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Demographic Risk Factors of Mortality among Non-Pregnant Adults with Invasive Group B Streptococcal Infection: Data from New Mexico Active Bacterial Surveillance, 2004-2009

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Abstract

Demographic Risk Factors of Mortality among Non-Pregnant Adults with Invasive Group B Streptococcal Infection: Data from New Mexico Active Bacterial Surveillance, 2004-2009

By Jessica R. Reno

Group B *Streptococcus* (GBS) has emerged as an important cause of invasive infection in non-pregnant adults since the 1970s. Active-, population-, and laboratory-based surveillance for GBS began in 1997 through Active Bacterial Core surveillance (ABCs), a core component of the Emerging Infections Program (EIP) network at the Centers for Disease Control and Prevention (CDC). In 2004, the state of New Mexico (NM) joined the EIP network. The purpose of this study was to determine demographic risk factors for mortality among non-pregnant NM adults with invasive GBS infection between January 1, 2004 and December 31, 2009 using NM's ABCs surveillance data. During this time period, there were 641 cases of invasive GBS infection among non-pregnant adults living in the state of NM. Of the 628 cases with known outcome, 68 (10.8%) died as a result of infection. The risk of mortality according to age, gender, health insurance status, race/ethnicity, and region of residence was assessed using SAS version 9.2. None of these demographic characteristics were significant ($p<0.05$) predictors of mortality in the univariate analysis of each characteristic or in the multivariate logistic regression including all demographic characteristics and known risk factors for mortality. The demographic groups with the highest mortality in NM from 2004 to 2009 were those without health insurance (16.7%), those living in the southeast (15.9%) or southwest (13.3%) region of the state, and those who were not American Indian (non-Hispanic White: 12.5%; Hispanic: 13.0%). In order to prevent deaths due to invasive GBS infection, it is important to further examine why these disparities exist and whether they exist in other populations.

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1. Background

1.1 Introduction

Group B *Streptococcus* (GBS) has emerged as an important cause of invasive infection in non-pregnant adults since the 1970s. Active-, population-, and laboratory-based surveillance for invasive GBS began in 1997 through Active Bacterial Core surveillance (ABCs), a core component of the Emerging Infections Program (EIP) network at the Centers for Disease Control and Prevention (CDC). In 2004, the state of New Mexico (NM) joined the EIP network. From 2004 through 2009, NM identified 641 cases of invasive GBS infection among non-pregnant adults living in NM. Of the 628 cases with known outcome, 68 (10.8%) died as a result of infection. During 2007, the mortality rate among non-pregnant adult GBS cases from all ten ABCs sites was 7.5% (1). The purpose of this study is to evaluate potential demographic risk factors of mortality among NM residents with invasive GBS infection.

1.2 Streptococcal Infections

In 1933, Lancefield first described the serological classification of hemolytic streptococci into groups, now called "Lancefield groups," on the basis of bacteria cell wall carbohydrate antigens (2). A few years later, the first cases of invasive GBS infection among elderly adults were reported (3). By this time, GBS had been recognized as an important, but occasional, pathogen causing postpartum sepsis, amnionitis, endocarditis, and septic abortion (4). In the 1960s, the incidence of invasive GBS infection began to increase, starting in the United States and Europe. GBS is a major cause of bovine mastitis, and spread from cattle to humans is thought to occur mainly via the hands of dairy workers. It can now exist as part of the normal flora in humans. It

may be transmitted from person to person by hands, through respiratory secretions and droplets.

Streptococcal species known to cause disease in humans are either part of the normal flora, i.e. enteric or oral, where they cause opportunistic infections, or pyogenic, meaning that they are not generally part of the normal flora and typically cause acute and often severe infections (4). Pyogenic streptococcal species include GBS, or *Streptococcus agalactiae*, *S. pyogenes*, (or group A *Streptococcus*), *S. equisimilis* (or group C *Streptococcus*), *S. equi* (group G *Streptococcus*), and *S. pneumoniae* (or pneumococcus). These Lancefield groups differ in colony morphology, laboratory identification, and common disease associations. Unlike groups A, C, and G, GBS has large, mucoid colonies with a narrow zone of hemolysis and produces a positive CAMP test in the laboratory. Groups are definitively identified in the laboratory with latex and similar particle agglutination kits. The carbohydrate antigens identified by these methods are M and T proteins (for groups A and G) and capsular polysaccharides (for groups B and pneumococci). Molecular identification methods are becoming more common, including rapid PCR testing for GBS. Currently, diseases most commonly associated with GBS are neonatal sepsis, meningitis, postpartum infections, endocarditis, and cellulitis.

In 2009, the incidence in the United States of GBS among adults ≥65 years was 23.5 cases per 100,000 population, which was lower than that of *S. pneumoniae* but more than twice as high as that of group A *Streptococcus* (5-7) (see Table 1). Each of these three pathogens has a high case-fatality rate among elderly patients with invasive

infection. In contrast, the incidence and mortality rates of the same species among cases age 50-64 years are much lower than their older counterparts, but follow a similar pattern.

Table 1. Invasive Infection Due to GBS and Other Gram-positive Pathogens among Elderly Adults ≥65 years in the United States, 2009.

Pathogen	Incidence Rate per 100,000 population (No. of Infections)		Mortality % (No. of Deaths)	
	50-64 years	≥65 years	50-64 years	≥65 years
Group B *Streptococcus*	10.6 (648)	23.0 (895)	5.7 (37)	10.9 (98)
Streptococcus pneumoniae	21.2 (1,138)	38.7 (1,317)	12.2 (139)	16.9 (223)
Group A *Streptococcus*	4.7 (276)	8.9 (328)	10.5 (29)	18.9 (62)

Note: Data are from (5-7).

1.3 Etiology of Invasive Group B Streptococcal Infection among Adults

GBS exists as normal flora within the female genital tract and the lower gastrointestinal tract, but can cause severe infection when introduced to sterile sites (4). Transmission occurs via person-to-person contact or fecal-oral transmission. A cross-sectional study of a convenience sample of healthy adults ≥65 years in Houston found that 21.7% of subjects were colonized with GBS when two collection sites were tested: rectal swab specimens and initial voided urine specimens from men or lower vaginal swab specimens from women. A similar prevalence of GBS colonization was found among healthy university students in Michigan (20% of men; 34% of women) (8). This study found that female gender and ever having had any type of sexual contact were predictors of being colonized with GBS. A gender disparity was not found among adults ≥65 years. Regarding fecal-oral transmission, a study of 914 food products from 595 food establishments in France observed that 1.2% of food products were contaminated with GBS (9).

1.4 Epidemiology of Invasive Group B Streptococcal Infection among Neonates

The highest GBS infection rate occurs among neonates, many of whom are exposed to the bacteria upon rupture of the placental membranes or in the vaginal tract during birth. The most commonly diagnosed clinical syndromes among neonates with invasive GBS infection are bacteremia without focus, pneumonia, and meningitis (10). In fact, GBS emerged as the leading cause of sepsis and meningitis in the first week of life in the 1970s in the United States (1, 10). Surveillance of populations consisting of more than 300,000 live births show that the incidence of invasive early-onset GBS (0-6 days after birth) remained unchanged between 1999 and 2001, but that there was a 31% decrease from 0.47 cases per 1,000 live births in 2001 to 0.34 in 2004 (10, 11). This decrease corresponded with the publication of revised early-onset disease prevention guidelines in 2002, recommending universal screening of pregnant women at 35-37 weeks' gestation for rectovaginal GBS colonization, and administration of intrapartum antibiotics for carriers. In this study, the overall mortality rate among early-onset GBS cases was 6.8%, and the mortality rate among late-onset (7-89 days after birth) was 4.7%. The incidence of late-onset GBS (7-89 days after birth) remained relatively stable at an average of 0.34 per 1,000 live births, and incidence of GBS infection among pregnant women also remained stable at an average of 0.12 per 1,000 live births. There are currently no strategies to prevent late-onset GBS, and the incidence of late-onset GBS surpassed that of early-onset GBS for the first time in 2003. The rates of both early-onset and late-onset GBS were more than twice as high among African American infants compared to White infants. However, cases outside the perinatal risk period account for

nearly 90% of the national burden of disease, and mortality rates are higher in these age groups (10).

