Contents lists available at ScienceDirect

# EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Commentary

# Pre-treatment HIV drug resistance testing cost-effectiveness

David AMC van de Vijver[a], Brooke E Nichols[b,c,*]

[a] Department of Viroscience, Erasmus Medical Center, Rotterdam, the Netherlands
[b] Department of Global Health, Boston University School of Public Health, Boston, United States
[c] Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

HIV drug resistance testing before initiation of antiretroviral treatment has been demonstrated to have clinical benefits in epidemiological studies across sub-Saharan Africa [1–3]. The largest epidemiological study on antiretroviral drug resistance in Africa was the PharmAccess African Studies to Evaluate Resistance Monitoring (PASER-M) which included 2579 individuals between 2007 and 2009 from six African countries [1,2]. PASER-M found that, compared to patients in whom no drug resistance was found, individuals infected with a drug resistant virus were twice as likely to experience virological failure after twelve months [1], and four times more likely to switch to a second-line regimen within three years [2]. Pre-treatment drug resistance was not associated with increased mortality or new AIDS events [2]. Although PASER-M provided important insights, more than 50% of the study participants used zidovudine or stavudine which are no longer recommended antiretroviral drugs. In this respect it is important to observe that a recent study from Kenya, in which participants used currently recommended drugs, found that guiding treatment based on drug resistance testing reduced virological failure by 1.2% and mortality by 1.8%, which was not statistically significant [3]. Patients are, however, unable to take advantage of these potential clinical benefits when a drug resistance test is not performed due to health system financial constraints.

In eClinicalMedicine, Duarte and colleagues modelled the cost-effectiveness of baseline resistance testing using two types of assays: a traditional consensus sequencing assay, and a low-cost point-mutation assay [4]. The authors concluded that pre-treatment drug resistance testing is unlikely to be cost-effective in Kenya given the current NNRTI-based first-line regimen used among women. Should Kenyan women switch to a dolutegravir-based first-line regimen in the future, pre-treatment drug resistance is even less likely to be considered cost-effective.

New antiretroviral drugs are, however, continuously being developed. In the coming years, long-acting antiretroviral drugs can become available which allow less frequent dosing and thereby reducing the burden of daily therapy. Of the long-acting formulations that are currently being developed, the two-drug injectable combination of cabotegravir and rilpivirine is in the most advanced stage of development [5,6]. New modeling studies should be performed in the future to assess the cost-effectiveness of pre-treatment drug resistance when long-acting antiretroviral drugs become available.

Even if new regimens and ART formulations become available, there may be other nuanced effects of implementing pre-treatment resistance testing, regardless of current or future regimen type. In particular, same-day ART initiation has become widely recommended to the majority of patients with a newly confirmed HIV diagnosis. Same-day ART initiation has been shown to increase uptake of ART by up to 36% [7,8]. Therefore, a delay in ART initiation due to waiting of results from a pre-treatment drug resistance results could result in a decrease in the proportion of people initiating ART, further hampering epidemic control.

Duarte and colleagues addressed HIV drug resistance as part of clinical care. HIV drug resistance testing, however, is also used for surveillance purposes in which the occurrence of resistance associated mutations is studied in a sample of people living with HIV that initiate treatment or who showed virological failure while on antiretroviral therapy. These surveillance programs allow the timely identification of wide-spread transmission and emergence of drug resistance which in turn could necessitate a change in treatment [6]. As a consequence, surveillance programs using drug resistance testing should be continued as part of public health programs.

The study by Duarte and colleagues further adds to the body of evidence that, given the regimens available now and the current rates of transmitted drug resistance, pre-treatment drug resistances testing is unlikely to be cost-effective. Resources should instead continue to focus on consistent annual viral load monitoring and a timely switch to second-line regimen if required.

## Declaration of Competing Interest

# References

[1] Hamers RL, Schuurman R, Sigaloff KC, Wallis CL, Kityo C, Siwale M, et al. Effect of pretreatment HIV-1 drug resistance on immunological, virological, and drug-resistance outcomes of first-line antiretroviral treatment in sub-Saharan Africa: a multicentre cohort study. Lancet Infect Dis 2012;12(4):307–17.

[2] Boender TS, Hoenderboom BM, Sigaloff KCE, Hamers RL, Wellington M, Shamu T, et al. Pretreatment HIV Drug Resistance Increases Regimen Switches in Sub-Saharan Africa. Clin Infect Dis 2015;61(11):1749–58.

[3] Chung MH, McGrath CJ, Beck IA, Levine M, Milne RS, So I, et al. Evaluation of the management of pretreatment HIV drug resistance by oligonucleotide ligation assay: a randomised controlled trial. Lancet HIV 2020;7(4):e104–12.

[4] Duarte HC, Babigumira JB, Enns EA, et al. Cost-effectiveness analysis of pre-ART HIV drug resistance testing in Kenyan women. EClinicalMedicine 2020. doi: 10.1016/j. eclinm.2020.100355.

[5] Orkin C, Arasteh K, Hernández-Mora MG, Pokrovsky V, Overton ET, Girard P-M, et al. Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection. N Engl J Med 2020;382(12):1124–35.

[6] Swindells S, Andrade-Villanueva J-F, Richmond GJ, Rizzardini G, Baumgarten A, Masiá M, et al. Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression. N Engl J Med 2020;382(12):1112–23.

[7] Rosen S, Maskew M, Larson BA, Brennan AT, Tsikhutsu I, Fox MP, et al. Simplified clinical algorithm for identifying patients eligible for same-day HIV treatment initiation (SLATE): results from an individually randomized trial in South Africa and Kenya. PLoS Med 2019;16(9):e1002912.

[8] Rosen S, Maskew M, Fox MP, Nyoni C, Mongwenyana C, Malete G, et al. Initiating antiretroviral therapy for HIV at a patient's first clinic visit: the RapIT randomized controlled trial. PLoS Med 2016;13(5):e1002015.