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The Impact of Obesity and Diabetes on the Risk of Disease and Death due to Invasive Group A *Streptococcus* Infections in Adults

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Abstract

Background.—Invasive group A *Streptococcus* (iGAS) infections cause significant morbidity and mortality worldwide. We analyzed whether obesity and diabetes were associated with iGAS infections and worse outcomes among an adult US population.

Methods.—We determined the incidence of iGAS infections using 2010–2012 cases in adults aged ≥18 years from Active Bacterial Core surveillance (ABCs), a population-based surveillance system, as the numerator. For the denominator, we used ABCs catchment area population estimates from the 2011 to 2012 Behavioral Risk Factor Surveillance System (BRFSS) survey. The relative risk (RR) of iGAS was determined by obesity and diabetes status after adjusting for age group, gender, race, and other underlying conditions through binomial logistic regression.

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Multivariable logistic regression was used to determine whether obesity or diabetes was associated with increased odds of death due to iGAS compared to normal weight and nondiabetic patients, respectively.

Results.—Between 2010 and 2012, 2927 iGAS cases were identified. Diabetes was associated with an increased risk of iGAS in all racial groups (adjusted risk ratio [aRR] ranged from 2.71 to 5.08). Grade 3 obesity (body mass index [BMI] ≥40) was associated with an increased risk of iGAS for whites (aRR = 3.47; 95% confidence interval [CI], 3.00–4.01). Grades 1–2 (BMI = 30.0–<40.0) and grade 3 obesity were associated with an increased odds of death (odds ratio [OR] = 1.55, [95% CI, 1.05, 2.29] and OR = 1.62 [95% CI, 1.01, 2.61], respectively) when compared to normal weight patients.

Conclusions.—These results may help target vaccines against GAS that are currently under development. Efforts to develop enhanced treatment regimens for iGAS may improve prognoses for obese patients.

Keywords

group A *Streptococcus* infections; obesity; diabetes

Invasive group A *Streptococcus* (iGAS) infections cause significant morbidity and mortality in the form of severe skin and soft tissue infections (SSTIs), bacteremic pneumonia, necrotizing fasciitis (NF), streptococcal toxic shock syndrome (STSS), bloodstream infections, and sepsis [1]. In 2013, an estimated 11 500 cases and 1100 deaths due to iGAS infections occurred in the United States [2]. Vaccines against invasive and noninvasive GAS infections are under development [3, 4], but currently there are limited strategies for disease prevention. Identifying factors that put people at risk for iGAS or impact their clinical prognosis is important for clinicians who must promptly recognize and treat these severe infections and for public health officials working on prevention efforts.

The proportion of obese adults in the United States increased substantially during the 1980s and 1990s and rose slightly in the last decade [5, 6]. In 2012, approximately 35% of adults were considered obese [7]. The proportion of adults diagnosed with diabetes has risen steadily from approximately 3% to approximately 8% between the 1980s and 2012 [8]. Obesity and diabetes have been linked to increased risk of surgical-site and other SSTIs, respiratory infections, bloodstream infections, and sepsis—all of which are common manifestations of iGAS [9–21]. Because obesity is a risk factor for diabetes [22], a common mechanism may at least partially explain why both are associated with an increased risk of these types of infections. There have been no known published reports looking at the impact of both obesity and diabetes on the incidence and outcomes of severe GAS infections. We used population-based surveillance for iGAS that includes individual-level data on underlying conditions in conjunction with population-based estimates of the frequency of obesity and diabetes to calculate incidence rates and to analyze whether obesity and diabetes are risk factors for iGAS infections and poor outcomes.

