Burden of Adults Hospitalized With Group B Streptococcal Infection

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Background. The burden of noninvasive group B Streptococcus (GBS) infections in adults is unknown. We determined population-based rates of hospitalization where invasive or noninvasive GBS infections were identified among US adults in a defined catchment area.

Methods. We identified adults with clinical and laboratory-confirmed evidence of GBS infection from January 2014 through December 2016 from 6 hospitals in Louisville, Kentucky. Invasive disease was defined as GBS isolated from a normally sterile site.

Results. Among 1076 adults with GBS infection, the median age was 52 years, 51% were male, and 89% had ≥1 chronic medical condition. The most prevalent infection sites were skin and soft tissue (39%), urinary tract (23%), bone and joint (16%), and bloodstream (11%). Forty percent of infections were polymicrobial. The annual incidence of GBS-associated hospitalization was 73 per 100,000 adults and 68 and 100 per 100,000 for patients aged 18–64 and ≥65 years, respectively. For every invasive GBS infection, 3.7 noninvasive infections occurred.

Conclusions. Our population-based study outlines the full burden of GBS-associated hospitalization in adults and found incidence rates comparable to those of pneumococcal disease, where vaccines are recommended. Noninvasive disease was 3–4 times more common than invasive disease, suggesting that the GBS burden among adults is considerably greater than previously recognized.

Keywords. Group B Streptococcus (GBS); noninvasive; incidence; adults; epidemiology; risk factor.

Group B Streptococcus (GBS) is a well-recognized cause of infection in neonates and pregnant women [1–3]. GBS also causes invasive infections in nonpregnant adults, especially among the elderly and adults with chronic medical conditions [4–8], resulting in significant morbidity and mortality rates [8–10]. Furthermore, contemporary reports from developed countries suggest that the incidence of invasive GBS disease in adults is increasing [5, 8, 11, 12].

Studies describing the burden of GBS in adults to date have primarily focused on invasive disease because existing surveillance systems rely on collection of blood cultures [8, 13]. However, GBS also causes many noninvasive infections of the skin and soft tissue, bone and joint, and urinary and respiratory tracts [11, 12]. Describing the incidence of these infections is more challenging because GBS may colonize skin and mucosal surfaces and may be isolated from infected sites along with other pathogens [14–17]. Thus, no studies to date have characterized the burden of noninvasive GBS infections in adults using a population-based approach. This type of study is needed to elucidate the full spectrum of the GBS disease burden in adults and inform future treatment and prevention strategies. We determined population-based rates of hospitalization where invasive or noninvasive GBS infections were identified among US adults living in a defined catchment area and extrapolated our results to the entire US population.

METHODS

Design, Setting, and Participants

We identified GBS infections among adults ≥18 years of age by retrospectively reviewing laboratory and medical records from 6 hospitals in Louisville, Kentucky, between 1 January 2014 and 31 December 2016. Data describing demographic and clinical characteristics (eg, chronic medical conditions) were collected for each patient. Institutional review board approval (no. 17.0542) was obtained by each participating center. The requirement for informed consent was waived.

Louisville is the largest city in Kentucky and sits on the Ohio River along the Indiana border. At the time of our study, Louisville’s population was generally similar to the United States in terms of demographics and the prevalence of underlying chronic medical conditions, including diabetes and obesity, based on data from the Behavioral Risk Factor Surveillance System (BRFSS). BRFSS is an annual survey conducted by the
Definition of GBS Infection
Patients had to have GBS isolated from culture obtained during hospitalization with (1) clinical or laboratory evidence of local signs and symptoms of infection or (2) systemic inflammatory response (Supplementary Table 2). Instances in which GBS was isolated from culture without local or systemic evidence of infection were categorized as colonization (only) and were excluded. Pregnant women meeting criteria for GBS infection were included (except for asymptomatic pregnant women with positive screening cultures). Infection sites were defined using clinical and laboratory criteria adapted from Mandell, Douglas, and Bennett’s Principles and Practice of Infectious Diseases [19] (Supplementary Table 2).

