AL. In this case, it is particularly noteworthy that patients considered very severe according to the z -score are younger than severe patients, and their mean age is even lower than the mean of the entire cohort. This finding is surprising, given the lung-function trajectories in COPD (5), as one would expect that lung function would deteriorate as patients age. Apart from these considerations, the analysis of the hazard ratio of death splines of our patients (Figure 2 of Reference 1) clearly shows that FEV₁ z -score values between -3 and -5 lose the exponential correlation with risk for mortality, which is a circumstance that does not occur for %Pred.

Finally, we believe it necessary to emphasize that our results are not intended to question the relevance of z -score as an essential parameter for interpreting lung function, much less the Global Lung Function Initiative. This is especially true after the recent irreparable loss of Professor Philip H. Quanjer, one of its main proponents (6). In our opinion, the identification of this prognostic limitation of the z -score in elderly patients with COPD could suggest the need to recalibrate reference values in elderly subjects by incorporating more groups of this age (7). ■

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Francisco García-Río, M.D., Ph.D.
Hospital Universitario La Paz
Madrid, Spain
CIBER de Enfermedades Respiratorias
Madrid, Spain
and
Universidad Autónoma de Madrid
Madrid, Spain

On behalf of all authors

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Is It Acceptable to Assess Prenatal Smoking Risk to Infants without Considering Socioeconomic Status?

To the Editor:

In a recent issue of the *Journal*, Morrow and colleagues reported that exposure to maternal smoking increases the odds of bronchopulmonary dysplasia (BPD) and persistent respiratory morbidities in preterm infants (1). The association is clear, but the causal relationship of antenatal smoke exposure to early childhood risk of BPD and respiratory disease needs to be dissected more carefully. In their models, the authors adjust for maternal race but not for the confounding role of socioeconomic determinants in tobacco exposure and respiratory health outcomes. This was discussed in the article's accompanying editorial (2), but we believe that the close link between tobacco use and other causes of respiratory health disparities needs further amplification.

There is a well-established association of socioeconomic status (SES) with lung function in the general population (3), particularly in patients with cystic fibrosis (CF) (4). Although it has been suggested that the primary driver of this is environmental tobacco exposure (5), we conducted an evaluation of the relative impact of several different measures of secondhand tobacco exposure (prenatal maternal smoking, postnatal maternal smoking, and exposure to other household smokers) before and after adjusting for a combination of markers of SES (maternal education, household income, and insurance type) on respiratory outcomes in young children with CF (6). All of our measures of smoke exposure showed highly significant associations with lung function, but these associations were severely attenuated, and some lost statistical significance, when adjusted for SES. Specifically, our initial estimate of a difference in FEV₁ percent predicted in children exposed to prenatal smoking was 4.6% (95% confidence interval, 2.7–6.4; $P < 0.0001$). This diminished by 45% to 2.5% (95% confidence interval, 0.43–4.65; $P = 0.02$) after adjustment for SES. We also found an adverse effect of prenatal and postnatal maternal smoke exposure on weight that lost significance when adjusted for SES.

Our findings in CF suggest that the complex relationship of SES with secondhand smoke exposure cannot be ignored in other chronic respiratory disease populations, such as infants at risk for BPD. Tobacco smoke exposure is an important social determinant of health, but it is found in parallel with other adverse exposures such as air pollution, stress, nutritional deficiencies, and poor health literacy. A complete understanding of the interplay of social and environmental determinants with respiratory health

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is vital to any attempt to address public health policies and anticipate family needs (7). ■

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Thida Ong, M.D.
University of Washington
Seattle, Washington

Michael S. Schechter, M.D., M.P.H.
Children's Hospital of Richmond at Virginia Commonwealth University
Richmond, Virginia

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Reply to Ong and Schechter

From the Authors:

Dr. Ong and Dr. Schechter refer to findings from a study of subjects with cystic fibrosis in which the strength of association between environmental tobacco smoke (ETS) exposure and lung function was attenuated after adjustment for socioeconomic status (SES) (1). Indeed, the scientific literature is replete with studies that examine long-standing questions regarding the complex and interactive associations of SES, smoking, other environmental exposures and lung function, often in the context of chronic obstructive pulmonary disease (2). These issues are highly relevant to our understanding of links between maternal smoking before birth

and the risk for bronchopulmonary dysplasia, which is multifactorial in origin, and late respiratory disease in preterm infants, in whom neonatal ICU and subsequent home environmental exposures, access to health care resources, and other factors are likely important determinants together with the nature or severity of prematurity-associated changes in underlying lung structure and function.

Strong associations between antenatal smoking and bronchopulmonary dysplasia, as reported by Morrow and colleagues (3), were not adjusted for SES, because this information was not collected. However, similar associations between ETS and late respiratory outcomes were reported in a recent large cohort of preterm infants in the NHLBI Prolonged Respiratory Outcomes of Prematurity study (4). In this latter study, maternal smoking and public insurance status were each associated with increased late respiratory morbidity, and intrauterine smoke exposure was retained in the late respiratory disease model that also included insurance status. Despite this confirmation, it is worth noting that SES and ETS are also likely associated, resulting in collinearity when both are included as predictors in a statistical model, making it difficult to separate the effects of each variable (5).

Most important, striking preclinical data have demonstrated dramatic adverse effects of antenatal smoke and nicotine exposure on lung structure and function, providing substantial biological mechanisms and plausibility to the clinical observations (as recently reviewed in Reference 6). On the strength of such mechanistic findings, McEvoy and coworkers have led exciting clinical studies in which maternal vitamin C attenuated the adverse effects of smoking on lung function in human infants (7). ■

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Steven H. Abman, M.D.
Peter Mourani, M.D.
Brandie Wagner, Ph.D.
University of Colorado Denver Anschutz Medical Center
Aurora, Colorado

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