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Performance evaluation of point-of-care CD4 cell counting devices compared with conventional laboratory methods

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Abstract

Background: CD4 cell counting is important for determining immune status and determining care for people living with HIV and in regions where laboratory CD4 cell testing is not easily available. While point-of-care devices can enhance access, acceptability of results needs to be ensured with the reference flow cytometry. The aim of this study was to assess the level of agreement and clinical classification performance of two point of care CD4 counting methods to the flow cytometry platform. **Methods:** In 240 patients, comparison between paired CD4 counts obtained from two point-of-care devices and reference flow cytometry using Pearson correlation, Lin's concordance correlation coefficient, Bland-Altman analysis and diagnostic performance at CD4 thresholds of 200 and 350 cells/µL in 240 patients. **Results:** Strong Pearson correlation between both devices and reference flow cytometry was demonstrated with Pearson r values of 0.974 for Device A and 0.992 for Device B and concordance of 0.960 and 0.989 respectively. The mean bias values were –34.2 cells/µL for Device A and –13.5 cells/µL for Device B. The sensitivity and specificity were 79% for Device A and 89% for Device B, and 94% for Device A and 97% for Device B, respectively, when counting below 200 cells/µL. The respectives overall misclassifications of Device A and Device B were 8.3% and 4.6%. **Conclusion:** Both point-of-care devices exhibited good degree of agreement with reference flow cytometry with Device B having a smaller bias and lower misclassification. Point-of-care testing can contribute to decentralisation of CD4 testing, but borderline results can be verified using reference testing.

Keywords: *CD4 count, Point-of-care testing, Flow cytometry, Method comparison, Bland-Altman, Concordance, HIV, Limits of agreement*

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1. Introduction

The enumeration of CD4 T lymphocytes has been, for the whole of the modern history of HIV medicine, one of the central measurements in the care of the infected patient. The count reflects the state of the immune system, and although the advent of universal antiretroviral treatment has shifted the emphasis of monitoring towards

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the viral load, the CD4 count retains a defined and important place: it identifies the patient with advanced disease, in whom the risk of opportunistic infection is high, and it guides the prophylaxis and the intensified care that such a patient requires (World Health Organization, 2021; Ford *et al.*, 2017; World Health Organization, 2017). A count below two hundred cells per microlitre marks severe immunosuppression and the need for prophylaxis, and a count below three hundred and fifty has historically defined the threshold for treatment and for the staging of disease, so that the decisions that follow from the count turn on these particular values.

The reference method for counting CD4 cells is flow cytometry, which is accurate and precise but demands a well-equipped laboratory, a stable supply of power and reagents, trained operators and, in the common situation where the laboratory is distant from the patient, the transport of blood samples with the delay and the loss that transport entails (Peeling *et al.*, 2015; Cassim *et al.*, 2021). In the decentralised and resource-limited settings in which much of the burden of HIV falls, these demands are often not met, and the patient may leave the clinic before the result returns, so that the count, however accurate, arrives too late to inform the decision it was meant to guide (Drain *et al.*, 2014; Vojnov *et al.*, 2016).

Point-of-care devices for counting CD4 cells have been developed to meet this difficulty. Small, portable and usable by a nurse or a technician at the bedside or in the clinic, they return a count within minutes from a drop of blood, and they promise to place the measurement where and when it is needed, improving the linkage of the patient to care (Reid *et al.*, 2020). A number of such devices have come into use, and their evaluation against the reference method has become an important task, for a portable count is of value only if it is accurate enough to support the same clinical decisions as the laboratory count it replaces (Mwau *et al.*, 2013; Jani *et al.*, 2011; Scott *et al.*, 2015; Coetzee *et al.*, 2016).

The evaluation of a measuring device against a reference is a question not of correlation but of agreement, and the two are not the same: two methods may correlate almost perfectly and yet disagree systematically, one reading consistently higher or lower than the other, a disagreement that correlation conceals but that the analysis of agreement, by the methods of Bland and Altman and of concordance, reveals (Bland and Altman, 1986; Lin, 1989; Giavarina, 2015). For a CD4 device the agreement that matters most is agreement at the clinical thresholds, for a device that classified a patient correctly as above or below two hundred or three hundred and fifty cells would serve the clinical purpose even if its individual counts were imperfect, whereas one that misclassified patients at these thresholds could mislead the decision to treat.

