The Feasibility of Using Screening Criteria to Reduce Clinic Visits for Stable Patients on Antiretroviral Therapy in South Africa

William B. MacLeod, ScD,* †‡ Mhairi Maskew, MBCh, MSc (Med), Dip HIV Man,*
Imogen A. Jaffray, RN, RM,§ A. Patrick MacPhail, MBCh, PhD,§|| Prudence D. Ive, MBCH, FCP(SA),
DTM&H, Dip HIV Man (SA),|| and Matthew P. Fox, DSc, MPH*†¶

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From the *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; †Center for Global Health and Development, Boston University, Boston, MA; ‡Department of International Health, Boston University School of Public Health, Boston, MA; §Right to AU3 Care, Johannesburg, South Africa; ||Clinical HIV Research Unit, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; and ¶Department of Epidemiology, Boston University School of Public Health, Boston, MA.

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Correspondence to: William B. MacLeod, ScD, Center for Global Health and Development, Boston University, 801 Massachusetts Avenue, CT3, Boston, MA 02118 (e-mail: wmacleod@bu.edu).

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INTRODUCTION

Since April 2010, the South African government has made changes to its antiretroviral therapy (ART) treatment program—expanding HIV counseling and testing and raising the CD4 cell count threshold for ART initiation—that have increased by 50% the patients eligible for ART.1–3 By 2016, the number of patients receiving ART therapy is projected to be 3.5 million,4 a challenge to the limited human resources and health service capacity and one which could overburden clinic staff currently working at capacity.5

In response, the South African government is looking at new ways of managing ART patients.6 The primary proposed strategy has been one of accreditation of PHC facilities and “task-shifting”: specifically, nurse initiated and managed ART care.7–10 A complimentary approach for reducing the burden on health facilities is the identification of stable patients presenting for medical visits who may be well enough that a full clinical consultation (either by a doctor or a nurse initiated and managed ART care–trained nurse) is unnecessary.6 Patients

and normal laboratory results for hemoglobin, alanine aminotransferase, and creatinine clearance.

Methods: We assessed the sensitivity and specificity of nonstable visits at predicting indicators of disease progression or needing additional care: (1) ART regimen change and (2) follow-up visits in <2 and <4 weeks from previous visit.

Results: Stable visits had a sensitivity of 88.9% (95% confidence interval: 88.2 to 89.7) and a specificity of 44.8% (44.5 to 44.1) at predicting ART therapy changes, and a sensitivity of 72.6% (71.8 to 73.4) and specificity of 45.1% (44.8 to 45.4) for predicting a follow-up visit interval of <2 weeks and similar results for predicting a follow-up visit interval of <4 weeks.

Conclusions: Our retrospective analysis suggests an approach to potentially reduce the number of medical visits while missing few visits in which changes in regimen or additional care would be needed. Evaluation of our criteria in a primary care setting is needed to determine whether they could safely reduce visits.

Key Words: HIV/AIDS, clinic management, stable patients, South Africa, antiretroviral therapy

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identified as stable by a screening tool would have a visit limited to monitoring tests and collecting ARVs. Successful screening for stable patients has the potential to target clinician visits to those most in need and reduce time patients spend in the clinic. To evaluate the feasibility and safety of using such a strategy, we set out to determine the likely reduction in medical visits and the ability of a screening tool to correctly identify “stable patients” at a large urban public-sector clinic in Johannesburg, South Africa.

METHODS

Themba Lethu is a high volume ART clinic in Johannesburg, South Africa, which has been described in detail elsewhere. During the 2009–2010 calendar years, over 13,000 patients were actively receiving ART: an average of 176 medical visits per day (increasing from 40,537 in 2009 to 47,467 in 2010).