If GBS was isolated from >1 clinical site, the most life-threatening or invasive site was considered the “most serious” infected site (eg, necrotizing fasciitis of the leg was considered the “most serious” site in a patient that also had cellulitis). To help establish these clear definitions of GBS infection, we consulted several experts (see Acknowledgments). Each case was reviewed by 2 infectious disease specialists (P. P. and J. R.). In instances where the type of GBS infection or the most serious site was not immediately clear, a third infectious disease expert was consulted (D. L. S.). For the most challenging cases, external experts who were not part of the study were also consulted (see Acknowledgments). Discrepancies between specialists were resolved through discussion until consensus was reached. Invasive disease was defined in accordance with CDC invasive bacterial surveillance criteria as GBS isolated from a normally sterile site, such as blood, bone, an internal body site (eg, specimen obtained from brain, lymph node, surgical site, or aspirate), or cerebrospinal, pleural, peritoneal, or pericardial fluid [20]. Infections such as osteomyelitis or necrotizing myositis were classified as noninvasive when the infection developed from another noninvasive contiguous site, such as an open wound. Polymicrobial infection was defined as the presence of GBS and ≥1 other organism in the same culture within the most serious site.

Clinical Outcomes
For each GBS infection, we recorded the length of hospital stay and the proportion that were admitted to the intensive care unit (ICU), required mechanical ventilation, or died from any cause during hospitalization (in-hospital mortality rate) or within 30 days after hospital admission if discharged alive. Hospital-acquired infections were defined as those that occurred ≥48 hours after admission and did not seem to be incubating at the time of admission.

Statistical Analysis
We compared invasive with noninvasive infections and monomicrobial with polymicrobial infections, using χ² tests. We estimated annual rates of GBS infection by dividing the number of GBS cases occurring among permanent residents of the catchment area (most serious site only) identified across the 5 hospitals used for calculating incidence by US Census population estimates for the catchment area. We adjusted the number of GBS infections for the estimated proportion of adult admissions in Louisville occurring in the 5 study hospitals (ie, market share). Age-specific market share data were obtained from the statewide Inpatient Records Database (Kentucky Cabinet for Health and Family Services).

We also adjusted incidence estimates for the shortened period for which the University of Louisville Hospital recruited study participants (Supplementary Table 1). For calculation of risk group–specific incidence rates, the prevalence of chronic medical conditions in the catchment area were obtained from the Louisville Metropolitan Statistical Area–specific BRFSS [18]. Incidence rates were not age standardized to the US population, because the age distribution of adults in Louisville was nearly identical to that of the United States. Rates were presented for GBS infections both including and excluding noninvasive polymicrobial infections (where the role of GBS as the primary cause of infection may not be clear [14–17]). All analyses were performed with SAS software, version 9.4 (SAS Institute), or Stata software, version 14.0 (StataCorp).

RESULTS
Description of GBS Infections
We identified positive GBS cultures in 1428 hospitalized patients, of which 352 (25%) were deemed colonization (only). Of the remaining 1076 patients with GBS infection, 549 (51%) were male, 786 (73%) were white, 263 (24%) were black, and 961 (89%) had ≥1 chronic medical condition, with diabetes (633; 59%), obesity (585; 54%), coronary artery disease (221; 21%), and chronic renal disease (217; 20%) the most common. The
median age was 52 years. Forty-five patients (4%) were pregnant or puerperal women. Only 38 (4%) were hospital acquired. The median hospital length of stay was 5 days. Twenty percent of patients (213 of 1076) were admitted to the ICU (Table 1). All-cause in-hospital deaths occurred in 30 of 1076 (3%). Six additional patients were discharged but died within 30 days of admission.

