taking ART and we acknowledge that ART-experienced persons with VL nonsuppression are at risk for cryptococcosis [5]. Yet, the authors failed to present data that a novel, VL-directed screening approach with an appropriate intervention clearly improved outcomes. We believe the evaluation of VL-directed CrAg screening and its impact on morbidity and mortality should be addressed prospectively. Also, operational matters need attention before changing guidelines (eg, VL results turnaround time) and ensuring anyone at risk of cryptococcal disease has rapid CD4 access, including those on ART with virological failure.

We commend the authors for their description of CrAg prevalence in those on ART with VL nonsuppression, however, more data would be needed to justify a recommendation that the WHO should change CrAg screening in PLHIV with an isolated high VL result.

Notes

Disclaimer. The findings and conclusions in this letter are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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References

- World Health Organization. Guidelines for the Diagnosis, Prevention and Management of Cryptococcal Disease in HIV-Infected Adults, Adolescents and Children: Supplement to the 2016 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. WHO Guidelines Approved by the Guidelines Review Committee. Geneva, Switzerland: WHO, 2018.
- World Health Organization. Guidelines for Managing Advanced HIV Disease and Rapid Initiation of Antiretroviral Therapy. WHO guidelines approved by the Guidelines Review Committee. Geneva, Switzerland: WHO, 2017.
- Mpoza E, Rajasingham R, Tugume L, et al. Cryptococcal antigenemia in HIV therapyexperienced Ugandans with virologic failure. Clin Infect Dis. 2020; 71:1726–31.
- Meya DB, Kiragga AN, Nalintya E, et al. Reflexive laboratory-based cryptococcal antigen screening and preemptive fluconazole therapy for cryptococcal antigenemia in HIV-infected individuals with CD4 <100 cells/µL: a stepped-wedge,

cluster-randomized trial. J Acquir Immune Defic Syndr **2019**; 80:182–9.

 Rhein J, Hullsiek KH, Evans EE, et al; ASTRO-CM Study Team. Detrimental outcomes of unmasking cryptococcal meningitis with recent ART initiation. Open Forum Infect Dis 2018; 5:ofy122.

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Reply to the Author

To THE EDITOR—We have read the commentary by Heather and Raizes on our recent publication with interest. Given that this was one of the first studies to determine cryptococcal antigen (CrAg) prevalence among individuals with suspected antiretroviral therapy (ART) with a viral load (VL) >1000 copies/mL in the public health system in Uganda, the conclusions we draw may have been overstated in relation to implementing this guidance for country programs.

We agree that we had small numbers of patients to demonstrate improvement in outcomes, however, despite the small numbers in our study, and based on prior studies in Uganda and South Africa, a CrAg prevalence of >0.6% followed by pre-emptive antifungal therapy for those with cryptococcal antigenemia is cost effective [1, 2]. We believe that a CrAg prevalence of 3% among individuals with VL >1000 copies/mL warrants the need to do larger evaluation studies, particularly in sub-Saharan Africa where cryptococcal disease remains a significant cause of AIDS-related mortality. Second, given that the proportion of HIV-infected individuals presenting with cryptococcal meningitis is increasingly skewed to those who are ART experienced, there is a need to do studies on CrAg prevalence among this population of individuals likely failing their ART regimen by using the VL test as a Crag screening entry point to define the Given the reasons above, we agree with the authors that further studies are needed to review viral load based CrAg screening in HIV patients with virologic failure in order to prevent and reduce cryptococcosis related mortality.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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References

- Meya DB, Manabe YC, Castelnuovo B, et al. Cost-effectiveness of serum cryptococcal antigen screening to prevent deaths among HIV-infected persons with a CD4+ cell count < or = 100 cells/ microL who start HIV therapy in resource-limited settings. Clin Infect Dis 2010; 51:448–55.
- Jarvis JN, Harrison TS, Lawn SD, Meintjes G, Wood R, Cleary S. Cost effectiveness of cryptococcal antigen screening as a strategy to prevent HIV-associated cryptococcal meningitis in South Africa. PLoS One 2013; 8:e69288.

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The Detrimental Effects of Oral Vancomycin

To THE EDITOR—In the 1 September 2020 issue of *Clinical Infectious Diseases*, Johnson and colleagues [1] evaluated oral vancomycin prophylaxis in a randomized trial for prevention of *Clostridioides difficile* infection (CDI). We agree with and wish to elaborate on 2 of Professor Garey's editorial comments that (1) one important concern for oral vancomycin as a prophylactic agent is its "profound effect on the microbiome that by itself decreases colonization resistance to *C. difficile*,