The study population consisted of all “on-ART” patient clinic visits between January 1, 2007 and September 7, 2011. We excluded visits in the first 6 months on ART, as we deemed patients should always be seen by a doctor during early ART. Laboratory results (CD4 count, viral load, alanine aminotransferase, creatinine clearance, and hemoglobin), clinical observations recorded during a visit (weight, pregnancy status, and comorbid conditions), and pharmacy records are captured and stored in an electronic patient record, TherapyEdge-HIV. Current South African Treatment guidelines recommend CD4 count and viral load testing during clinical visits, once in the first 6 months and annually thereafter. We defined a “stable patient” by asking HIV clinicians to identify a set of criteria that would cause concern if identified at a clinical visit. Many of these criteria are used to define treatment failure (or nonresponsiveness to treatment), change in World Health Organization (WHO) stage, or identify drug side effects and/or toxicity. Based on these recommendations, we defined a medical visit to be “stable” if the following criteria are met:

- On ART for ≥6 months
- Most recent CD4+ value >75% of previous CD4+ measurement (if absolute CD4+ value <200 cells/mm³ in the presence of a HIV viral load ≥400 copies/mL) within 12 months (within 6 months for patients with <12 months on ART)
- Most recent HIV viral load (<400 copies/mL) within 12 months (within 6 months for patients with <12 months on ART)
- Weight change ≤5% since previous medical visit (within 6 months for all patients) (Weight gain per se is not a concern, but rapid weight gain since the previous visit could be an indicator of a drug side effect such as hyperlactaemia.)
- Not pregnant
- No comorbid conditions
- On current ART regimen ≥3 months
- No laboratory values indicating a possible side effect or adverse event:
  - Haemoglobin <8 g/dL (on zidovudine)
  - Alanine aminotransferase >100 U/L (on nevirapine)
  - Creatinine clearance <50 mL/min (on tenofovir)

Nonstable patient visits are defined as the opposite of stable patient visits. Because in our data set, the standard of care is for all patients to see a doctor at each visit, to assess the ability of our definition to identify patients who did not need to be seen by a clinician, we compared our definition of a nonstable patient visit against 3 measures of doctor behavior that likely indicated a need to see a clinician: (1) change in antiretroviral regimen at the current visit, (2) follow-up medical visit that occurs in less than 14 or 28 days from the current visit, and (3) composite measures combining both. We calculated sensitivities, specificities, and positive predictive values (PPV) and negative predictive values (NPVs), and exact 95% confidence interval (CI) comparing nonstable visits to the “gold standard” of the doctor behavior. The ethics committees of the University of the Witwatersrand and Boston University approved the study.

RESULTS

A total of 14,054 patients were on ART for at least 6 months between January 1, 2007 and September 7, 2011. These patients had 139,685 medical visits for an average of 9.9 medical visits (range, 1–46). Of these, 46,532 (33.3%) were defined as stable. Nearly 75% (10,458/14,054) of patients had at least one stable patient visit. Patients with one or more stable visits were more likely to be female, have been on ART for more than double the time, and had a higher WHO stage at initiation as compared with subjects with no stable visits (Table 1).

Detectable viral load (26.8%), gain or loss in weight greater than 5% (18.6%), CD4+ decline (12.9%), comorbid conditions (11.3%) and ARV therapy change in the past 3 months (9.3%) were the most common reasons for not being stable (Table 2). The most common 10 comorbid conditions were lipodystrophy, polynuropathy, hyperlactaemia, hyperlipidaemia, hypertension, acute upper respiratory tract infection, diarrhoea, urinary tract infection, anogenital warts, and rash. These conditions comprised >50% of all the conditions reported. Pregnancies (2.1%) were less common and abnormal laboratory values (0.1%) were rare. For individual criteria predicting an ARV change at a visit, sensitivity ranged from 0.7% to 73.9% and specificity ranged from 73.5% to 99.9%. When meeting any one of these, individual criteria were considered nonstable, 56.9% of all visits would be defined as nonstable, and the sensitivity of a nonstable visit predicting ARV change during a medical visit is 88.9% (95% CI: 88.2% to 89.7%), the specificity is 44.8% (44.5% to 45.1%), the PPV is 8.1 (95% CI: 7.9 to 8.3), and the NPV is 98.7 (98.6 to 98.8).