METHODS

Surveillance Population

We identified nonpregnant adults (≥18 years old) with iGAS infections between 1 January 2010 and 31 December 2012 through the Active Bacterial Core surveillance (ABCs) system. ABCs, a part of the Centers for Disease Control and Prevention's (CDC) Emerging Infections Program (EIP), conducts active, laboratory- and population-based surveillance for iGAS at 10 sites located throughout the United States, covering approximately 32 million persons (approximately 10% of the US population). ABCs methods have been previously described [23]. Briefly, ABCs staff routinely contacts all microbiology laboratories that serve patients residing in the ABCs catchment area. A case is defined as isolation of GAS from a normally sterile site or from a wound in a patient with NF or STSS who is also a resident of the surveillance area. The ABCs areas included in this analysis were: California (3 county San Francisco Bay area); Colorado (5 county Denver area); Connecticut; Georgia (20 county Atlanta area); Maryland (6 county metropolitan Baltimore area); Minnesota; New Mexico; New York (15 county Rochester and Albany areas for the years 2011 and 2012 only); Oregon (3 county Portland area); and Tennessee (20 urban counties). Patient demographics (eg, age, gender, race), height, weight, and clinical data (eg, underlying conditions, infection type, outcome) were obtained from medical record reviews based on a standardized case report form. Race groups were divided into white, black, and other (includes American Indian/Alaska Natives and Asian/Other Pacific Islanders) races. We could not further categorize persons into Hispanic and non-Hispanic ethnicity because of a high degree of missing data. All available isolates were collected and *emm* typed at the CDC's *Streptococcus* Laboratory [24].

Determination of Obesity and Diabetes Status for iGAS Cases

We used body mass index (BMI) to determine obesity status for iGAS patients. For cases that had height and weight recorded in the medical record, BMI was calculated by the standard formula (BMI=weight (kilograms)/height (meters^2)). For each patient missing height and weight or whose calculated BMI was thought to be implausible (≤12 or >100), BMI was imputed 30 times using a regression model that included demographics (age, race, gender, insurance status), year, location, presence of underlying conditions, clinical syndrome, and height (if available) and weight (if available). Thirty imputations were selected based on the average amount of missing data [25, 26]. Patients were categorized into standard BMI categories: underweight (BMI < 18.5), normal weight (BMI 18.5–<25.0), overweight (25.0–<30.0), grades 1–2 obesity (BMI: 30.0–<40.0), and grade 3 obesity (BMI: ≥40.0) [27]. A person was considered to have diabetes if it was recorded in the medical record by a healthcare provider. All types of diabetes were included except gestational diabetes.

Incidence and Relative Risk Calculation

We estimated the incidence of iGAS for demographic groups (age, race, gender) and underlying conditions of interest (obesity status, diabetes, and heart disease) using ABCs cases as numerators and ABCs catchment area population estimates from the Behavioral Risk Factor Surveillance System (BRFSS) surveys as denominators. BRFSS [28] is a cross-

sectional cellular and landline telephone survey of noninstitutionalized adults administered by state health departments using a standardized questionnaire developed in conjunction with the CDC. Data collected include self-reported height and weight and self-reported chronic health conditions such as diabetes. The survey is designed to determine the state-specific prevalence of certain health conditions and risk behaviors. We used small area estimation for BRFSS denominators by a method previously described to determine the prevalence of health conditions in the ABCs catchment area which includes entire states or only certain counties within states as delineated above [29]. To account for bias known to exist from self-reported heights and weights, we derived ratios that compared national estimates of calculated BMIs from the 2011 to 2012 BRFSS self-reported heights and weights to calculated BMIs from the 2011 to 2012 National Health and Nutrition Examination Survey (NHANES), which obtains measured heights and weights, stratified by age group (18–49 year olds, 50–64 year olds, and 65 years and older), race (white, black, and other) and gender [30]. The ratios were used to adjust individual BMIs used in the denominators of the incidence estimates. We used multilevel binomial logistic regression with county-level random effects to estimate the relative risk (RR) with 95% confidence intervals (CIs) of iGAS by BMI category and diabetes status after controlling for gender, age group, county, the presence of heart disease, and the presence of one or more other underlying conditions thought to be risk factors for iGAS (includes asthma/chronic obstructive pulmonary disease [COPD], current smoking, cancer, chronic kidney disease, and stroke). In sum, 95% CIs that did not include 1.0 were considered significant relative risks. Data were stratified by race to account for differences across racial groups. The RR was approximated from the odd ratios (ORs) because iGAS is a relatively rare disease.

