patients. Regardless of the outcome, each scenario in which AZM is added to tobramycin, whether during an acute PEx, for eradication, or for chronic maintenance therapy, should be carefully considered and requires evaluation by robust studies.

In conclusion, AZM and tobramycin are commonly prescribed concurrently in both the acute and chronic setting, with combinations occurring in at least half of patients with CF over their lifetime. Both the study in this issue and others before it enforce the concept that "too much of a good thing" may be an accurate adage in select CF populations and that "add-on" therapy should be reevaluated over time. ■

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Social Inequities and Cystic Fibrosis Outcomes: We Can Do Better

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Social hierarchy is intuitively recognized by researchers and lay people alike. While one's status in society is easily gauged by professional title, clothing, or residential address, there is not an agreed-upon definition or measure denoting social status. Nevertheless, it cannot be denied that social status is a powerful predictor of health status. At every point across the life course, lower socioeconomic position is associated with poorer health and higher mortality (1–4).

Three possible explanations for the relationship between socioeconomic status (SES) and health should be considered. First, it could be a spurious association resulting from the separate relationships of SES and health outcomes to genetically based factors. For instance, lower intellectual capacity and smaller physical size might lead concurrently to low SES and poor health. Although plausible, this explanation is improbable. In the Whitehall study of mortality (5), for example, the association between job status and health persisted after adjustment for height and body mass index. The second explanation for the association between SES and health status is offered by the health selection (or drift) hypothesis, according to which the association reflects the influence of illness on SES rather than of SES on illness (6). In other words, poverty is a result of poor health, not the other way around. The third explanation of the SES–health relationship is the social causation hypothesis, stating that SES directly and indirectly affects biological functions, which in

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turn influence health status. Although evidence supporting the drift hypothesis is limited compared with evidence supporting the social causation hypothesis (7), establishing causality in the SES–health relationship is often a challenge. This is why the paper by Tumin and colleagues (pp. 290–299) in this issue of *AnnalsATS*, "Patterns of Health Insurance Coverage and Lung Disease Progression in Adolescents and Young Adults with Cystic Fibrosis," makes an important contribution to this field (8).

Analyzing data from the Cystic Fibrosis Foundation Patient Registry for 2000–2015, the authors report that, during the transition to adulthood, public health insurance status is associated with accelerated lung function decline among patients with cystic fibrosis (CF) but not with differences in outpatient care utilization. What distinguishes their analysis from other similar reports (9–12) is that they show a temporal relationship between health insurance status and lung function; the authors measure insurance status over a 6-year period that precedes the respiratory decline over the subsequent 6 years after the insurance status categorization. The establishment of temporality is a powerful argument for causation in epidemiologic studies (13) and a strong evidence against the drift hypothesis. Ruling out a potential reverse causation (illness leading to public health insurance) is particularly pertinent in adults with CF, as many states have a "medically needy" eligibility program that makes sicker and disabled patients more likely to qualify for Medicaid benefits (14). However, given the chronicity of lung disease in CF, it is plausible that some degree of reverse causation continues to contribute to the relationship between public insurance status and disease severity, particularly in adults.

The study by Tumin and colleagues illustrates both the potential and the challenges of research on the social

determinants of health. Despite an increased interest in the role of socioenvironmental factors for clinical outcomes, patient registries and medical records rarely include detailed and complete patient-level data on SES indicators such as income, education, and occupation. Consequently, investigators resort to ecologic measures that approximate such indicators, including area-level estimates from the U.S. Census, the American Community Survey, and other publicly available data. The concordance of such proxy measures with individual-level SES, however, decreases with the size and rurality of the area (15, 16). Unfortunately, the Cystic Fibrosis Foundation Patient Registry records only the ZIP code of residence rather than the full address, limiting investigators to the of use of less-accurate ZIP-code measures of SES instead of more precise Census tract or block group measures. Thus, attempting to control for SES independently of insurance status, Tumin and colleagues include in their models a composite score of SES on a ZIP-code level. However, the original score was developed for a different geographic unit (Census block groups) and patient sample (participants 45–64 yr of age sampled from Forsyth County, North Carolina; Jackson, Mississippi; the northwestern suburbs of Minneapolis; and Washington County, Maryland) (17). We would also point out that, unlike health insurance, SES score was not measured prior to but simultaneously with the outcome of lung function decline, introducing the possibility of reversed causality.

In the study, public health insurance status primarily functions as an indicator of lower SES rather than of inferior medical care for CF. Publicly ensured patients in the sample had worse pulmonary outcomes, but there is no indication that this was due to less care as measured by outpatient visits, and they had more hospitalizations. These findings corroborate previous reports that in the United States, disparities in CF outcomes cannot be explained by differences in medical treatment, including differential use of health services, prescribed therapies, treatment of pulmonary exacerbations, or hospitalizations for CF (9–12). More worrisome, perhaps, is the finding that individuals with gaps in insurance coverage had worse lung function but fewer outpatient visits and variable differences in hospitalizations, adding to previous work reporting that this is a high-risk population (18).

Although medical care is a relatively small contributor to the overall health status of individuals in the United States (19–21), much of the national health policy for addressing disparities in health outcomes has focused on improving access to care. Although such efforts may be beneficial for some populations, their impact in CF would be small, per Tumin and colleagues' findings. As the authors aptly note, the differential lung function decline by health insurance status in adolescents and young adults with CF is likely related to a complex set of social factors that are correlated with the use of public insurance. Disparities in health outcomes rooted in social and economic circumstances may be reduced but not eliminated solely via clinical means in clinical settings; they must be addressed with social and economic policies. Nevertheless, the transition from pediatric to adult CF care is a high-risk period for losing health insurance. In this sample, 3% of adolescents but 8% of young adults with CF (ages 24–29 yr) had gaps in coverage. Therefore, universal health insurance is critical for improving access to CF care, especially in adults.

Regardless of its limitations, the study adds to a literature that now goes back over 20 years documenting social inequities in CF outcomes (22–28). Although not as clearly shown in this paper, racial and ethnic disparities also exist. The growing Hispanic population with CF and the overdue recognition of the importance of institutional and implicit racial bias call for our attention to the special needs of these groups. It is also time to move on to next steps: developing a better understanding of the mechanisms mediating the relationship between SES and CF outcomes that would allow us to devise effective interventions. There are already CF-specific studies showing that low-SES groups experience differential exposure to tobacco smoke (26, 29), infectious agents (30, 31), access to transplantation (32), enrollment in clinical trials (33), incidence of depression (34), unmet supportive care needs (35), and decreased maintenance of daily therapies (36). There are some socially constructed inequities that are beyond the immediate reach of the healthcare system, but as we clearly elucidate the mechanisms of disparities, we can begin to develop and test effective interventions that may be feasibly delivered in the current healthcare setting. That is the next step. We can do better. ■

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