1.5 Epidemiology of Invasive Group B Streptococcal Infection among Adults

GBS exists as normal flora within the female genital tract and the lower gastrointestinal tract as a result of person-to-person contact or fecal-oral transmission, but can cause severe infection when introduced to sterile sites (4). Analyses of multicenter surveillance of GBS among over 26 million United States residents have revealed extreme increases in incidence of infection in the past two decades. In an analysis of invasive GBS infection cases among non-pregnant adults ≥18 years, the incidence doubled from 3.6 to 7.3 cases per 100,000 population between 1990 and 2007 (1). During the time period when the neonatal GBS infection rate was rapidly decreasing due to updated prevention recommendations, the overall incidence of invasive GBS infection among non-pregnant adults ≥15 years increased by 32%, from 6.0 per 100,000 population in 1999 to 7.9 in 2005 ($p<0.001$) (10). During this time, the incidence among adults ≥65 years increased significantly by 20% (from 21.5 cases per 100,000 population to 26.0), while the incidence of invasive GBS infection increased significantly by 48% among persons 15 to 64 years old (from 3.4 per 100,000 population to 5.0). This increase in incidence among younger adults indicates that the overall rate is not increasing primarily because of ageing of the population. Furthermore, the studies reported consistent age distributions among cases of infection throughout the study periods. The increase could be partly explained by the increasing prevalence of adults with chronic medical conditions, but not completely, as the incidence has risen very sharply over a relatively short period of time. This increase is also unlikely to be due to increased surveillance as

the data used in both of these studies come from the same established surveillance network started in 1990. While the population of the surveillance area has increased, the methods of surveillance have remained the same.

The rising incidence of GBS infection among adults has been noted internationally as well. A retrospective study in Japan found a nearly 3-fold increase in the number of adult GBS cases from the time period of 1998-2002 to 2003-2007 (12). The researchers mentioned an increase in the number of diabetic and pre-diabetic patients in the surveillance population from 13.7 million to 18.7 million during the same time period, and hypothesize that there might have also been an increase in the incidence of diabetes, which may have been linked to the increased incidence of invasive GBS infection.

1.6 Treatment of Invasive Group B Streptococcal Infection

Penicillin is the front-line antibiotic for treatment of GBS infection (13). For patients who are allergic to penicillin, erythromycin or clindamycin are typically used. While GBS remains susceptible to penicillin, resistance to the second-line antimicrobials has increased since 1996 (14). In the United States, between 2005 and 2006, resistance to tetracycline, erythromycin, and clindamycin was common (83.3%, 40.0%, and 20.2%, respectively) (10). All of the isolates in this study were susceptible to ampicillin, cefotaxime, penicillin, and vancomycin. In Japan, between 1998 and 2007, 2% of GBS isolates were resistant to erythromycin, 3% to clindamycin, and 31% to levofloxacin (12). There are currently no guidelines for the prevention of invasive GBS infection among adults like there are for neonates (1).

1.7 Prevention of Invasive Group B Streptococcal Infection

The major surface antigens of GBS are capsular polysaccharides (CPS) (4). Nine capsular types of GBS have been identified: Ia, Ib, and II through VIII. Types Ia, Ib, II, and III are the "classical" types, types IV and V are newer but becoming more common, and types VI, VII, and VIII are relatively uncommon. A tenth capsular type, type IX, has recently been proposed. According to surveillance data covering counties from 10 states between 2005 and 2006, the most prevalent types identified among cases of GBS infection among adults ≥18 years in the United States were V (29.2%) and Ia (24.3%) (1) (see Table 2). A quadrivalent vaccine that included types Ia, II, III, and V could have potentially prevented 78.5% of these cases because this proportion of case isolates belonged to one of these type groups. Most reported cases of GBS in the surveillance areas (78.7%) were analyzed for serotype identification during this time period. A similar study concluded that a pentavalent conjugate vaccine that included types Ia, Ib, II, III, and V could have prevented up to 88% of adult invasive GBS infection in the United States from 1999 to 2006 (10).

Table 2. Distribution of GBS Capsular Polysaccharide Types among Non-Pregnant Cases of Invasive GBS Infection ≥18 years in the United States, 2005-2006.

Type	No. of Isolates (%) N=1,933
Ia	470 (24.3)
Ib	182 (9.4)
II	261 (13.5)
III	221 (11.4)
IV	110 (5.7)
V	565 (29.2)
VI	1 (0.1)
VII	2 (0.1)
Nontypeable	121 (6.3)

Note: Data are from (1).

Clinical trials have begun for vaccines that prevent infection by types Ia, Ib, II, III, and V(15-20). These vaccines, which are typically conjugated with tetanus toxoid for optimal antibody production, have been shown to be well tolerated in healthy adults between 18 and 40 years of age, produce higher concentrations of type-specific antibodies, and lead to the opsonophagocytic killing of type-specific GBS in vitro. Impaired immune responses in older adults may make vaccination a less effective prevention strategy among older adults than it would be in pregnant women neonates, but one study has shown that type V CPS-specific antibodies are safe and immunogenic when administered to adults 65-85 years (16). A cross-sectional study found that GBS colonization among adults ≥65 years was dominated by type V (47.3%), so a vaccine preventing infection by this type is particularly important (21). Unfortunately, 12.3% of the study subjects were colonized with non-typeable GBS types.

1.8 Known Risk Factors of Invasive Group B Streptococcal Infection among Adults

An estimated 16,700 cases of invasive GBS infection occurred among non-pregnant adults in the United States in 2007 (1). The primary clinical syndromes among

these cases included bacteremia and skin and/or soft-tissue infection. Table 3 lists the most recently reported distribution of clinical syndromes among cases of invasive GBS infection from this ABCs multistate, population-based analysis.

Table 3. **Clinical Syndromes of Non-Pregnant Adults with Invasive GBS Disease in the United States, 2007.**

Clinical Syndrome	Cases (%) N=1,546
Bacteremia without focus	607 (39.3)
Skin and/or soft-tissue infection	395 (25.5)
Pneumonia	194 (12.5)
Osteomyelitis	146 (9.4)
Joint infection	121 (7.8)
Abscess	61 (3.9)
Endocarditis	46 (3.0)
Peritonitis	42 (2.7)
Streptococcal Toxic Shock Syndrome	24 (1.6)
Meningitis	24 (1.6)
Necrotizing fasciitis	17 (1.1)
Other	48 (3.1)

Note: Data are from (1).

Invasive GBS disease occurs in African Americans more frequently than in White Americans, a trait common to other streptococcal pathogens (1, 10, 22, 23). Between 1990 and 2007, multicenter surveillance data from ABCs found that the average incidence difference between the African American population and the White population in the United States was 4.6 cases per 100,000 persons (1). Between 1995 and 2005, the same surveillance system determined that African Americans were twice as likely to be infected with GBS than White Americans (95% CI 1.5-2.6) (10). Similar results were found throughout the United States between 1993 and 1998 (RR 2.0, $p<0.001$, 95% CI 1.7-2.3) (23), and in Maryland in 1995 (RR 1.6, $p<0.001$) (22). Race could be a surrogate for factors which increase the risk of disease, such as socioeconomic status, nutritional

differences, educational disparities, access to health care, or underlying medical conditions.

Other commonly observed risk factors for GBS infection are age, diabetes mellitus and cancer. Active-, population-based, multistate surveillance during 2008 found that the incidence of GBS infection among adults ≥65 years (22.0 per 100,000 population) was at least twice as high as that of any other adult age group in the United States (24). Between 1990 and 2007 in the United States, incidence increased in all age groups, although the largest increase was observed among case patients aged 65 to 79 years (114.7%) and among case patients aged 40 to 64 years (92.7%) (1). Both diabetes and age ≥65 years increase the risk for infection because they affect the immune system negatively by interfering with cell-mediated immunity, delayed-type hypersensitivity responses, humoral immunity, and immunoglobulin levels (25). Diabetes is the most common comorbid condition among patients with invasive GBS infection. A review of the literature stated that this association is at least in part due to the altered integrity of anatomical barriers to GBS among people with diabetes mellitus and related complications (13, 26). In 2007, 44.4% of invasive GBS cases among non-pregnant adults in the United States were diabetic, while only 10.7% of the adult population was diabetic (1). Diabetes has been reported as a risk factor for GBS infection in three separate multistate, population-based studies analyzing ABCs surveillance data in metropolitan areas of the United States since 1982, with risk ratios as high as 10.5 (95% CI 7.8-14.4) (27-29). Trends in the incidence of invasive GBS infection incidence may continue to parallel trends in the prevalence of diabetes in the United States population. The same three multistate, population-based studies also found cancer to be a significant

risk factor for infection, with risk ratios as high as 16.4 (95% CI 11.5-23.3). The study conducted in Atlanta, Georgia in 1989, however, only found this to be a significant risk factor for adults under the age of 70 years (28).