Analysis of Outcomes

Multivariable logistic regression was used to calculate ORs with 95% CIs for intensive care unit (ICU) admission and death by BMI category and diabetes status. Besides BMI category and diabetes status, other factors included in the model were age group, gender, race, state of residence, presence of specific underlying conditions (skin conditions, heart disease, current smoker, asthma/COPD, immunosuppression, malignancy and alcohol abuse), *emm* type and syndrome (eg, SSTI, pneumonia, NF, meningitis, STSS/septic shock). SSTIs included cellulitis, erysipelas, wound infections, phlebitis, lymphangitis, lymphadenitis, and gangrene but excluded NF. Patients who had multiple syndromes were classified into the syndrome (“primary syndrome”) with the highest case fatality. Death was considered GAS-associated if it occurred during the hospitalization for iGAS. If the outcome status was unknown during initial medical record review, site staff reviewed state vital records to determine if the patient died during their hospitalization for iGAS. Factors associated ($P < .20$) with obesity and diabetes and that were associated with the severe outcomes (ICU admission or death) were included in the initial multivariable logistic regression model. Factors were dropped from the model if they were not significantly ($P < .05$) associated with the outcomes and did not significantly change the results for the main factors being evaluated (ie, obesity and diabetes). Two-way interactions were also considered. The 95% CIs that did not include 1.0 were considered significant.

Human Subject Considerations

These activities were considered part of public health surveillance and determined to be "non-research" by CDC's Institutional Review Board (IRB). Where required, IRB approval was obtained at ABCs site health departments or academic institutions.

RESULTS

Between 2010 and 2012, 2927 iGAS cases were identified through ABCs. The median age of patients was 56 years, and they were fairly equally distributed among the age groups (Table 1). A majority of patients (55%) were male and most (76%) were white. BMI was multiply imputed for 516 (18%) patients. Thirty-nine percent of patients were obese (grades 1–3) with about one-third of those being extremely (grade 3) obese (Table 1). Most (87%) patients had at least one underlying condition—the most common being diabetes, skin conditions, current smoking, and heart disease. The most common primary syndromes associated with iGAS were SSTIs, bacteremia without a focus, STSS/septic shock, and pneumonia. Isolates were available for *emm* typing from approximately 76% of patients (Table 1).

Approximately 24.8 million adults resided in the catchment area. The crude incidence of iGAS was higher in grade 3 obese patients compared to normal and overweight patients across all race groups (Table 2). The highest incidence of iGAS occurred in underweight patients. Patients with diabetes had higher incidences of iGAS compared to nondiabetic patients overall and across all race groups (Table 2).

After adjusting for age, gender, obesity status, heart disease, and the presence of one or more other underlying conditions, the RR of iGAS was significantly higher in diabetic patients than nondiabetic patients with the point estimate ranging from 2.71 in blacks, 3.37 in whites, and 5.08 in other races (Table 3). Grade 3 obesity compared to normal weight was associated with an increased risk of iGAS in whites and other races. Rates of iGAS were lower for overweight persons compared to normal weight persons (in both whites and blacks). Being underweight compared to being normal weight was associated with a higher incidence of iGAS for both whites and blacks but not for other races. Age ≥65 years (except for blacks), male gender, and heart disease (except for other races) were also associated with higher rates of iGAS infections compared to younger ages (18–49 years), being female, and the absence of heart disease, respectively (Table 3).

On univariate analysis, factors associated ($P < .20$) with death included older age group (>50 years), state of residence, higher BMI category, heart disease, chronic renal disease/dialysis, malignancy, alcohol abuse, or STSS/septic shock as was having *emm* type 1 or 3. Factors associated ($P < .20$) with ICU admission included all those associated with death as well as having COPD/asthma, pneumonia or NF.

