Published in final edited form as:
J Acquir Immune Defic Syndr. 2013 March 1; 62(3): e82–e86. doi:10.1097/QAI.0b013e318278e976.

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

William B. MACLEOD[1,2,3,¶], **Mhairi MASKEW**[1], **Imogen JAFFRAY**[4], **A. Patrick MACPHAIL**[4,5], **Prudence IVE**[5], and **Matthew P. FOX**[1,2,6]

[1]Health Economics and Epidemiology Research Office, Department of Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

[2]Center for Global Health and Development, Boston University, Boston, MA, USA

[3]Department of International Health, Boston University School of Public Health, Boston, MA, USA

[4]Right to Care, Johannesburg, South Africa

[5]Clinical HIV Research Unit, Department of Medicine, University of the Witwatersrand, Johannesburg, South Africa

[6]Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA

Abstract

Objective—South African HIV care providers are exploring ways to reduce the intensity of patient visits while maintaining high quality of care. We used routinely collected data to model whether a simple screening tool could identify stable patients who would not need to see a doctor during a scheduled medical visit.

Design—We identified stable and non-stable visits from January 2007 to September 2011 at a large HIV clinic in Johannesburg, SA. Stable medical visits were defined as having all of the following: stable CD4 count, undetectable viral load, stable weight, not pregnant, no comorbidity, no regimen change within three months, and normal lab results for hemoglobin, ALT, and creatinine clearance.

Methods—We assessed the sensitivity and specificity of non-stable visits at predicting indicators of disease progression or needing additional care: a) ART regimen change; and b) follow-up visits in <2 and <4 weeks from previous visit.

Results—Stable visits had a sensitivity of 88.9% (95% CI 88.2–89.7) and a specificity of 44.8% (44.5–44.1) at predicting ART therapy changes, and a sensitivity of 72.6% (71.8–73.4) and specificity of 45.1% (44.8–45.4) 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

Corresponding Author Details: William B. MacLeod, Center for Global Health and Development, Boston University, 801 Massachusetts Avenue, CT3, Boston, MA 02118, USA, Phone: +1-617-414-1260, Fax: +1-617-414-1261, wmacleod@bu.edu.

Data will be presented at (CROI 2012) and published as abstract in Proceedings from the CROI. Seattle, Washington; 2012.

Designed study: MM APM WBM MPF IJ PI. Analyzed data: WBM MPF MM. Wrote first draft of paper: WBM MM MPF. Wrote paper: WBM MM IJ APM PI MPF.

needed. Evaluation of our criteria in a primary care setting is needed to determine whether they could safely reduce visits.

Introduction

Since April 2010 the South African government has made changes to its 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 (NIMART).(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 NIMART trained nurse) is unnecessary.(6) Patients 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 employing such a strategy, we set out to determine the likely reduction in medical visits and 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. (11) 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, ALT, creatinine clearance and hemoglobin), clinical observations recorded during a visit (weight, pregnancy status, co-morbid 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 six months and annually thereafter. (3)

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 non-responsiveness to treatment), change in WHO stage, or identify drug side effects and/or toxicity. (12–14)

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/mm^3 in the presence of a HIV viral load ≥400 copies/ml) within 12 months (within 6 months for patients with less than 12 months on ART)

- Most recent HIV viral load (<400 copies/ml) within 12 months (within 6 months for patients with less than 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 hyperlactaetemia.)
- Not pregnant
- No comorbid conditions
- On current ART regimen ≥3 months
- No lab values indicating a possible side effect or adverse event:
  - Haemoglobin <8g/dl (on zidovudine)
  - ALT >100 (on nevirapine)
  - Creatinine clearance <50ml/min (on tenofovir)

Non-stable patient visits are defined as the opposite of stable patient visits.