Among the 1076 patients with GBS infection, GBS was isolated from 1784 samples. Most GBS isolations (983 of 1784 [55%]) were taken from skin and soft tissue, followed by urinary tract (269 of 1784 [15%]), bone and joint (248 of 1784 [14%]), and bloodstream (141 of 1784 [8%]) (Table 2). When analyses were restricted to the most serious site, skin and soft-tissue infections were still most common (423 of 1076 [39%]). Urinary tract (252 of 1076 [23%]), bone and joint (173 of 1076 [16%]), and bloodstream (115 of 1076 [11%]) infections comprised the remaining majority (Table 2). The 10 most common diagnoses were skin abscess, treated bacteriuria (abnormal urinalysis and antibiotic prescribed), osteomyelitis, secondary bacteremia, skin ulcer, necrotizing myositis, pyelonephritis, cystitis, necrotizing fasciitis, and community-acquired pneumonia, accounting for 84% (Table 3 and Supplementary Table 2). Results were similar when pregnant or puerperal women were excluded from the analyses (data not shown).

**Invasive Versus Noninvasive Infections**

Of the most serious infections, 21% (227 of 1076) were invasive. The most common invasive sites were bacteremia (115 of 227 [51%]), bone and joint (45 of 227 [20%]), skin and soft tissue (27 of 227 [12%]; eg, necrotizing fasciitis or myositis with samples collected during operative procedures), and the cardiovascular system (27 of 227 [12%]) (Supplementary Table 3). Invasive infections were more likely than monomicrobial infections to be skin and soft-tissue or bone and joint infections (331 of 428 polymicrobial infections [77%] vs 265 of 648 monomicrobial infections [41%]) and less likely to be bacteremia (18 of 428 [4%] vs 97 of 648 [15%, respectively) or urinary tract infections (42 of 428 [10%] vs 210 of 648 [32%]) (all P < .001; Supplementary Table 3). Polymicrobial infections were more likely than monomicrobial infections to occur in patients with noninvasive infections (375 of 428 [88%] vs 474 of 648 [73%], respectively; P < .001), in men (248 of 428 [58%] vs 301 of 648 [46%]; P < .001), and in those with diabetes (292 of 428 [68%] vs 341 of 648 [53%]; P < .001), peripheral vascular disease (79 of 428 [18%] vs 68 of 648 [10%]; P < .001), or stroke (51 of 428 [12%] vs 50 of 648 [8%]; P = .02), but were less common in those with liver disease (19 of 428 [4%] vs 55 of 648 [8%]; P < .01) (Supplementary Table 5). Among monomicrobial infections only, 2.7 noninvasive infections occurred for every invasive GBS infection.

**Incidence of GBS Infection**

Among the 1076 hospitalizations in which GBS was identified, 684 were eligible for calculating incidence, corresponding to an annual rate of 73 (95% confidence interval [CI], 68–78) per 100,000 in all adults. Rates were 68 (95% CI, 63–74) and 100 (85–117) per 100,000 in adults 18–64 and ≥65 years of age, respectively. Rates for older adults were similar over time, but there was an annual increase in GBS rates among adults <65 years of age, from 52 (95% CI, 44–61) to 82 (72–94) per 100,000. The highest rate of GBS-associated hospitalization was seen among adults <65 years of age with diabetes, at 486 (95% CI, 437–540) per 100,000 annually (Table 4).

Black adults were 2.6 (95% CI, 2.2–3.1) times more likely than whites to acquire GBS, with a rate of 157 per 100,000
Table 1. Characteristics of Patients With Group B Streptococcus Infections

