From the authors:

We thank J.P. de Torres and co-workers for their interest in our recently published paper regarding the effect of body weight gain on systemic inflammation in subjects with chronic obstructive pulmonary disease (COPD) [1]. Their comments highlight important issues concerning the sex discrepancies reported in the literature on the effect of systemic inflammation and COPD outcomes. First, we believe that this is still a subject of controversy; the potential prognostic advantage of females with COPD reported in some clinical studies has not been confirmed by other reports [2]. There are multiple reasons for these conflicting findings. In clinical settings, under diagnosis of COPD in females is well described, which may be a source of bias and relatively fewer females compared with males are included in therapeutic trials on COPD, thus limiting power [3].

By contrast, epidemiological studies benefit from a more representative sample of the population. Beyond survival, several of these studies have shown poorer outcomes in females on many aspects. For example, when considering lung function over time, DOWNS *et al.* [4] reported that females with airway obstruction experienced a greater smoking-related decline in lung function than males. In terms of health care use, hospitalisation rates for COPD were increased in elderly females [5]. We can hypothesise that the relative lower prevalence of classical cardiovascular risk factors in females within the general population allows the possibility of COPD and systemic inflammation becoming major risk factors of cardiovascular disease, which is the main cause of death in females [6]. Full explanations about the potential differences between females and males with COPD deserve further studies specifically designed for this purpose.

Secondly, our definition of COPD, based on accelerated forced expiratory volume in 1 s (FEV_1) decline, captures the essence of COPD, as discussed by FLETCHER *et al.* [7]. Absence of reversibility tests with bronchodilators is a frequent limitation in population studies. Despite the lack of bronchodilation, the term COPD is used in epidemiology because it helps clinicians and researchers to better understand the disease [8]. Misclassification of COPD in studies missing bronchodilation is associated with a younger age [9]. Mild obstruction may also play a role [10]. Our subjects were rather old (mean $\pm$ SD 57 ± 10 yrs), and those with fast FEV_1 decline were more than 10 times more likely to have stage 2–4 disease, thus reducing the risk of misclassification.

Lastly, we would like to comment on the concern raised by the use of only two time points. The statistical validity of the FEV_1 decline measurement increases with the length of follow-up (11 yrs in our study). If the measurement error is of the same order of magnitude as the average decline, a reliable estimation would not be possible at an individual level. However, by having a large sample, we can confidently rely on the statistical law stating that random errors average out. Thus, the final point made by J.P. de Torres and co-workers is of minor concern.

Findings from our population-based cohort contribute to the ongoing discussion concerning sex differences in systemic inflammation in individuals with COPD.

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