The present study was undertaken to evaluate the performance of two point-of-care CD4 counting devices against reference flow cytometry in a single cohort of patients tested in parallel by all three methods. Its objectives were to quantify the correlation and the concordance of each device with the reference; to characterise their agreement by the analysis of the bias and its limits, overall and across the range of the count; and to determine their diagnostic performance, the sensitivity, specificity and misclassification, at the clinically critical thresholds of two hundred and three hundred and fifty cells per microlitre, and thereby to judge their fitness for clinical use and to compare the two devices.

2. Materials and methods

2.1. Design and participants

This was a cross-sectional method-comparison study in which 240 patients attending an HIV clinic were tested for their CD4 count in parallel by two point-of-care devices and by reference laboratory flow cytometry. Reporting follows the recommendations for observational studies (Vandenbroucke *et al.*, 2007). A single venous blood sample from each patient was divided and analysed by all three methods on the same day by operators unaware of the results of the other methods, to minimise measurement and observer bias.

2.2. Measurements

The reference CD4 count was measured by laboratory flow cytometry, the established method, following the standard protocol with appropriate controls. The two point-of-care devices, designated Device A and Device B, were operated according to the manufacturers' instructions by trained staff at the clinic, each returning an absolute CD4 count from the same sample. The two devices represent the two broad classes of portable analyser in current use, and were chosen to allow a comparison not only of each against the reference but of the two against each other.

2.3. Statistical analysis

The agreement of each device with the reference was assessed in three complementary ways. The strength of the linear relationship was quantified by the Pearson correlation coefficient and, because correlation does not capture systematic difference, the agreement proper by Lin's concordance correlation coefficient. The bias, the mean difference between the device and the reference, and its ninety-five percent limits of agreement were determined by the method of Bland and Altman, and the bias was examined separately within strata of the reference count to detect any dependence of the bias on the magnitude of the count.

2.4. Ethical considerations

The study was approved by the Institutional EthicsCommittee before commencement and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from every participant, participation was voluntary, and all records were anonymised and identified only by a study code.

3. Results

3.1. Patient characteristic

The 240 patients had a reference CD4 count with a median of 350 cells per microlitre and a wide range, and the count was distributed across the clinically relevant range, about a sixth of the patients having a count below two hundred, more than half between two hundred and five hundred, and the remainder above five hundred, so that the comparison spanned the range over which clinical decisions are made. The distribution of the reference count is set out in Table 1.

Table 1: Distribution of the reference CD4 count in the 240 patients

Characteristic	Value
Reference CD4, median (IQR)	350 (238-528)
CD4 < 200 cells/uL	38 (16%)
CD4 200-499 cells/uL	133 (55%)
CD4 >= 500 cells/uL	69 (29%)

3.2. Correlation and agreement

Both devices correlated very strongly with the reference flow cytometry, the Pearson coefficient being 0.974 for Device A and 0.992 for Device B, and the concordance, which additionally penalises systematic difference, was high for both, at 0.960 and 0.989 respectively, a little higher for Device B. The analysis of agreement, however, showed that both devices underestimated the count relative to the reference, the mean bias being −4.2 cells per microlitre for Device A and -13.5 for Device B, and the limits of agreement were correspondingly wider for Device A than for Device B. Both devices, that is, read systematically a little low, and Device A more so and with more scatter than Device B. The measures of correlation and agreement presented in Table 2, the correlation displayed in Figure 1 and the agreement in Figure 2.

Table 2: Correlation, concordance and Bland-Altman agreement of each device with reference flow cytometry

Device	Pearson r	Lin CCC	Bias	95% LOA	Slope	Intercept
Device A	0.974	0.960	-34.2	-153 to 85	0.88	23
Device B	0.992	0.989	-13.5	-80 to 53	0.95	15