| Patient Characteristics | All Patients (n = 1076) | Invasive Infection (n = 227) | Noninvasive Infection (n = 849) | P Value |
|-------------------------|-------------------------|-----------------------------|-------------------------------|---------|
| Demographics            |                         |                             |                               |         |
| Year of study           |                         |                             |                               |         |
| 2014                    | 293 (27)                | 60 (26)                     | 233 (27)                      | .88     |
| 2015                    | 388 (36)                | 85 (37)                     | 303 (36)                      |         |
| 2016                    | 395 (37)                | 82 (36)                     | 313 (37)                      |         |
| Age group, y            |                         |                             |                               |         |
| 18–49                   | 452 (42)                | 68 (30)                     | 384 (45)                      | <.001   |
| 50–64                   | 388 (36)                | 101 (44)                    | 287 (34)                      |         |
| 65–74                   | 138 (13)                | 25 (11)                     | 113 (13)                      |         |
| ≥75                     | 98 (9)                  | 33 (15)                     | 65 (8)                        |         |
| Sex                     |                         |                             |                               |         |
| Female                  | 527 (49)                | 85 (37)                     | 442 (52)                      | <.001   |
| Male                    | 549 (51)                | 142 (63)                    | 407 (48)                      |         |
| Raceb                   |                         |                             |                               |         |
| White                   | 786 (73)                | 175 (77)                    | 611 (72)                      | .29     |
| Black                   | 263 (24)                | 47 (21)                     | 216 (26)                      |         |
| Other                   | 24 (2)                  | 4 (2)                       | 20 (2)                        |         |
| Ethnicityc              |                         |                             |                               |         |
| Hispanic or Latino      | 26 (2)                  | 3 (1)                       | 23 (3)                        | .47     |
| Not Hispanic or Latino  | 1043 (98)               | 223 (99)                    | 820 (97)                      |         |
| Body mass indexd        |                         |                             |                               |         |
| Underweight             | 40 (4)                  | 6 (3)                       | 34 (4)                        | .72     |
| Normal weight           | 218 (20)                | 48 (21)                     | 170 (20)                      |         |
| Overweight              | 228 (21)                | 45 (20)                     | 183 (22)                      |         |
| Obesity                 | 585 (54)                | 127 (56)                    | 458 (54)                      |         |
| Class 1                 | 216 (20)                | 45 (20)                     | 171 (20)                      |         |
| Class 2                 | 155 (14)                | 30 (13)                     | 125 (15)                      |         |
| Class 3                 | 214 (20)                | 52 (23)                     | 162 (19)                      |         |
| Chronic medical conditions |                         |                             |                               |         |
| Any                     | 961 (89)                | 209 (92)                    | 752 (89)                      | .13     |
| Diabetes mellitus       | 633 (59)                | 118 (52)                    | 515 (61)                      | .02     |
| Chronic renal disease   | 217 (20)                | 57 (25)                     | 160 (19)                      | .04     |
| Congestive heart failure| 163 (15)                | 51 (22)                     | 112 (13)                      | <.001   |
| Coronary artery disease | 221 (21)                | 51 (22)                     | 170 (20)                      | .42     |
| Peripheral vascular disease | 147 (14) | 32 (14) | 115 (14) | .83 |
| Stroke                  | 101 (9)                 | 17 (7)                      | 84 (10)                       | .27     |
| COPD                    | 139 (13)                | 28 (12)                     | 111 (13)                      | .77     |
| Liver disease           | 74 (7)                  | 29 (13)                     | 45 (5)                        | <.001   |
| Neoplastic disease      | 70 (7)                  | 19 (8)                      | 51 (6)                        | .20     |
| HIV/AIDS                | 13 (1)                  | 3 (1)                       | 10 (1)                        | .74     |
| Health behaviors        |                         |                             |                               |         |
| Nursing home resident   | 66 (6)                  | 20 (9)                      | 46 (5)                        | .06     |
| Current smoker          | 305 (28)                | 59 (26)                     | 246 (29)                      | .37     |
| Alcoholism              | 54 (5)                  | 17 (7)                      | 37 (4)                        | .06     |
| Intravenous drug use    | 29 (3)                  | 4 (2)                       | 25 (3)                        | .49     |
| Severity of infection   |                         |                             |                               |         |
| ICU admission           | 213 (20)                | 69 (30)                     | 144 (17)                      | <.001   |
| Mechanical ventilation  | 129 (12)                | 42 (19)                     | 87 (10)                       | <.001   |
| Hospital acquired       | 38 (4)                  | 10 (4)                      | 28 (3)                        | .42     |
| Pathogen results        |                         |                             |                               |         |
| Monomicrobial           | 648 (60)                | 174 (77)                    | 474 (56)                      | <.001   |
| Polymicrobial           | 428 (40)                | 53 (23)                     | 375 (44)                      |         |

Abbreviations: AIDS, acquired immunodeficiency syndrome; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; ICU, intensive care unit.

