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Accuracy of Pima point-of-care CD4 analyzer in routine use in public health clinics in Uganda

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To the Editor

We read with interest the article by Larson et al.,¹ and we would like to summarize findings of point-of-care CD4 testing in a multi-site, real-world setting at seven Kampala Capital City Authority (KCCA) health facilities in Uganda under general clinic conditions.

Venous blood samples (n=225) were run onsite by trained clinic staff using the PimaTM Analyser (Alere). Excess portions of the same plasma specimen were sent to the Makerere University-Johns Hopkins University (MU-JHU) laboratory for testing within 24 hours via a BD FACSCaliburTM flow cytometer. The MU-JHU lab is accredited by the College of American Pathologists and participates in external quality assurance testing. Daily calibrations are performed with commercial controls. The sampled population was 80% female, and comprised of HIV-infected persons whose median age was 27.

The overall correlation between Pima CD4 and the referent FACSCalibur CD4 result was excellent (Spearman's rho=0.953). However, the correlation strength decreased as patient CD4 counts increased (Figure 1-a). Among all paired samples, the Pima Analyser under-reported the CD4 count relative to the FACSCalibur result by a mean of 48 cells/mL (median -31 CD4/mL, IQR: -85 to +6). One-half (49.8%) of Pima results were within ± 50 CD4 cells/mL of the FACSCalibur result. Among FACSCalibur CD4<350 cells/mL (n=76), 75% of Pima test results were within ± 50 CD4 cells/mL of the FACSCalibur (median difference -2 CD4/mL, IQR: -31 to +20). Among FACSCalibur CD4<200 cells/mL (n=37), 73% and 86.5% of Pima results were within ± 25 and ± 50 cells/mL of the FACSCalibur, respectively. The median relative difference between the two tests was +1 CD4/mL of Pima above FACSCalibur (IQR: -8 to +15). Additionally, the direction of the difference between the two tests was inconsistent. Among all paired samples, 30% of Pima results were above the FACSCalibur, and 70% were below.

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These results reinforce what other research has shown in clinical settings and under research conditions. The Alere Pima™ Analyser performs with increasing accuracy as CD4 decreases and is reasonably able to correctly classify patients at clinical thresholds, e.g. <350 cells/mL. This research included a small number of patients with CD4<100 (n=15), which limits our ability to evaluate Pima's accuracy among severely immunocompromised patients. However, it illustrated three points. First, the Pima test performed very well in capturing patients with <100 CD4 (100% sensitivity, >99% specificity). Second, two-thirds of patients tested had CD4>350 cells/mL, which reflects Pima's significant usage in pregnant women. Third, without thoughtful point-of-care integration, the magnitude of point-of-care CD4 testing impact may be quite modest in urban settings with regular access to standard flow cytometry.

Based on its diagnostic performance, Pima is currently not an optimally reliable method for longitudinal monitoring.^{2,3} Point-of-care CD4 analyzers – including the Pima machine – are however useful in identifying severely immunocompromised patients at high risk of adverse HIV-related clinical events. Furthermore, South African pilot data indicate that point-of-care testing can increase linkages to HIV care – specifically, increased likelihood of completing a secondary referral visit post-CD4 testing.¹ Point-of-care CD4 testing may also decrease the time to ART initiation. More operational research is needed establish how Pima may be used in a targeted fashion to ensure maximal utility.

Using point-of-care technology is at HIV-clinic intake for first time patients may be one effective method of utilizing point-of-care CD4 technology. However, this may present considerable challenges for staff in high-volume clinics. The time to obtain a single Pima CD4 was ~20 minutes, resulting in a maximum of 24 sample analyses per machine in an 8-hour workday. Among high patient volume clinics involved in this research, 24 samples would represent only ~45% of specimens sent to the referral laboratory daily. During the course of this research, we also observed that higher volume clinics were less likely to use point-of-care CD4 analyzers as part of integrated ART care, due possibly in part to time constraints of the laboratory staff.

At an operational level, implementation of point-of-care CD4 or any new technology should be done in consultation with clinical staff. Implementation without consultation and training may result in increased burdens on health workers, incomplete understanding of how a new technology can be valuable, and the resulting underutilization of a new technology. Further research on the improvements in patient care via point-of-care diagnostics in resource-limited settings will be valuable in building the case for appropriate implementation of this new technology.

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Figure 1. Diagnostic performance of the Pima Analyser

a) Scatter plot and linear prediction of Pima venous blood samples versus BD FACSCalibur standard, including 100, 200, 350 CD4 cells/μL thresholds (n=225). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for Pima results are presented in the tablet at <200, <350, and >350 CD4 cell/μL thresholds. b) Bland-Altman Plot showing divergence of Pima and FACSCalibur CD4 Counts (n=225). Pima Analyser reported on average 48 CD4 cells/μL below FACSCalibur results (dotted horizontal). Limits of agreement (solid horizontal lines) plotted at -218 and 122 cells/μL, or two standard deviations from mean difference.