On multivariable analysis, grades 1–2 obesity and grade 3 obesity were associated with an increased odds of death compared with normal weight (Table 4). Diabetes was not associated with an increased odds of death. There was no interaction between diabetes and obesity and death in the multivariable model. The same percentage (9%) of normal weight

patients both with and without diabetes died ($P = .93$), and almost the same percentage of obese patients both with (11%) and without diabetes (12%) died ($P = .17$). Other factors that were independently associated with death included older age, heart disease, malignancy, and alcohol abuse. Among the primary syndromes, the odds of death was elevated among patients who had STSS/septic shock compared to those without those syndromes. Patients with SSTIs had a reduced odds of death compared to those who did not have SSTIs. When subset to patients with SSTIs, patients with grade 3 obesity had an increased odds of death compared to normal weight patients (OR = 9.21; 95% CI, 1.06–79.64), but diabetic patients did not have an increased odds of death compared to nondiabetic patients (OR = 0.58, 95%CI, .17–1.94). There was no increase odds of death based on obesity or diabetes status for those who had syndromes other than SSTIs.

The odds of ICU admission was higher in obese patients compared to those with normal weight. However, there was no appreciable difference in the mean or median length of stay between patients who had grade 1–2 obesity (mean 10.6 days, median 7 days), grade 3 obesity (mean 10.8 days, median 7 days), were underweight (mean 11.0 days, median 7 days), or were normal weight (mean 10.3, median 8 days). Diabetes was not associated with an increased odds of ICU admission, and length of stays were similar between diabetic (mean 10.9 days, median 8 days) and nondiabetic patients (10.2 and median 7 days). There was no interaction between diabetes and obesity and ICU admission in the multivariable model. About the same percentage of normal weight patients with (38%) and without (37%) diabetes required ICU ($P = .16$).

The distribution of primary syndromes associated with iGAS infections did not appreciably differ by BMI category or diabetes status, with one important exception. A higher proportion of patients with grade 3 obesity (45.3%) had SSTIs compared to normal weight patients (29.2%, $P < .001$) as did diabetic patients (37.3%) compared to nondiabetic patients (31.1%, $P < .001$) (Figure 1). There was a higher odds of SSTIs among grade 3 obese compared to normal weight patients among whites (OR = 1.83; 95% CI, 1.38–2.42), blacks (OR = 2.36; 95% CI, 1.89–4.71), and patients of other races (OR = 4.62, 95% CI, 2.08–10.56). The odds of SSTI was higher among diabetic compared to nondiabetic patients for whites (OR = 1.28, 95% CI, 1.05–1.55). The relationship between SSTIs and diabetes was not statistically significant among blacks (OR = 1.16, 95% CI, .72–1.9) or other races (OR = 1.53, 95% CI, .92–2.56).

DISCUSSION

We found diabetes to be a risk factor for iGAS infections among all race groups and extreme obesity to be a risk factor for iGAS infections among whites and other races. Obesity was also associated with an increased risk of ICU admission and death, although there were no associations between diabetes and poorer outcomes. Understanding who is at increased risk for iGAS infections and poorer outcomes has implications for recognizing severe infections, administering timely and appropriate treatments, and targeting public health prevention efforts.

Obesity and diabetes have been previously shown to be risk factors for syndromes often associated with iGAS, including SSTIs [9–11, 14–15, 16, 18, 20–21], pneumonia [12, 17, 21], bloodstream infections, and sepsis [13, 19, 31]. A case-control study from the late 1990s did show diabetes to be a risk factor for iGAS (relative risk = 2.27, $P = .03$), but the study did not assess obesity as a potential risk factor [32]. Our results showing an increased risk of iGAS among extremely obese whites and other races and diabetic patients across all races are consistent with these findings. SSTI was the only primary syndrome that was positively associated with obesity and diabetes, although the relationship between diabetes and SSTIs varied by race. Likewise, the increased risk of death was seen in obese patients with SSTIs but was not present for other syndromes. Differences in the occurrence of SSTIs seem to be driving much of the increased risk of iGAS and poorer outcomes. We did not find an overall association between extreme obesity and the incidence of iGAS infections among blacks. Biologic differences in body composition may vary across races and ethnicities, so BMI may not be measuring the same level of adiposity across the different demographic groups [33]. Mechanisms thought to increase an obese person's susceptibility to severe infections include alterations in immune system functions, impaired skin barrier functions and altered lung mechanics [34–35]. Likewise, diabetes may alter immune system function and wound healing beyond the effects of obesity [36].

