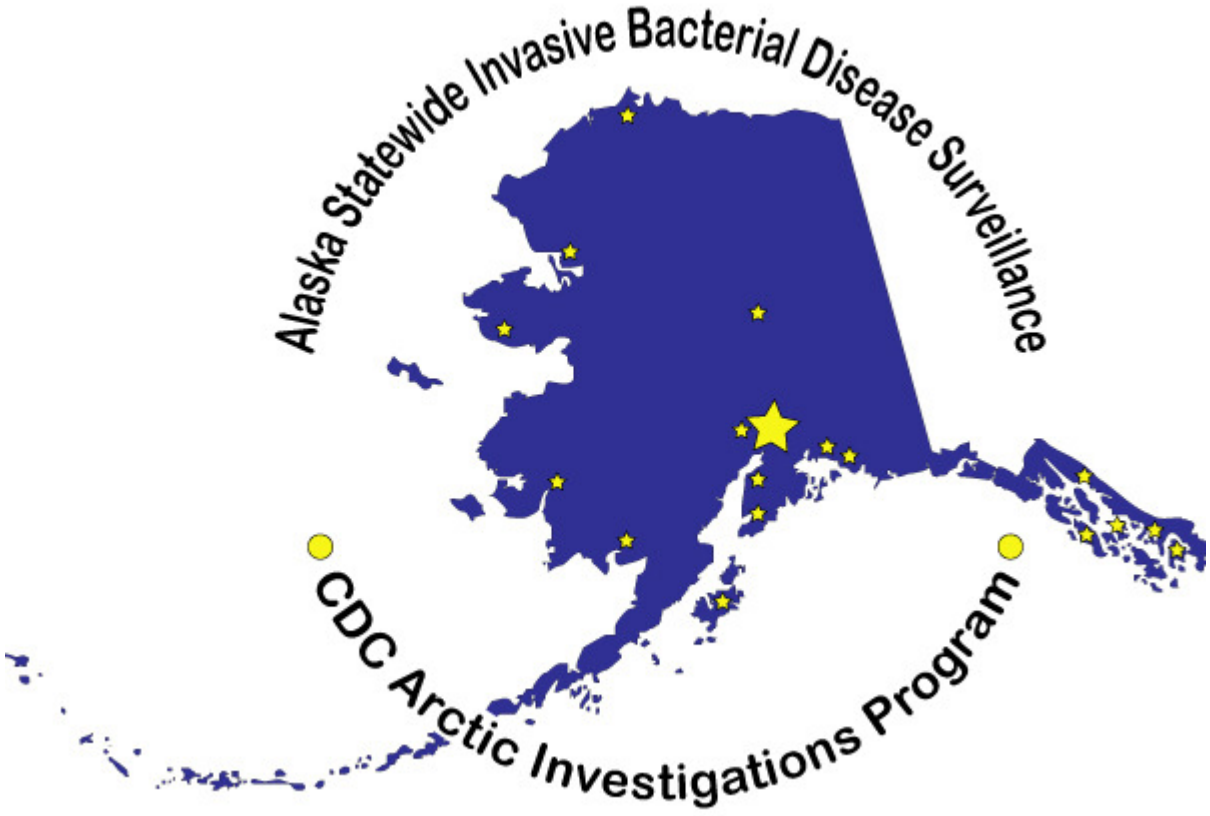

Surveillance of Invasive Bacterial Disease in Alaska, 2016

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Alaska Statewide Invasive Bacterial Disease

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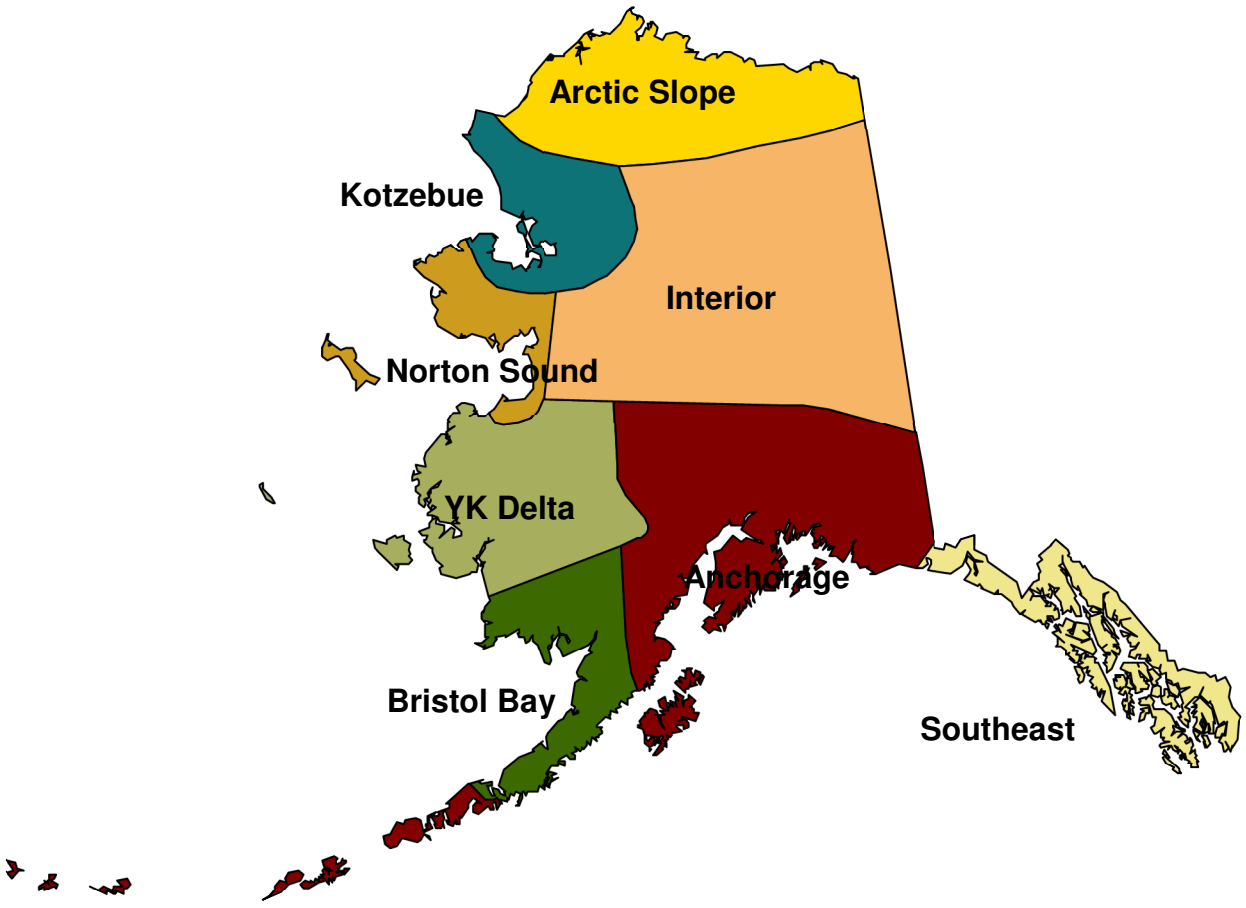
Summary

The Centers for Disease Control and Prevention's Arctic Investigations Program (AIP) in Anchorage, Alaska, maintains a statewide surveillance system for invasive diseases caused by *Streptococcus pneumoniae*, *Haemophilus influenzae, Neisseria meningitidis,* and groups A and B streptococci. Laboratories throughout the state are requested to send to AIP any isolates of these organisms recovered from blood, CSF, or other normally sterile site in an Alaska resident. Isolate identification is confirmed and, when appropriate, isolates are serotyped/serogrouped and tested for antimicrobial susceptibility. The objectives of this system are to provide information on disease rates within the state, monitor the emergence of antimicrobial resistance, and to monitor the effectiveness of implemented vaccine programs, such as the 23-valent pneumococcal polysaccharide vaccine, the pneumococcal conjugate vaccine and *Haemophilus influenzae* type b vaccines.

Figure 1: Invasive Bacterial Disease Surveillance Regions – Alaska, 2016



In 2016, the total numbers of cases of invasive disease caused by these organisms reported to AIP were 131 *S. pneumoniae*, 19 *H. influenzae*, 7 *N. meningitidis*, 145 group A *Streptococcus* (GAS) and 68 group B *Streptococci* (GBS). Alaska Native people had higher rates of disease overall than non-Native people for all surveillance organisms. Rates of invasive pneumococcal disease were highest in the YK Delta and Kotzebue regions. Rates for each organism by region are presented in the following table.

