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🔓 Reply to Zhao *et al.*

From the Authors:

We appreciate the response by Zhao and colleagues and their interest in our work, and we welcome the opportunity to present some additional details about our data (1). To begin, we wish to echo their concerns that 2-year follow-up may not be sufficient for subsolid nodules (SSNs). In fact, a closer examination of our data reveals that clinical practice at Vanderbilt University Medical Center is even more aggressive than this.

Zhao and colleagues correctly point out that our methods section states that "two-year longitudinal imaging follow-up showing no signs of growth for benign nodules" is sufficient to establish benign disease. We admit that this general criterion is likely insufficient for SSNs, but many of our patients were in fact either diagnosed via invasive procedures or followed for much longer than 2 years, including several who were followed for up to 5 years before showing signs of growth necessitating invasive diagnoses. Among the 170 patients from Vanderbilt University Medical Center, 18 (10%) had SSNs (7 pure ground-glass opacities), and 14 of those 18 (78%) received diagnoses of cancer (11 adenocarcinoma, 2 squamous cell carcinoma, and 1 small-cell lung cancer). Of the 18 SSNs, half were suspicious enough on their first computed tomography scans to trigger diagnostic bronchoscopy, leading to cancer diagnoses in 8 patients and a benign diagnosis in 1 patient. The benign nodule had a pretest Mayo Clinic Model probability of cancer of 74% and a combined biomarker model risk of 57%, so although the combined biomarker model did provide a decrease in risk, it would not have delayed the diagnostic procedure. The other 3 benign SSNs were followed for 280, 748, and 1,887 days. Only the patient followed for 1,887 days was finally marked "benign" after only surveillance; the patient followed for 280 days received a diagnosis of histoplasmosis infection by fungal serology, and diagnosis was made on bronchoscopy in the patient followed for 748 days. These lengthy surveillance timelines did not affect our reported clinical outcomes of time to diagnosis among cancers and number of procedures among those with benign disease.

The limitation to this analysis is that our role as a tertiary care center generates some selection bias within our sample population; many less suspicious SSNs that are stable over time likely are never referred to us. In addition, clinical practice in our region is likely more aggressive, with disposition toward tissue diagnosis among pulmonary nodules, including SSNs, considering the prevalence of histoplasmosis infections. ∎

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Contribution of Chronic Obstructive Pulmonary Disease as a Mediator for the Association Between Air Pollution and Lung Cancer

To the Editor:

We read with interest the recent article by Huang and colleagues (1), its accompanying editorial (2), and correspondence (3, 4). The long-term impact of air pollution on lung diseases, particularly chronic obstructive pulmonary disease (COPD) and lung cancer, has drawn substantial research interest in the context of worsening air pollution