Since, in our dataset the standard of care is for all patients to see a doctor at each visit, in order 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 non-stable 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 (PPV) and negative (NPV) predictive values, and exact 95% CI comparing non-stable 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–September 7, 2011. These patients had 139,685 medical visits for an average of 9.9 medical visits (range 1–46). 46,532 (33.3%) of these 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 to 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%), co-morbid 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, polyneuropathy, hyperlactaetemia, hyperlipidaemia, hypertension, acute upper respiratory tract infection, diarrhoea, urinary tract infection, anogenital warts, and rash. These conditions comprised over 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 are considered non-stable, 56.9% of all visits would be defined as non-stable and the sensitivity of a non-stable visit predicting ARV change during a medical

visit is 88.9% (95% CI: 88.2–89.7%), the specificity is 44.8% (44.5–45.1%), the PPV is 8.1 95% CI: 7.9–8.3) and the NPV is 98.7 (98.6–98.8).

Table 2 compares different "gold standards" to a non-stable visit. The first two 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 non-stable 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 3.3–17.4%, and NPV ranged from 93.4 to 97.4%.

We explored two additional criteria for identifying non-stable visits by substituting these criteria for the CD4 decline criteria as the definition of this criterion was most discussed by out team of doctors. The first was defined as CD4+ count within 12 months < then previous CD4+count. This criterion identified 35.4% of the patient visits as being non-stable. The criteria had a higher specificity, 91.5 (95% CI: (90.8 – 92.1)), but lower sensitivity 34.7 (34.4 – 34.9) than our preferred criteria presented in Table 2.

The second is called CD4% decline and is defined as a CD4% drop greater than 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 (88.8–90.3) and specificity 36.0 (35.7–36.3).

Discussion

In this study we defined and modeled a set of criteria that we applied to retrospective data for ART patients on treatment 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 non-stable 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. Nonetheless, even the lowest specificity of 43.9% would result in a reduction of over 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 "non-stable" were a detectable viral load, declining CD4+ count, and weight change more than 5% since the last recorded weight. These three criteria likely overstate non-stable 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 couldn't 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. Over-classifying patients as non-stable 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 pre-clinical 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 the specificity of any criterion. Strengths of the study include the large number of visits that we were able to include in our model using a comprehensive clinical database.

We modeled criteria to identify stable patients with the potential of reducing total doctor visits by over 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 this criteria in a primary care setting is needed to determine the extent to which the criteria could reduce visits without compromising safety or increasing loss to follow-up.

Acknowledgments

Funding for this study was provided by the South Africa Mission of the US Agency for International Development (USAID) under the terms of Cooperative Agreement 674-A-00-09-00018-00 to Boston University (WBM) and Cooperative Agreement 674-A-00-02-00018 to Right to Care (MM, APM, IJ, IS) and by Award Number K01AI083097 from the National Institute of Allergy and Infectious Diseases (NIAID) (MPF time). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The opinions expressed herein are those of the authors and do not necessarily reflect the views of the funders or the study site.

We thank the staff of the study Themba Lethu Clinic, who helped us to collect and interpret the data, and the Gauteng Department of Health for the participation of its clinic.

References

1. WHO, UNAIDS, UNICEF. Towards universal access: Scaling up priority HIV/AIDS interventions in the health sector--Progress Report 2010. Geneva: 2010.
2. South African National AIDS Council. National Strategic Plan on HIV, STIs, and TB: 2012–2016. 2011.
3. South African National Department of Health. The South African Antiretroviral Treatment Guidelines 2010. 2010.
4. Meyer-Rath, G.; Pillay, Y.; Blecher, M.; Brennan, A.; Long, L.; Johnson, L.; Moultrie, H.; Sanne, I.; Fox, M.; Rosen, S. Total cost and potential cost savings of the national antiretroviral treatment (ART) programme in South Africa 2010 to 2017. XVIII International AIDS Conference; Vienna. 2010.
5. Treatment Action Campaign. Time for task-shifting: 999 days to close the HIV/AIDS treatment gap [Internet]. Treament Action Campaign Website. 2011. [cited 2011 Oct 28] Available from: http://www.tac.org.za/community/node/2529
6. Harries AD, Zachariah R, Lawn SD, Rosen S. Strategies to improve patient retention on antiretroviral therapy in sub-Saharan Africa. Tropical medicine & international health: TM & IH. 2010 Jun; 15(Suppl 1)(june):70–5. [PubMed: 20586963]
7. Colvin CJ, Fairall L, Lewin S, Georgeu D, Zwarenstein M, Bachmann MO, Uebel KE, Bateman ED. Expanding access to ART in South Africa: The role of nurse- initiated treatment. South African

medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 2010 Apr; 100(4):210–2. [PubMed: 20459957]