Table 1: Surveillance Organisms Reported by Region – Alaska, 2016

Region	*S. pneumoniae* n (rate*)	*H. influenzae* n (rate*)	*N. meningitidis* n (rate*)	GAS n (rate*)	GBS n (rate*)
Anchorage	86 (17.5)	10 (2)	2 (0.4)	100 (20.3)	50 (10.2)
Arctic Slope	0 (0)	0 (0)	0 (0)	2 (22.8)	0 (0)
Bristol Bay	0 (0)	1 (14.1)	0 (0)	1 (14.1)	0 (0)
Interior	20 (17.8)	0 (0)	0 (0)	15 (13.4)	11 (9.8)
Kotzebue	2 (23.2)	0 (0)	2 (23.2)	4 (46.4)	1 (11.6)
Norton Sound	2 (19.8)	1 (9.9)	0 (0)	1 (9.9)	1 (9.9)
Southeast	9 (12.2)	2 (2.7)	1 (1.4)	3 (4.1)	5 (6.8)
YK Delta	12 (45.3)	5 (18.9)	2 (7.5)	19 (71.7)	0 (0)
Total	131 (17.7)	19 (2.6)	7 (1.0)	145 (19.6)	68 (9.2)

*Cases per 100,000 population

Introduction

AIP conducts statewide surveillance of invasive *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, and groups A and B *Streptococcus*. This program is part of a passive, laboratory-based surveillance system in which laboratories from all hospitals throughout the state are encouraged to participate. The population included in the AIP surveillance is the State of Alaska, which totaled 739,828 persons in 2016 [1]. Case detection occurs year-round as participating laboratories send isolates recovered from sterile sites to the AIP laboratory in Anchorage; materials and forms for isolate shipment and data collection are provided to each laboratory by AIP. Demographic and clinical information on the cases are collected from a review of medical records. At year-end, AIP asks that each laboratory review their records and provide information on any cases that may have been overlooked. In 2016, 22 laboratories in Alaska participated in the invasive disease surveillance system, either by sending isolates to the AIP laboratory throughout the year, conducting year-end record reviews, or both. Invasive *S. pneumoniae*, *H. influenzae*, *N. meningitidis*, GAS and GBS are reportable conditions to the State of Alaska Division of Public Health (DPH). Reports of cases of disease received by DPH are shared with AIP; these reports are used to identify potential cases and request isolates if not received by AIP. If an isolate is not available but was laboratory-confirmed and meets the case definition, the report is included as a case.

AIP defines a case of invasive *S. pneumoniae, H. influenzae*, *N. meningitidis*, GAS or GBS as an isolate of the bacteria from a normally sterile site, including blood, cerebrospinal fluid, pleural fluid, peritoneal fluid or joint fluid that has been taken from a resident of Alaska. In addition, for GAS, laboratories are asked to submit isolates obtained from deep tissue infections (e.g., collected from surgical debridement of patients with necrotizing fasciitis).

Invasive Pneumococcal Disease (IPD)

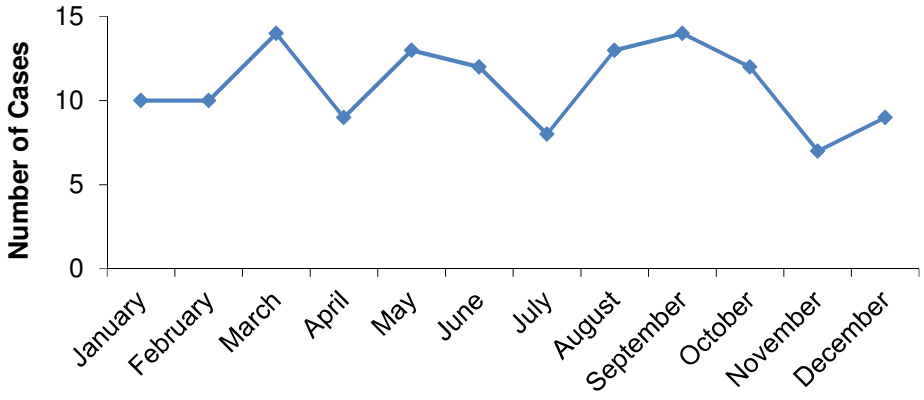
Overall Incidence

A total of 116 pneumococcal isolates were received at AIP in 2016. An additional 13 cases were detected through shared surveillance with the State DPH and 2 cases were reported by laboratories during the annual audit for a total of 131 cases of invasive pneumococcal disease. The overall rate for invasive pneumococcal disease in 2016 was 17.7 cases per 100,000 persons per year. Alaska rates for 2016 were higher than the 2016 national projected rate of 9.4/100,000 [2] for Active Bacterial Core Surveillance (ABCs), a surveillance system that operates in 10 states and covers a population of up to 42 million persons.

Month of Culture

Invasive *Streptococcus pneumoniae* cases were identified in each month of 2016. The largest number of cases (n=14) were reported in March and September.

Figure 2: Invasive Pneumococcal Disease, by Month of Culture - Alaska, 2016



Race

In 2016, the state population was comprised of 20% Alaska Native (AN) people *(Alaska Native persons alone or in combination 147,699 non-Native persons 592,129)* [1]. Of all reported *S. pneumoniae* cases in 2016, 56 (43%) occurred in Alaska Native people; the age-adjusted rate was 41.3/100,000 persons per year. Seventy-five cases occurred in non-Native (NN) people, for an age-adjusted rate of 11/100,000 persons per year. The rate ratio of age-adjusted rates of *S. pneumoniae* disease for the Alaska Native population compared with the non-Native population in 2016 was 3.8.

Table 2: IPD Cases by Race – Alaska, 2016

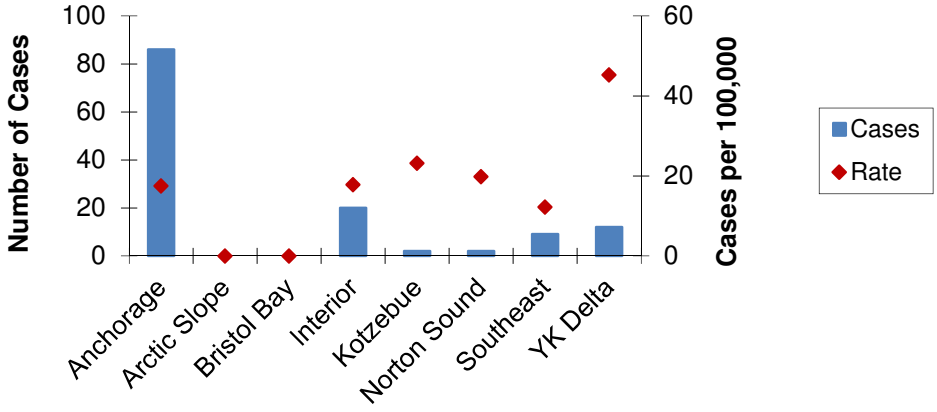
Race	Cases n (%)	Age Adjusted Rate*	% Male	Deaths n (%)
Alaska Native Persons	56 (43)	41.3	59%	2 (4)‡
Non-Native Persons†	75 (57)†	11.0	53%	11 (15)‡
Total	131		56%	13 (10)

*Cases per 100,000 per percent distribution of Alaska 2010 population
†Includes 10 cases for which race was unknown
‡Outcome unknown in 1 AK Native case, 1 non-Native case

Region

The highest percentage (66%) of IPD cases occurred in the Anchorage area in 2016. Rates of disease, however, were highest in the YK Delta (45.3/100,000 persons per year) and the Kotzebue region (23.2/100,000 persons per year).

Figure 3: Invasive Pneumococcal Disease, Cases & Rates by Region - Alaska, 2016

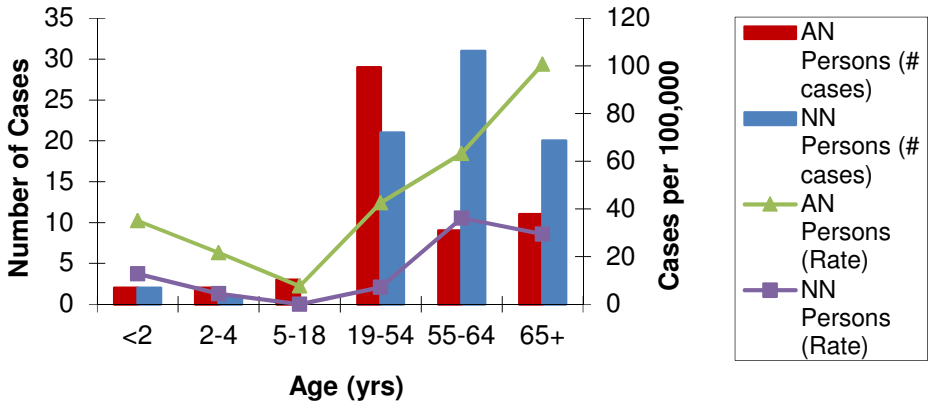


Age

Cases occurred in all age groups in 2016, with age ranging from 9 months to 89 years and a median age of 56 years. Overall, the highest rates of disease occurred in adults aged 55-64 years and 65 years and older.

When stratified by age and race, the highest rates of disease in 2016 occurred in Alaska Native adults 65 years and older (100.7/100,000 persons per year).