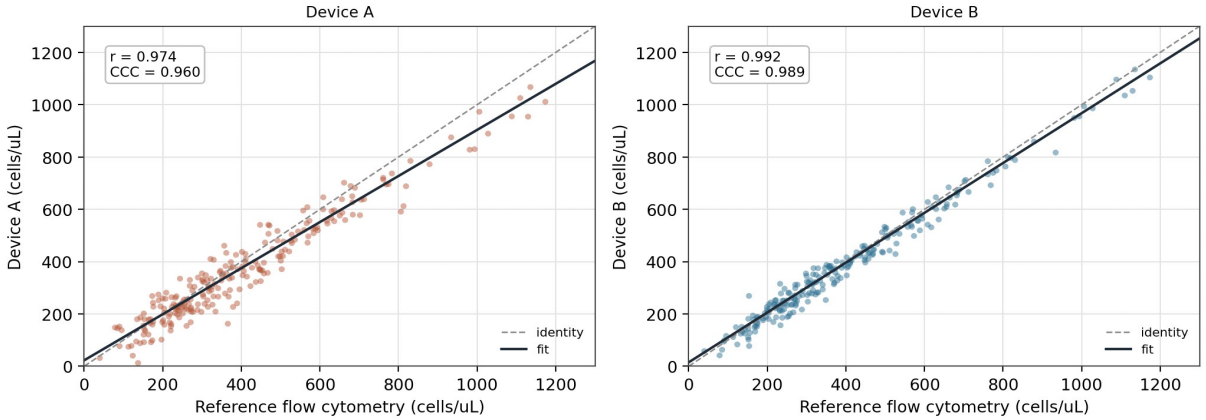


Figure 1: Correlation of each point-of-care device with reference flow cytometry

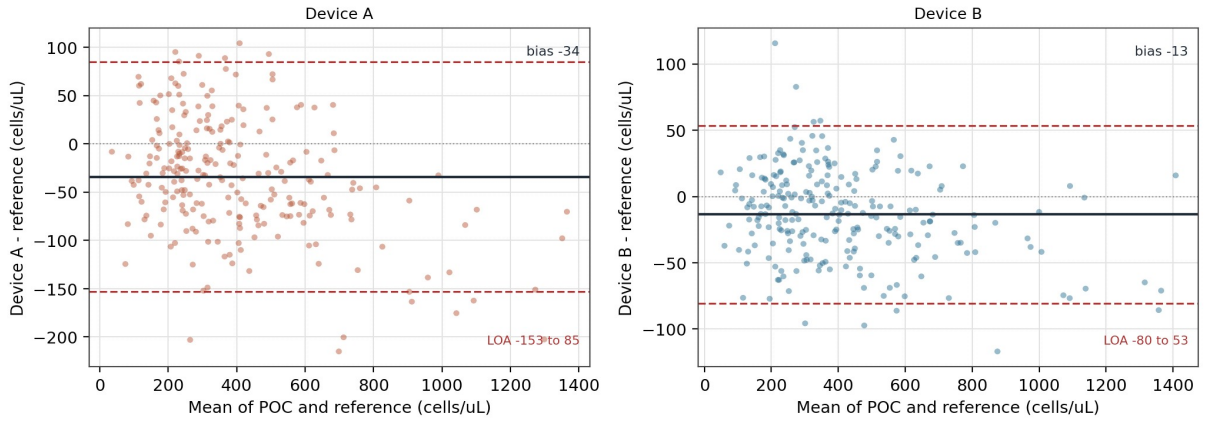


Figure 2: Bland-Altman agreement of each device with reference flow cytometry

3.3. Bias across the range of the count

The magnitude of bias varied across CD4 count strata. At counts below 200 cells/μL, the mean bias was minimal for both devices (+0.4 cells/μL for Device A and –2.9 cells/μL for Device B). Bias increased at higher counts, reaching –71.7 cells/μL for Device A and –28.9 cells/μL for Device B among patients with counts ≥500 cells/μL. Thus, both devices showed their closest agreement in the lowest CD4 stratum, although the magnitude of agreement specifically at the 350-cell/μL threshold was not separately estimated.

Table 3: Mean bias of each device relative to the reference, by CD4 stratum (cells/uL)

Device	CD4 < 200 cells/μL	CD4 200-499	CD4 >= 500
Device A	+0.4	-24.5	-71.7
Device B	-2.9	-8.5	-28.9

3.4. Diagnostic performance at clinical thresholds

The results indicated that device B achieved higher sensitivity and specificity than device A at 200 cells/μL: 89% vs 79% and 97% vs 94%, respectively. The sensitivity of both devices was high at 350-cells/μL level (96% and 95% for Device A and Device B, respectively), and specificity remained at 88% and 93% respectively. Misclassification was lower with Device B compared to Device A at both thresholds of 200 cells/μL (4.6%, 8.3%) and 350 cells/μL (5.8%, 8.3%). Therefore, Device B had overall less misclassification than Device B although the relative sensitivity and specificity of the two devices were dependent on the threshold.