Table 2 compares different “gold standards” to a nonstable visit. The first 2 standards measure time to the next visit (<28 days and <14 days). Sensitivity ranged from 72.6% to 75.6% and specificity ranged from 43.9% to 45.1% for nonstable visit criteria predicting a shorter than expected interval between medical visits. When combining change in ART regimen and a shorter than expected interval between visits, sensitivity ranged from 77.6% to 84.6%, specificity ranged from 45.2% to 46.1%, PPV ranged from 3.3% to 17.4%, and NPV ranged from 93.4% to 97.4%.

We explored 2 additional criteria for identifying nonstable visits by substituting these criteria for the CD4 decline

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criteria as the definition of this criterion was most discussed by our team of doctors. The first was defined as CD4+ count within 12 months less than previous CD4+ count. This criterion identified 35.4% of the patient visits as being nonstable. The criteria had a higher specificity, 91.5 (95% CI: 90.8 to 92.1), but lower sensitivity 34.7 (34.4 to 34.9) than our preferred criteria presented in Table 2.

The second is called CD4% decline and is defined as a CD4% drop ≥5% from the previous visit or an overall CD4% less than 14%. The CD4% criterion showed very similar results to the CD4 decline criterion [sensitivity, 89.6 (88.8 to 90.3) and specificity, 36.0 (35.7 to 36.3)].

**DISCUSSION**

In this study, we defined and modeled a set of criteria that we applied to retrospective data for ART patients on treatment for at least 6 months to determine whether they needed a clinician visit. We tested these criteria against doctor behavior in the clinic as measured by ART regimen change at the medical visit and the interval between medical visits. The criteria selected to identify stable patients are used to define treatment failure in studies, national treatment guidelines, WHO stage, and drug side effects and toxicities.11–13 Some were also chosen on the basis of good clinical practice: seeing pregnant patients to determine if a regimen needs to be changed, monitoring newly initiated ARV patients closely during the first 6 months, and closely monitoring patients whose treatment regimen recently changed.

The limited set of clinical and laboratory signs that defined nonstable patients showed high sensitivity (ranging from 72.6% to 88.9%) and low specificity (ranging from 43.9% to 46.1%). The high sensitivity indicates that use of these criteria would likely miss a small proportion of patients who needed a clinical visit, but the moderate specificity results in a limited effect on reducing the number of clinical visits.
visits. Nonetheless, even the lowest specificity of 43.9% would result in a reduction of >40% of the clinical visits at this clinic, approximately 14,000 per year—a significant reduction in clinic congestion. PPV values were low, but NPV values were high meaning that the criteria captured only a small percentage of false negatives.

The most common reasons for being classified as “nonstable” were a detectable viral load, declining CD4+ count, and weight change >5% since the last recorded weight. These 3 criteria likely overstate nonstable visits as missing, and out-of-date test data would trigger a visit. Six percent of the visits were accompanied by CD4 tests that were too old and for 2.8% of visits only one CD4 test was available, so a difference could not be evaluated. For 6.8% of visits, a viral load test was out of date. Only 2% of visits had an out-of-date or missing weight value. Overclassifying patients as nonstable will reduce the efficiency of this approach but should increase sensitivity and miss fewer patients who should see a clinician. The data we used to determine a stable-patient visit was collected prospectively by nurses and doctors at a full clinic visit. In the actual application, all of the information for the determination of a stable patient would have to be collected during a preclinical interview and review of test results. We conducted this study at a large well-run ARV clinic with regular laboratory testing. High-quality care at this clinic has ensured a stable-patient population that return for regular appointments. The applicability of these criteria in less-resourced ARV clinics is unknown, as many lack the resources to conduct regular laboratory testing and patient populations may be less stable. An additional criterion to be considered is the minimum visit full schedule for patients that are always stable. Including this a criterion will reduce resources to conduct regular laboratory testing and patient appointments.

We modeled criteria to identify stable patients with the potential of reducing total doctor visits by >40%. Our retrospective analysis suggests an approach to reduce the number of doctor visits while missing few visits in which changes in regimen or additional care would be needed. Implementation of these criteria in a primary care setting

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is needed to determine the extent to which the criteria could reduce visits without compromising safety or increasing loss to follow-up.

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REFERENCES