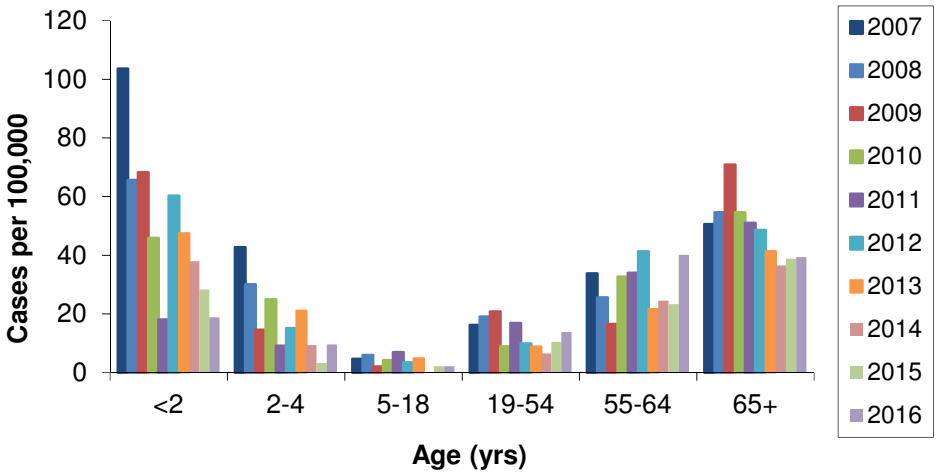
Figure 4: Invasive Pneumococcal Disease, Cases & Rates by Age Group & Race - Alaska, 2016



Since the initiation of a pneumococcal 7-valent conjugate vaccine (PCV7) program in 2001, overall rates of invasive disease declined dramatically in children less than 2 years of age [3]. In 2008, the rate of IPD in children less than 2 years declined to 65.6/100,000 which was the lowest rate observed in this age group since introduction of the 7-valent vaccine. Following introduction of a 13-valent conjugate vaccine (PCV13) in 2010, rates of disease observed in children less than 2 years old declined to 18/100,000 in 2011. In 2012, however,

disease rates in this age group increased to 60.3/100,000 due to disease caused by serotypes not included in the current vaccine. In 2016, rates declined to 18.8/100,000.

Figure 5: Invasive Pneumococcal Disease by Age Group - Alaska, 2007-2016



Although pneumococcal disease rates dropped initially in AK Native and non-Native children less than 2 years of age after introduction of PCV7, the rates of disease in AK Native children less than 2 years trended upward from a low of 93.6/100,000 in 2001 to 335.9/100,000 in 2006 (data not shown, historical trend). This increase in rates was due primarily to disease caused by serotypes not contained in PCV7 [4,5]. In 2009, rates of disease in AK Native children less than 2 years declined to 87.1/100,000 which was the lowest rate since the introduction of PCV7. After introduction of PCV13 in 2010, rates declined to 30.7/100,000 in 2011, however, increased to 177.5/100,000 in 2012. Rates have since declined to 35.1/100,000 in 2016. Rates of invasive disease in non-Native children less than 2 years declined during the same time period reaching 26.8/100,000 in 2005, and following an increase to 64.4/100,000 in 2007, declined in 2008 to 6.2/100,000. In 2009, the rate of disease in non-Native children less than 2 years increased to 60.3/100,000, but declined to 13/100,000 in 2012 with use of PCV13. Following an increase in 2013 (26.3/100,000), rates in non-Native children less than 2 years were similar in 2014 (25.9/100,000), but declined in 2015 to 12.8/100,000 and remained the same in 2016 (12.8/100,000).

Figure 6: Invasive Pneumococcal Disease in Alaska Native Persons, by Age Group - Alaska, 2007-2016

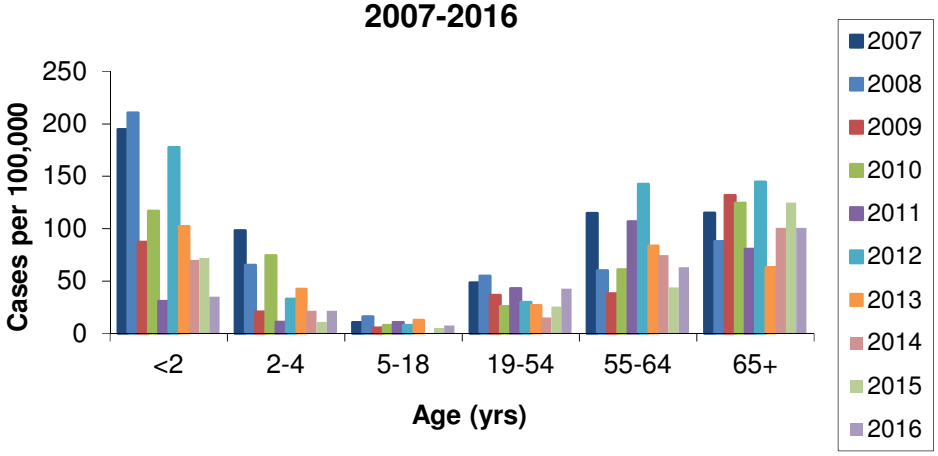
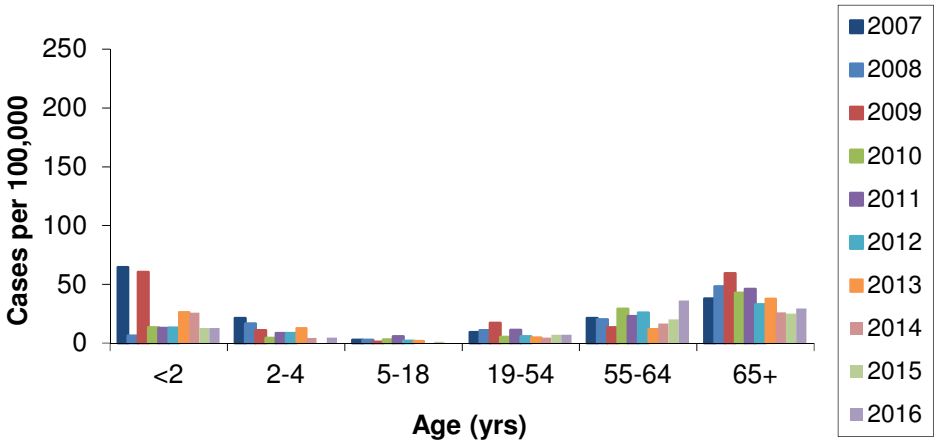


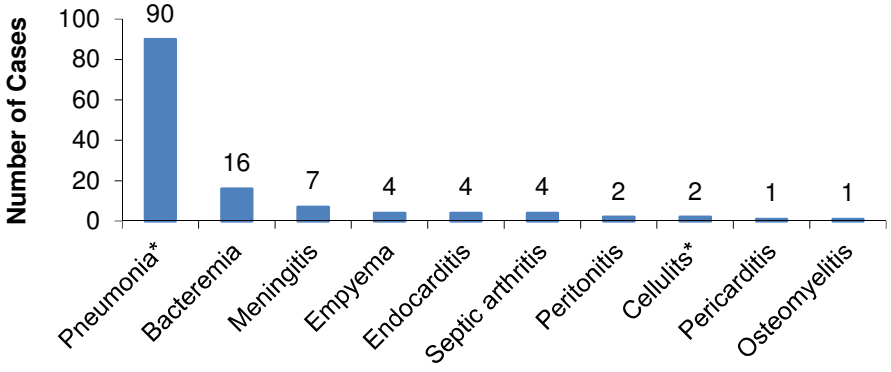
Figure 7: Invasive Pneumococcal Disease in Non-Native Persons, by Age Group - Alaska, 2007-2016



Clinical Presentation

The primary clinical presentation was determined by a review of the discharge diagnoses associated with the invasive bacterial illness in each patient's individual medical record. In patients with multiple discharge diagnoses, the most serious diagnosis related to the pneumococcal infection was recorded as the primary clinical presentation. Pneumonia with bacteremia was the most common primary clinical presentation in 2016 (69%) followed by bacteremia (12%). Thirteen patients had a secondary pneumococcal-related diagnosis in 2016, including pneumonia with bacteremia (7), cellulitis (3), streptococcal toxic shock syndrome (1), cellulitis and necrotizing fasciitis (1), and cellulitis and osteomyelitis (1).

Figure 8: Primary Clinical Presentations of Invasive Pneumococcal Disease - Alaska, 2016



*with bacteremia

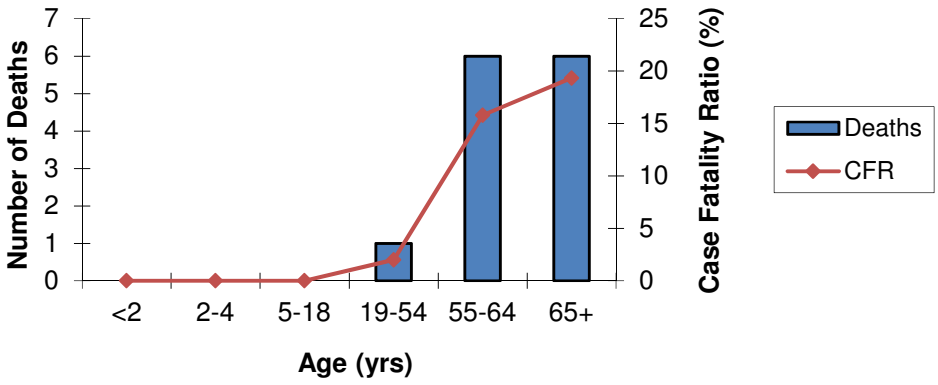
In 2016, blood, which was used to identify 127 (97%) of 131 cases, was the most common source of a positive culture. Two cases each were identified from cerebrospinal fluid and joint fluid.

Mortality

In 2016, the overall case fatality ratio for *S. pneumoniae* in Alaska was 10% (13 deaths out of 129 cases for which outcome was known). The case fatality ratio for non-Natives was higher (15%, 11 deaths) than for AK

Natives (4%, 2 deaths). The highest case fatality ratio occurred in the 65 and older age category: 6 deaths, CFR 19.4%.

Figure 9: Invasive Pneumococcal Deaths & Case Fatality Ratios by Age Group - Alaska, 2016



Serotype

Serotyping of IPD isolates is performed at AIP using internationally standardized methods. Serotype identification is based on the organism's polysaccharide capsule, which is a principal virulence factor for pneumococci. This information provides a way to categorize organisms and to determine if the infection was due to a type that could be prevented by use of one of the available pneumococcal vaccines. Serotyping was performed on all of the *S. pneumoniae* cases for which an isolate was available. AIP received 116 isolates in 2016 and 3 of those isolates were non-viable; 113 isolates were serotyped.