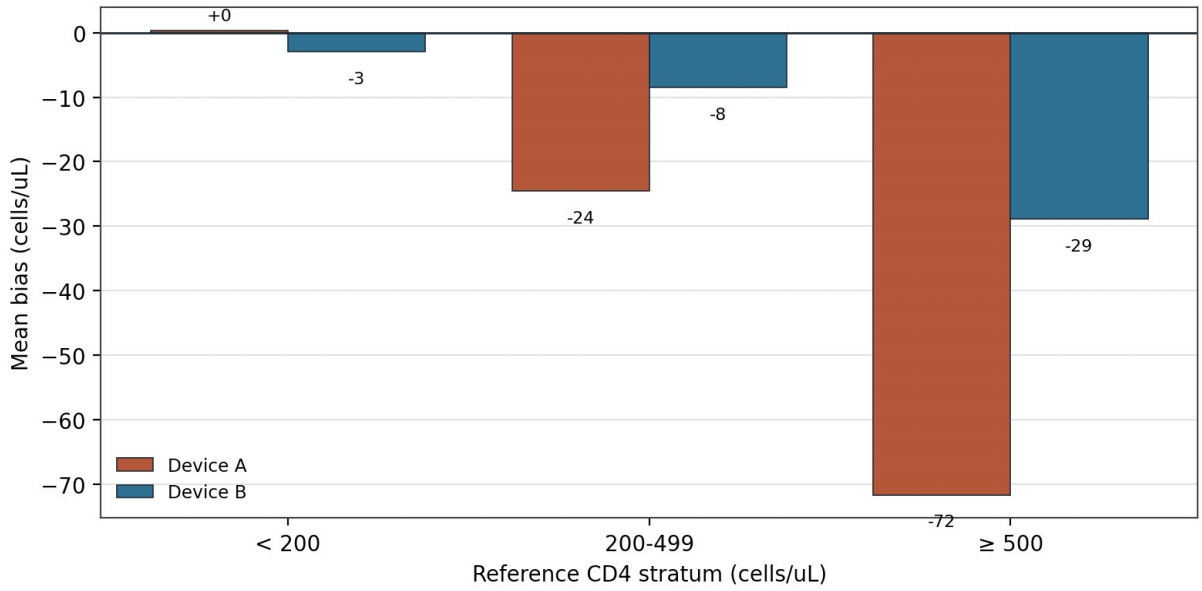


Figure 3: Mean bias of each device relative to the reference, by CD4 stratum

Table 4: Diagnostic performance of each device at the 200 and 350 cell/uL thresholds (percent)

Device (threshold)	Sensitivity	Specificity	PPV	NPV	Misclass
Device A (<=200)	79	94	71	96	8.3
Device B (<=200)	89	97	83	98	4.6
Device A (<=350)	96	88	88	95	8.3
Device B (<=350)	95	93	93	95	5.8

