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# Prognostic factors associated with mortality and major in-hospital complications in patients with bacteremic pneumococcal pneumonia
## Population-based study

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## Abstract

Bacteremic pneumococcal pneumonia (BPP) causes considerable mortality and morbidity. We aimed to identify prognostic factors associated with mortality and major in-hospital complications in BPP.

A prospective, population-based clinical registry of 1636 hospitalized adult patients (≥18 years) with BPP was established between 2000 and 2010 in Northern Alberta, Canada. Prognostic factors for mortality and major in-hospital complications (e.g., cardiac events, mechanical ventilation, aspiration) were evaluated using multivariable logistic regression.

Average age was 54 (standard deviation 18) years, 57% males, and 59% had high case-fatality rate (CFR) serotypes. Overall, 14% (226/1636) of patients died and 22% (315/1410) of survivors developed at least 1 complication. Independent prognostic factors for mortality were age (adjusted odds ratio [aOR], 1.5 per decade; 95% confidence interval [CI], 1.3–1.7), nursing home residence (aOR, 3.7; 95% CI 1.8–7.4), community-dwelling dementia (aOR 3.7; 95% CI, 1.6–8.6), alcohol abuse (aOR, 2.2; 95% CI, 1.4–3.4), acid-suppressing drugs (aOR, 1.5; 95% CI, 1.0–2.3), guideline-discordant antibiotics (aOR, 3.4; 95% CI, 2.4–4.8), multilobe pneumonia (aOR, 2.6; 95% CI, 1.8–3.6), and high CFR serotypes (aOR, 1.8; 95% CI, 1.2–2.8). Similar prognostic factors were observed for major in-hospital complications. Pneumococcal vaccination was associated with reduced in-hospital mortality (aOR, 0.2; 95% CI, 0.05–0.9) but not major complications ($P = 0.2$).

Older and frailer patients, and those who abuse alcohol or take acid-suppressing drugs, are at increased risk of BPP-related mortality and complications, as are those with high CFR serotypes. Beyond identifying those at highest risk, our findings demonstrate the importance of guideline-concordant antibiotics and pneumococcal vaccination in those with BPP.

**Abbreviations:** AIDS = acquired immune deficiency syndrome, aOR = adjusted odds ratio, ARDS = acute respiratory distress syndrome, BPP = bacteremic pneumococcal pneumonia, CAP = community-acquired pneumonia, CFR = case-fatality rate, CI = confidence interval, GI = gastrointestinal, IPD = invasive pneumococcal disease, MACE = major adverse cardiovascular events, SD = standard deviation.

**Keywords:** complications, mortality, pneumococcus, pneumonia, prognostic factors

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## 1. Introduction

Community-acquired pneumonia (CAP) is a significant cause of morbidity and mortality worldwide.[1]*Streptococcus pneumoniae* (hereafter, "pneumococcus") remains the most commonly identified pathogen in CAP, and is responsible for 30% to 40% of all diagnostically confirmed cases.[2] It has been estimated that 25% of cases of pneumococcal pneumonia are associated with bacteremia.[3] Complications of bacteremic pneumococcal pneumonia (BPP) are diverse and range from adult respiratory distress syndrome to septic shock and death.[4] Case-fatality rates (CFRs) in adults with BPP are 15% to 36% despite continued advances in antibiotic therapy and supportive care.[5–7] Furthermore, major complications (e.g., need for mechanical ventilation, heart failure, acute kidney injury) occur in a large proportion of patients who survive pneumococcal bacteremia.[8] Thus, there is interest in identifying novel prognostic markers to identify those at highest risk of adverse events associated with BPP before they occur.