Several other risk factors of GBS infection have been reported, although less commonly. A study of GBS infection patients in Maryland found living in a nursing home to be a risk factor for infection among adults over the age of 65 years (RR 4.1, 95% CI 2.6-6.7) (22). This is plausible, due to the fact that a closed institutional environment favors regular exposure to GBS through contact with health care workers, other residents, and staff when hand hygiene is deficient (13). An additional ABCs study conducted in three metropolitan areas in the United States found several underlying illnesses, besides diabetes and breast cancer, to contribute significantly to the risk of infection when compared to hospital-matched controls: cirrhosis (OR 9.7, $p<0.001$, 95% CI 3.5-26.9), stroke (OR 3.5, $p<0.001$, 95% CI 1.9-6.4), decubitus ulcer (OR 4.0, $p=0.002$, 95% CI 1.6-9.8), and neurogenic bladder (OR 4.6, $p=0.01$, 95% CI 1.4, 15.1]) (29). Two ABCs studies of GBS cases in metropolitan Atlanta, Georgia in the 1980's found other risk factors for infection when compared to the general population: living in Fulton County (RR 2.9, $p<0.001$, 95% CI 2.1-4.0), HIV infection (RR 30, $p<0.001$, 95% CI 11-78) (28), and male gender (RR 2.0, $p=0.01$) (27). Alcoholism may also be a risk factor for GBS infection, which was demonstrated in a rat model in which chronic ethanol ingestion was associated with greater incidence (30). Alcohol is known to deplete antioxidants, cause macrophage dysfunction, reduce macrophage killing of internalized bacteria, and damage the barrier integrity of the lungs.

1.9 Evidence-Based Risk Factors of Mortality among Adult Cases of Invasive Group B Streptococcal Infection

The mortality among non-pregnant adults with invasive GBS infection has been decreasing since its emergence in the United States. In 1990, multicenter surveillance data from ABCs reported a mortality of 23.7%, which fell to 8.8% in 1994, rose again to 13.0% the following year, and decreased until 2007, when the mortality was 7.5%, resulting in an estimated 1,200 deaths among cases that year (1). Multicenter ABCs data of 11,662 cases over 15 years in the United States determined that African American race is associated with increased mortality compared to White race among those ≥45 years ($p<0.05$) (10). The same study found that being infected with serotype Ia was significantly associated with mortality among cases of all ages (RR 1.3, 95% CI 1.3-2.1). An analysis of earlier data from this multicenter surveillance system also found that African American cases were more likely to die than White cases (RR 1.9, $p<0.001$, 95% CI 1.7-2.4) (23). In addition, this study found an association between meningitis and mortality (RR 2.1, $p=0.003$, 95% CI 1.4-3.2). A multicenter case-control study in the United States reported an increased mortality for those 65 years and older among 219 non-pregnant adult cases of GBS ($p=0.008$) (29). In Japan, 52 non-pregnant adult GBS patients with bacteremia had a significantly increased mortality rate compared to those without bacteremia (RR 4.79, $p<0.05$) (12). Bacteremia was also associated with mortality in a study of 32 non-pregnant adults with invasive GBS infection in Spain ($p=0.041$) (31). Another Spanish study of 150 non-pregnant adults infected with GBS concluded that the patients with shock at diagnosis (OR 23.96, $p=0.001$, 95% CI 3.44-166.57) or cancer (OR 4.96, $p=0.012$, 95% CI 1.43-17.20,) had an increased risk of

mortality (32). Shock at diagnosis was also associated with mortality in a study of 32 patients with GBS-related bacteremia in the United States (RR 3.94, p=0.01) (33). A South African study of 40 non-pregnant adults with GBS infection reported that clinical manifestations of bacteremia (RR=6.00, p=0.0009) and pneumonia (RR=4.00, p=0.012) were independently associated with mortality (34).

Several studies have identified risk factors of mortality among cases of bacterial infections that include, but are not limited to, Group B Streptococcal infection. A study conducted in Spain among 185 adult bacterial meningitis cases found that pneumonia as focus (OR 25.9, 95% CI 2.6-257), coma on admission (OR 9.9, 95% CI 2.8-34.1), and seizures after therapy (OR 6.8, 95% CI 1.7-27) were related with mortality in multivariate analysis, while intracranial pressure therapy (OR 0.21, 95% CI 0.04-0.996) was a protective factor (35). However, less than 10 of the 185 cases in this particular study were caused by GBS, and none of them ended in fatality. A study conducted in Finland found that obesity (RR 6.4, p=0.03, 95% CI 1.2-34.4) and smoking (RR 23.0, p=0.02, 95% CI 1.7-321.6) were significantly associated with case fatality among 149 bacteremia patients, of which 23 were infected with β-hemolytic streptococcal species such as GBS (36).

2. Methods

2.1 Study Design

The purpose of this study was to determine demographic risk factors for mortality among non-pregnant NM adults with invasive GBS infection between January 1, 2004 and December 31, 2009. A retrospective analysis of all reported invasive GBS cases in NM from 2004 through 2009 was conducted using data collected by ABCs. ABCs, as previously described, is an active-, population-, and laboratory-based surveillance system housed under the Emerging Infections Program (EIP) at the Centers for Disease Control and Prevention (CDC).

2.2 Study Setting

The NMEIP is one of ten surveillance systems established by the CDC throughout the United States. The other EIP sites are located in California (3-county Bay area), Colorado (5-county Denver metro area), Connecticut (statewide), Georgia (20-county metro Atlanta area), Maryland (5-county metro Baltimore area), Minnesota (statewide), New York (11 counties), Oregon (3-county Portland area), and Tennessee (20-county surveillance area). The NMEIP is administered by the New Mexico Department of Health (NMDOH) and the University of New Mexico's Institute for Public Health. EIPs investigate certain invasive bacterial diseases (through ABCs), as well as foodborne diseases, influenza hospitalizations, and healthcare associated infections.

The invasive bacterial infections under surveillance by ABCs include infections by six bacterial organisms: groups A and B *Streptococcus*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, and methicillin-resistant *Staphylococcus aureus*. GBS was added to NM's notifiable conditions list in August

2003, and clinical laboratories are required by state statute to report all cases of culture-confirmed infections by these organisms to the NMDOH. When a case has been identified, laboratories which process a relatively high volume of clinical tests typically fax the hospital identifier, medical record number, patient name, date of birth, and clinical test date to the NMDOH at least once every two weeks. In addition, laboratory audits are conducted in laboratories which process a relatively low volume of clinical tests at least once every six months and usually involve either running EIP-specific queries of the laboratory's electronic records or manually scanning handwritten log books of clinical tests for reportable cases.

2.3 Study Subjects

Adult GBS infection was defined as culture-confirmed isolation of GBS from a normally sterile site in a non-pregnant, non-post-partum NM resident ≥18 years of age collected between January 1, 2004 and December 31, 2009. Subjects were considered to be post-partum if they had given birth ≤30 days before the time of the specimen collection.

2.4 Data Source

Cases of invasive GBS were reported to NMABCs by laboratories throughout NM, or identified by routine audits of these laboratories. NMABCs surveillance officers reviewed medical records of each of these cases throughout the six years of this study. If source of specimen collection, age, or culture date could not be determined using the medical records and laboratory reports, then follow-up was conducted by the ABCs surveillance staff by contacting hospital or laboratory staff. If this information was still

not able to be obtained through follow-up, then the subject was excluded from the ABCs database.

NMABCs surveillance staff abstracted data from medical records using a standard data collection form (Appendix A). Data used for this study included information about region of residence, age, sex, race, ethnicity, type of insurance, outcome at time of hospital discharge, pregnancy status, clinical illness, source, date of specimen collection, and underlying medical conditions or illnesses.