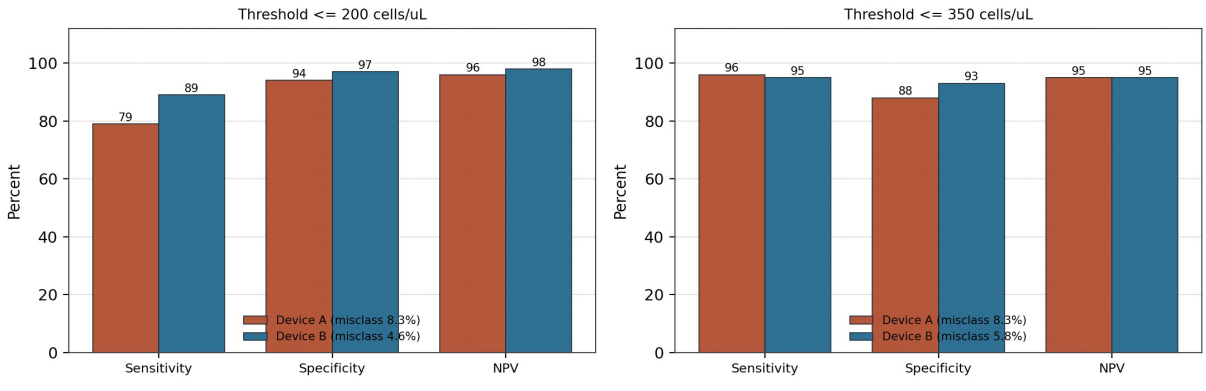


Figure 4: Diagnostic performance of each device at the clinical CD4 thresholds

4. Discussion

This study highlighted good correlation and concordance of two point-of-care CD4 counting devices compared to the reference flow cytometry. Blind biases and limits of agreement were small without systematic underestimation of both devices, with Device B having a smaller blind bias and narrower limits of agreement than Device A, and the overall level of misclassification of either device at clinically relevant thresholds was generally good.

The distinction between correlation and agreement, which the analysis was designed to draw, proved to be the substance of the matter. The very high correlation of both devices with the reference, taken alone, might have suggested near-perfect interchangeability, but the analysis of agreement revealed a systematic underestimation that the correlation had concealed, a reminder that the evaluation of a measuring device requires the methods of agreement and not correlation alone. The negative bias of both devices, of the order of a few tens of cells, is consistent with the reports of the portable analysers now in use, which have generally been found to read a little low against flow cytometry, and the smaller bias of Device B accords with the better performance reported for the more recent instruments.

The dependence of bias on the magnitude of the CD4 count is clinically relevant. Both devices showed minimal bias in the lowest CD4 stratum (<200 cells/μL), while greater underestimation occurred at higher counts. This pattern is reassuring for identification of patients with severe immunosuppression, although the present analysis did not estimate bias specifically at the 350-cell/μL threshold. The threshold-specific diagnostic results nevertheless showed good classification performance for both devices.

The diagnostic performance at the thresholds confirms this judgement in the terms that matter clinically. Both devices classified most patients correctly as above or below the thresholds, with high sensitivity and negative predictive value, so that a patient with a low count would seldom be missed, and the misclassification that did occur was modest and, for the better device, uncommon. The superiority of Device B, evident in its smaller bias, tighter limits of agreement and lower misclassification, illustrates that the portable analysers are not all equivalent and that the choice of device matters, the more accurate instrument being preferable where it is available (Bwana *et al.*, 2018).

The findings support the potential use of point-of-care CD4 testing in decentralised HIV care, particularly where access to conventional flow cytometry is limited. However, the observed negative bias means that results close to clinically relevant thresholds should be interpreted cautiously. Confirmation by reference testing may be appropriate when a result is close to a treatment- or prophylaxis-related decision threshold, particularly where the consequences of misclassification are substantial.

5. Strengths and limitations

This study has multiple strengths such as same-day paired POC testing and flow as our reference standard, blinded operators, and analysis with correlation, concordance, Bland–Altman agreement, and clinically-defined diagnostic thresholds. However, the study was carried out at a single centre where trained operators obtained venous blood samples for testing; in the field, testing might often be performed at point-of-care either in the field or at the care takers premises, and capillary blood might be the preferred sample type. There are further inherent analytical variability for the reference method and the two devices examined could not be generalized to other devices and settings. Multicentre trials with larger number of field operators with capillary specimens should be performed.

6. Conclusion

In this method-comparison study, two point-of-care CD4 counting devices were evaluated against reference flow cytometry, and both were found to be accurate enough for clinical use, with the better of the two, Device B, performing distinctly well. Both devices correlated very strongly with the reference, but the analysis of agreement showed that both underestimated the count by a small margin, Device A by more than Device B, a systematic difference that correlation alone had concealed. The underestimation was least at the low counts and greatest at the high, so that the devices agreed most closely with the reference precisely at and below the thresholds of two hundred and three hundred and fifty cells at which clinical decisions are made, and their diagnostic performance at these thresholds was accordingly good, with high sensitivity and negative predictive value and a modest misclassification that was lower for Device B. The point-of-care devices are therefore a sound basis for the decentralised measurement of the CD4 count, provided that the more accurate device is preferred where available and that a result falling just above a clinical threshold, where the small negative bias could mislead, is confirmed by the reference method.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from every participant.