Several studies have reported prognostic factors associated with mortality in patients with BPP including extremes of age, alcohol abuse, certain comorbidities, severity of presenting illness, late antibiotic treatment, and CAP guideline-discordant therapy.[9–12] However, the findings from these studies are often contradictory, and the generalizability of 3 of these studies is limited due to small study sample sizes (all <150 patients),[9–11] missing data,[12] or uncontrolled confounding. Furthermore, studies examining in-hospital complications in BPP patients are even more limited,[8,13] and to our knowledge prognostic factors associated with in-hospital complications in patients with BPP have yet to be examined in detail.

Therefore, we used a large clinically rich prospective population-based cohort to evaluate potential prognostic factors associated with mortality and major in-hospital complications in adults with BPP.

## 2. Methods

### 2.1. Setting and subjects

Since 1998, all cases of invasive pneumococcal disease (IPD) in the province of Alberta are classified as notifiable diseases and therefore are reported to the Provincial Health Office. As a result of this reporting requirement, identified *S pneumoniae* isolates from IPD cases in Alberta are forwarded to the Provincial Laboratory for Public Health in Edmonton, Alberta, for serotyping and antimicrobial susceptibility trend analysis.[14,15] The definition of IPD followed the Canadian national case definition: isolation of *S pneumoniae* from a nonsterile site such as blood, cerebrospinal fluid, pleural fluid, biopsy tissue, joint aspiration, pericardial fluid, or peritoneal fluid.[16] The database used for this survey encompassed IPD cases that occurred in Northern Alberta, Canada (population: 2,060,039[17]) between January 1, 2000 and December 31, 2010. From this population, we restricted our study to adult patients (≥18 years) with clinically diagnosed pneumonia who had pneumococcal bacteremia (Fig. 1). This study was approved by the University of Alberta Health Research Ethics Board panel B (Pro00001314), and received a waiver for the need for written informed consent.

### 2.2. Data collection

All identified cases of BPP were reviewed in detail by trained research nurses was prior experience in this field
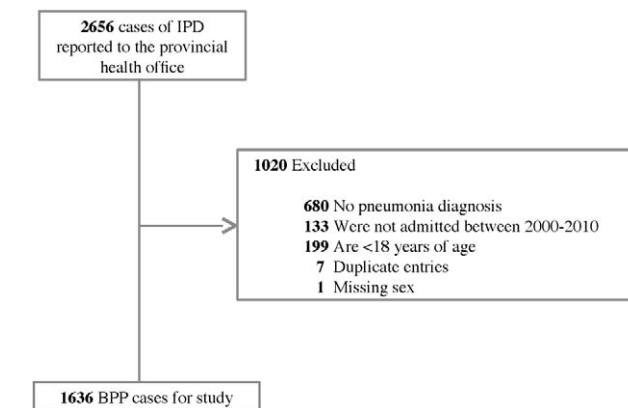


**Figure 1.** Selection of adult patients admitted to northern Alberta hospitals with bacteremic pneumococcal pneumonia (BPP).

using a data collection tool previously described.[18,19] Information collected included sociodemographic data, pre-existing comorbid conditions, and prescription drug history, lifestyle factors (e.g., smoking status, alcohol intake, illicit drug use), and clinical data (e.g., chest radiograph findings, antibiotic treatments). We classified antibiotic treatments according to whether or not they were concordant or discordant with clinical practice guidelines for the empiric treatment of CAP.[20,21]

### 2.3. Streptococcus pneumoniae characterization

Optochin susceptibility and bile solubility assays were used to confirm that isolates were *S pneumoniae*.[14,15] Serotyping of all isolates was performed using the Quellung reaction[22] and grouped according to previous literature into: low CFR serotypes (1, 4, 5, 7F, 8) versus high CFR serotypes (3, 6A, 6B, 9N, 9V, 12F, 14, 19A, 19F, 22F, 23F).[12,23] All "other" serotypes identified from cases in our survey (2, 7C, 9L, 10A, 10F, 11A, 11B, 11F, 13, 15A, 15B, 15C, 16F, 17F, 18A, 18B, 18C, 18F, 20, 22A, 23A, 23B, 28A, 29, 31, 33A, 33F, 34, 35A, 35B, 35C, 35F, 37, 38, 40, 42) were subsequently classified as high CFR category because there were similar patient characteristics and nearly identical CFRs as observed with the high CFR serotypes (22% in high CFR serotypes vs 17% in low CFR serotypes). Supplementary Tables 1 to 3, http://links.lww.com/MD/B414, present a stratification of all pneumococcal serotypes into vaccine-related or nonvaccine related serotypes, respectively.