2.5 Analysis

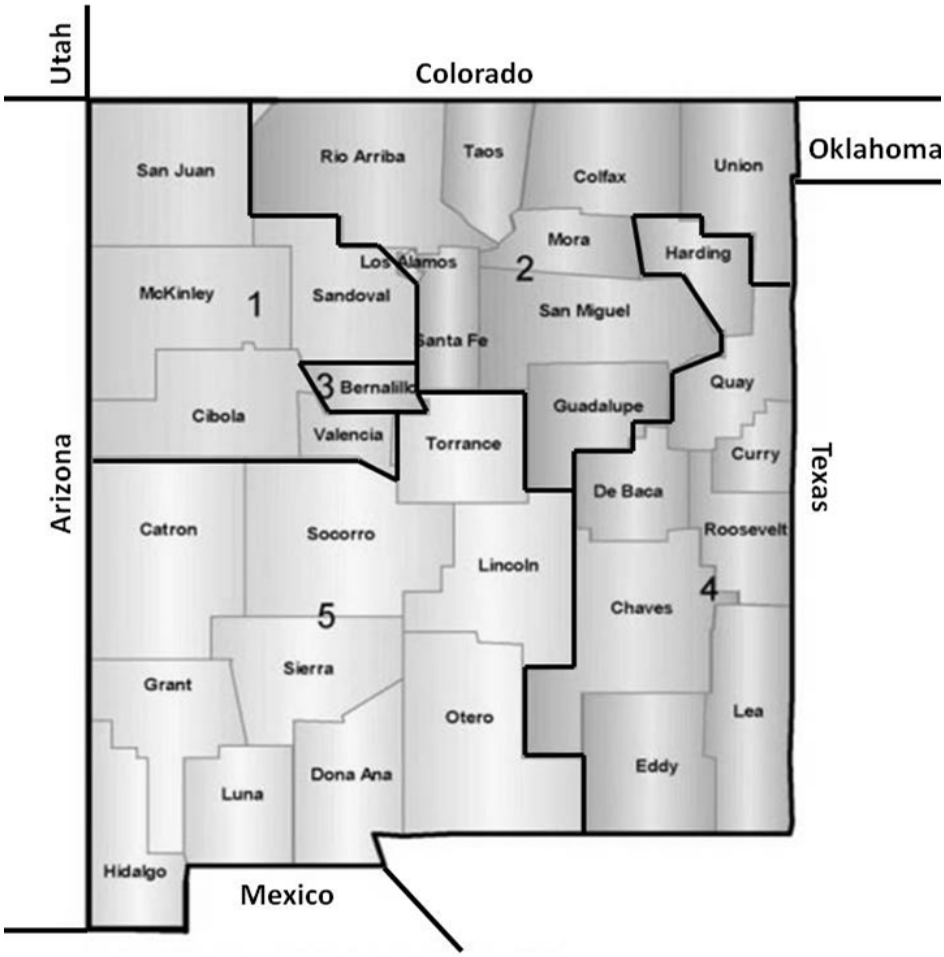
Non-pregnant or non-postpartum cases of invasive GBS isolated from a normally sterile site ≥18 years of age between the dates of January 1, 2004 and December 31, 2009 were included in the analysis. NM residency was determined using the address listed in the medical chart. Specimen source and culture date were recorded as written in the medical or laboratory records.

Initially, outcome was classified as having survived if the case was discharged from the hospital, or as a death if the case died during the hospital visit when GBS was collected. After classifying outcome based on medical records, NMABCs matched surviving cases with the death certificate database maintained by the NMDOH Bureau of Vital Records and Health Statistics. Cases that died within three days of discharge were re-classified as a death.

Demographic variables analyzed included region of residence, age, sex, race, ethnicity, and type of insurance. Residence was classified using NM public health regions determined by the NMDOH (see Figure 1). Public health region 1 consists of

five counties in the northwest section of the state. Public health region 2 consists of nine counties in the northeast section of the state. Public health region 3 is Bernalillo County, the most populous county, which is located in the center of the state. Public health region 4 consists of eight counties in the southeast section of the state. Public health region 5 consists of the ten counties in the southwest section of the state.

Figure 1. Public Health Regions of New Mexico.



Source: New Mexico Department of Health. Ibis.health.state.nm.us. Accessed January 14, 2011.

Age was calculated by subtracting the subject's date of birth from the culture date, and assigned to two age groups: <65 years and ≥65 years. Gender was classified as

male or female. Race was collected as White, African American, American Indian, Asian, or Native Hawaiian or Other Pacific Islander. Ethnicity was collected as Hispanic or Latino, or Not Hispanic or Latino. For the purposes of this analysis, race and ethnicity were combined and classified as Hispanic (White Hispanic or unknown race Hispanic), non-Hispanic White, African American, American Indian, or Asian, Native Hawaiian or Other Pacific Islander. Type of insurance was collected as Medicare, Military/VA, Medicaid/state assistance program, Indian Health Service, Private/HMO/PPO/managed care plan, other, or no health care coverage. For the purposes of this analysis, insurance was further classified as private or Military/VA, government assisted (Medicare, Medicaid/state assistance program, and Indian Health Service), or none.

Potentially confounding variables were determined by identifying predictors of mortality among GBS cases in the literature and available in the NMABCs dataset. Risk factors for mortality among GBS infection cases reported in the literature are African American race (compared to White race); ≥65 years of age; pneumonia, bacteremia, meningitis, and streptococcal toxic shock syndrome (STSS) as clinical manifestations; infection by GBS serotype Ia; and cancer as an underlying condition. All of these data points were collected by NMABCs. Risk factors for mortality were also identified from studies of subjects infected by a variety of bacterial organisms, including GBS. These factors were considered potentially confounding variables and included the following: coma on admission, seizures after therapy, obesity, smoking, and intracranial pressure therapy (a protective factor). Coma on admission, seizures after therapy, and intracranial pressure therapy were not collected by NMABCs and could not be included in the statistical analysis.

SAS® version 9.2 was used for all statistical analyses. A two-sided p-value < 0.05 was designated as the level for statistical significance. The χ^2 test was used in univariate analysis to examine the mortality rates between groups of demographic characteristics. The Fisher's Exact test was used to examine associations when data were sparse (<5 in any cell). Multivariate conditional logistic regression was used to identify associations adjusted for potentially confounding variables identified in the literature.

3. Results

3.1 Population Characteristics

There were 782 reported GBS infections in NM residents from 2004 through 2009. Of these, 651 were at least 18 years of age. Six of these infections were isolated from pregnant or post-partum patients at the time of the infection and were excluded from the study. Four had culture-confirmed specimens which were isolated from non-sterile or unknown sites: one from muscle tissue (which is only considered a sterile site among cases of group A streptococcal infection according to ABCs), two from wounds, and one from an unknown source. Thus, there were 641 infections eligible for inclusion in the study. Among the 628 (98.0%) infections with known outcome, 68 (10.8%) died before the infection was resolved. Mortality varied from 7.6% at its lowest in 2008 to 14.6% at its highest in 2006, but appears to be relatively stable (see Table 4).

Table 4. Mortality among Nonpregant Adults with Invasive GBS Infection in New Mexico by Year.

Year	Deaths (Infections)	Mortality %
2004	9 (101)	8.9
2005	11 (91)	12.1
2006	15 (103)	14.6
2007	9 (89)	10.1
2008	8 (106)	7.6
2009	16 (138)	11.6
Total	68 (628)	10.83

Table 5 describes the study subjects by demographic characteristics, and by potentially confounding characteristics to be considered in the multivariate analysis. Variables for health insurance and obesity had missing values for the 101 (16.1%)

subjects who had infections in 2004 because ABCs began collecting these data in 2005. Only 300 (47.7%) isolates were tested for serotype, so this variable will not be included in the multivariate analysis as a potential confounder. Only 5 (0.8%) subjects were diagnosed with meningitis during the infection, so meningitis was not included in the multivariate analysis. Similarly, STSS was not considered as a potential confounder because no subjects were diagnosed with STSS during the study period.

Table 5. Characteristics of Non-Pregnant Adult GBS Infections in New Mexico by Evidence-based and Potential Risk Factors of Mortality, 2004-2009.