Table 3: IPD Serotype Distribution by Race and Age Group – Alaska, 2016

		Alaska Native					Non-Native				
Serotype	Total n (%)	<2	2-4	5-18	19-64	65+	<2	2-4	5-18	19-64	65+
03	9 (8)	-	-	-	1	-	-	-	-	7	1
04	1 (1)	-	-	-	-	-	-	-	-	-	1
06C	4 (4)	-	-	-	1	-	-	-	-	1	2
07C	1 (1)	-	-	-	-	-	-	-	-	-	1
07F	2 (2)	-	-	-	1	-	-	-	-	1	-
08	10 (9)	-	-	1	-	1	-	-	-	8	-
09N	10 (9)	-	-	-	3	1	-	-	-	6	-
10A	9 (8)	1	-	-	5	3	-	-	-	-	-
11A	3 (3)	-	-	-	1	-	-	-	-	-	2
12F	6 (5)	-	-	-	5	-	-	-	-	1	-
15A	3 (3)	1	-	-	-	-	-	-	-	2	-
15C	3 (3)	-	-	-	1	-	-	-	-	-	2
16F	5 (4)	-	1	-	2	-	-	-	-	1	1
17F	3 (3)	-	1	-	1	-	-	-	-	1	-
19A	4 (4)	-	-	-	-	2	-	-	-	2	-
19F	3 (3)	-	-	-	-	-	-	-	-	3	-
20	11 (10)	-	-	-	7	1	-	-	-	3	-
21	1 (1)	-	-	-	-	-	-	-	-	-	1
22F	10 (9)	-	-	1	2	1	-	-	-	4	2
23A	3 (3)	-	-	-	2	-	-	-	-	1	-
23B	3 (3)	-	-	-	-	-	-	-	-	2	1
31	2 (2)	-	-	-	2	-	-	-	-	-	-
33F	3 (3)	-	-	1	-	-	2	-	-	-	-
35B	2 (2)	-	-	-	-	-	-	1	-	-	1
38	2 (2)	-	-	-	-	-	-	-	-	-	2
Total	113	2	2	3	34	9	2	1	0	43	17

In 2016, the most common pneumococcal serotypes were 20, (11 isolates, 10%), 8 (10 isolates, 9%), 9N (10 isolates, 9%) and 22F (10 isolates, 9%). From 1986 through 2001, serotype 14 was the most common invasive pneumococcal serotype ranging from 7.4% to 23.5% of isolates. Following introduction in 2001 of PCV7 which includes serotype 14, the proportion of serotype 14 isolates dropped to 1.5% of serotyped isolates in 2006 and there were no serotype 14 cases in 2016. Disease caused by serotypes 7F and 19A, which are not included in the 7-valent conjugate vaccine, continually increased until the introduction of PCV13 in 2010 which does include these two serotypes. Although cases caused by 7F and 19A continue to occur, they are no longer the most common serotypes. The majority (73%) of serotype 20 cases, serotype 8 cases (80%), serotype 9N (80%) and serotype 22F cases (50%) occurred in the Anchorage area in 2016.

Table 4: IPD Serotype Distribution by Region – Alaska, 2016

Serotype	Anchorage	Arctic Slope	Bristol Bay	Interior	Kotzebue	Norton Sound	Southeast	YK Delta
03	6	-	-	2	-	-	-	1
04	1	-	-	-	-	-	-	-
06C	2	-	-	2	-	-	-	-
07C	1	-	-	-	-	-	-	-
07F	2	-	-	-	-	-	-	-
08	8	-	-	1	-	-	-	1
09N	8	-	-	1	-	-	1	-
10A	1	-	-	1	2	-	-	5
11A	2	-	-	1	-	-	-	-
12F	2	-	-	-	-	-	4	-
15A	3	-	-	-	-	-	-	-
15C	2	-	-	1	-	-	-	-
16F	2	-	-	2	-	1	-	-
17F	2	-	-	1	-	-	-	-
19A	3	-	-	-	-	-	1	-
19F	2	-	-	-	-	-	1	-
20	8	-	-	-	-	-	-	3
21	1	-	-	-	-	-	-	-
22F	5	-	-	2	-	-	2	1
23A	2	-	-	1	-	-	-	-
23B	2	-	-	1	-	-	-	-
31	1	-	-	1	-	-	-	-
33F	3	-	-	-	-	-	-	-
35B	2	-	-	-	-	-	-	-
38	2	-	-	-	-	-	-	-
Unknown	13	-	-	3	-	1	-	1
Total	86	0	0	20	2	2	9	12

Vaccine Serotypes

In 2001, PCV7 was included in the Alaska childhood vaccination schedule. This vaccine provided protection against the 7 most common pneumococcal serotypes causing invasive disease among children (types 4, 6B, 9V, 14, 18C, 19F, 23F). In early 2010, PCV13 was introduced into the Alaska childhood vaccination schedule. This vaccine provided protection against the 7 pneumococcal serotypes contained in PCV7 plus six additional

serotypes (1, 3, 5, 6A, 7F, 19A) that have caused invasive disease since the introduction of PCV7. The table below shows the proportion of invasive infections from 2016 that were due to serotypes found in PCV13. There were no cases of pneumococcal disease caused by serotypes contained in PCV13 in children less than 5 years of age, the age group for which the vaccine is recommended.

Table 5: Proportion of Invasive Isolates Contained in the PCV13 Vaccine by Age Group and Race – Alaska, 2016

Age (yrs)	Alaska Native (%)	Non-Native (%)	Total (%)
<2	0 (0%) of 2	0 (0%) of 2	0 (0%) of 4
2-4	0 (0%) of 2	0 (0%) of 1	0 (0%) of 3
5+	4 (9%) of 46	15 (25%) of 60	19 (18%) of 106
Total	4 (8%) of 50	15 (24%) of 63	19 (17%) of 113

For the year covered by this report, the 23-valent polysaccharide vaccine (Ps23V) was recommended in Alaska for all persons 65 years and older, and for persons over age 2 who are at higher risk for pneumococcal disease [5]. In addition, one dose of PCV13 was also recommended for persons 65 years and older. In 2016, for persons 65 years and older, 9 (35%) of 26 cases serotyped were potentially vaccine preventable invasive pneumococcal illnesses.

Vaccine Failures

In 2016, pneumococcal vaccine status was known for 125 (95%) of the 131 cases; 45% (n=56) of patients with known vaccine status did receive a pneumococcal vaccine prior to illness and 69 patients (55%) had no record of a pneumococcal vaccine.

A PCV13 vaccine failure is defined as invasive pneumococcal disease caused by a serotype contained in PCV13 in a child less than five years old who has had at least two doses of vaccine. There were no vaccine failures in 2016.

Potentially Preventable Deaths

Overall, 46% of all pneumococcal-related mortality in 2016 was potentially preventable with the use of the 23-valent polysaccharide vaccine in persons over 5 years old; 46% of deaths were due to disease caused by serotypes not contained in pneumococcal vaccines.

Table 6: Potentially Vaccine Preventable IPD Deaths – Alaska, 2016

Serotypes	< 2 years	2-4	5-18	19-54	55-64	65+	Total
PCV13	0	0	0	0	0	0	0
Ps23V	0	0	0	0	4* (67%)	2* (33%)	6 (46%)
Non-Vaccine	0	0	0	1 (100%)	1 (17%)	4 (67%)	6 (46%)
Unknown	0	0	0	0	1 (17%)	0	1 (8%)
Total	0	0	0	1	6	6	13

*One case was serotype 3 which is also contained in PCV13

Six of the 13 deaths in 2016 from invasive *S. pneumoniae* were caused by serotypes contained in the Ps23V vaccine; two of the deaths were in individuals eligible for the vaccine. Both deaths occurred in a vaccinated individual; time since vaccination was 13 years for one case and 5 years for the second.

Table 7: IPD, Serotypes of Fatal Cases – Alaska, 2016

Serotype	Deaths n (%)	Serotype Frequency (n)
03†*	2 (22)	9
07C	1 (100)	1
08*	1 (10)	10
10A*	1 (11)	9
12F*	1 (17)	6
16F	1 (20)	5
17F*	1 (33)	3
21	1 (100)	1
23B	2 (67)	3
35B	1 (50)	2

†Serotypes contained in the 13-valent conjugate vaccine
*Serotypes contained in the 23-valent polysaccharide vaccine

Reported Risk Factors

The presence of one or more associated risk factors was reported in 82% of IPD cases in 2016. Cigarette smoking was the most prevalent risk factor observed in adults, followed by alcohol abuse and diabetes.