Although increases in the adult prevalence of obesity (from approximately 31% to approximately 35%) and diabetes (from approximately 5% to approximately 8%) in the United States have been noted over the past 17 years [6–8], there has been no significant increase in the overall incidence of iGAS as detected by ABCs during the same time period [37]. The prevalence of grade 3 obesity has doubled from 3% to 6%. Absolute changes in the proportions of adults with these conditions were still relatively small, so a major impact on overall iGAS rates is not expected.

This analysis has some limitations. First, we imputed BMI for approximately 18% of cases, but values were based on predictive variables in a regression analysis. BRFSS uses self-reported heights and weights, and we attempted to adjust for known biases in self-reporting. It is possible that both obese and nonobese persons had undiagnosed diabetes, but we found an increased risk among the extremely obese even after controlling for patients whose diabetes was diagnosed. However, we were only able to measure the direct impact of obesity on iGAS infections because we controlled for diabetes in the model. We did not measure the indirect effect that obesity has on iGAS through its association with diabetes [22]. We did not collect measures of glucose control, like hemoglobin A1C, which may affect a diabetic person's risk of iGAS. Although we found obesity (except in blacks) and diabetes to be risk factors for iGAS after controlling for other factors, it is possible that we did not control for other unknown factors. Finally, the ABCs catchment area includes a more urban population than the United States as a whole, so the findings may not be representative of the entire US population.

There are few strategies for preventing iGAS infections or their severe outcomes. Current approaches include prevention of secondary cases in healthcare and household settings [38]. Curbing obesity and diabetes has been a major focus of the medical and public health communities for decades, and reductions in the prevalence of these conditions may

help reduce overall rates of iGAS. Additionally, vaccines against GAS are currently under development [3–4]. These results, if confirmed, may help target vaccines to patients with diabetes or obesity should they become available. However, one also must consider that obese persons may have reduced responses to vaccinations [39]. More needs to be done to understand how obesity may impact outcomes—particularly whether different treatment regimens, such as altered antibiotic dosing, would improve prognoses.

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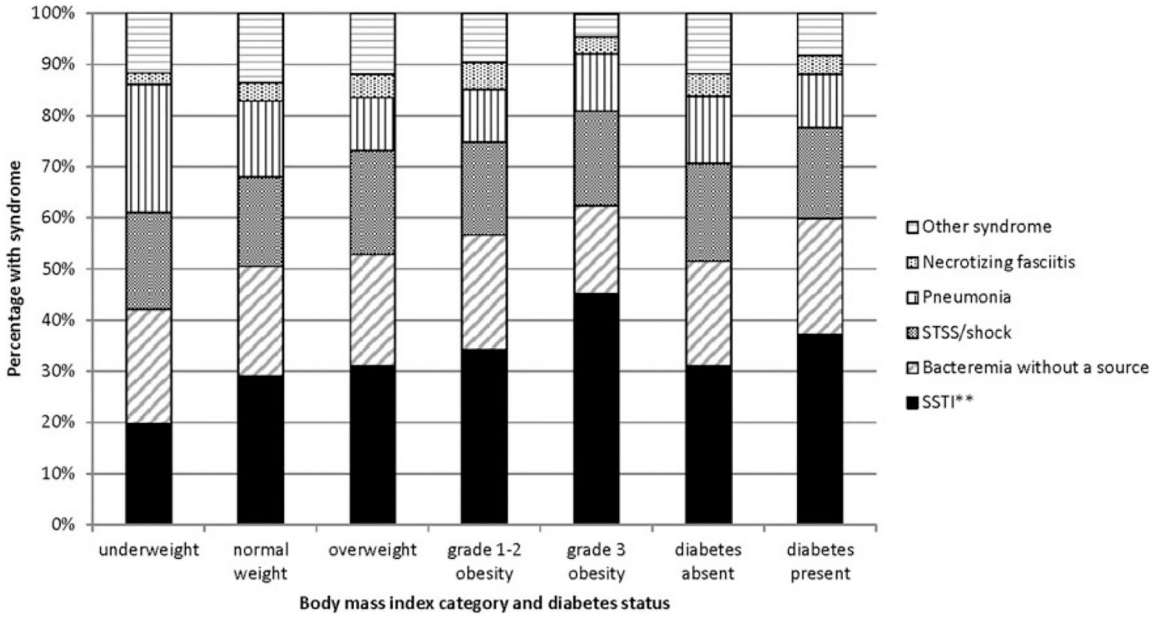

Figure 1.