Potential Risk Factors	No. With Characteristic (%)	N (% Known of 628)
Age ≥65 years	272 (43.3)	628 (100.0)
Female Gender	246 (39.2)	628 (100.0)
Insurance		503 (80.1)
Private or Military	217 (43.1)	
Government Assisted	256 (50.9)	
No Insurance	30 (6.0)	
Race/Ethnicity		571 (90.9)
White Non-Hispanic	208 (36.4)	
Hispanic	208 (36.4)	
American Indian	142 (24.9)	
African American	11 (1.9)	
Asian/Pacific Islander	2 (0.4)	
Region		628 (100.0)
1 (Northwest)	190 (30.3)	
2 (Northeast)	79 (12.6)	
3 (Central)	192 (30.6)	
4 (Southeast	69 (11.0)	
5 (Southwest)	98 (15.6)	
Evidence-based Risk Factors		
Bacteremia	258 (41.1)	628 (100.0)
Cancer	58 (9.2)	628 (100.0)
Current Smoking	79 (12.6)	628 (100.0)
Meningitis	5 (0.8)	628 (100.0)
Obesity (BMI≥30)	82 (15.6)	527 (83.9)
Pneumonia	92 (14.7)	628 (100.0)
Serotype Ia	69 (23.0)	300 (47.8)
STSS	0 (0.0)	628 (100.0)

3.2 Univariate Analysis

Table 6 shows the mortality among GBS infections by demographic groups. Cases ≥65 years had a slightly higher mortality (11.8%) than younger cases (10.1%). This difference was not significant. Similarly, males had a slightly higher mortality (11.0%) than females (10.6%).

Mortality for cases without health insurance (16.7%) were 64% higher than those with private or military health insurance(10.1%), while those with government assisted health insurance had a similar mortality (10.2%) to those with private or military health insurance. ABCs began collecting health insurance information in 2005; 125 (19.9%) of the cases in this study did not have health insurance information, 101 of which occurred in 2004.

The racial/ethnic group with the highest mortality was the Hispanic group (13.0%), and the American Indian group had the lowest mortality (6.3%) besides the African American and Asian/Pacific Islander groups, which consisted of only 11 and 2 cases, respectively, and no deaths. Sixty-one (9.5%) cases were not identified by racial/ethnic group on their medical records.

The southeast (15.9%) and southwest (13.3%) regions of NM had the highest mortality, and the northwest region had the lowest mortality (6.8%).

There were no significant differences among any of these demographic characteristics.

Table 6. χ^2 Tests for Association of Demographic Characteristics with Outcome of GBS Infection among Non-Pregnant Adult Cases of Invasive GBS Infection in New Mexico, 2004-2009.

Characteristic	Infections (%)	Mortality (%)	Relative Risk	p-value
Age (N=628)				
Under 65 years	356 (56.7)	10.1	1.00	-
65+ years	272 (43.3)	11.8	1.16	0.5094
Gender (N=628)				
Female	246 (39.2)	10.6	1.00	-
Male	382 (60.8)	11.0	1.04	0.8670
Insurance (N=503)				
Private or Military	217 (43.1)	10.1	1.00	-
Government Assisted	256 (50.9)	10.2	1.00	0.9949
No Insurance	30 (6.0)	16.7	1.64	0.2837
Race/Ethnicity (N=571)				
White Non-Hispanic	208 (36.4)	12.5	1.00	-
Hispanic	208 (36.4)	13.0	1.04	0.8832
American Indian	142 (24.9)	6.3	0.51	0.0595
African American	11 (1.9)	0.0	0.33*	0.3689**
Asian/Pacific Islander	2 (0.4)	0.0	1.31*	1.0000**
Region (N=628)				
1 (Northwest)	190 (30.3)	6.8	0.57	0.0862
2 (Northeast)	79 (12.6)	10.1	0.85	0.6638
3 (Central)	192 (30.6)	12.0	1.00	-
4 (Southeast)	69 (11.0)	15.9	1.33	0.4025
5 (Southwest)	98 (15.6)	13.3	1.11	0.7538

*Added 0.5 to one cell populated with 0 cases in order to calculate statistics.
**Fisher's Exact Test was used because at least one cell was populated with <5 cases.

3.3 Multivariate Analysis

A logistic regression model was used to calculate odds ratios of mortality by demographic groups while controlling for possible confounders. Variables for the interaction between demographic characteristics of interest and potential confounders were screened by running all possible models including one demographic variable, one potential confounder variable, and a product term of the two. Seven of the interaction

terms caused quasi-separation of data points and were excluded. None of the remaining interaction terms were significant within their respective models, so all interaction terms between a demographic variable and a potential confounder variable were excluded from the full model.

Variables for the interaction between two demographic factors were assessed by including all ten possible interaction terms in the model. Two of these variables caused quasi-separation of data points and were excluded. Multicollinearity between variables in the full model was assessed by calculating condition indices for a model containing all five demographic variables, all six potential confounding variables, and the remaining eight interaction terms. The highest condition index was 30.5, and three of the corresponding variance-decomposition proportions were ≥0.50. These results indicated that there was multicollinarity between the variables for age, gender, and the interaction between the two. Condition indices were calculated again excluding the interaction term between the variables for age and gender, and the highest condition index was only 20.1.

The seven interaction terms left in the model were assessed using backwards elimination. The term with the highest p-value was excluded from the model until only significant interaction terms were left. All interaction terms were excluded with this method. Interaction was not considered for the rest of the analysis.

Confounding variables for the final model were assessed using backwards elimination with a 10% change in estimate as evidence of confounding. The term that changed the estimated odds ratio the least, without changing it by 10% or more, was excluded from the model each time. Pneumonia as a clinical manifestation was the only

confounding variable remaining in the final model. However, the precision of the estimated odds ratio did not change meaningfully when the other potentially confounding variables were excluded, so all six potentially confounding variables were included in the final model.

The final model included variables for the five demographic characteristics (age, gender, health insurance, race/ethnicity, and region) and the six potential confounders (bacteremia, cancer, current smoking, meningitis, obesity, and pneumonia). Neither African American nor Asian/Pacific Islander cases were included in the logistic regression analysis because the absence of mortality in both groups caused quasi-separation of the data points. None of the odds ratios comparing the mortality rates by demographic groups calculated by the logistic regression model were significant. This was confirmed by a backwards elimination of exposure variables conducted using Wald chi-square tests with a significance level of 95%.

Table 7 shows the odds ratios calculated by the full model. Most notably, the odds of dying were twice as high among subjects who did not have insurance as compared to those who had private or military insurance (OR=2.31, 95% CI 0.69-7.75). Also, the odds of dying among American Indian subjects were only half the odds for non-Hispanic White subjects (OR=0.54, 95% CI 0.18-1.62). Similarly, those living in the northwest region of the state had only half the odds of dying as those living in the central region (OR=0.58, 95% 0.23-1.50). Age and gender had very small effects on mortality in this population. None of the relationships between mortality and demographic characteristics were significant in the multivariate model.

Table 7. Odds of Mortality among Non-Pregnant Adults in New Mexico with Invasive GBS Infection by Demographic Characteristics Controlled for Demographic Characteristics and Potentially Confounding Variables, 2004-2009.

Characteristic	Odds Ratio	95% Confidence Interval
Age		
Under 65 years	1.00	-
65+ years	1.03	[0.532,1.992]
Gender		
Female	1.00	-
Male	0.99	[0.516,1.894]
Insurance		
Private or Military	1.00	-
Government Assisted	1.31	[0.668,2.583]
No Insurance	2.31	[0.688,7.749]
Race/Ethnicity		
White Non-Hispanic	1.00	-
Hispanic	0.97	[0.485,1.920]
American Indian	0.54	[0.181,1.616]
Region		
1 (Northwest)	0.58	[0.225,1.497]
2 (Northeast)	0.99	[0.391,2.498]
3 (Central)	1.00	-
4 (Southeast)	0.66	[0.224,1.936]
5 (Southwest)	0.80	[0.318,2.004]

4. Discussion

4.1 Results

The overall mortality among non-pregnant adult GBS cases in NM from 2004 through 2009 was 10.8%, while the mortality among cases in all ten ABCs sites was 7.5% in 2007 (1). This analysis of active-, population-, and laboratory-based surveillance data suggests that the cases at highest risk of death in NM were in the following demographic groups: ≥65 years, uninsured, not American Indian, or residing in the southern regions of the state. However, none of the demographic characteristics were significantly associated with outcome in the univariate analysis or in the logistic model including all demographic characteristics and potential confounding variables. Because of this, the results of this study cannot be generalized to other populations. However, given that the data were collected through statewide surveillance, they can be used to identify groups in NM who experienced the highest mortality when infected with GBS. The identification of these groups using univariate analysis can inform GBS treatment and prevention protocols in the state and allow health care professionals can recognize high-risk GBS patients using standard demographic information found in medical records.