Table 8: Reported Risk Factors* Identified in IPD Cases – Alaska, 2016

Risk Factor	Adult Cases (≥ 18 years) n=121, Cases (%)
Cigarette smoking	46 (38)
Alcohol abuse	40 (33)
Diabetes	20 (17)
Chronic lung disease	16 (13)
Injection drug use	6 (5)
Immunosuppressive treatment	5 (4)
Asplenia	0 (0)

*More than one risk factor was identified in several cases

Antibiotic Resistance

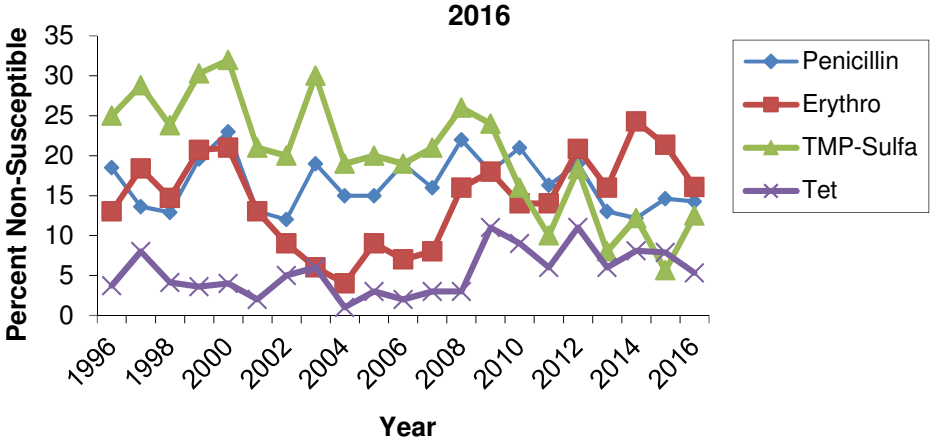
Susceptibility testing was performed on 113 isolates received in 2016. Cut points from the Minimum Inhibitory Concentration (MIC) Interpretive Standards were used to determine if an isolate was 'susceptible', 'intermediate', or 'resistant' to the antibiotic being tested [7]. The MIC Interpretive Standards definitions of 'susceptible', 'intermediate', and 'resistant' can be found in the Appendix. Results of the testing are presented in the following table.

Table 9: Antibiotic Resistance in Invasive *Streptococcus pneumoniae* Isolates – Alaska, 2016

Antibiotic	Susceptible	Intermediate	Resistant	I + R	Total Tested
Penicillin	96 (85%)	13 (11.5%)	4 (3.5%)	17 (15%)	113
TMP-sulfa	99 (88%)	13 (11%)	1 (1%)	14 (12%)	113
Erythromycin	94 (83%)	0 (0%)	19 (17%)	19 (17%)	113
Ceftriaxone	109 (96%)	2 (2%)	2 (2%)	4 (4%)	113
Tetracycline	107 (95%)	1 (1%)	5 (4%)	6 (5%)	113
Chloramphenicol	112 (99%)	0 (0%)	1 (1%)	1 (1%)	113
Vancomycin	113 (100%)	0 (0%)	0 (0%)	0 (0%)	113
Levofloxacin	113 (100%)	0 (0%)	0 (0%)	0 (0%)	113
Clindamycin	108 (96%)	0 (0%)	5 (4%)	5 (4%)	113

Serotypes found in PCV7 and PCV13 are more likely to be non-susceptible to penicillin and erythromycin than non-vaccine serotypes. One potential benefit of the use of these vaccines was an anticipated decline in antibiotic resistance among circulating pneumococci. Following the initiation of the PCV7 vaccine in 2001, antibiotic resistance among invasive pneumococci dropped. During 2003, TMP-sulfa and penicillin resistance increased, however, following an increase in disease caused by serotype 19A. This serotype is included in the PCV13 vaccine; decreasing proportions of isolates resistant to most antibiotics tested may be due to the introduction of the vaccine. However, the proportion of isolates resistant to erythromycin has increased which is a trend that was also seen after the introduction of PCV7 [8].

Figure 10: Trends in Antibiotic Non-Susceptibility Among Invasive Pneumococcal Isolates - Alaska, All Ages, 1996 - 2016



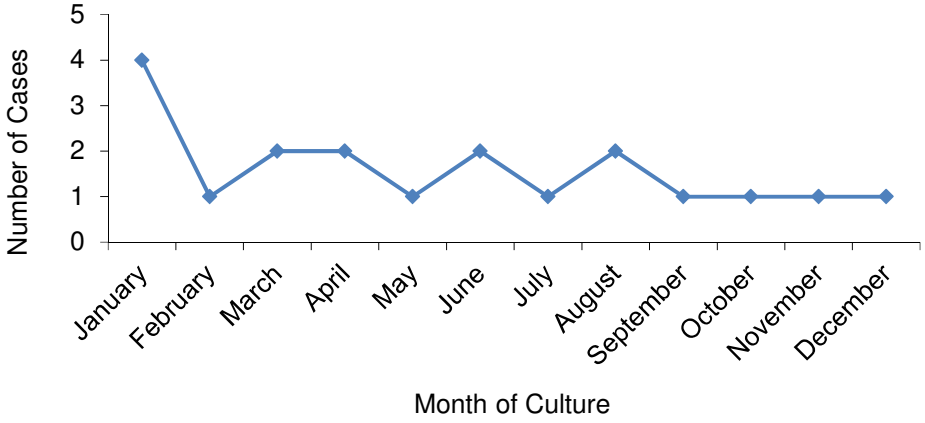
Invasive *Haemophilus influenzae*

Overall Incidence

In 2016, there were 19 cases of invasive *Haemophilus influenzae* in Alaska, for a statewide rate of 2.6/100,000 persons per year. This rate is higher than the ABCs 2016 national projected rate of 1.99/100,000 persons per year [9]. There were 5 deaths associated with *H. influenzae* in 2016, for a case fatality ratio of 26%.

Month of Culture

Figure 11: *Haemophilus influenzae* Disease by Month of Culture - Alaska, 2016

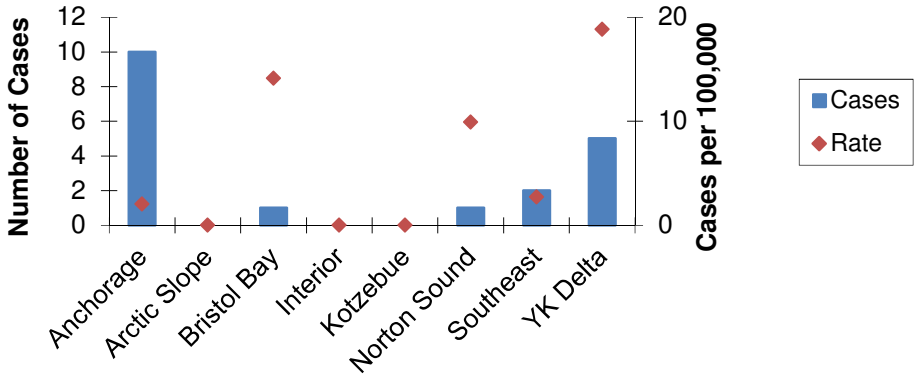


Cases of invasive *H. influenzae* occurred throughout 2016; the largest number of cases (n=4) occurred in January.

Region

The highest rates of disease caused by invasive *H. influenzae* in 2016 were in the YK Delta region, 18.9/100,000 (5 cases), and the Bristol Bay region, 14.1/100,000 (1 case). Although a large number of cases occurred in the Anchorage area (10 cases), the rate was much lower (2/100,000).

Figure 12: Invasive *Haemophilus influenzae*, Cases & Rates by Region - Alaska, 2016



Race

Table 10: Invasive *Haemophilus influenzae* Cases by Race – Alaska, 2016

Race	Cases n (%)	Age Adjusted Rate*	% Male	Deaths n (%)
Alaska Native Persons	10 (53%)	6.0	70%	3 (30%)
Non-Native Persons	9 (47%)	1.4	44%	2 (22%)
Total	19		58%	5 (26%)

*Cases per 100,000 per percent distribution of Alaska 2010 population

In 2016, 53% of the cases occurred in Alaska Native persons. Age-adjusted rates were calculated for Alaska Native and non-Native persons. The age-adjusted rate ratio of *H. influenzae* disease for the Alaska Native population compared with the non-Native population in 2016 was 4.3.

Age

H. influenzae patients ranged in age from 1 month to 87 years in 2016 (median 28.6 years). Overall, the highest rates of disease occurred in children less than 2 years old (32.8/100,000).

Rates of disease in Alaska Native versus non-Native populations by age group were variable; overall numbers of cases and rates by race and age group are presented in Figure 14. The highest rates of disease occurred in Alaska Native children less than two years of age and Alaska Native adults 65+ years of age, 105.4/100,000 persons per year and 18.3/100,000 persons per year, respectively.

