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Reply to Parker

From the Authors:

We welcome the interest shown by Dr. Parker in our recent publication that described the yield and efficiency of novel intensified tuberculosis (TB) case-finding algorithms for people living with HIV (1). We agree that sputum mycobacterial culture has imperfect sensitivity for active pulmonary TB. Nonetheless, culture is the best available microbiological reference standard for evaluation of novel TB diagnostics. The addition of clinical follow-up can be helpful but also has limitations. For example, in the context of our study, initiation of antiretroviral therapy complicates assessment of whether clinical and radiological improvements are a result of TB treatment. Furthermore, in most TB-endemic areas, culture is not routinely available for TB diagnosis, and Xpert MTB/RIF (Xpert) is used as the confirmatory TB test. In such settings, all patients with a positive Xpert result are in fact regarded as a TB case and initiated on TB treatment.

If we consider all Xpert-positive patients to be true positives, as suggested by Dr. Parker and as occurs in routine clinical practice, our study conclusions would remain unchanged: *1*) CRP (C-reactive protein)-based TB screening followed by Xpert confirmatory testing would identify a similar proportion of TB cases as the current intensified case-finding (ICF) algorithm (54% [95% confidence interval (CI), 45–63] vs. 58% [95% CI, 49–66]; difference in yield 4% [95% CI, −9% to +16%]; $P = 0.57$); *2*) CRP-based ICF would use less than half as many Xpert assays (9 vs. 4); and *3*) the addition of a single culture would substantially increase ICF yield, detecting ⩾77% of all TB cases, regardless of the screening strategy used. Thus, we believe HIV programs should first consider implementation of CRP-based TB screening, which may then enable the routine use of more sensitive confirmatory tests, such as culture, to improve ICF yield. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reference

1. Yoon C, Semitala FC, Asege L, Asege L, Katende J, Mwebe S, *et al*. Yield and efficiency of novel intensified tuberculosis case-finding algorithms for people living with HIV. *Am J Respir Crit Care Med* [online ahead of print] 7 Sept 2018; DOI:10.1164/rccm.201803-0490OC . Published in final form as *Am J Respir Crit Care Med* 2019; 199:643–650 (this issue).

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Considerations in the Diagnosis of Idiopathic Pulmonary Fibrosis

To the Editor:

The clinical practice guideline on diagnosis of idiopathic pulmonary fibrosis (IPF) by Raghu and colleagues has been helpful in addressing the complexities of radiological and pathological features in diagnosing IPF (1). The heterogeneity of features and limited understanding of the pathogenesis and progression of fibrotic lung disease as well as the option of antifibrotic therapy have made this a timely article (2). The latest iteration has reduced the number of diagnostic subtypes to three groups: IPF, probable IPF, and uncertain IPF (1). However, despite these improvements from previous versions (3), further explanation is required to improve the clarity of this article.

The introduction of "early UIP" on high-resolution computed tomography imaging (Table 4 from Reference 1) requires context. The authors need to discuss what exactly is meant by early usual interstitial pneumonia (UIP), because features such as reticulation, ground-glass opacities (GGO), and distortion are also found in probable UIP. What is the clinical, radiological, and pathological evidence that these features of early UIP indeed progress to UIP?

The authors have added mild GGO to probable IPF. It would be useful to define in numerical terms the extent of mild and predominant GGO (Table 3 from Reference 1).

The term "some histologic features from column 1 are present but to an extent that precludes a definite diagnosis of UIP/IPF" in Table 5 from Reference 1 is broad but open to different interpretations by clinicians and institutes.

The authors should comment on how to handle potential overlap of nonspecific interstitial pneumonia that shares inflammatory and fibrotic features of probable and uncertain UIP on radiology and pathology (4). It is likely that most nonspecific interstitial pneumonia may fall into probable or indeterminate UIP.

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