### 2.4. Outcomes

Our primary outcome of interest was in-hospital mortality. The secondary end-point of interest was any major in-hospital complication, defined as the presence of 1 or more of need for mechanical ventilation, acute respiratory distress syndrome not needing mechanical ventilation, major adverse cardiovascular events (MACE, including unstable angina, myocardial infarction, heart failure, or cardiac arrest), liver failure, acute kidney injury, stroke, seizure, or acute aspiration associated with the presenting illness. All outcomes were obtained by detailed chart review and adjudicated by medical experts as previously described.

## 2.5. Statistical analysis

Descriptive data using appropriate statistical tests were undertaken. Adjusted odd ratios were estimated using multivariable logistic regression. All potential prognostic variables listed in Table 1 were adjusted for in our analysis with exception to the Charlson Comorbidity Index.[26] The c-statistic (area under the receiver-operating characteristic) was used to describe overall predictive model accuracy and the Hosmer–Lemeshow test statistic was used to assess the model's goodness-of-fit. All analyses were performed with Stata SE, version 12.1 (Stata, College Station, TX).

## 2.6. Sensitivity analyses

We conducted several sensitivity analyses to evaluate the robustness of our study results. First, we restricted analyses to those 65 years and older because these patients are at a substantially increased risk of mortality.[24] Second, we stratified by sex, because females with IPD have a much higher risk of mortality than males.[25] Third, we stratified our analysis based on low versus high CFR serotypes.[23] Fourth, we reclassified our CFR serotypes as low versus high versus "other" rather than collapsing the latter 2 categories. Lastly, to ensure differences in comorbidities were not driving our results, we further adjusted our analyses for the Pitt Bacteremia Score, which has been shown to have high accuracy predicting mortality in patients with BPP.[27]

## 3. Results

Our cohort consisted of 1636 adults with BPP; mean age was 54 (standard deviation 18) years, 434 (27%) were over the age of 65 years, and 931 (57%) were male. Chronic obstructive pulmonary disorder, mental health disorders, and cardiac disease were the most frequent comorbidities, and in terms of lifestyle factors, 51% of patients were nonsmokers and 25% abused alcohol (Table 1). Overall, 41% had low CFR serotypes and only 4% had been vaccinated with the polysaccharide pneumococcal vaccine prior to presentation.

### 3.1. In-hospital mortality

Overall, 226 (14%) patients died in hospital. Compared with those who survived, patients who died were older, more likely to reside in a nursing home, and sicker (e.g., more comorbidities and medications) and they had more severe BPP (e.g., multilobe pneumonia, high CFR serotypes, see Table 1). Moreover, patients who died were also more likely to have suffered 2 or more major complications than those who survived (41% vs 8%, $P < 0.001$ for difference).

In the multivariable analysis, the most important independent prognostic factors for death were older age, nursing home residence, community-dwelling dementia, alcohol abuse, and the use of acid-suppressing drugs as well as some characteristics of BPP itself and its treatment such as multilobe pneumonia and use of CAP guideline-discordant antibiotics (Table 2). Of note, even though <5% of patients were vaccinated, pneumococcal vaccination was independently associated with lower mortality (adjusted odds ratio, 0.2; 95% confidence interval, 0.05–0.9; $P = 0.03$).