*aIf group B Streptococcus was isolated from >1 clinical site in the same patient, the most life-threatening or deepest site of infection was considered the most serious infected site.

*bRace was missing for 3 patients.

*cEthnicity was missing for 7 patients.

*dUnderweight was defined as body mass index (BMI) calculated as weight in kilograms divided by height in meters squared <18.5, normal weight as BMI 18.5–24.9, overweight as BMI 25.0–29.9, obesity as BMI ≥30.0, class 1 obesity as BMI 30.0–34.9, class 2 obesity as BMI 35.0–39.9, and class 3 obesity as BMI ≥40.0. BMI was missing for 8 patients.
The annual incidence of hospitalization where GBS was identified from any source was 73 per 100,000 for adults 18-64 and reached 100 per 100,000 in adults ≥65 years of age. The in-hospital mortality rate was 3%. Applying these rates of infection and case fatality to the 2020 US adult population corresponds to an estimated 188,570 (95% CI, 175,290–202,710) GBS-related hospitalizations and 5,660 (5,260–6,080) deaths annually. If noninvasive, polymicrobial infections (where the role of GBS as the primary cause of infection may not be clear [14–17]) were excluded, rates were 48 (95% CI, 43–52) and 72 (59–87) per 100,000 among adults ≥18 years and ≥65 years of age, respectively (Table 4). Annual rates among adults with chronic medical conditions were also higher. Rates for all GBS-associated hospitalizations and after exclusion of noninvasive, polymicrobial infections, respectively, were as follows, all per 100,000: chronic renal disease, 421 and 276; diabetes mellitus, 409 and 241; coronary artery disease, 259 and 158; history of stroke, 171 and 90; obesity, 129 and 83; chronic obstructive pulmonary disorder, 98 and 65; and current smoker status, 98 and 64.

Rates increased linearly with increasing levels of obesity, with rates for all GBS-associated hospitalizations and after exclusion of noninvasive, polymicrobial infections of 87 and 57 per 100,000, respectively, for class 1 obesity, 126 and 82 per 100,000 for class 2 obesity, and 263 and 165 per 100,000 for class 3 obesity (Tables 4 and 5 and Supplementary Table 6). Overall, the rate of GBS excluding noninvasive, polymicrobial infections was 48 (95% CI, 43–52) per 100,000 among all adults and 43 (39–48) and 72 (59–87) per 100,000 among adults 18–64 and ≥65 years of age, respectively (Table 5 and Supplementary Table 6). The rate of invasive GBS was 15 (95% CI, 13–17) per 100,000 per year, with rates of 13 (11–16) and 25 (18–35) per 100,000 in adults aged 18–64 and ≥65 years, respectively (Supplementary Table 6).

**DISCUSSION**

To our knowledge, this is the first population-based study to determine the total burden of hospitalization where both invasive and noninvasive GBS infection was identified among adults. Previous studies have described the adult burden of invasive GBS, but hospitalization with noninvasive GBS disease was 3–4 times more common in our study. This finding suggests that the adult burden of GBS is considerably greater than previously recognized.
### Table 4. Cases, Annual Incidence Rates, and Rate Ratios of the Most Serious Group B Streptococcus Infections by Patient Characteristics

