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Yes, genotype testing is cost-effective for primary resistance in Brazil

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We thank Ramos and colleagues for giving us the opportunity to help readers understand and interpret our findings of the per person life expectancy and average cost estimates of population-based interventions, such as genotype testing for HIV resistance mutations. While the per person gains we reported may appear small (7.3 days, \$330), the benefits of genotype resistance testing are not allocated on a per person basis. A small number of individual patients – those in whom non-nucleoside reverse-transcriptase inhibitors (NNRTI) resistance is detected and treatment is optimized accordingly – will experience substantial benefits: LE gains for these select individuals will be measured in months and cost savings measured in the thousands of dollars. When conducting a cost-effectiveness analysis, we do not know ahead of time which patients will benefit from the test. Consequently, we spread those benefits across a denominator that includes the entire population of patients who undergo testing, most of whom will be found to have no resistance and will therefore not personally benefit from the intervention. Hence, the answer to Ramos and colleagues' question – namely, “Is there any significant clinical or economical difference in a gain of 7.3 days of life and in savings of \$330 over a lifetime time horizon?” – is a resounding “yes”. Compared to the life expectancy gains from other interventions¹, these values are large, clinically significant, and represent excellent value.

We also thank the writers for noting that we restricted our attention to NNRTI resistance. Given that resistance to other drug classes (nucleoside reverse-transcriptase and protease inhibitors, for example) can be assessed in a single test, accounting for the other possible

resistances would only serve to strengthen our findings and further support the case for genotype resistance testing as a cost-effective investment.

Genotype resistance testing has been consistently offered in Brazil since 2001 and current approaches for transporting samples and results between existing genotyping facilities and all states are established and functioning. Additionally, the technology and infrastructure available in both the public and private sectors could serve to enhance the country's capacity for genotype resistance testing, if needed. Moreover, we find that the cost-effectiveness result is robust, even in the face of a 50% increase in our base case assumption about the costs of genotype resistance testing, an increase which could be interpreted as accounting for higher-than-expected transportation costs. As to the deferral of treatment while waiting for test results: if lengthy delays are really unavoidable, it may be that patients with the lowest CD4 counts should be started empirically on first-line ART², which could be changed if needed upon receipt of genotype resistance testing results.

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