Correspondence

Adjustment for baseline value in the analysis of change in FEV_1 over time

To the Editor:

In a recent issue of the *Journal*, an interesting editorial by Tantisira[1] accompanying an article by Marcon et al[2] on the association of body mass index (BMI) and weight gain with lung function decrease in the European Community Respiratory Health Survey (ECRHS) asthma cohort was published. Although we basically agree with the content of the editorial, some observations by Tantisira deserve a further comment.

The main finding of Marcon et al[2] was that in subjects with asthma, a decrease in FEV_1 was associated with BMI gain during the follow-up period and that this association was stronger in men than in women. Moreover, Marcon et al noted that when compared with relatively underweight or obese subjects, individuals with intermediate values of baseline BMI had the greatest decrements of FEV_1 over time. Because these subjects also had the highest levels of baseline FEV_1, Tantisira[1] argued that the most likely reason for this inverted U-shaped association between baseline BMI and FEV_1 decrease was regression to the mean and that adjusting the analyses for the baseline level of FEV_1 would have been optimal.

As originally documented by Peto,[3] in any prospective study of the evolution of any numeric quantity (eg, FEV_1), a correlation between the true absolute value and the true rate of change is expected, just as in a race between fast and slow horses one would expect to find the faster horse out in front halfway through the race ("the horse-racing effect"). Referring to the observational study by Marcon et al,[2] baseline FEV_1, which had been measured in the age range of 20 to 44 years (ie, a point in the already descending curve of FEV_1 during a lifetime), might have been low *because of* fast FEV_1 decrease. In this situation adjustment for the baseline value is inappropriate and might mask true differences.[4] An "intermediate step in the causal path,"[5] such as baseline FEV_1 in the proposed association between BMI and decrease in FEV_1, should not be adjusted for in the analyses because this might artificially decrease the differences among the subjects compared (subjects with different baseline BMI in this case). Accordingly, other articles in the ECRHS avoided adjusting for baseline FEV_1 when analyzing change in FEV_1.[6]

Finally, given the general debate on the topic, we wanted to clear up the doubt raised by Tantisira.[1] The analysis of decrease in FEV_1 questioned by the author was repeated when adjusting for baseline FEV_1. Moreover, as proposed by Barnett et al,[7] we analyzed FEV_1 at follow-up when including the mean-centered baseline value of FEV_1 as a covariate. These alternative analyses (data available on request) did not alter the findings of Marcon et al[2] and left the inference made in the article unchanged. We conclude that regression to the mean is not a likely explanation for the results observed by Marcon et al and that the inverted U-shaped association between baseline BMI and FEV_1 decrease in subjects with asthma requires different hypotheses and further investigation.

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