Among NM cases of invasive GBS infection, adults ≥65 years had a 16% higher mortality than those <65 years of age (11.8% and 10.1%, respectively). A mortality among older subjects is expected, because age has a deteriorating effect on the immune system. However, the difference in mortality between age groups was relatively small. This may be due to the fact that the younger subjects became infected because they have similarly debilitated immune systems. Compared to infection cases identified by all ten

ABCs sites between 1990 and 2007, the NM subjects had a very similar median age (63 and 61 years, respectively) and age range (18-105 and 20-98 years, respectively) (1). However, the mortality among age groups in NM GBS cases did not appear to follow the same pattern as that shown by all ten ABCs sites in 2009. The national data for 2009 in Table 8 indicate that mortality among non-pregnant adult GBS cases increases with age; furthermore, a report on national data between 1995 and 2005 confirmed that infection cases between the ages of 15 and 64 years had a mortality of 7.3%, while the older cases had a mortality of 13.1%, for a risk ratio of 1.80. However, among NM GBS cases, the mortality of those between the ages of 35 and 49 years was very similar to that among those ≥65 years, and the risk ratio comparing subjects over and under 65 years was only 1.16. Overall, NM non-pregnant adult GBS cases had a higher mortality than the general United States population, and the difference increased inversely with age. The reason for this has not yet been explored. The high mortality among non-pregnant adult GBS cases <65 of age years may have contributed to NM's high overall mortality among residents with invasive GBS infection.

Table 8. **Mortality by Age among New Mexico GBS Infections (2004-2009) and GBS Infections Identified by All ABCs Sites (2009).**

Age (years)	Mortality in New Mexico (%)	Mortality in All ABCs Sites (%)
18-34	7.7	1.6
35-49	11.4	4.3
50-64	9.7	5.7
65+	11.8	11.0

Note: Data for all ABCs sites are from (CDC 2010) (5).

NM non-pregnant adults GBS cases with no health insurance had a mortality 64% higher than those with private or military insurance (16.7% and 10.1%, respectively).

GBS cases without health insurance likely belonged to lower socioeconomic groups and may have had less access to transportation. These characteristics may encourage a longer waiting period between first symptoms of infection and seeking medical treatment. This hesitance could have contributed to the high mortality of those without insurance. However, it is unknown how long these subjects waited to seek treatment, as a variable for onset of symptoms was not available in this dataset.

The incidence of GBS in the American Indian populations of the United States and the mortality among those cases has not previously been described. National surveillance of GBS cases reported that only 4.1% of the non-pregnant adult cases occurring in 2007 were neither African American nor White (1). In NM, American Indians made up 24.9% of all non-pregnant adult GBS cases between 2004 and 2009, and had a mortality at least 49% lower than White non-Hispanic and Hispanic cases (6.3%, 12.5%, and 13.0%, respectively). While a quarter of the infection cases were American Indian, only 10% of the population of NM was American Indian during the study period (see Table 9). It is interesting to note that while American Indian cases had a low mortality compared to other racial and ethnic groups, they may have had a higher incidence of infection. The reason for these disparities has not been explored, but the literature suggests that African Americans tend to have both a higher incidence and a higher associated mortality than White Americans (1). Race may be a surrogate for underlying medical conditions which affect the risk of infection, such as diabetes, and perhaps for factors which determine the severity and outcome of the infection.

The southeast and southwest regions of the state had the highest mortality among non-pregnant adult GBS cases (15.9% and 13.3%, respectively), while the northwest

region had the lowest, at least 48% lower than the southern regions (6.8%). There are at least two factors which may have contributed to the high mortality among cases of adult GBS infection in the southern regions. First, the disparities in mortality between different regions may have been determined by other factors which differed between regions, such as race and ethnicity or socioeconomic status. For example, the mortality by region changed inversely with the proportion of the population that identifies as American Indian (see Table 9). As previously discussed, American Indian GBS cases had the lowest mortality in NM. The northwest region, which had the highest proportion of American Indians in 2009 (31.4%), had the lowest associated mortality of all five regions. The southeast region, which had the lowest proportion of American Indians (1.9%), had the highest associated mortality. Furthermore, the results from the multivariate analysis also suggest that the higher mortality among non-pregnant adult cases in the southern regions may be closely related to other demographic characteristics of the people living there. The effect of race and ethnicity on mortality was similar in both the univariate and multivariate anlyses, while the effect of region of residence on mortality was reversed in the multivariate analysis. The cases in the southern regions had the highest crude mortality, but the central region had the highest mortality when all demographic variables and potential confounders were included in a model. This leads to the second possible reason for disparities in GBS-associated mortality between regions in NM: The central region has the highest population density, which may be a risk factor for mortality. Figure 1 shows that the central region is by far the smallest out of the five public health regions, and Table 9 shows that it has the largest population. This is due to the fact that the state's largest city, Albuquerque, is located in the central region. A

similar phenomenon involving incidence of GBS infection was reported among residents of Atlanta, Georgia in 1989 (28). The surveillance data revealed that residents of Fulton County, the urban center of Atlanta, were almost three times as likely to be infected with GBS as residents of any other county in the metropolitan area (RR 2.9, $p<0.001$, 95% CI 2.1-4.0). The authors hypothesize that this may be due to the lower socioeconomic status often observed among residents of dense urban centers. This theory might apply to mortality among GBS cases in NM as well, since there was also a disparity in mortality between those with insurance and those without.

Table 9. **Population and Mortality Among Non-Pregnant Adults with Invasive GBS Infection by Public Health Region in New Mexico, 2009.**

Public Health Region	Population (%)	Proportion of Population Identified as American Indian (%)	Proportion of Cases Reported as American Indian (%)	Mortality (%)
1 (Northwest)	324,117 (20.5)	101,685 (31.4)	115 (61.8)	6.8
2 (Northeast)	238,781 (15.1)	12,470 (5.2)	12 (15.4)	10.1
3 (Central)	510,877 (32.3)	26,919 (5.3)	12 (7.1)	12.0
4 (Southeast)	192,774 (12.2)	3,662 (1.9)	1 (1.6)	15.9
5 (Southwest)	315,504 (19.9)	10,515 (3.3)	3 (3.5)	13.3
Total	1,582,053 (100.0)	155,251 (9.8)	143 (24.7)	10.8

Note: Population estimates are from the University of New Mexico Bureau of Business and Economic Research.

These findings suggest that older patients, patients without health insurance, non-American Indian patients, and patients residing in the southern part of the state should be recipients of more aggressive therapy when presenting with invasive GBS infection in NM. These demographic groups should also be given special consideration during any future vaccine prevention efforts against GBS, in addition to those at high risk of GBS infection, such as diabetic patients.

4.2 Strengths and Weaknesses

Active-, laboratory-, and population-based surveillance of invasive GBS infection conducted by the NMABCs has created opportunities to study a unique population in the United States. Statewide mandatory reporting of GBS infections makes it possible to report accurate incidence and subsequent outcome information for the state of NM by certain characteristics. Furthermore, the race and ethnicity distribution of NM allow for the analysis of disparities in mortality besides that between African Americans and White Americans. Finally, the NMABCs's established relationships with hospitals and laboratories throughout the state gives them access to the large amount of data available in medical records for each case of invasive GBS infection.

This analysis of risk factors of mortality among cases of invasive GBS infection in NM was limited by certain characteristics of the surveillance process. The information available is limited to the medical charts and laboratory worksheets of each infection case. Surveillance officers complete a data abstraction form using medical charts that are not standardized and varies from hospital to hospital. For example, race and ethnicity may be assessed differently by different hospitals. Some may in fact ask the patient their ethnicity and their race, while others may only ask one or the other. In some cases, the staff member may simply guess the race and ethnicity of the patient based on their experience with the population, the last names, or physical appearance. Abstracting data from medical charts also means that certain items may not be recorded for every case because data are not universally collected for each person who is admitted to a hospital. For example, a health care provider may not consider current smoking or obesity to be important to write down in the notes for the patient's hospital visit. To demonstrate this

limitation, body mass index (BMI) was calculated for the 248 (39.5%) cases of GBS infection for whom weight and height were available. Only 33.3% of cases who were obese (BMI >30) were designated as obese in the medical chart notes. Unfortunately, height and weight information were only available for this small portion of the subjects because these measurements are not taken at every hospital visit.

