Use of Population-Based Cohort Data to Assess Community-Acquired Pneumonia: A Powerful Approach

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(See the article by Jackson et al. on pages 1642-50)

The first step toward a cure is to know what the disease is.

Latin proverb [1]

Understanding the epidemiology of a disease is essential to designing optimal strategies for diagnosis, prevention, and treatment. Nowhere is this truer than for pneumonia. There are few estimates of the true burden of community-acquired pneumonia (CAP), especially in subsets of patients defined by age and risk group. Application of definitive diagnostic evaluations to large, diverse populations to measure pneumonia incidence is not practical. However, the development of solid case definitions and their application to population-based data from large, linked databases facilitates measurement of the pneumonia disease burden and movement toward disease control strategies. Linked information systems, including microbiologic surveillance data, private and public vaccination records, and administrative health data, are a powerful population-based resource for investigations of disease incidence and of the impact of specific interventions, such as the introduction of vaccines or targeted educational programs.

The study in this issue of Clinical Infectious Diseases by Jackson et al. [2] illustrates the power of using such data for detailed descriptions of the epidemiology of a common problem, CAP, in an important demographic group, seniors aged ≥65 years. With use of health maintenance organization data from 46,000 seniors in Washington State with >122,000 person-years of observation, Jackson et al. [2] defined hospitalized episodes of CAP using specific International Classification of Diseases, Ninth Revision, Clinical Modification codes for pneumonia coupled with the requirement of a clinical diagnosis of pneumonia. The definition of pneumonia in outpatients also required that the patient both underwent chest radiography and was given a prescription of antibiotics within 14 days after onset of the pneumonia episode. The authors identified >2400 hospitalizations and 3100 outpatient encounters for presumptive pneumonia, reviewed an impressive 97% of medical charts, and confirmed that 60%-70% of subjects had CAP. Rates of pneumonia were higher in men and older seniors, with 1 in 20 persons aged ≥85 years developing pneumonia annually. More than 12% of persons who were hospitalized with pneumonia died within 30 days after hospital admission. Markers of comorbid illness, such as underlying malignancy, preexisting pulmonary disease, and increased use of health care services (including home oxygen), were independently associated with increased risks of both CAP and hospitalization.

This study provides important comprehensive population-based data on the incidence of CAP in a growing segment of the population: noninstitutionalized seniors. The majority (59.3%) of episodes of pneumonia in the study population were treated in the outpatient setting. Omission of these cases in any description of the epidemiology of CAP would overestimate the impact of chronic comorbid illnesses on overall pneumonia rates and underestimate the burden of disease.

Another useful feature of such cohort studies is the ability to provide population-based assessments of the “attributable risk” for specific conditions—how much
of the disease burden is caused by the specific condition, and what would be the burden if the condition was lessened or eliminated? For example, Jackson et al. [2] tried to estimate the role of smoking in the development of pneumonia in senior adults. However, in spite of these attempts, the impact of smoking was likely underestimated for 2 reasons. First, incomplete medical record information on smoking likely resulted in misclassification of smoking status, likely biasing the risk ratio towards the null. Second, smoking-related diseases were evaluated as independent risk factors in the same models as smoking, which would minimize the full effect of smoking.

Although it is often described as a risk factor for invasive pneumococcal disease [3] and CAP [4, 5], tobacco use is difficult to accurately ascertain from many administrative data systems. In an earlier study describing the association of tobacco use with invasive pneumococcal disease, Nuorti et al. [3] conducted extensive telephone interviews to adequately ascertain details on each subject’s history of tobacco use. Use of prospectively collected data, as found in the Group Health Cooperative cohort [2], allows for more accurate ascertainment of tobacco use than is available in many administrative databases. In the study by Jackson et al. [2], current smokers comprised 9.4% of the senior adult population, but data on current smoking was missing for 12%. The reference group for evaluating the risk of current smokers included former smokers who may also have had an elevated risk of pneumonia. Nonetheless, the risk of developing pneumonia was significantly higher in current smokers than in those who were not currently using tobacco. The attributable risk percentage for current tobacco use was 30.8%, suggesting that nearly one-third of pneumonia episodes in senior adult smokers were associated with smoking.

Although the estimated impact of smoking on smokers was substantial, the authors estimated that only 4.4% of all cases of pneumonia were due to smoking. However, the population-attributable risk of smoking was likely underestimated by their calculations, because smoking is the major cause of chronic lung disease and lung cancer and is a major contributor to other comorbid conditions, such as receipt of home oxygen therapy. Controlling for chronic obstructive pulmonary disease (COPD), lung cancer, and other smoking-related conditions in their analyses, each of which increased the pneumonia risk, minimized the role of tobacco, because these conditions are on the causal pathway between smoking and pneumonia. Because ~10% of the study population had COPD, which increased the risk of pneumonia 2.4-fold, the population-attributable risk of COPD is ~9%, suggesting that smoking contributes far more to the disease burden of pneumonia than the 4.4% estimate indicates.

The power of population-based databases is enhanced by linkage to and comparison with other population-based systems, again illustrated by Jackson et al. [2]. Linkage to the regional cancer registry allowed for a more exact ascertainment of underlying malignancy than would be expected through the use of administrative diagnostic coding alone. In addition, comparison of incidences of CAP and annual trends in pneumonia and influenza mortality illustrated that pneumonia was seasonal, mirroring annual trends of influenza activity. Bacterial pneumonia is a well-described and potentially fatal sequela that occurs after influenza [6], and influenza virus neuraminidase potentiates the in vitro development of pneumonia due Streptococcus pneumoniae, the most common cause of bacterial pneumonia, by mediating improved bacterial adherence [7]. Interventions designed to reduce the burden of bacterial respiratory pathogens are now being found to decrease the rate of viral-associated pneumonias. The use of a nonavalent pneumococcal conjugate vaccine in South African infants was recently shown to reduce the incidence of laboratory-confirmed viral pneumonia by 31% [8].

The increase in the rate of CAP during periods of high influenza activity also suggests that influenza vaccination might substantially reduce the incidence of CAP. However, the burden of CAP was still striking, despite impressive annual vaccination rates of >70% in the Washington State study population, suggesting that further increasing influenza vaccination of seniors may not have dramatic results. It will be important to determine whether new recommendations for influenza vaccination of young children [9] will influence adult disease. This was suggested by a publication from Japan that showed that, as more school children were vaccinated, the mortality rates in the elderly significantly decreased [10]. In addition, other respiratory viruses may play a role in the seasonal peaks of CAP in seniors. Infection with respiratory syncytial virus (RSV), a seasonal respiratory virus traditionally considered a pathogen among young children, has been increasingly associated with dramatic morbidity and mortality in adults [11–17]. The potential for newer vaccines targeted at other respiratory pathogens, such as RSV, to decrease the burden of pneumonia will require randomized, controlled clinical trials. However, once new vaccines are shown to be safe and effective, these types of population-based cohorts are needed to examine whether the targeted prevention of one pathogen affects overall pneumonia disease burden.

The utility and power of population-based databases can be realized only through the allocation of substantive resources required to develop, maintain, and analyze these data systems. Ensuring accuracy and validity of the captured data is essential. In addition, extensive programming is often needed to integrate multiple data sources, and researchers with training in epidemiology and statistics are needed for data analysis. Ongoing support for such research is vital for epidemiologists, physicians, and public policy makers to
continue to “know” the burden and trends of specific diseases, such as CAP, and to plan optimal approaches to reduce this burden.

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References