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# Reconsidering Cryptococcal Antigen Screening in the U.S. among persons with CD4<100 cells/mcL

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Dear Editor,

The 2012 International AIDS Conference was themed around the need for an "AIDS free generation." The concept is that the HIV virus is not yet curable, but with medications, we can prevent those who are HIV-infected from developing complications of AIDS and opportunistic infections. Cryptococcal meningitis is one such opportunistic infection that causes 20-25% of AIDS-related mortality in Africa [1]. Cryptococcal antigen (CRAG) can be detected in a subclinical phase, weeks prior to onset of symptomatic infection, and can be screened and preemptively treated with fluconazole to prevent overt cryptococcal meningitis. The new FDA-approved point-of-care CRAG lateral flow assay (LFA) (Immy, Inc., Norman, OK) has fundamentally changed the cost-effectiveness of CRAG screening to prevent cryptococcal meningitis from occurring in those with subclinical infection. The CRAG LFA assay cost is $2.00 in resource limited regions and $5.00 in high-income countries, which translates to a probable real world cost of approximately $2.50-$5.00 in resource limited settings and $10 in high-income countries when including labor, shipping, and overhead costs. This screen and preemptive treatment strategy has the potential to vastly diminish and eliminate cryptococcal meningitis from occurring after ART initiation and reduce the 20-25% of early ART mortality caused by cryptococcosis [2-4].

Previously Meya *et al* showed the value of CRAG screening in a prospective cohort, using the CRAG latex agglutination at a cost of $16.75 in Uganda [3]. Now with a real world cost of the CRAG LFA at $2.50, the cost per life saved with CRAG screening and pre-emptive fluconazole therapy is $39.73 in Uganda among persons with CD4<100 cells/μL, and $2.21 per quality adjusted life year saved (QALY) [5]. In contrast to the cost of cryptococcal meningitis hospitalization, CRAG screening and targeted preemptive treatment of those CRAG+ is cost saving to healthcare systems at $\geq$1% CRAG+ prevalence (Figure 1).

But is this program only relevant to Africa? While early HIV testing is key, the U.S. reality is that 38% of newly HIV diagnosed Americans received an AIDS diagnosis concurrently or within 1 year of their HIV diagnosis between 1996-2005 [6]. In North America, our opinion is CRAG screening should also be considered among those who do present with advanced AIDS and CD4<100. The US cost of cryptococcal meningitis hospitalization is extraordinarily high, in contrast to CRAG screening (~$10) followed by pre-emptive treatment with 10 weeks of fluconazole per WHO guidelines ($30.24) at 800mg daily for 2 weeks followed by 8 weeks of 400mg daily [7]. The approximate cost of hospitalization for cryptococcosis from one Boston hospital including room and board ($700/day), liposomal amphotericin (~$350/day), and flucytosine (~$500/day) for 14 days is on average $50 000. For this cost, assuming that the LFA would cost $10 in high-income settings, one could screen approximately 5000 persons for asymptomatic antigenemia.

Thus while the prevalence of cryptococcal antigenemia among those with CD4<100 cells/μL is likely much lower in North America than in Sub-Saharan Africa or Asia, the cost of cryptococcal meningitis treatment is astronomically higher. CRAG screening is likely cost saving in the U.S. if screened population prevalence was >0.1%. Thus, U.S. CRAG prevalence data are needed. Given the improved cost considerations, the U.S. DHHS Opportunistic Infection guidelines should reexamine the benefit of routine pre-ART CRAG screening for those with CD4<100 or among persons hospitalized shortly after ART initiation [8]. While ideally in the future this population of late HIV presenters will be eliminated, among those who do present late, CRAG screening in the U.S. may not only be cost saving, but life saving.