Conflict of interest

The authors declare that no conflict of interest exists in relation to this work.

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Data availability

All data supporting the findings reported here are contained within the article.

References

Bland, J.M. and Altman, D.G. (1986). Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*, 1(8476): 307-10.

Bwana, P., Ageng'o, J. and Mwau, M. (2018). Performance and usability of the Visitect CD4 semiquantitative point-of-care test in Kenya. *PLoS One*, 13(11): e0207977.

Cassim, N., Coetzee, L.M., Kalk, E. and Glencross, D.K. (2021). Timely delivery of CD4 results supports linkage to HIV care: A comparison of laboratory and point-of-care approaches. *Afr J Lab Med*, 10(1): a1315.

Coetzee, L.M., Cassim, N. and Glencross, D.K. (2016). Analytical performance of the Becton Dickinson FACSPresto near-patient CD4 instrument in a laboratory and typical field clinic setting in South Africa. *PLoS One*, 11(6): e0156266.

Drain, P.K., Hyle, E.P., Noubary, F., Freedberg, K.A., Wilson, D., Bishai, W.R. *et al.* (2014). Diagnostic point-of-care tests in resource-limited settings. *Lancet Infect Dis*, 14(3): 239-49.

Fajardo, E., Metcalf, C.A., Chaillet, P., Aleixo, L., Pannus, P., Panunzi, I. *et al.* (2014). Prospective evaluation of diagnostic accuracy of dried blood spots from finger prick for point-of-care CD4. *J Clin Microbiol*, 52(11): 3899-905.

Ford, N., Meintjes, G., Vitoria, M., Greene, G. and Chiller, T. (2017). The evolving role of CD4 cell counts in HIV care. *Curr Opin HIV AIDS*, 12(2): 123-8.

Giavarina, D. (2015). Understanding bland altman analysis. *Biochem Med (Zagreb)*, 25(2): 141-51.

Jani, I.V., Sitoe, N.E., Chongo, P.L., Alfai, E.R., Quevedo, J.I., Tobaiwa, O. *et al.* (2011). Accurate CD4 T-cell enumeration and antiretroviral drug toxicity monitoring in primary healthcare clinics using point-of-care testing. *AIDS*, 25(6): 807-12.

Lin, L.I. (1989). A concordance correlation coefficient to evaluate reproducibility. *Biometrics*, 45(1): 255-68.

Mwau, M., Adungo, F., Kadima, S., Njagi, E., Kirwaye, C., Abubakr, N.S. *et al.* (2013). Evaluation of PIMA point of care technology for CD4 T cell enumeration in Kenya. *PLoS One*, 8(6): e67612.

Peeling, R.W., Sollis, K.A., Glover, S., Crowe, S.M., Landay, A.L., Cheng, B. *et al.* (2015). CD4 enumeration technologies: A systematic review of test performance for developing world settings. *PLoS One*, 10(3): e0115019.

Reid, A., Dhairyawan, R., Devan, D., Wandeler, G. and Ford, N. (2020). The role of point-of-care CD4 testing in the era of universal antiretroviral therapy: A re-evaluation. *Afr J Lab Med*, 9(1): a1088.

Scott, L.E., Campbell, J., Westerman, L., Kestens, L., Vanham, G., Peter, T. *et al.* (2015). A meta-analysis of the performance of the PIMA CD4 for point of care testing. *BMC Med*, 13: 168.

Vandenbroucke, J.P., von Elm, E., Altman, D.G., Gotzsche, P.C., Mulrow, C.D., Pocock, S.J. *et al.* (2007). Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and elaboration. *PLoS Med*, 4(10): e297.

Vojnov, L., Markby, J., Boeke, C., Harris, L., Ford, N. and Peter, T. (2016). POC CD4 testing improves linkage to HIV care and timeliness of ART initiation in a public health approach: A systematic review and meta-analysis. *PLoS One*, 11(5): e0155256.

World Health Organization. (2017). WHO guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. WHO, Geneva.

World Health Organization. (2021). Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: Recommendations for a public health approach. WHO, Geneva.

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