Response

To the Editor:

We appreciate the interest that Drs. Miller and Mann have taken in our article.1 They have made several insightful observations that warrant consideration. The relationship between bronchodilator responsiveness and change in lung function between examinations has already been clarified.2 Significant predictors of greater average decline in lung function between examinations were a lack of bronchodilator responsiveness at examination 1 and weight gain. We agree that the distribution of average changes in lung function between examinations shown in Figure 1 of our article3 is not skewed toward excessive loss. Indeed, the majority of those patients studied had a normal decline in lung function. It is noteworthy, however, that a subset of responders in our population (n = 131) were “rapid fallers” since they lost >300 mL/yr in FVC. We are currently clinically characterizing these individuals to better understand their accelerated lung function decline.

We reported results from all World Trade Center responders who presented for examination, understanding that those with respiratory symptoms may have been more likely to participate. It is true that if we were able to evaluate all individuals who worked at Ground Zero regardless of symptoms, then the spirometry abnormality rates we reported might have been lower.

The issues related to bronchodilator responsiveness are indeed intriguing. Although some participants had a significant response only at the second examination, this does not mean that this was the “onset” of their responsiveness. There is great variability in bronchodilator response even in those with significant disease. It does not seem justifiable to conclude that those with a robust response only at examination 2 did not have pulmonary dysfunction that was related to exposure at the World Trade Center disaster.

We agree that one limitation of a retrospective review of spirometric quality is that the total lung capacity, expiratory reserve volume, and residual volume are unknown. The reduction in FVC could be due to a “less than full inspiratory capacity” due to patient errors in technique or alternatively to true restrictive lung disease, loss of the expiratory reserve volume due to body habitus or due to airtrapping (increased residual volume). Our technicians were trained to focus on inspiratory maneuvers as well as expiratory maneuvers. This training should have reduced the rate of artificially low FVC. Our results are indeed consistent with the development of reactive airway dysfunction syndrome among some responders with clinical recovery in the majority.

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Predictors of Success in Pulmonary Rehabilitation for Patients With Interstitial Lung Disease

To The Editor:

We read with interest the recent study in CHEST (February 2009) by Ferreira et al,1 which provides further evidence supporting the beneficial effects of pulmonary rehabilitation (PR) in patients with interstitial lung diseases (ILDs). The aim of this observational study was also to identify patient characteristics that are predictors of benefit for patients receiving PR.

Although nine potential variables were identified a priori, baseline 6-min walk test distance (6MWD) was the only predictor of benefit. Specifically, the results of the study by Ferreira et al indicate that a lower 6MWD at baseline is a predictor of greater improvement in 6MWD following PR. Caution is needed when assessing predictors of success for any intervention. Participants with a very low baseline 6MWD are more likely to have an increase in walking distance even without any actual benefit from the intervention since they are unlikely to or cannot do worse. Similarly, participants with a higher baseline 6MWD will be more apt to experience the opposite effect because they are starting at the “ceiling” of the measured outcome and are not expected to improve any further beyond their baseline values. This phenomenon, often referred to as the regression to the mean, might result in misleading conclusions about the mean change and predictors of success when the values of participants are at the extremes of the range of an outcome.

A careful visual examination of the scatterplot graph in Figure 1 of the article by Ferreira et al1 supports this concept. It is established that “outliers” that are located at either extreme of the range of values will have an appreciable effect in changing the slope of the best-fitted regression line.2 In Figure 1, there are outlier values for patients with very low baseline 6MWDs (ie, <100 m) who were among the participants with the largest change in 6MWD following PR. Similarly, at the other extreme there are participants with very high baseline 6MWDs (ie, approaching 600 m) who had little to no change following PR, likely due to a “ceiling effect.” If these outlier values were omitted from the model, we hypothesize that the best-fitted regression line would most likely be close to a horizontal line, indicating no overall relationship.

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2 Miller A. A simple spirometric clue to asthma: airways obstruction suggested by a negative or reduced forced expiratory reserve volume despite normal FEV1/FVC ratio. Mt Sinai J Med 1990; 57:85–92

References

2 Erratum. Chest 2009; 135:1114
More prospective studies are needed to assess the predictors of benefit for PR in patients with ILD (and COPD) that are hypothesis driven as opposed to data driven. Unfortunately, this study does not provide strong enough evidence to support prescribing PR for patients with ILD based on their characteristics such as baseline values for 6MWD.

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Response

To the Editor:

We agree completely with Drs. Al-Ghimlas and Todd that caution is needed when interpreting the results of studies such as ours that identify the predictors of response to an intervention. Their concern that patients with low baseline walk distances are more likely to get better and that patients with high baseline walk distances are more likely to get worse is reasonable, although not supported by the limited evidence available for patients with pulmonary fibrosis. A more careful look at the predictive value of supported by the limited evidence available for patients with pulmonary fibrosis: prognostic value of changes in physiology and critical revision of the manuscript.

The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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Flawed Comparative Groups Lead to Flawed Conclusions

To the Editor:

In a recent issue of CHEST (May 2009), Winchester et al concluded that not prescribing antibiotics on the day of the diagnosis of lower respiratory tract infections (LRTIs) resulted in more deaths and hospital admissions. Investigating large populations (as this team did) on whether limiting antibiotic use causes harm is very important. Unfortunately, because of flawed comparative groups and design, this study leaves the reader with false impressions and misleading conclusions. The authors imply that if public health messages

Table 1—Relationship of Baseline Walk Distance to Change in Walk Distance After Pulmonary Rehabilitation in Various Subgroups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Baseline Walk Distance, m</th>
<th>Patients, No.</th>
<th>Point Estimate</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire study group</td>
<td>30–618</td>
<td>99</td>
<td>-0.23</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Subgroup 1 (P5–P95)</td>
<td>116–568</td>
<td>91</td>
<td>-0.17</td>
<td>0.003</td>
</tr>
<tr>
<td>Subgroup 2 (P10–P90)</td>
<td>138–487</td>
<td>84</td>
<td>-0.22</td>
<td>0.002</td>
</tr>
<tr>
<td>Subgroup 3 (P25–P75)</td>
<td>247–430</td>
<td>51</td>
<td>-0.16</td>
<td>0.03</td>
</tr>
</tbody>
</table>

P5 = 5th percentile; P95 = 95th percentile; P10 = 10th percentile; P90 = 90th percentile; P25 = 25th percentile; P75 = 75th percentile.