition is "meningitis, no organism specified", "bacterial meningitis" without naming the bacteria…),
- Category C: Patients found only in IDRIS with a MID condition, not found in LaHIDD,
- Category D: Patients found only in LaHIDD with a MID condition and not found in IDRIS

Category	In IDRIS		In LaHIDD		
	Condition	Number	Condition	Number	
A	MID	218	MID	218	Names matching in both IDRIS & LaHIDD
B	MID	54	MID*	54	Names matching in both IDRIS & LaHIDD
C	MID	235	Not found	0	In IDRIS but not found in LaHIDD
D	Not found	0	MID	200	In LaHIDD with MID but not found in IDRIS

MID = Classified as a condition close to Meningococcal Invasive Disease, like Meningitis, Not Otherwise Specified, Bacterial Meningitis...*

A and B Patients were Concordant

Patients in category A were a perfect match. Those in category B can be considered to represent the patients whose condition was not perfectly coded in LaHIDD, they were not identified as MID but there were meningitis with a coding for the condition slightly off.

Examining C and D Patients

How to explain categories C and D? These were a total mismatch. To understand these discrepancies, the medical records of a sample of recent (2008 to 2010) C and D patients were examined: this sample was 52% of category C patients and 53% of category D patients.

Who Are Category C Patients (in IDRIS but not in LaHIDD)?

Category C were 235 patients reported in IDRIS but not found in LaHIDD. This is unusual since one would expect all patients to have been hospitalized. The medical record review showed:

C1	Patients who were indeed in IDRIS and LaHIDD but their names were misspelled causing them not to match	20%
C2	Patients who were in the Emergency department but died before admission in the hospital,	40%
C3	Patients who were dead on arrival at the Emergency Department who were diagnosed at autopsy,	10%
C4	Patient who were in the Emergency Department, diagnosed clinically with no bacterial confirmation, not hospitalized but whose contacts were treated prophilactically as contacts of MID	10%
C5	Patients resident of Louisiana but hospitalized out of state, therefore not hospitalized in Louisiana and not in LaHIDD	10%
C6	Patients hospitalized for MID in Louisiana but not appearing in LaHIDD (About 10 to 15% of hospitalizations are not reported in LaHIDD for miscellaneous reasons	10%

In summary, except for category C4 patients (MID suspects only) from category C (reported in IDRIS only) are indeed validated MID.

Who are Category D Patients (in LaHIDD but not in IDRIS)?

Category D were 200 patients reported in LaHIDD but not found in IDRIS. This would indicate that neither the Infection Preventionist nor the lab reported these cases. The medical record review showed:

D1	Patients who were indeed in IDRIS and LaHIDD but their names were misspelled causing them not to match	22%
D2	Patients who were miscoded in LaHIDD, there were not MID, not even close	73%
D3	Patients who were indeed MID in their hospital record but never reported in IDRIS	5%

In summary the following are estimates based on computer review of 707 records and estimation based on a sample of mismatched records:

IDRIS Only			IDRIS and LaHIDD	LaHIDD Only	
Suspect	**Not Hospitalized**	**Missing in LaHIDD**		**MID missed by IDRIS**	**Miscoded in LaHIDD**
24	141	23	363	10	146

1-Using LaHIDD as a quality assurance tool for IDRIS is not an acceptable approach given the high percentage of coding errors in LaHIDD. LaHIDD has a 28% false positive rate.

2-IDRIS captured 527 out of 537 real cases for a sensitivity of 98.1%

Category	Description	Number	Percent
A	Perfect match between IDRIS and LaHIDD	**218**	**30.8**
B	MID in IDRIS with compatible coding in LaHIDD but mot exact coding in LaHIDD	**54**	**7.6**
C1	Patients who were indeed in IDRIS and LaHIDD but their names were misspelled causing them not to match	47	6.6
C2	Patients who were in the Emergency Department but died before admission in the hospital	94	13.3
C3	Patients who were dead on arrival at the Emergency Department who were diagnosed at autopsy	23	3.2
C4	Patient who were in the Emergency Department, diagnosed clinically with no bacterial confirmation, not hospitalized but whose contacts were treated prophilactically as contacts of MID	24	3.4
C5	Patients resident of Louisiana but hospitalized out of state, therefore not hospitalized in Louisiana and not in LaHIDD	24	3.4
C6	Patients hospitalized for MID in Louisiana but not appearing in LaHIDD (About 10 to 15% of hospitalizations are not reported in LaHIDD for miscellaneous reasons	23	3.2
C	**Subtotal**	**235**	**33.2**
D1	Patients who were indeed in IDRIS and LaHIDD but their names were misspelled causing them not to match	44	6.2
D2	Patients who were miscoded in LaHIDD, there were not MID, not even close	146	20.7
D3	Patients who were indeed MID in their hospital record but never reported in IDRIS	10	1.4
D	**Subtotal**	**200**	**28.4**
	Grand Total	**707**	**100.0**

Numbers in Category C and D are estimates based on a sample of medical records