Another limitation to this study is that while GBS infection reporting is mandatory for hospitals and laboratories inside the state border, it may not necessarily be reported in the surrounding states, or in Mexico. Just as there are some residents of other states who were identified by the NMABCs because they sought treatment at a facility in NM, some cases among residents of NM may have crossed state, or even country, borders to seek the most convenient medical facility. Because of this, some GBS infections among NM residents may not have been identified by NMABCs. Fortunately, the NMABCs has relationships with hospitals in Lubbock County and El Paso, Texas, who report cases among NM residents living near the Texas border. However, this is not true of all border areas.

4.3 Future Directions

There are several ways that variables could have been chosen and categorized for this analysis. This study categorized variables similarly to other studies of GBS infection and associated mortality, such as the binary outcome and age variables. However, these variables could have been categorized differently in order to explore other associations that may exist. The age variable could have been linear or categorized into several groups of increasing age. The outcome variable could have been categorical and represented severity of infection by accounting for length of hospital stay as well as

death. Also, additional demographic characteristics that could have been explored in regard to mortality are county population density and healthcare worker density. This analysis would shed light on the disparity between different public health regions. Finally, diabetes as an underlying condition was not accounted for in this analysis because other studies found no association between diabetes and mortality. However, because NM has a unique population and American Indians in the state typically have a higher prevalence of diabetes than other residents (9.5% and 7.8%, respectively, in 2008), it may be necessary to account for the existence of this illness in cases of GBS infection (37). It is possible that because diabetic patients require more frequent medical attention than their peers, invasive infections are detected and treated earlier. Furthermore, diabetes and invasive infections have similar risk factors, such as smoking and obesity. This would help explain the association between American Indian race and low mortality observed in this study.

The results of this analysis brought up additional questions about mortality among cases of GBS infection that could be answered with future studies and additional data. First, in order to determine if any of the demographic variables are true risk factors for mortality and can be generalized to other populations, the same analysis could be conducted with a larger population after more years of data collection. Race and ethnicity as well as region of residence were approaching significance in the univariate analysis. Second, although these surveillance data identified and monitored racial and ethnic differences, both are likely a surrogate for social determinants of health that contribute more broadly to disease disparities. Unfortunately, ABCs can not capture socioeconomic status and access to health care. However, geocoding, an exploration into

the census track and social economic distribution, may be feasible for future exploration of the impact of socioeconomic status and access to health care on the outcome of GBS infection.

4.4 Conclusions

GBS has emerged as an important cause of invasive infection in non-pregnant adults since the 1970s. ABCs has been able to estimate the burden of this pathogen on the United States population with surveillance of ten catchment areas, including NM. In this state, approximately 10.8% of 628 cases ended in death between 2004 and 2009. This study explored the associations between demographic characteristics and death among those cases, and found that there may be disparities in mortality between socioeconomic and racial/ethnic groups. It appears that individuals without health insurance and those living in the southern half of the state require more aggressive treatment when presenting with invasive GBS infection. Future protocol recommendations and prevention efforts should take into account the high mortality that may be associated with these groups.

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Appendices

Appendix A: ABCs Case Report Form

– ACTIVE BACTERIAL CORE SURVEILLANCE CASE REPORT –

Patient's Name: _____ (Last, First, M.I.) Phone No.:( ) _____

Address: _____ (Number, Street, Apt. No.) Patient Chart No.: _____

_____ (City, State) _____ (Zip Code) Hospital: _____

– Patient identifier information is not transmitted to CDC –

DEPARTMENT OF HEALTH & HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
ATLANTA, GA 30333

ACTIVE BACTERIAL CORE SURVEILLANCE (ABCs) CASE REPORT

A CORE COMPONENT OF THE EMERGING INFECTIONS PROGRAM NETWORK

– SHADED AREAS FOR OFFICE USE ONLY –

1. STATE: (Residence of Patient) ☐☐

2. COUNTY: (Residence of Patient) _____

3. STATE I.D.: ☐☐☐☐☐☐

4a. HOSPITAL/LAB I.D. WHERE CULTURE IDENTIFIED: ☐☐☐☐☐

4b. HOSPITAL I.D. WHERE PATIENT TREATED: ☐☐☐☐☐

5. WAS PATIENT HOSPITALIZED? 1 ☐ Yes 2 ☐ No

If YES, date of admission: Mo. ☐☐ Day ☐☐ Year ☐☐☐☐

Date of discharge: Mo. ☐☐ Day ☐☐ Year ☐☐☐☐

6a. Was patient transferred from another hospital? 1 ☐ Yes 2 ☐ No 9 ☐ Unk

6b. If YES, hospital I.D. ☐☐☐☐☐

7a. Was patient a resident of a nursing home or other chronic care facility at the time of first positive culture? 1 ☐ Yes 2 ☐ No 9 ☐ Unk

7b. If yes, name _____

8. DATE OF BIRTH: Mo. ☐☐ Day ☐☐ Year ☐☐☐☐

9a. AGE: ☐☐☐

9b. Is age in day/mo/yr? 1 ☐ Days 2 ☐ Mos. 3 ☐ Yrs.

10. SEX: 1 ☐ Male 2 ☐ Female

11a. ETHNIC ORIGIN: 1 ☐ Hispanic or Latino 2 ☐ Not Hispanic or Latino 9 ☐ Unk

11b. RACE: (*Check all that apply*) 1 ☐ White 1 ☐ Black 1 ☐ American Indian or Alaska Native 1 ☐ Asian 1 ☐ Native Hawaiian or Other Pacific Islander 1 ☐ Unk

12a. WEIGHT: _____ lbs _____ oz **OR** _____ kg ☐ Unk

12b. HEIGHT: _____ ft _____ in **OR** _____ cm ☐ Unk

13. TYPE OF INSURANCE: (*check all that apply*)
1 ☐ Medicare; 1 ☐ Military/VA; 1 ☐ Medicaid/state assistance program; 1 ☐ Indian Health Service (IHS); 1 ☐ Private/HMO/PPO/managed care plan; 1 ☐ Other (*specify*) _____; 1 ☐ No health care coverage; 1 ☐ Unk

14. OUTCOME: 1 ☐ Survived 9 ☐ Unk 2 ☐ Died

15a. At time of first positive culture, patient was: 1 ☐ Pregnant 2 ☐ Post-partum 3 ☐ Neither 9 ☐ Unk

15b. If pregnant or post-partum, what was the outcome of fetus: 1 ☐ Survived, no apparent illness 2 ☐ Survived, clinical infection 3 ☐ Live birth/neonatal death 4 ☐ Abortion/stillbirth 5 ☐ Induced abortion 9 ☐ Unk

16. If patient <1 month of age: Gestational age: ☐☐ (wks) Birthweight: ☐☐☐☐ (gms)

17. TYPES OF INFECTION CAUSED BY ORGANISM: (*Check all that apply*)
1 ☐ Bacteremia without Focus; 1 ☐ Meningitis; 1 ☐ Otitis media; 1 ☐ Pneumonia; 1 ☐ Cellulitis; 1 ☐ Epiglottitis; 1 ☐ Hemolytic uremic syndrome (HUS); 1 ☐ Abscess (not skin); 1 ☐ Peritonitis; 1 ☐ Pericarditis; 1 ☐ Septic abortion; 1 ☐ Chorioamnionitis; 1 ☐ Septic arthritis; 1 ☐ Osteomyelitis; 1 ☐ Empyema; 1 ☐ Endocarditis; 1 ☐ Endometritis; 1 ☐ STSS; 1 ☐ Necrotizing fasciitis; 1 ☐ Puerperal sepsis; 1 ☐ Other (*specify*) _____; 1 ☐ Unk

18a. BACTERIAL SPECIES ISOLATED FROM ANY NORMALLY STERILE SITE:
1 ☐ *Neisseria meningitidis*; 2 ☐ *Haemophilus influenzae*; 3 ☐ Group B streptococcus; 4 ☐ *Listeria monocytogenes*; 5 ☐ Group A streptococcus; 6 ☐ *Streptococcus pneumoniae*