Distribution of select syndromes* among invasive group A *Streptococcus* patients, by body mass index category and diabetes status: Active Bacterial Core surveillance (2010–2012). *Persons with more than one syndrome were categorized into the most severe type based on the likelihood of death for persons with a single syndrome. **Skin/soft tissue infection (SSTI) includes cellulitis, erysipelas, wound infections, phlebitis, lymphangitis, lymphadenitis and gangrene but excludes necrotizing fasciitis. Abbreviations: STSS, streptococcal toxic shock syndrome; SSTI, skin and soft tissue infection.

Table 1.

Characteristics of Patients With Invasive Group A *Streptococcus* Infection: Active Bacterial Core surveillance (2010–2012)

Characteristic	Number (%) N = 2927
Age group in years:	
18–49	1102 (37.6)
50–64	852 (29.1)
≥65	973 (33.2)
Male gender	1611 (55.0)
Race	
White	2222 (75.9)
Black	432 (14.8)
Other race[a]	273 (9.3)
Body mass index (BMI) category	
Underweight (<18.5)	131 (4.5)
Normal weight (18.5–<25.0)	836 (28.6)
Overweight (25.0–<30.0)	818 (27.9)
Obesity grade 1–2 (30.0–<40.0)	743 (25.4)
Obesity grade 3 (≥40)	399 (13.6)
Underlying conditions	
Diabetes	859 (29.3)
Skin conditions[b]	836 (28.6)
Current smoker	548 (18.7)
Heart disease	544 (18.6)
Chronic renal disease/dialysis	375 (12.8)
Immunosuppression[c]	310 (10.6)
Malignancy[d]	303 (10.4)
Alcohol abuse	277 (9.5)
Chronic obstructive pulmonary disease (COPD)/asthma	272 (9.3)
Any underlying condition[e]	2539 (86.7)
Primary syndrome[f]	
Skin/soft tissue infection[g]	976 (33.3)
Bacteremia without a focus	629 (21.5)
STSS/septic shock	533 (18.2)
Pneumonia	352 (12.0)
Necrotizing fasciitis	123 (4.2)
Meningitis/other central nervous system infection	29 (1.0)
Other syndrome	314 (10.7)
emm types[h]	
*emm*1	480 (16.4)

Characteristic	Number (%) N = 2927
*emm*89	222 (7.6)
*emm*12	195 (6.7)
*emm*28	140 (4.8)
*emm*3	139 (4.7)
Other *emm* types	1062 (36.3)
emm type unknown	689 (23.5)

Abbreviation: STSS, streptococcal toxic shock syndrome.

[a]Includes American Indian/Alaska Natives (6.0%) and Asian/Other Pacific Islanders (3.3%).

[b]Skin condition includes chronic skin breakdown or recent (within 7 days of culture) varicella infection, penetrating or blunt trauma, surgical wound or burn.

[c]Includes patients with immunoglobulin deficiencies, nephrotic syndrome, organ transplantation, receipt of immunosuppression therapy, AIDS and asplenia.

[d]Excludes malignancies of the skin.

[e]Includes conditions listed and other underlying conditions.

[f]Patients with more than one syndrome were categorized into the most severe one based on the likelihood of death for patients with a single syndrome.

[g]Skin/soft tissue infection includes cellulitis, erysipelas, wound infections, phlebitis, lymphangitis, lymphadenitis and gangrene but excludes necrotizing fasciitis.

[h]Five most common *emm* types are listed individually.

Table 2.