### 3.2. Major in-hospital complications

Among the 1410 BPP survivors, most patient-level characteristics were similar to those we noted for mortality (Table 3). The most

| **Table 1** | | | |
|---|---|---|---|

**Characteristics of 1636 adult patients with bacteremic pneumococcal pneumonia, stratified by mortality.**

| | Mortality, N (%) or mean (SD) | | |
|---|---|---|---|
| **Characteristics** | **No (n = 1410)** | **Yes (n = 226)** | **P** |
| Age | 52 (17) | 65 (18) | <0.001 |
| Sex, male | 801 (56.8) | 130 (57.5) | 0.8 |
| Aboriginal | 186 (13.2) | 26 (11.5) | 0.5 |
| Nursing home | 22 (1.6) | 26 (11.5) | <0.001 |
| Nonsmoker | 663 (47.0) | 164 (72.6) | <0.001 |
| Underlying condition | | | |
| Dementia | 16 (1.1) | 15 (6.6) | <0.001 |
| Mental health disorder | 241 (17.1) | 40 (17.7) | 0.8 |
| Stroke | 48 (3.4) | 17 (7.6) | 0.003 |
| Cardiac disease | 205 (14.5) | 65 (28.8) | <0.001 |
| Anemia | 93 (6.6) | 27 (11.9) | 0.004 |
| Diabetes | 180 (12.8) | 38 (16.8) | 0.096 |
| Asplenia | 11 (0.8) | 1 (0.4) | 0.6 |
| Auto-immune disorder | 147 (10.4) | 27 (11.9) | 0.6 |
| AIDS | 76 (5.4) | 9 (4.0) | 0.4 |
| Cancer | 161 (11.4) | 52 (23.0) | <0.001 |
| Immunosuppressive therapy | 96 (6.8) | 30 (13.3) | 0.001 |
| Musculoskeletal disorder | 211 (15.0) | 51 (22.6) | 0.004 |
| Asthma | 174 (12.3) | 21 (9.3) | 0.2 |
| COPD | 282 (20.0) | 64 (28.3) | 0.004 |
| Hepatic cirrhosis | 58 (4.1) | 19 (8.4) | 0.005 |
| GI bleed | 33 (2.3) | 12 (5.3) | 0.011 |
| Renal disorder | 56 (4.0) | 25 (11.1) | <0.001 |
| Charlson index | | | |
| Low (0) | 560 (39.7) | 38 (16.8) | Ref. |
| Intermediate (1–2) | 581 (41.2) | 100 (44.2) | <0.001 |
| High (>3) | 269 (19.1) | 88 (38.9) | <0.001 |
| ≥3 Other comorbidities | 203 (14.4) | 58 (25.7) | <0.001 |
| Alcoholism | 346 (24.5) | 67 (29.6) | 0.1 |
| Illicit drug use | 315 (22.3) | 35 (15.5) | 0.021 |
| Multilobe pneumonia | 309 (21.9) | 91 (40.3) | <0.001 |
| Guideline-discordant antibiotics | 242 (17.2) | 91 (40.3) | <0.001 |
| ≥3 Nonantibiotic medications | 549 (38.9) | 139 (61.5) | <0.001 |
| Acid suppressing drugs | 223 (15.8) | 72 (31.9) | <0.001 |
| Bronchodilators | 270 (19.1) | 60 (26.5) | 0.01 |
| Bronchio anti-inflammatories | 65 (4.6) | 15 (6.6) | 0.2 |
| Pneumococcal vaccine | 69 (4.9) | 2 (0.9) | 0.006 |
| Serotypes by case-fatality rates | | | |
| Low | 624 (44.3) | 44 (19.5) | Ref. |
| High | 786 (55.7) | 182 (80.5) | <0.001 |

AIDS = acquired immune deficiency syndrome, COPD = chronic obstructive pulmonary disorder, GI = gastrointestinal, SD = standard deviation.

common in-hospital complications were need for mechanical ventilation (16%), acute aspiration (6%), and MACE (5%) (Table 4). In the multivariable analysis, the most important prognostic factors independently associated with nonfatal complications were stroke, alcohol abuse, multilobe pneumonia, and having a high CFR serotype (Table 5).