| Patient Characteristics | Patients Aged 18–64 y | | | Patients Aged ≥65 y | | | Patients Aged ≥18 y | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | Cases | Annual Rate per 100 000 | Rate Ratio (95% CI) | Cases | Annual Rate per 100 000 | Rate Ratio (95% CI) | Cases | Annual Rate per 100 000 | Rate Ratio (95% CI) |
| All patients | 542 | 68 | ... | 142 | 100 | ... | 684 | 73 | ... |
| Demographics | | | | | | | | | |
| Year of study | | | | | | | | | |
| 2014 | 136 | 52 | 1.0 | 49 | 109 | 1.0 | 185 | 60 | 1.0 |
| 2015 | 203 | 72 | 1.4 (1.1–1.7) | 45 | 95 | 0.9 (1.6–1.3) | 248 | 82 | 1.4 (1.1–1.6) |
| 2016 | 203 | 82 | 1.6 (1.2–2.0) | 48 | 104 | 0.9 (1.6–1.4) | 251 | 78 | 1.3 (1.1–1.6) |
| Sex | | | | | | | | | |
| Female | 259 | 64 | 1.0 | 74 | 91 | 1.0 | 333 | 69 | 1.0 |
| Male | 283 | 72 | 1.1 (0.9–1.3) | 68 | 112 | 1.2 (0.8–1.6) | 351 | 77 | 1.1 (0.9–1.3) |
| Race* | | | | | | | | | |
| White | 346 | 54 | 1.0 | 112 | 89 | 1.0 | 458 | 60 | 1.0 |
| Black | 178 | 152 | 2.8 (2.3–3.4) | 27 | 199 | 2.2 (1.5–3.4) | 205 | 157 | 2.6 (2.2–3.1) |
| Other | 18 | 40 | .7 (0.5–1.2) | 2 | ... | ... | 20 | 41 | .7 (0.4–1.1) |
| Ethnicity** | | | | | | | | | |
| Not Hispanic or Latino | 525 | 69 | 1.0 | 139 | 98 | 1.0 | 664 | 74 | 1.0 |
| Hispanic or Latino | 16 | 41 | .6 (0.4–1.0) | 1 | ... | ... | 17 | 43 | .6 (0.4–1.1) |
| Body mass indexd | | | | | | | | | |
| Underweight | 16 | 132 | 3.4 (1.9–6.0) | 7 | ... | ... | 23 | 170 | 3.8 (2.4–6.1) |
| Normal weight | 115 | 39 | 1.0 | 31 | 102 | 1.0 | 146 | 45 | 1.0 |
| Overweight | 117 | 45 | 1.1 (0.9–1.5) | 35 | 77 | 0.8 (1.5–2.1) | 153 | 50 | 1.1 (0.9–1.4) |
| Obesity | 330 | 117 | 3.0 (2.4–3.8) | 72 | 232 | 2.3 (1.5–3.5) | 402 | 129 | 2.9 (2.4–3.5) |
| Class 1 | 119 | 77 | 2.0 (1.5–2.6) | 33 | 161 | 1.6 (0.9–2.6) | 152 | 87 | 1.9 (1.5–2.5) |
| Class 2 | 83 | 111 | 2.8 (2.1–3.8) | 20 | 308 | 3.0 (1.7–5.3) | 103 | 126 | 2.8 (2.2–3.7) |
| Class 3 | 128 | 247 | 6.3 (4.9–8.2) | 19 | 476 | 4.6 (2.6–8.3) | 147 | 263 | 5.9 (4.6–7.4) |
| Chronic medical conditions | | | | | | | | | |
| Diabetes mellitus | | | | | | | | | |
| No | 216 | 30 | 1.0 | 66 | 60 | 1.0 | 282 | 34 | 1.0 |
| Yes | 326 | 486 | 16.1 (13.5–19.1) | 76 | 240 | 4.0 (2.9–5.6) | 402 | 409 | 12.0 (10.3–14.0) |
| Chronic renal disease | | | | | | | | | |
| No | 441 | 57 | 1.0 | 95 | 72 | 1.0 | 536 | 59 | 1.0 |
| Yes | 100 | 401 | 7.0 (5.6–8.7) | 47 | 473 | 6.6 (4.7–9.4) | 147 | 421 | 7.1 (5.9–8.5) |
| Coronary artery disease | | | | | | | | | |
| No | 460 | 60 | 1.0 | 81 | 70 | 1.0 | 541 | 62 | 1.0 |
| Yes | 82 | 279 | 4.6 (3.7–5.8) | 61 | 236 | 3.4 (2.4–4.7) | 143 | 259 | 4.2 (3.5–5.1) |
| Stroke | | | | | | | | | |
| No | 503 | 65 | 1.0 | 112 | 89 | 1.0 | 615 | 68 | 1.0 |
| Yes | 39 | 165 | 2.5 (1.8–3.5) | 30 | 181 | 2.0 (1.4–3.0) | 69 | 171 | 2.5 (1.9–3.2) |
| COPD | | | | | | | | | |
| No | 491 | 67 | 1.0 | 112 | 94 | 1.0 | 603 | 70 | 1.0 |
| Yes | 51 | 86 | 1.3 (1.0–1.7) | 30 | 129 | 1.4 (0.9–2.1) | 81 | 98 | 1.4 (1.1–1.8) |
| Neoplasm | | | | | | | | | |
| No | 515 | 67 | 1.0 | 132 | 114 | 1.0 | 647 | 73 | 1.0 |
| Yes | 27 | 86 | 1.3 (0.9–1.9) | 10 | 39 | 0.3 (0.2–0.7) | 37 | 66 | .9 (0.6–1.3) |
| Health behaviors | | | | | | | | | |
| Current smoker | | | | | | | | | |
| No | 353 | 58 | 1.0 | 127 | 100 | 1.0 | 480 | 65 | 1.0 |
| Yes | 189 | 98 | 1.7 (1.4–2.0) | 15 | 100 | 1.0 (0.6–1.7) | 204 | 98 | 1.5 (1.3–1.8) |
| Alcoholism | | | | | | | | | |
| No | 511 | 69 | 1.0 | 136 | 99 | 1.0 | 647 | 74 | 1.0 |
| Yes | 31 | 56 | 0.8 (0.6–1.2) | 6 | ... | ... | 37 | 60 | 0.8 (0.6–1.1) |