Incidence (per 100 000) of Invasive Group A *Streptococcus* Infection by Age, Gender, Body Mass Index Category, Underlying Conditions and Race: Active Bacterial Core Surveillance (2010–2012)

Characteristic	Incidence for Whites (95% CI)	Incidence for Blacks (95% CI)	Incidence for Other Race[a] (95% CI)	Incidence for All Races (95% CI)
Age group in years				
18–49	2.4 (2.2, 2.5)	3.2 (2.8, 3.7)	2.6 (2.2, 3.1)	2.5 (2.4, 2.7)
50–64	4.3 (3.9, 4.6)	5.2 (4.4, 6.2)	5.6 (4.5, 7.0)	4.5 (4.2, 4.8)
≥65	8.2 (7.7, 8.8)	6.8 (5.4, 8.5)	8.7 (6.8, 11.1)	8.1 (7.6, 8.6)
Gender				
Female	3.4 (3.2, 3.6)	3.6 (3.1, 4.1)	3.4 (2.9, 4.1)	3.4 (3.2, 3.6)
Male	4.5 (4.2, 4.7)	4.6 (4.1, 5.3)	4.4 (3.7, 5.1)	4.5 (4.3, 4.7)
Body mass index category				
Normal weight (18.5–<25.0)	3.4 (3.2, 3.7)	4.7 (3.9, 5.7)	2.1 (1.7, 2.7)	3.4 (3.2, 3.6)
Underweight (<18.5)	17.3 (14.1, 21.2)	37.8 (26.4, 54.1)	3.3 (1.6, 6.9)	15.7 (13.2, 18.6)
Overweight (25.0–<30.0)	3.1 (2.9, 3.4)	2.9 (2.4, 3.6)	3.6 (2.9, 4.6)	3.1 (2.9, 3.4)
Obese grade 1–2 (30.0–<40.0)	3.8 (3.5, 4.2)	3.3 (2.7, 3.9)	7.0 (5.6, 8.7)	3.9 (3.6, 4.2)
Obese grade 3 (≥40)	11.4 (10.1, 12.7)	6.3 (4.9, 8.0)	18.7 (13.7, 25.5)	10.4 (9.4, 11.5)
Diabetes				
Absent	3.1 (2.9, 3.2)	3.3 (2.9, 3.6)	2.5 (2.2, 2.9)	3.0 (2.9, 3.2)
Present	13.8 (12.8, 15.0)	9.8 (8.2, 11.6)	19.9 (16.5, 24.0)	13.5 (12.7, 14.5)
Heart disease				
Absent	3.6 (3.4, 3.8)	3.7 (3.4, 4.1)	3.5 (3.1, 4.0)	3.6 (3.5, 3.8)
Present	8.8 (7.9, 9.9)	9.7 (7.5, 12.7)	12.2 (8.7, 17.2)	9.2 (8.3, 10.1)

Abbreviation: CI, confidence interval.

[a]Other race includes American Indian/Alaska Natives (6.0%) and Asian/Other Pacific Islanders (3.3%).

Table 3.

Adjusted Relative Risk of Invasive Group A *Streptococcus* Infection by Age, Gender, Body Mass Index Category, Underlying Conditions and Race: Active Bacterial Core Surveillance (2010–2012)

Characteristic	Relative Risk[a] for Whites (95% CI)	Relative Risk[a] for Blacks (95% CI)	Relative Risk[a] for Other Race[b] (95% CI)
Age group			
18–49 years-old	reference	Reference	reference
50–64 years-old	1.52 (1.36,1.70)	1.21 (.95,1.54)	1.39 (1.02,1.89)
≥65 years-old	2.69 (2.41,3.01)	1.29 (.95,1.75)	1.86 (1.30,2.65)
Gender			
Female	reference	reference	reference
Male	1.41 (1.29,1.54)	1.33 (1.10,1.62)	1.35 (1.05,1.74)
Body mass index category			
Normal weight (18.5–<25.0)	reference	reference	reference
Underweight (<18.5)	4.82 (3.73,6.24)	7.32 (4.67,11.5)	1.57 (.64,3.86)
Overweight (25.0–<30.0)	0.77 (.68,.88)	0.60 (.45,.81)	1.23 (.86,1.77)
Obese grade 1–2 (30.0–<40.0)	1.02 (.90,1.16)	0.65 (.49,.86)	2.02 (1.41,2.89)
Obese grade 3 (≥40)	3.47 (3.00,4.01)	1.29 (.93,1.79)	4.34 (2.76,6.81)
Diabetes			
Absent	reference	reference	reference
Present	3.37 (3.05,3.71)	2.71 (2.15,3.42)	5.08 (3.81,6.77)
Heart disease			
Absent	reference	reference	reference
Present	1.50 (1.32,1.71)	1.99 (1.45,2.72)	1.29 (.84,1.98)
Any other chronic condition[c]			
Absent	reference	reference	reference
Present	1.05 (.96,1.14)	0.91 (.74,1.1)	0.66 (.5,.87)