18b. OTHER BACTERIAL SPECIES ISOLATED FROM ANY NORMALLY STERILE SITE: (*specify*) _____

19. STERILE SITES FROM WHICH ORGANISM ISOLATED: (*Check all that apply*)
1 ☐ Blood; 1 ☐ CSF; 1 ☐ Pleural fluid; 1 ☐ Peritoneal fluid; 1 ☐ Pericardial fluid; 1 ☐ Joint; 1 ☐ Bone; 1 ☐ Muscle; 1 ☐ Internal body site (*specify*) _____; 1 ☐ Other normally sterile site (*specify*) _____

20. DATE FIRST POSITIVE CULTURE OBTAINED: (Date Specimen Drawn) Mo. ☐☐ Day ☐☐ Year ☐☐☐☐

21. OTHER SITES FROM WHICH ORGANISM ISOLATED: (*Check all that apply*)
1 ☐ Placenta; 1 ☐ Amniotic fluid; 1 ☐ Wound; 1 ☐ Other (*specify*) _____; 1 ☐ Middle ear; 1 ☐ Sinus

– ACTIVE BACTERIAL CORE SURVEILLANCE CASE REPORT –

Page 1 of 2

– IMPORTANT – PLEASE COMPLETE THE BACK OF THIS FORM –

22. UNDERLYING CAUSES OR PRIOR ILLNESS: *(Check all that apply)* *(If none or chart unavailable, check appropriate box)* 1 ☐ None 1 ☐ Unknown

1 ☐ Current Smoker
1 ☐ Multiple Myeloma
1 ☐ Sickle Cell Anemia
1 ☐ Splenectomy/Asplenia
1 ☐ Immunoglobulin Deficiency
1 ☐ Immunosuppressive Therapy (Steroids, Chemotherapy, Radiation)
1 ☐ Leukemia
1 ☐ Hodgkin's Disease
1 ☐ Asthma
1 ☐ Emphysema/COPD
1 ☐ Systemic Lupus Erythematosus (SLE)
1 ☐ Diabetes Mellitus
1 ☐ Nephrotic Syndrome
1 ☐ Renal Failure/Dialysis
1 ☐ HIV Infection
1 ☐ AIDS or CD4 count <200
1 ☐ Cirrhosis/Liver Failure
1 ☐ Alcohol Abuse
1 ☐ Atherosclerotic Cardiovascular Disease (ASCVD)/CAD
1 ☐ Heart Failure/CHF
1 ☐ Obesity
1 ☐ CSF Leak
1 ☐ IVDU
1 ☐ Cerebral Vascular Accident (CVA) / Stroke
1 ☐ Complement Deficiency
1 ☐ Cochlear Implant
1 ☐ Deaf/Profound Hearing Loss
1 ☐ Other Malignancy *(specify)* _____
1 ☐ Organ Transplant *(specify)* _____
1 ☐ Other Prior Illness *(specify)* _____

– *IMPORTANT* – PLEASE COMPLETE FOR THE RELEVANT ORGANISMS:

HAEMOPHILUS INFLUENZAE

23a. If <15 years of age and serotype 'b' or 'unk' did patient receive *Haemophilus influenzae* b vaccine? 1 ☐ Yes 2 ☐ No 9 ☐ Unk
If YES, please complete the list below.

DOSE	DATE GIVEN (Mo. Day Year)	VACCINE NAME	MANUFACTURER	LOT NUMBER
1				
2				
3				
4				

23b. Were records obtained to verify vaccination history? *(<5 years of age only)*
1 ☐ Yes 2 ☐ No

If yes, what was the source of the information? *(check all that apply)*
1 ☐ Vaccine Registry
1 ☐ Healthcare Provider
1 ☐ Other *(specify)* _____

24. What was the serotype?
1 ☐ b 2 ☐ Not Typeable 3 ☐ a 4 ☐ c 5 ☐ d 6 ☐ e 7 ☐ f 8 ☐ Other *(specify)* _____ 9 ☐ Not Tested or Unk

NEISSERIA MENINGITIDIS

25. What was the serogroup?
1 ☐ A 3 ☐ C 5 ☐ W135 9 ☐ Unk
2 ☐ B 4 ☐ Y 6 ☐ Not groupable 8 ☐ Other *(specify)* _____

26. Is patient currently attending college?
(15 – 24 years only)
1 ☐ Yes 2 ☐ No 9 ☐ Unk

27. Did patient receive meningococcal vaccine?
1 ☐ Yes 2 ☐ No 9 ☐ Unk
If YES, please complete the following information:

VACCINE NAME/MANUFACTURER	DATE GIVEN (List most recent date for each vaccine) (Mo. Day Year)	LOT NUMBER
☐ Menomune, tetravalent meningococcal polysaccharide vaccine		
☐ Menactra, tetravalent meningococcal conjugate vaccine		
☐ Other *(specify)* _____		
☐ Not Known		

STREPTOCOCCUS PNEUMONIAE

28. If <15 years of age did patient receive pneumococcal conjugate vaccine?
1 ☐ Yes 2 ☐ No 9 ☐ Unk
If YES, please complete the following information:

DOSE	DATE GIVEN (Mo. Day Year)	VACCINE NAME/MANUFACTURER	LOT NUMBER
1			
2			
3			
4			

GROUP A STREPTOCOCCUS

(#29–31 refer to the 7 days prior to first positive culture)

29. Did the patient have surgery ? 1 ☐ Yes 2 ☐ No 9 ☐ Unk
If YES, date of surgery: Mo. Day Year

30. Did the patient deliver a baby (vaginal or C-section)?
1 ☐ Yes 2 ☐ No 9 ☐ Unk
If YES, date of delivery: Mo. Day Year

31. Did patient have:
1 ☐ Varicella
1 ☐ Penetrating trauma
1 ☐ Blunt trauma
1 ☐ Surgical wound (post operative)
1 ☐ Burns

32. COMMENTS: _____

– SURVEILLANCE OFFICE USE ONLY –

33. Was case first identified through audit?
1 ☐ Yes 2 ☐ No
9 ☐ Unk

34. CRF Status:
1 ☐ Complete
2 ☐ Incomplete
3 ☐ Edited & Correct
4 ☐ Chart unavailable after 3 requests

35. Does this case have recurrent disease with the same pathogen?
1 ☐ Yes 2 ☐ No
9 ☐ Unk
If YES, previous (1st) state I.D.

36. Date reported to EIP site (Mo. Day Year)

37. Initials of S.O.

Submitted By: _____ Phone No.:( ) _____ Date: ____/____/____
Physician's Name: _____ Phone No.:( ) _____

Appendix B: Emory IRB Letter of Exemption

EMORY UNIVERSITY | Institutional Review Board

TO: Jessica McCoury
Principal Investigator

DATE: June 1, 2010

RE: Notification of Submission Determination: No IRB Review Required
IRB00044240

TITLE: RISK FACTORS OF NOTIFIABLE BACTERIAL INFECTION IN NEW MEXICO

The above-referenced study has been vetted by the Institutional Review Board (IRB), and it was determined that it does not require IRB review because it does not meet the definition of "Research involving Human Subjects" or the definition of "Clinical Investigation" under applicable federal regulations. Based on the proposal information submitted by the study team and the permission letter submitted from the University of New Mexico Institute for Public Health, all identifiers will be removed from the data collected by the New Mexico Emerging Infections Program prior to providing the data to the Principal Investigator for use in her thesis. Accordingly, IRB review is not required.

45 CFR Section 46.102(f) defines "Research involving Human Subjects" as follows:

> Human Subject means a living individual about whom an investigator (whether professional or student) conducting research obtains:
>
> (1) data through intervention or interaction with the individual, or
> (2) identifiable private information
>
> Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

In addition, the IRB has determined that the study is not a "Clinical Investigation" under applicable Food & Drug Administration regulations because it does not involve a test article and does not otherwise meet the requirements of the definition of "Clinical Investigation" as set forth in 21 CFR Section 50.3(c).

Please note that any changes to the protocol could conceivably alter the status of this research under the federal regulations cited above. Accordingly, any substantive changes in the protocol should be presented to the IRB for consideration prior to their implementation in the research.

Sincerely,

LaShawn Martin
Research Protocol Analyst
Emory University Institutional Review Board
This letter has been digitally signed

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