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease.

*aIf group B Streptococcus (GBS) was isolated from >1 clinical site in the same patient, the most life-threatening or deepest site of infection was considered the most serious infected site. Rates were not calculated if the number of GBS cases was <10.

*bRace was missing for 3 patients.

*cEthnicity was missing for 7 patients.

*dUnderweight was defined as body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) <18.5, normal weight as BMI 18.5–24.9, overweight as BMI 25.0–29.9, obesity as BMI ≥30.0, class 1 obesity as BMI 30.0–34.9, class 2 obesity as BMI 35.0–39.9, and class 3 obesity as BMI ≥40.0; BMI was missing for 8 patients.
of age, respectively. These rates still translate to an estimated 122,960 (95% CI, 112,260–134,420) GBS-related hospitalizations and 3,690 (95% CI, 3,370–4,030) deaths each year in the United States.

Rates for older adults were similar over the 3-year study period, but there was an increase in GBS rates among adults <65 years of age during the study. Consistent with previous reports [4–6], most GBS infections (89%) occurred in adults with chronic medical conditions, most commonly diabetes, obesity, coronary artery disease, and chronic renal disease. Compared with the general population, rates of GBS were 2–6 times higher in these patients, with incidence rates of GBS infection between 129 and 421 per 100,000. The highest rate of GBS-associated hospitalization was seen among adults <65 years of age with diabetes, reaching almost 500 per 100,000 annually. Patients in this age group were 16 times more likely to be hospitalized with GBS than those without diabetes. Although these conditions have previously been identified as risk factors for invasive GBS [4–6], our population-based study allowed us to evaluate rates of both invasive and noninvasive disease and to construct detailed age-specific and risk group–specific rates of GBS infection. Future studies should evaluate the interaction between potentially related chronic medical conditions (e.g., diabetes, obesity, and renal disease) and rates of GBS infection.

Rates of GBS-related hospitalization in older adults and in adults with chronic medical conditions were comparable to or even higher than rates of pneumococcal disease for which vaccines are recommended. For example, the rate of hospitalization for invasive and noninvasive vaccine-type pneumococcal infection in adults ≥65 years of age was estimated to be 144 per 100,000 [21] in 2014 when 13-valent pneumococcal conjugate vaccine was universally recommended in this age group [22].