Figure 13: Invasive *Haemophilus influenzae* by Age Group - Alaska, 2016

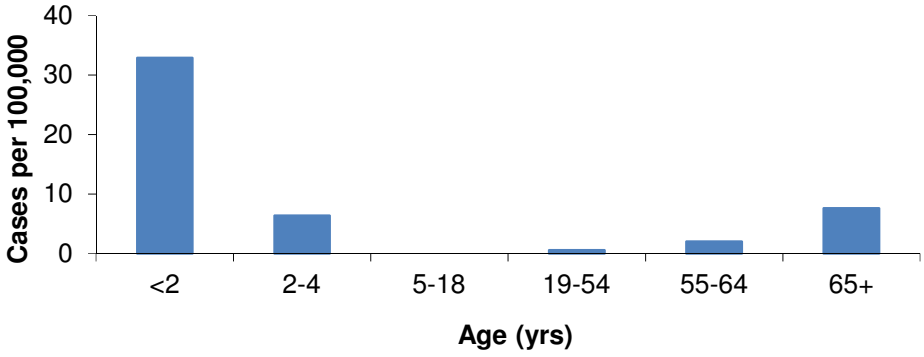
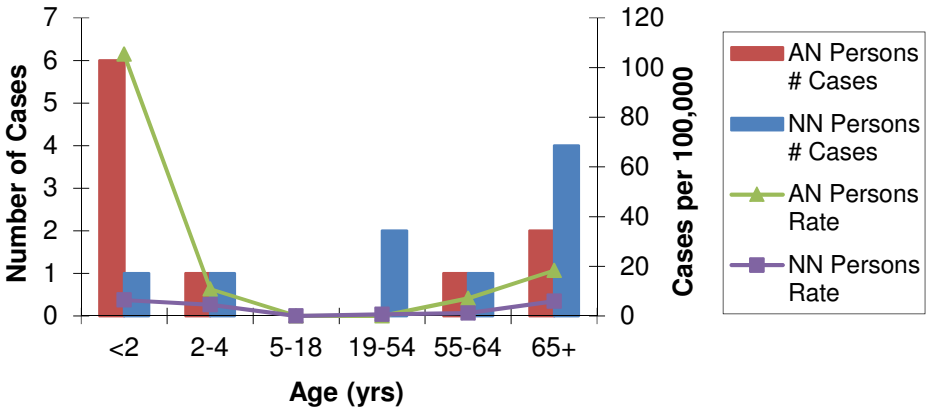


Figure 14: Invasive *Haemophilus influenzae*, Cases & Rates by Age Group & Race - Alaska, 2016



Clinical Presentation

The primary clinical presentation was determined by a review of the discharge diagnoses in each patient's individual medical record associated with the invasive bacterial illness. For cases with more than one diagnosis, the most serious *H. influenzae*-related diagnosis was recorded as the primary clinical presentation. In 2015, pneumonia with bacteremia was the most common presentation (47% of cases).

Sixteen (84%) *H. influenzae* isolates were from blood samples in 2016, two were from cerebrospinal fluid and one was from peritoneal fluid.

Table 11: Primary Clinical Presentation of Invasive *Haemophilus influenzae* - Alaska, 2016

Primary Presentation	n (%)
Pneumonia*	9 (47%)
Bacteremia	4 21%)
Meningitis	3 (16%)
Peritonitis	2 (11%)
Cellulitis*	1 (5%)
Total	19

*with bacteremia

Serotypes

All isolates received at AIP are serotyped; 18 (95%) cases in 2016 had isolates and were serotyped. The bacterial capsule is the basis for serotyping and is the primary virulence factor. Serotype b was the most common serotype in the past, but its prevalence has decreased with use of the childhood Hib vaccine. Surveillance of serotypes is important for monitoring vaccine effectiveness and emergence of non-vaccine serotypes.

Table 12: Serotypes of Invasive *Haemophilus influenzae* Cases by Race – Alaska, 2016

		Alaska Native Persons				Non-Native Persons			
Serotype	Total n (%)	<2	2-18	19-64	65+	<2	2-18	19-64	65+
a	6 (32)	4	-	-	1	-	1	-	-
b	1 (5)	1	-	-	-	-	-	-	-
f	3 (16)	1	-	-	-	1	-	1	-
NT*	8 (42)	-	1	-	1	-	-	2	4
Unknown	1 (5)	-	-	1	-	-	-	-	-
Total	19	6	1	1	2	1	1	3	4

*Non-typeable

Hib

In recent years, the prevalence of *H. influenzae* type b has declined due to increased use of a childhood vaccine against this serotype. There was one case of Hib in a child less than 5 years old in 2016; the child was 2 months old and had not yet received any vaccine.

Hia

Prior to 2002, *H. influenzae* type a (Hia) had not been detected in Alaska. Following an outbreak in 2003 [10], cases have occurred sporadically until 2010 when an outbreak began in the YK Delta and continued through 2011 [11]. Six cases of Hia were detected in 2016; 83% occurred in AK Native people. The rate of invasive disease caused by Hia in AK Native children less than 2 years old for 2016 was 70.2/100,000.

Antibiotic Resistance

Eighteen *H. influenzae* isolates received at AIP were tested for susceptibility to ampicillin, chloramphenicol, ceftriaxone and TMP/sulfa. All isolates tested were susceptible to ceftriaxone and chloramphenicol, 6 isolates were resistant to ampicillin (1 intermediate, 5 fully resistant), and 9 isolates were resistant to TMP/sulfa (4 intermediate and 5 fully resistant).

Invasive *Neisseria meningitidis*

Overall Incidence

Seven cases of invasive *Neisseria meningitidis* were reported to AIP in 2016, for an overall rate of 1/100,000. The Alaska rate is higher than the ABCs 2016 national projected rate of 0.12/100,000 [12]. There were 3 invasive *N. meningitidis*-related deaths in Alaska in 2016, for a case fatality ratio of 43%.

Race

Table 13: Invasive *Neisseria meningitidis* Cases by Race – Alaska, 2016

Race	Cases n (%)	Age Adjusted Rate*	% Male	Deaths n (%)
Alaska Native Persons	5 (71)	2.8	60	3 (60)
Non-Native Persons	2 (29)	0.3	100	0 (0)
Total	7		71	3 (43)

*Cases per 100,000 per percent distribution of Alaska 2010 population

In 2016, 71% of the cases occurred in Alaska Native persons. Age-adjusted rates were calculated for Alaska Native and non-Native persons. The age-adjusted rate ratio of *N. meningitidis* disease for the Alaska Native population compared with the non-Native population in 2016 was 9.3.

Invasive group A *Streptococcus*

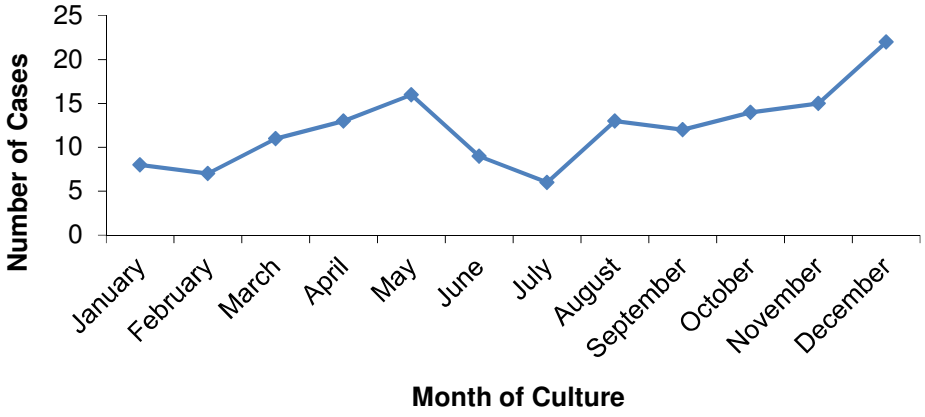
Overall Incidence

A total of 146 cases of invasive group A *Streptococcus* (GAS) were reported to AIP in 2016. The overall rate of invasive GAS disease in the state of Alaska was 19.7/100,000 persons per year. The Alaska rate is higher than the ABCs 2016 national projected rate of 5.8/100,000 [13]. In 2016, there were 16 GAS-related deaths for a case fatality ratio of 11%.

Month of Culture

Cases of group A *Streptococcus* occurred throughout the year in 2016; the largest number of cases (n=22) occurred in December.

Figure 15: Invasive group A *Streptococcus*, by Month of Culture - Alaska, 2016



Race

In 2016, 64% of invasive GAS cases in Alaska occurred in the Alaska Native population. The age-adjusted rate ratio of invasive GAS disease for the Alaska Native population compared with the non-Native population in 2016 was 8.2.

Table 14: Invasive group A *Streptococcus* Cases by Race – Alaska, 2016

Race	Cases n (%)	Age Adjusted Rate*	% Male	Deaths n (%)
Alaska Native Persons	93 (64%)	68.2	62%	10 (11%)
Non-Native Persons	53† (36%)	8.3	63%	6 (11%)
Total	146		64%	16 (11%)

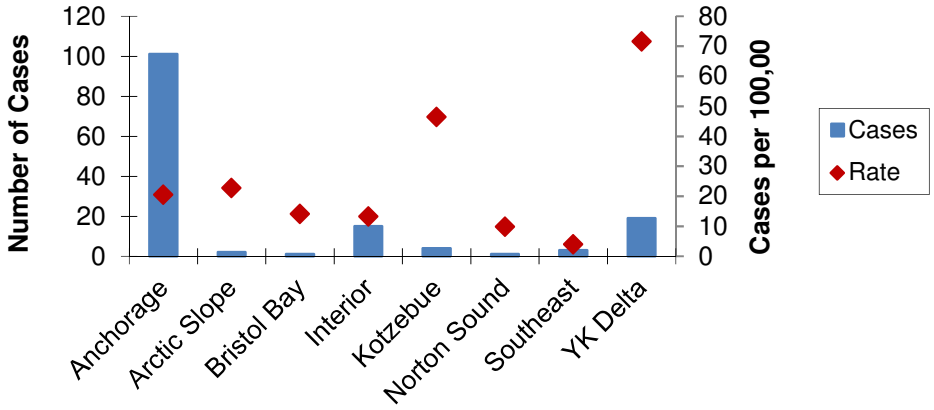
*Cases per 100,000 per percent distribution of Alaska 2010 population
†Includes 5 cases for which race is unknown

Region

One hundred one (69%) of the 146 invasive group A *Streptococcus* cases in 2016 were reported in the Anchorage area, 19 cases in the YK Delta, 15 cases in the Interior, Southeast, 4 cases in the Kotzebue region, 3

cases in the Southeast, 2 cases in the Arctic Slope and one case each in Bristol Bay and Norton Sound. The highest rates of disease occurred in the YK Delta (71.6/100,000) and the Kotzebue region (46.4/100,000).

