In a large multicenter, retrospective cohort study by Gupta et al,1 no association of alcohol use disorder (AUD) with pneumonia prognosis was found for short-term mortality in hospitalized adults after adjustment for comorbid illnesses and antimicrobial resistance. Alcohol withdrawal, however, was associated with poorer outcomes. Alcohol use remains a significant public health issue. In the United States alone, 70% of persons aged 18 years or older will have consumed some alcohol during the past year, and approximately 90 000 people will die from an alcohol-related cause.2

The spectrum of AUD is wide ranging, from the otherwise “healthy” college student with acute alcohol intoxication to the older person with the manifestations of long-term alcohol use, including withdrawal and cirrhosis, who is frequently in and out of the health care setting. Alcohol use disorder is defined by 11 criteria related to the inability to stop or control alcohol use in the past year despite significant social, occupational, or health consequences. Severity of AUD ranges from mild to severe depending on the presence of 2 to 6 symptoms. Binge-drinking involves consumption of 5 or more drinks for men and 4 or more drinks for women within several hours at least once in the preceding month; heavy alcohol use involves binge-drinking for 5 or more days in the preceding month.2 Intense binge-drinking has been noted in 27% of alcohol users; these individuals are mostly young adults between the ages of 18 and 24 years.2 Seven percent of drinkers are considered heavy alcohol users.2 In the study by Gupta et al,1 AUD was based on International Classification of Diseases Ninth Revision, Clinical Modification diagnosis codes; the diagnosis of alcohol use in remission was excluded from the study. Major diagnostic categories included acute alcoholic intoxication, alcohol dependence, alcohol abuse, and alcohol withdrawal syndrome. Continuous use vs episodic use was reported in 28% of individuals.

Regardless of differences in patterns of alcohol use, pneumonia and poor outcomes have been well described in individuals with AUD in the medical literature, and direct toxic effects of alcohol on the lung also have been described. The effects of long-term alcohol use on lung function have been studied more often than the more recently described short-term binge drinker. The sedating effects of alcohol use impair cough and gag reflexes, leading to aspiration. Long-term alcohol use diminishes ciliary function and bacterial clearance; these functions may be increased in short-term alcohol use. Long-term alcohol use also directly impedes the ability of alveolar macrophages to ingest bacteria, release cytokines and chemokines, and recruit neutrophils into the lung. Long-term alcohol use has also been shown to independently pose a 2-fold to 4-fold increased risk for acute respiratory distress syndrome, with alterations in alveolar macrophage oxidative metabolism, reduced clearance of bacteria, and increased permeability of epithelial and endothelial cells.3,5

The underlying bacterial etiology is determined in only a fraction of patients with pneumonia. This study was no exception, with 71% of patients having no bacterial isolate identified and 17% of patients diagnosed as having an aspiration event.1 In this study, microbiological cultures needed to be obtained by the first day of hospitalization. Patients with AUD were significantly more likely to have a causative organism identified than were patients without AUD. However, patients with AUD were also significantly more likely to be admitted to larger teaching hospitals and to require intensive care
with mechanical ventilation and pressure support, a setting that might facilitate acquisition of a sputum specimen.

More patients with AUD had *Streptococcus pneumoniae* infection compared with patients without AUD.\(^1\) *Streptococcus pneumoniae* remains the most important cause of bacterial pneumonia in the community and in patients with predisposing conditions. In this study, patients with and without AUD had significant predispositions for pneumococcal infection, but their risk factors were different. Patients with AUD were significantly younger, more likely to be economically disadvantaged, and found to have other comorbid illnesses, especially smoking, liver disease, and chronic obstructive pulmonary disease. In contrast, patients without AUD were more likely to be older and have congestive heart failure, diabetes, and neurologic disorders, which also pose an increased risk for pneumonia.\(^6\)

The authors point out that, compared with patients without AUD, the burden of pneumonia due to gram-negative bacilli and *Klebsiella pneumoniae* was reduced.\(^1\) Community-acquired pneumonia due to *Klebsiella* species was well described in the early 20th-century literature and often occurred in individuals with alcoholism. As the authors point out, this “classic presentation” is now uncommon and, with the exception of some parts of Asia, most infections occur in health care settings. Reduced saliva production, or xerostomia, a scenario known to contribute to gingival disease and colonization with gram-negative bacilli in patients with many kinds of underlying conditions, is not unique to individuals with alcoholism.\(^4,7\)

Both groups had different risk factors for antimicrobial-resistant organisms, but no differences in resistance rates between patients with and without AUD were seen.\(^1\) Patients without AUD were significantly more likely to have risk factors that included recent stays in skilled nursing facilities and hospitals, the need for dialysis, or recent immunosuppression. In patients with AUD, significant risk factors for antimicrobial resistance included drug abuse and the presence of other chronic diseases, such as cirrhosis, that might serve as a marker for increased exposure to the health care setting. In any regard, no significant differences were seen for the treatment of community-acquired or health care–acquired pneumonia or for adherence to treatment guidelines to account for differences in outcomes. The frequent use of piperacillin-tazobactam and treatments directed against methicillin-resistant *Staphylococcus aureus* might be a reflection of increased risk of substance use and the predisposition for aspiration and the need for intensive care in the AUD group.

Initially, the data from Gupta et al\(^1\) seemed to confirm that AUD was an independent risk factor for increased mortality from pneumonia and the need for intensive care, with resulting increased length of stay and cost. Those findings persisted when adjusted for age, demographics, and economic vulnerability alone. However, many of these outcomes were no longer significant when adjusted for comorbidities and antimicrobial resistance. The main association of AUD with pneumonia outcomes appeared to be related to acute alcohol withdrawal.

In the end, do we believe that alcohol use is an independent risk factor for pneumonia and poor outcomes? Years of clinical experience seem to support this contention, but it remains difficult to prove. The strengths of this study are that it was a large multicenter cohort study with a standardized database. The AUD population is a heterogeneous one, and impairments in the patient’s ability to function, including blackouts, withdrawal, hepatitis, cirrhosis, and portal hypertension, can be objectively measured and correlated with the short-term and long-term effects of alcohol. There is evidence that alcohol has direct toxic effects on the lung and other host defenses. Duration and intensity of patient exposure may have different effects on the respiratory tract that are not so easily quantitated. Comorbidities in patients with AUD and exposure to health care settings and antibiotics may complicate the interpretation of outcome data as well. Obtaining sputum samples from chronically ill older adults remains difficult. More information about how pneumonia risk and outcomes change is needed as the patient evolves from the intermittent or binge drinker to the heavy drinker or individual with alcoholism to the patient with end-stage liver disease.
REFERENCES