### 3.3. Sensitivity analyses with respect to mortality

Restricting analyses to persons 65 years and older, stratifying by sex, categorizing according to high CFR serotypes, or reclassifying CFR as low versus high versus other did not materially alter the strength of association or statistical significance of any of the prognostic factors described in the main analysis for in-hospital mortality or nonfatal complications (Supplemental Figs. 1–3, http://links.lww.com/MD/B414).

## Table 2

Characteristics independently associated with in-hospital mortality: multivariable logistic regression.

| Characteristics | Adjusted OR (95% CI)[*] | P |
|---|---|---|
| Age (per decade) | 1.5 (1.3–1.7) | <0.001 |
| Nursing home | 3.7 (1.8–7.4) | <0.001 |
| Nonsmoker | 1.9 (1.3–2.7) | 0.002 |
| Alcoholism | 2.2 (1.4–3.4) | <0.001 |
| Underlying condition | | |
| Dementia | 3.7 (1.6–8.6) | 0.003 |
| Cancer | 1.5 (1.0–2.3) | 0.076 |
| Guideline-discordant antibiotics | 3.4 (2.4–4.8) | <0.001 |
| Acid suppressing drugs | 1.5 (1.0–2.3) | 0.036 |
| Multilobe pneumonia | 2.6 (1.8–3.6) | <0.001 |
| High CFR serotype | 1.8 (1.2–2.8) | 0.003 |
| Pneumococcal vaccine | 0.2 (0.05–0.9) | 0.033 |

CFR = case-fatality rate, CI = confidence interval, OR = odds ratio.

[*] Adjusted for all other variables presented in Table 1 with exception to the Charlson Comorbidity Index; only those variables with $P < 0.1$ included in table; Hosmer–Lemeshow goodness-of-fit test $P = 0.6$ and c-statistic = 0.83.

## 4. Discussion

Using a large clinically rich population-based cohort we found that in-hospital mortality and major in-hospital complications associated with BPP are still common (14% and 22%, respectively). Older age and other markers of frailty along with acid suppressing drugs were independently associated with in-hospital mortality while alcohol abuse, pneumonia severity, and guideline-discordant antibiotic treatments were independently associated with both in-hospital mortality and complications. Of note, high CFR serotypes were independently associated with both increased mortality and increased complications. Though fewer than 1-in-20 patients were documented to have received polysaccharide pneumococcal vaccine, it was associated with reduced mortality although it did not affect rates of in-hospital complications.

Previous studies have identified older age,[10] guideline-discordant antibiotic therapy,[9,11] and multilobe pneumonia,[11] as independent factors associated with increased BPP mortality. Our work confirms this and extends these findings to other markers of frailty beyond older age such as nursing home residence and community-dwelling dementia. Though acid-suppressing drugs are associated with an increased risk of pneumonia and an increased risk of recurrent pneumonia,[19] our findings that acid-suppressing drugs are associated with increased mortality was somewhat unexpected. It has been suggested that these medications may intensify the severity of an infection by promoting acid-suppression and bacterial overgrowth, which would increase the risk for mortality particularly among elderly patients.[19]

Our study also highlights the potential role of serotypes on adverse outcomes, which has been a controversial topic.[23,28] Although we found an association between high CFR serotypes and adverse in-hospital events, a recent comparable study involving 1580 adult patients with BPP by Naucler et al found that the effect of serotypes on mortality was mitigated after adjusting for age, sex, and Charlson Index.[12] Conversely, a study by Harboe et al composed of 18,858 patients with IPD found that specific pneumococcal serotypes increased the risk of IPD associated mortality after adjusting for age and comorbidity.[29] Our study is consistent with the larger study of Harboe

## Table 3

Characteristics of 1410 surviving adult patients with bacteremic pneumococcal pneumonia, stratified by in-hospital complications.