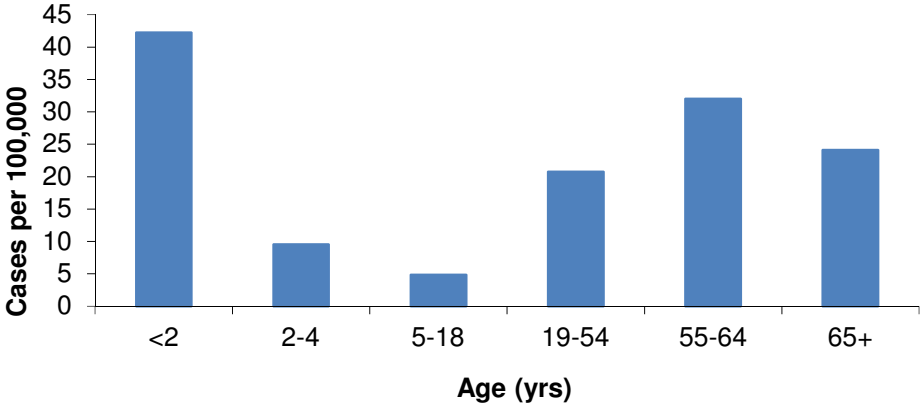
Figure 16: Invasive GAS Disease, Cases & Rates by Region - Alaska, 2016



Age

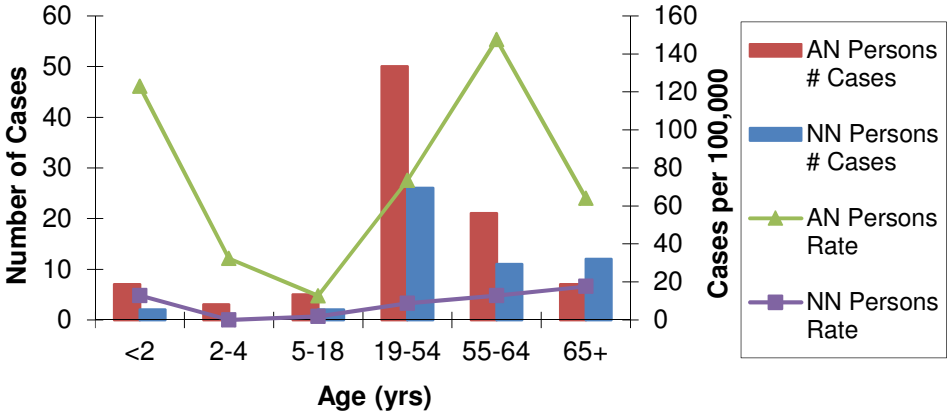
Patients with invasive group A *Streptococcus* reported in 2016 ranged in age from 3 months to 92 years old; the median age was 50.9 years. Highest rates of disease occurred in children less than 2 years old (42.2/100,000).

Figure 17: Invasive group A *Streptococcus* by Age Group - Alaska, 2016



When stratified by race, the highest rates of invasive group A streptococcal disease occurred in Alaska Native adults 55-64 years old (147.5/100,000 persons per year). The highest GAS disease rate in the non-Native population occurred in adults 65 years and older (17.6/100,000 persons per year).

Figure 18: Invasive group A *Streptococcus*, Cases & Rates by Age Group & Race - Alaska, 2016



Clinical Presentation

The primary clinical presentation was determined by a review of the discharge diagnoses in each patient's individual medical record associated with the invasive bacterial illness. In cases with multiple discharge diagnoses, the most serious diagnosis related to the GAS infection was recorded as the primary clinical presentation. Table 18 shows the primary clinical presentations of invasive group A *Streptococcus* in Alaska for 2016.

Group A *Streptococcus* was isolated from blood samples in 78 (53%) of 146 cases, 43 (29%) from surgical specimens, 10 from joint fluid, 4 each from bone, pleural fluid and abscesses, 2 from wounds, and one from CSF.

Table 15: Primary Clinical Presentations of Invasive group A *Streptococcus* – Alaska, 2016

Primary Presentation	n (%)
Cellulitis*	45 (31%)
Pneumonia*	22 (15%)
Necrotizing fasciitis	19 (13%)
Bacteremia	19 13%)
Septic arthritis	11 (8%)
Osteomyelitis	8 (5%)
Strep toxic shock	7 (5%)
Meningitis	2 (1%)
Peritonitis	1 (<1%)
Empyema	1 (<1%)
Endocarditis	1 (<1%)
Bursitis	1 (<1%)
Other	9 (6%)
Total	146

*with bacteremia

Reported Risk Factors

The presence of one or more associated risk factors was reported in 86% of invasive GAS cases in 2016. Alcohol abuse was the most prevalent risk factor observed in adults, followed by cigarette smoking and diabetes.

Table 16: Reported Risk Factors Identified in Invasive GAS Cases – Alaska, 2016*

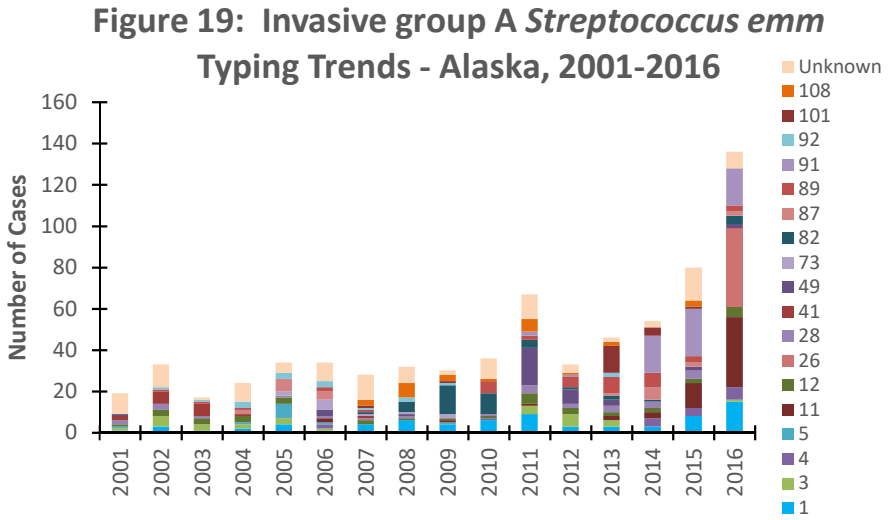
Medical Condition/Risk Factor	Adult Cases (≥ 18 years) n=128, Cases (%)
Alcohol abuse	65 (51%)
Cigarette smoking	53 (42%)
Diabetes	18 (14%)
Chronic lung disease	17 (13%)
Injection drug use	15 (12%)
Immunosuppressive treatment	6 (5%)
Asplenia	0 (0%)

*More than one risk factor was identified in several cases

Molecular Typing

Strain characterization of GAS has traditionally been based on serological identification of the M protein which is a major surface protein and an important GAS virulence factor. In the mid-1990s, many reference labs started using a molecular approach based on sequencing of the N-terminal region of the M protein gene (*emm* gene). To date, more than 200 different *emm* types have been reported. While there are currently no vaccines available to protect against invasive GAS disease, baseline data on the burden of GAS disease to include *emm* typing are critical to evaluate the potential utility of any candidate vaccines.

In 2016, 137 invasive GAS isolates were *emm* typed at AIP. The most common *emm* types were *emm* 26 (28%) and *emm* 11 (25%). The isolates identified as *emm* 26 were part of an outbreak that occurred in Alaska beginning in 2016 [14]. The following graph shows *emm* typing trends over time. Strains that totaled ≤ 10 isolates over the time period were not included.



Antibiotic Resistance

One hundred thirty-seven GAS isolates received at AIP were tested for susceptibility to penicillin, ceftriaxone, erythromycin, vancomycin, levofloxacin and clindamycin. All isolates tested were susceptible to penicillin, ceftriaxone, and vancomycin and levofloxacin. Thirty-six isolates were resistant to erythromycin; 33 of those

were *emm* type 11, two were *emm* type 91 and one was *emm* type 80. Three *emm* type 11 isolates and one *emm* type 91 isolate were also resistant to clindamycin.

Invasive group B *Streptococcus*

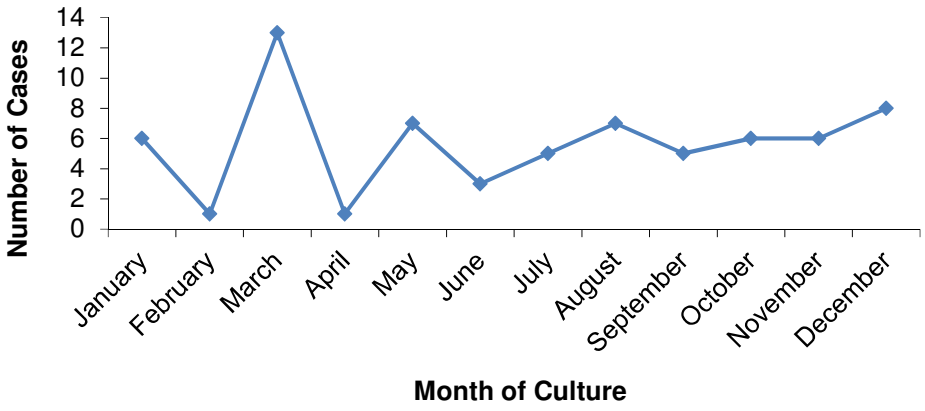
Overall Incidence

A total of 68 cases of invasive group B *Streptococcus* (GBS) were reported to AIP in 2016. The overall rate of invasive GBS disease in the state of Alaska was 9.2/100,000 persons per year. The Alaska rate is similar to the ABCs 2016 national projected rate of 9.6/100,000 [15]. In 2016, there were four GBS-related deaths for a case fatality ratio of 6.1%.