NOTES

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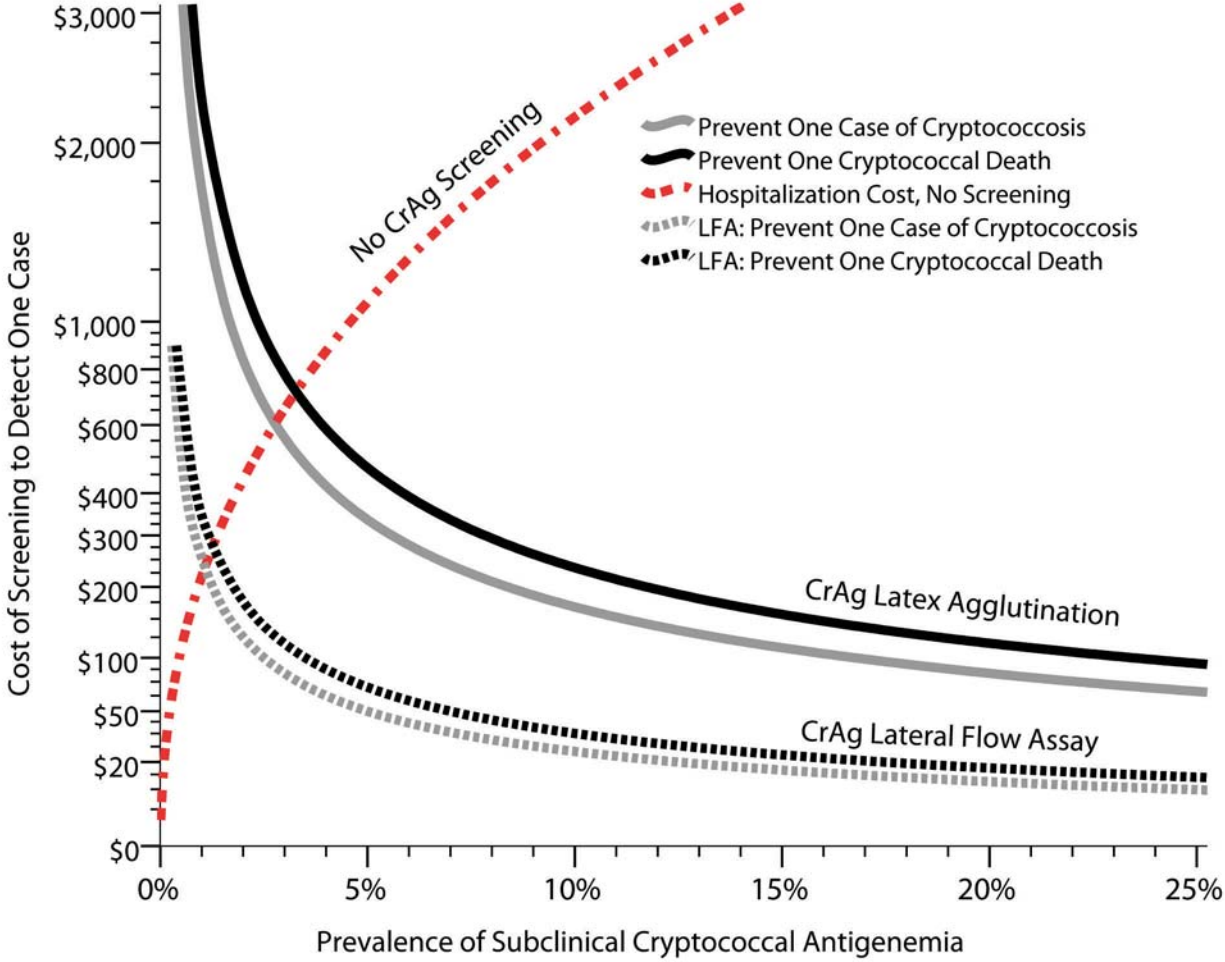
$3,000
$2,000
$1,000
$800
$600
$400
$300
$200
$100
$50
$20
$0
Cost of Screening to Detect One Case
0%
5%
10%
15%
20%
25%
Prevalence of Subclinical Cryptococcal Antigenemia
No CrAg Screening
Prevent One Case of Cryptococcosis
Prevent One Cryptococcal Death
Hospitalization Cost, No Screening
LFA: Prevent One Case of Cryptococcosis
LFA: Prevent One Cryptococcal Death
CrAg Latex Agglutination
CrAg Lateral Flow Assay