| Characteristics | In-hospital complications, N (%) or mean (SD) | | P |
|---|---|---|---|
| | No (n = 1095) | Yes (n = 315) | |
| Age | 51 (17) | 55 (16) | <0.001 |
| Sex, male | 614 (56.1) | 187 (59.4) | 0.3 |
| Aboriginal | 137 (12.2) | 49 (15.6) | 0.2 |
| Nursing home | 13 (1.2) | 9 (2.9) | 0.035 |
| Nonsmoker | 582 (53.2) | 165 (52.4) | 0.8 |
| Underlying condition | | | |
| Dementia | 11 (1.0) | 5 (1.6) | 0.4 |
| Mental health disorder | 174 (15.9) | 67 (21.3) | 0.025 |
| Stroke | 27 (2.5) | 21 (6.7) | <0.001 |
| Cardiac disease | 128 (11.7) | 59 (18.7) | 0.001 |
| Anemia | 65 (5.9) | 28 (8.9) | 0.063 |
| Diabetes | 129 (11.8) | 51 (16.2) | 0.039 |
| Asplenia | 6 (0.5) | 5 (1.6) | 0.065 |
| Auto-immune disorder | 115 (10.5) | 32 (10.2) | 0.9 |
| AIDS | 61 (5.6) | 15 (4.8) | 0.6 |
| Cancer | 141 (12.9) | 20 (6.3) | 0.001 |
| Immunosuppressive therapy | 70 (6.4) | 26 (8.3) | 0.248 |
| Musculoskeletal disorder | 93 (8.5) | 40 (12.7) | 0.024 |
| Asthma | 142 (13.0) | 32 (10.2) | 0.182 |
| COPD | 187 (17.1) | 95 (30.2) | <0.001 |
| Hepatic cirrhosis | 38 (3.5) | 20 (6.3) | 0.023 |
| GI bleed | 23 (2.1) | 10 (3.2) | 0.266 |
| Renal disorder | 38 (3.5) | 18 (5.7) | 0.072 |
| Charlson index | | | |
| Low (0) | 463 (42.3) | 97 (30.8) | Ref |
| Intermediate (1–2) | 433 (39.5) | 148 (47.0) | 0.001 |
| High (>3) | 199 (18.2) | 70 (22.2) | 0.003 |
| ≥3 Other comorbidities | 134 (12.2) | 69 (21.9) | <0.001 |
| Alcoholism | 221 (20.2) | 125 (39.7) | <0.001 |
| Illicit drug use | 244 (22.3) | 71 (22.5) | 0.9 |
| Multilobe pneumonia | 183 (16.7) | 126 (40.0) | <0.001 |
| Guideline-discordant antibiotics | 174 (15.9) | 68 (21.6) | 0.018 |
| ≥3 Nonantibiotic medications | 391 (35.7) | 158 (50.2) | <0.001 |
| Acid suppressing drugs | 157 (14.3) | 66 (21.0) | 0.005 |
| Bronchodilators | 207 (18.9) | 63 (20.0) | 0.7 |
| Bronchio anti-inflammatories | 49 (4.5) | 16 (5.1) | 0.7 |
| Pneumococcal vaccine | 55 (5.0) | 14 (4.4) | 0.7 |
| Serotypes by case-fatality rates | | | |
| Low | 534 (48.8) | 90 (28.6) | Ref |
| High | 561 (51.2) | 225 (71.4) | <0.001 |

AIDS = acquired immune deficiency syndrome, COPD = chronic obstructive pulmonary disorder, GI = gastrointestinal, SD = standard deviation.

et al[29] and supports the idea that pneumococcal serotypes are an important prognostic factor for in-hospital adverse events in BPP patients; however, not all studies have found this association. Potential reasons for discrepancies between other studies and ours may include the categorization of pneumococcal serotypes into 3 categories (low, medium, or high) compared to 2 categories (low or high),[12,23] differences in the numbers of individual serotypes present,[12] or residual confounding (i.e., insufficient adjustment for host factors).[30,31]

Despite its strengths, our study is not without limitations. First, we do not have cause-specific mortality. Second, we had little information on the severity of in-hospital complications, only whether they occurred or not. Third, our findings may not be generalizable to patients with pneumococcal bacteremia without pneumonia or cases of nonpneumonia IPD such as meningitis.