Month of Culture

Cases of group B *Streptococcus* occurred throughout the year; the largest number of cases (n=13) occurred in March.

Figure 20: Invasive group B *Streptococcus*, by Month of Culture - Alaska, 2016



Race

In 2016, 28% of invasive group B *Streptococcus* cases in Alaska occurred in the Alaska Native population. The age-adjusted rate ratio of invasive GBS disease for the Alaska Native population compared with the non-Native population in 2016 was 1.9.

Table 17: Invasive group B *Streptococcus* Cases by Race – Alaska, 2016

Race	Cases n (%)	Age Adjusted Rate*	% Male	Deaths n (%)
Alaska Native Persons	19 (28)	14.3	47	2 (11)
Non-Native Persons	49 (72)‡	7.5	61	2 (4)†
Total	68		57	4 (6)

*Cases per 100,000 per percent distribution of Alaska 2010 population
†Outcome unknown in 2 cases
‡Includes 5 cases for which race was unknown

Region

In 2016, 50 (74%) of the 68 reported GBS cases occurred in Anchorage; 11 cases were reported in the Interior, five cases in Southeast and one case each in the Kotzebue and Norton Sound regions. The highest rates of disease occurred in the Kotzebue region (11.6/100,000) and Anchorage (10.2/100,000).

Age

Patients with invasive group B *Streptococcus* reported in 2016 ranged in age from newborn to 88 years old; the median age was 55.2 years. Highest rates of disease overall occurred in persons 65 years and older (27.9/100,000 persons per year).

Figure 21: Invasive group B *Streptococcus* by Age Group - Alaska, 2016

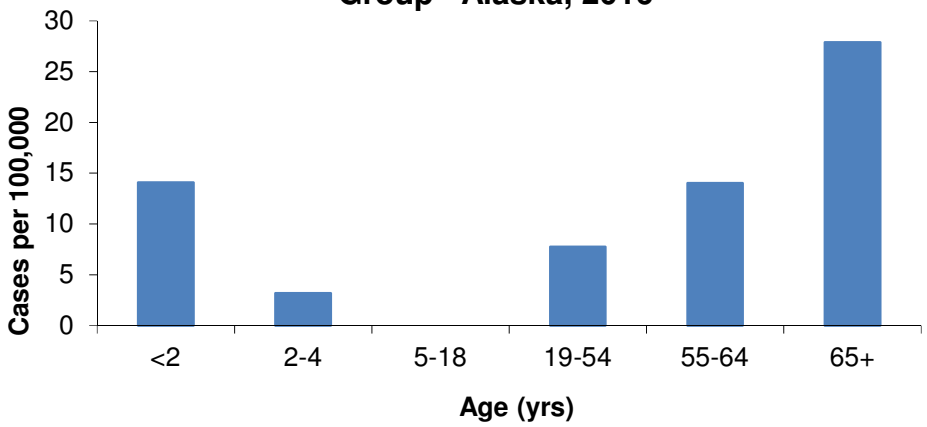
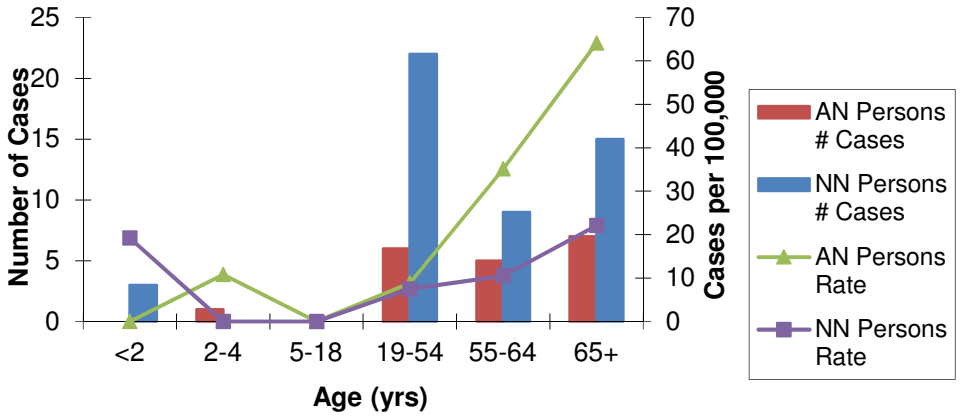


Figure 22: Invasive group B S*treptococcus*, Cases & Rates by Age Group & Race - Alaska, 2016



When stratified by race, the highest rates of disease occurred in AK Native persons 55-64 years old and 65 years and older, 35.1/100,000 persons per year and 64.1/100,000 persons per year, respectively. There was one case of early-onset disease (less than 7 days old) for a rate of 0.1 cases per 1,000 live births.

Clinical Presentation

The primary clinical presentation was determined by a review of the discharge diagnoses in each patient's individual medical record associated with the invasive bacterial illness. In cases with multiple discharge

diagnoses, the most serious diagnosis related to the GBS infection was recorded as the primary clinical presentation. In 2016, the most common clinical presentations were cellulitis and bacteremia which occurred in 24 (35%) and 15 (22%) cases, respectively.

Group B *Streptococcus* was isolated from blood in 49 (72%) of 68 cases in 2016; 8 cases were isolated from surgical specimens, 6 cases from joint fluid, and one each from peritoneal fluid, pericardial aspirate, placenta, abscess and bone.

Table 18: Primary Clinical Presentations of Invasive group B *Streptococcus* – Alaska, 2016

Primary Presentation	n (%)
Cellulitis*	24 (35)
Bacteremia	15 (22)
Pneumonia*	9 (13)
Osteomyelitis	8 (12)
Septic arthritis	5 (7)
Meningitis	2 (3)
Endocarditis	1 (1.5)
Pericarditis	1 (1.5)
Amnionitis	1 (1.5)
Septic abortion	1 (1.5)
Peritonitis	1 (1.5)
Total	68

*with bacteremia

Associated Risk Factors

The presence of one or more associated risk factors was reported in 91% of invasive GBS cases in 2016. Diabetes was the most prevalent risk factor observed in adults followed by chronic lung disease and cigarette smoking.

Table 19: Associated Risk Factors Identified in Adult Invasive GBS Cases – Alaska, 2016*

Medical Condition/Risk Factor	Adult Cases (≥ 18 years) n=64, Cases (%)
Diabetes	38 (59%)
Chronic lung disease	14 (22%)
Cigarette smoking	10 (16%)
Alcohol abuse	7 (11%)
Immunosuppressive treatment	2 (3%)
Asplenia	1 (2%)
Injection drug use	0 (0%)

*More than one risk factor was identified in several cases

Antibiotic Resistance

Susceptibility testing was performed on 59 GBS isolates received in 2016. Results of the testing are presented in the following table.

Table 20: Antibiotic Resistance in Invasive group B *Streptococcus* Isolates – Alaska, 2016

Antibiotic	Susceptible	Intermediate	Resistant	I + R	Total Tested
Penicillin	59 (100%)	0 (0%)	0 (0%)	0 (0%)	59
Ceftriaxone	59 (100%)	0 (0%)	0 (0%)	0 (0%)	59
Erythromycin	30 (51%)	0 (0%)	29 (49%)	29 (49%)	59
Vancomycin	59 (100%)	0 (0%)	0 (0%)	0 (0%)	59
Levofloxacin	59 (100%)	0 (0%)	0 (0%)	0 (0%)	59
Clindamycin	40 (68%)	1 (2%)	17 (29%)	18 (31%)	59

All isolates tested were susceptible to penicillin, ceftriaxone, vancomycin and levofloxacin. Resistance to erythromycin and clindamycin was seen in 49% and 31%, respectively, of isolates tested. The one early onset cases did not have an isolate available for testing.

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Appendix

MIC Interpretive Standards Definitions:

CLSI [7] provides recommended interpretive categories for various Minimum Inhibitory Concentration values (cut points) for each organism/antibiotic combination which are defined as follows:

1. Susceptible (S):

The "susceptible" category implies that isolates are inhibited by the usually achievable concentrations of antimicrobial agent when the recommended dosage is used for the site of infection.

2. Intermediate (I):

The "intermediate" category includes isolates with antimicrobial agent MICs that approach usually attainable blood and tissue levels and for which response rates may be lower than for susceptible isolates. The "intermediate" category implies clinical efficacy applicability in body sites where the drugs are physiologically concentrated (e.g., quinolones and β-lactams in urine) or when a higher dosage of a drug can be used (e.g., β-lactams). The "intermediate" category also includes a buffer zone which should prevent small, uncontrolled technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins.

3. Resistant (R):

Resistant strains are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules, and/or that demonstrate MICs or zone diameters that fall in the range where specific microbial resistance mechanisms are likely (e.g., β-lactamases) are likely, and clinical efficacy of the agent against the isolate has not been reliably shown in treatment studies.