Abbreviations: BMI, body mass index; CI, confidence interval.

[a]Relative risk is adjusted for all other characteristics listed.

[b]Other race includes American Indian/Alaska Natives (6.0%) and Asian/Other Pacific Islanders (3.3%).

[c]Other chronic conditions include asthma/chronic obstructive pulmonary disease, current smoking, cancer (excluding nonmelanoma skin cancer) chronic kidney disease and stroke, and exclude obesity (BMI ≥ 30), diabetes and heart disease.

Table 4.

Adjusted Odds Ratios for Characteristics Associated With Intensive Care Unit (ICU) Admission and Death for Patients with invasive Group A *Streptococcus* infection: Active Bacterial Core surveillance (2010–2012)

Characteristic	Adjusted OR[a] for ICU Admission (95% CI)	Adjusted OR[a] for Death (95% CI)
Age group		
18–49 years-old	reference	reference
50–64 years-old	1.27 (1.01,1.60)	2.02 (1.41,2.88)
≥65 years-old	1.31 (1.05,1.63)	3.38 (2.36,4.83)
Race		
White	reference	reference
Black	1.27 (.97,1.66)	0.84 (.56,1.26)
Other	0.90 (.63,1.29)	0.95 (.56,1.62)
BMI category		
Normal weight (18.5–<25.0)	reference	reference
Underweight (<18.5)	1.10 (.68,1.78)	1.63 (.84,3.15)
Overweight (25.0–<30.0)	1.36 (1.05,1.75)	1.38 (.94,2.03)
Obese grade 1–2 (30.0–<40.0)	1.46 (1.12,1.90)	1.55 (1.05,2.29)
Obese grade 3 (≥40)	2.07 (1.50,2.86)	1.62 (1.01,2.61)
Other conditions	Reference: absence of condition	Reference: absence of condition
Diabetes	1.06 (.86,1.30)	0.77 (.57,1.04)
Heart disease	1.29 (1.02,1.64)	1.50 (1.10,2.04)
Malignancy	*b*	1.50 (1.05,2.17)
Alcohol abuse	2.34 (1.73,3.16)	1.94 (1.28,2.96)
Current smoker	1.24 (.98,1.56)	0.65 (.44,.98)
Primary syndrome[c]	Reference: absence of syndrome	Reference: absence of syndrome
Skin/soft tissue infection[d]	0.53 (.41,.64)	0.26 (.17,.40)
Pneumonia	1.95 (1.51,2.54)	*b*
Necrotizing fasciitis	4.13 (2.75,6.19)	*b*
STSS/shock	17.03 (12.57,23.08)	4.82 (3.67,6.35)

Abbreviations: BMI, body mass index; CI, confidence interval; ICU, intensive care unit; OR, odds ratio; STSS, streptococcal toxic shock syndrome.

[a]The models are adjusted for the variables listed unless otherwise indicated and are also adjusted for state of residency.

[b] These factors were not included in the model because they were not significant ($P > .20$) on univariable analysis for the outcome (ICU admission or death) or did not change the results for the primary factors being considered (BMI category or diabetes status) and were not significant in multivariable analysis (95% confidence limits of the odds ratio included 1.0).

[c] Persons with more than one syndrome were categorized into the most severe type based on the likelihood of death for persons with a syndrome.

[d] Skin/soft tissue infection includes cellulitis, erysipelas, wound infections, phlebitis, lymphangitis, lymphadenitis and gangrene but excludes necrotizing fasciitis.

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