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## Ⓐ How Much Does the United States Spend on Respiratory Diseases?

Respiratory conditions are associated with significant morbidity and mortality costs in the United States and around the world. Allergic rhinitis, asthma, chronic obstructive pulmonary disease (COPD), lower respiratory tract infections, interstitial lung disease, tuberculosis, and other respiratory diseases cause substantial health, quality of life, and economic burdens to patients, payers, and society (1–8).

But what if a disease magically disappeared? How might we put to the best use all the resources formerly devoted to it? Imagine that we could drastically reduce hospitalizations and emergency department visits caused by chronic bronchitis; where, instead, might we most efficiently invest the savings? And what is the value of increased productivity at work or school from getting a good night's sleep, uninterrupted by nighttime asthma symptoms? These questions can be answered by analyzing all direct and indirect costs of the illness (2), also called the “opportunity cost” (9).

Healthcare expenditure in the United States is greater than in any other country in the world, reaching 17.7% of the gross domestic product in 2018, a large increase from 5% in 1960 (10). Respiratory diseases are among the leading contributors to overall healthcare costs (11). The amount paid for all medical and pharmaceutical services associated with an illness, called expenditure, is one of the largest parts of the healthcare cost. Payments are made by public and private insurances and by the patient or the patient's caregiver as out-of-pocket payments. Studies quantifying the cost of respiratory illnesses may inform prioritization of programs, policy development, and efficient management of resources.

Evaluation of disease expenditure reveals how much each payer spends on healthcare services associated with the disease or, as it also could be said, the amount that could be saved if the disease were eliminated. It identifies the different components of the cost and the contribution of each component to the overall expenditure. Such information can help identify funding priorities by highlighting inefficiencies and potential savings (12).

In this issue of the *Journal*, Duan and colleagues (p. 183–192) provide a comprehensive analysis of medical and pharmaceutical expenditures for respiratory diseases (13). On the basis of data from the Disease Expenditure Project (DEX), the authors derived expenditures by payer, type of care, and demographics. The study

also analyzed trends in spending changes from 1996 to 2016 and associations between these changes and five factors: population growth, population aging, disease prevalence, healthcare utilization, and service price and intensity.

On the basis of their analysis, the total expenditure for all respiratory diseases was \$170.8 billion, with asthma being the most expensive among all respiratory conditions, followed by COPD. The largest contribution to the total spending for asthma was prescribed pharmaceuticals (48.0%); for COPD, it was inpatient services (28.8%) and prescription medications (28.5%). For interstitial lung disease, hospitalization costs were the largest part, constituting almost 62.8% of total spending. Ambulatory (58.1%) and emergency department (21.7%) services were the largest costs for upper respiratory tract infections. Although almost all spending for COPD occurred for persons age 45 and older, asthma expenditures were spread evenly over all age groups. Slightly more than half of asthma spending came from private payers (51.5%), whereas almost 70% of spending for COPD was paid by public insurers.

The paper also focuses on the rate of change in spending from 1996 to 2016. On the basis of the analysis, pharmaceutical spending not only was the most expensive type of service for asthma and COPD but also had the highest annual growth rate of 2.7% and the largest absolute increase in spending among all respiratory conditions, adjusted for inflation. The rate of growth in pharmaceutical spending for asthma and COPD remained constant throughout the study period. Spending increase in prescription medications was strongly associated with the price of inhalers, which, according to the authors, “became more expensive over time with minimal clinical innovation, driven by extended patent protections on new delivery devices, new combination inhalers, and the 2008 change from chlorofluorocarbon to hydrofluoroalkane propellants” (p. 189–190). It appears also that the rate of increase in spending from 1996 through 2016 was the highest for public insurance compared with private payers and out-of-pocket payments.

Using decomposition analysis, the authors of the study investigated the drivers of spending growth for respiratory conditions. They determined that the effect of service price and intensity on the rate of growth in spending is larger than the effect of an aging population, contrary to a common perception in the popular media (14).

The paper has some limitations. The authors focus on the aggregate spending and, unlike in the original DEX study (11), per-person spending was not included in the paper's scope. Analyzing per-person spending brings important insights regarding the spending change over time and the factors associated with per-person expenditure, including sex, age, race and ethnicity, geographic

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location, income, education, and the benefit plan design of the individual's health insurance. The paper's findings on aggregate spending tell us about the magnitude of healthcare payments by Medicare, Medicaid, and private insurance but obscure the details of health plan designs that may affect the scale of spending on respiratory disease and reveal the causes of spending differences among health plans. Indirect costs of respiratory conditions, such as productivity losses associated with allergic rhinitis or the mortality costs of COPD, were also excluded, leaving out essential components of economic burden of the disease. For chronic respiratory conditions with no currently existing cure, a more practical focus would be the cost of uncontrolled category of the disease rather than the cost of both controlled and uncontrolled categories, similarly to the cost of uncontrolled asthma (7).

Despite these limitations, the paper substantially contributes to a relatively small body of literature on the cost of respiratory illness by providing a comprehensive analysis of spending for respiratory diseases. To my knowledge, for the first time in the literature, the authors used DEX data to provide a detailed analysis of expenditures on respiratory diseases, how expenditures varied by demographic group, how they changed over time, and how various factors drive changes.

The results of this study suggest development and implementation of effective programs and policies to improve the quality of care for respiratory diseases while reducing its costs. ■

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Tursynbek A. Nurmagambetov, Ph.D., M.S., M.A.  
Division of Environmental Health Science and Practice  
Centers for Disease Control and Prevention  
Atlanta, Georgia

ORCID ID: 0000-0001-5755-1290 (T.A.N.).

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## Ⓔ To Err Is Human, to Forgive Is Pharmacodynamic

It was not long after completion of the first controlled clinical trial of a new treatment for tuberculosis (TB) that drug-resistant strains of TB developed (1), dampening the enthusiasm generated by the mortality improvement that had been observed after 6 months of streptomycin (2). This discovery initiated a period of sustained research to identify combination regimens for the treatment of TB

that were effective at curing disease and preventing the acquisition of drug resistance (3, 4). Despite a number of options for the treatment of both drug-sensitive and drug-resistant TB, there are large gaps between the proportion of individuals cured when allocated to standard of care in clinical trials (5–8) and comparable figures published annually in the World Health Organization global surveillance reports (9). How robust a new treatment regimen is likely to perform in a programmatic setting in the presence of nonadherence is a critical aspect of drug development; in this issue of the *Journal*, the work by Stagg and colleagues (p. 193–205) to compare the forgiveness of 6- and 4-month regimens using data from clinical trials is welcome (10).

As the authors note, the relationship between dose-taking and treatment outcomes is complex, but they are to be commended for

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