The overall annual rate of invasive GBS was 15 per 100,000 and is consistent with, albeit slightly higher than, previous estimates from other population-based studies of adults using similar laboratory-based surveillance methods, which ranged from 3 to 11 per 100,000 [4, 5, 8, 11, 18]. Our rate of invasive GBS infection among adults ≥65 years of age was 25 per 100,000, which is identical to estimates from the CDC Active Bacterial Core Surveillance program in the same age group and during the same time period [18]. In addition, our risk group–specific rates of invasive GBS among patients with diabetes and obesity were similar to rates in a recently published CDC report [6], further confirming the robustness of our estimates.

Polymicrobial infection was common, occurring in 40% of GBS infections. Most (77%) polymicrobial infections were skin and soft-tissue or bone and joint infections. S. aureus, which is also frequently associated with skin infection, was the most commonly identified pathogen in polymicrobial infections, occurring in 39%. The exact role of GBS in the pathogenesis of polymicrobial infections is not clear [14–17]. For this reason, we presented our results both including and excluding polymicrobial noninvasive infections, and we are planning future research to better characterize the nature of polymicrobial GBS infections.

Our study has limitations. Our study population was limited to a single US city and may not be generalizable. The adult population in Louisville, however, is generally similar to the US adult population in terms of demographics and the prevalence of underlying chronic medical conditions, including diabetes and obesity, with few exceptions (e.g., higher smoking prevalence and fewer Hispanics) [18]. Although the network of Louisville hospitals included in our study have produced reliable estimates of pneumonia surveillance in the past [23], we included only 5 of 9 hospitals in the catchment area. However, we adjusted for market share to account for this limitation. Thus, our estimates should be unbiased if patients with GBS infection were not disproportionately referred to a particular hospital or group of hospitals in Louisville, which seems unlikely.

Our rates of GBS may be underestimated, given that GBS cases were identified via routine culture, and many patients may have been treated without cultures being performed. In addition, given the retrospective nature of our study, long-term follow-up was not conducted to assess rates of relapse or recurrence of GBS infection. Furthermore, there is an additional outpatient burden of noninvasive GBS disease that was not measured in our study and warrants future research.

It is unknown whether GBS infection was the primary reason for hospitalization in all cases with community-onset, which
accounted for 96% of GBS infections. This distinction, however, is rarely made in studies of infectious disease incidence (eg, studies to define the burden and etiology of adult pneumonia) [24]. Nevertheless, we admit that determining the burden of noninvasive GBS is challenging, because distinguishing between GBS colonization and infection can be difficult, and because GBS may be one of several pathogens isolated from a given culture (ie, polymicrobial infections occur frequently).

These complicating factors are key reasons the noninvasive burden of GBS in adults has never been described. To address these concerns and establish clear definitions of GBS infection, we consulted numerous experts. In addition, we collected exhaustive data describing clinical and laboratory findings for each patient, and each case was reviewed by multiple infectious disease specialists. Moreover, rates of GBS infections were presented both including and excluding noninvasive polymicrobial infections to ensure a range of plausible GBS incidence estimates was available. A final limitation is that GBS isolates were not serotyped, and future research is needed to determine the proportion of GBS disease that could be vaccine preventable. However, multivalent polysaccharide conjugate vaccines currently in development broadly target the most prevalent GBS serotypes [25].

Our population-based study outlines the full burden of hospitalization in adults in whom GBS infection was identified and found incidence rates comparable to those of pneumococcal disease where vaccines are recommended. Although previous studies have highlighted the growing burden of invasive GBS in adults, our study suggests for every invasive GBS infection requiring hospitalization, at least 3–4 hospitalized noninvasive infections also occur. Our results emphasize the importance of developing approaches for preventing GBS, especially among the growing population of adults who are older or have chronic medical conditions.

**Supplementary Data**

Supplementary materials are available at The Journal of Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

**Notes**

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