**Table 4**

**Major in-hospital complications from bacteremic pneumococcal pneumonia according to mortality.**

| Complication | Mortality, N (%) or mean (SD) | | P |
|---|---|---|---|
| | No (n = 1410) | Yes (n = 226) | |
| Mechanical ventilation | 229 (16.2) | 116 (51.3) | <0.001 |
| Acute aspiration | 81 (5.7) | 46 (20.4) | <0.001 |
| MACE | 71 (5.0) | 63 (27.9) | <0.001 |
| Acute kidney injury | 38 (2.7) | 28 (12.4) | <0.001 |
| Seizure | 24 (1.7) | 14 (6.2) | <0.001 |
| Liver failure | 17 (1.2) | 15 (6.6) | <0.001 |
| Stroke | 4 (0.3) | 6 (2.7) | 0.001 |
| ARDS without ventilation | 3 (0.2) | 5 (2.2) | <0.001 |
| Any major complication | 315 (22.3) | 158 (70.0) | <0.001 |
| ≥2 Complications | 111 (7.9) | 92 (40.7) | <0.001 |

ARDS = acute respiratory distress syndrome, MACE = major adverse coronary event, SD = standard deviation.

Fourth, our data represent adults with BPP prior to the era of recommendations to use conjugated vaccines in addition to just pneumococcal polysaccharide vaccine in this patient population.[32,33] Fifth, we did not have information about antibiotic therapy, including timing, route, dose, frequency, or antimicrobial susceptibilities. Lastly, our serotypes were grouped based on serotype-specific CFRs reported by previous meta-analysis and it is possible that certain serotypes were misclassified.[23] If this were the case; however, it would tend to bias to the null and suggests that, if anything, the associations between serotypes and outcomes are stronger than we reported.

The impact of BPP on mortality and in-hospital complications is substantial. Although we discovered only 2 potentially modifiable factors (current use of acid-suppressing drugs and treatment with CAP guideline-discordant antibiotics), we have established the importance of recognizing frailty and lifestyle factors and our results suggest that more rapid availability of pneumococcal serotypes might aid frontline clinicians by helping them select out a subgroup of patients destined to have poor outcomes who might benefit from more intense monitoring and more rapid intensification of supportive care and treatments for their pneumonia.

**Table 5**

**Characteristics independently associated with suffering any in-hospital complication.**

| Complication | Adjusted OR (95% CI)* | P |
|---|---|---|
| Alcoholism | 3.2 (2.3–4.6) | <0.001 |
| Underlying condition | | |
| Stroke | 2.3 (1.1–4.6) | 0.020 |
| AIDS | 0.5 (0.3–1.0) | 0.050 |
| Cancer | 0.3 (0.2–0.5) | <0.001 |
| COPD | 2.0 (1.3–2.9) | 0.001 |
| Guideline-discordant antibiotics | 1.7 (1.2–2.4) | 0.005 |
| ≥3 Other nonantibiotic medications | 1.7 (1.2–2.4) | 0.006 |
| Multilobe pneumonia | 3.9 (2.9–5.4) | <0.001 |
| High CFR serotype | 2.8 (2.0–2.9) | <0.001 |

AIDS = acquired immune deficiency syndrome, CFR = case-fatality rate, CI = confidence interval, COPD = chronic obstructive pulmonary disorder, OR = odds ratio.
* Adjusted for all other variables presented in Table 1 with exception to the Charlson Comorbidity Index; only those variables with P < 0.1 included in table; Hosmer–Lemeshow goodness-of-fit test P = 0.3 and c-statistic = 0.78.

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