8. Sanne I, Orrell C, Fox MP, Conradie F, Ive P, Zeinecker J, Cornell M, Heiberg C, Ingram C, Panchia R, Rassool M, Gonin R, Stevens W, Truter H, Dehlinger M, van der Horst C, McIntyre J, Wood R. Nurse versus doctor management of HIV-infected patients receiving antiretroviral therapy (CIPRA-SA): a randomised non-inferiority trial. Lancet. 2010 Jul; 376(9734):33–40. [PubMed: 20557927]
9. Long L, Brennan A, Fox MP, Ndibongo B, Jaffray I, Sanne I, Rosen S. Treatment Outcomes and Cost-Effectiveness of Shifting Management of Stable ART Patients to Nurses in South Africa: An Observational Cohort. PLoS Medicine. 2011 Jul.8(7):e1001055. [PubMed: 21811402]
10. Callaghan M, Ford N, Schneider H. A systematic review of task- shifting for HIV treatment and care in Africa Review. Human Resources for Health. 2010
11. Fox MP, Maskew M, Macphaila P, Long L, Brennan AT, Westreich D, Macleod WB, Majuba P, Sanne IM. Cohort Profile: The Themba Lethu Clinical Cohort, Johannesburg, South Africa. International journal of epidemiology. 2012 Mar.:6–8.
12. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. 1992.
13. WHO. WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva: 2007.
14. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. 2011.

Table 1

Clinical and demographic parameters of subjects by stable patient visit status

Parameter of Individual Patients	Had at least 1 stable patient visit	Had no stable patient visit	All Subjects
Male %, (n/N)	33.9% (3,543/10,458)	35.9% (1,272/3,596)	34.3% (4,815/14,054)
Mean Age at ART Initiation in Years, (SE)	37.3 (0.08)	37.2 (0.15)	37.2 (0.07)
Mean Time on ART in Days, (SE)	1366 (6.47)	670.8 (8.00)	1,188 (5.82)
Mean CD4 at Initiation (SE)	132.1 (7.00)	139.5 (2.46)	133.7 (5.45)
WHO Stage at ART Initiation			
WHO Stage I %, (n/N)	34.0% (3,574/10,458)	23.2% (823/3,596)	31.3% (4,397/14,054)
WHO Stage II %, (n/N)	14.0% (1,465/10,458)	15.9% (564/3,596)	14.5% (2,038/14,054)
WHO Stage III %, (n/N)	23.3% (2,441/10,458)	18.0% (636/3,596)	22.0% (3,089/14,054)
WHO Stage IV %, (n/N)	7.5% (783/10,458)	8.6% (303/3,596)	7.7% (1,088/14,054)
WHO Stage Missing % (n/N)	21.2% (2,218/10,458)	34.3% (1,215/3,596)	24.5% (3,442/14,054)
Total Number of Medical Visits per Subject			
Mean Number of Well Visits, (SE)	4.5 (0.03)	0.0 (0.00)	3.4 (0.03)
Mean Number of Visits, (SE)	11.8 (0.07)	4.6 (0.08)	9.9 (0.06)

Years on ART Completed for All Patient Medical Visits	Stable Patient Visit % (n)	Not Stable Patient Visit % (n)	
0.5–0.99	26.4% (2,439)	73.6% (6,795)	6.6% (9,234)
1–1.99	30.2% (5,404)	69.8% (12,504)	12.8% (17,908)
2–2.99	33.3% (7,836)	66.7% (15,670)	16.8% (23,506)
3–3.99	35.1% (7,894)	64.9% (14,579)	16.1% (22,473)
4–4.99	34.5% (9,656)	65.5% (18,293)	20.0% (27,949)
5–5.99	34.6% (7,369)	65.4% (13,940)	15.3% (21,309)
6–6.99	34.3% (5,934)	65.7% (11,361)	12.4% (17,295)
Total	33.3% (46,532)	66.7% (93,142)	100.0% (139,674)

Table 2

Frequency, prevalence, sensitivity, specificity, PPV and NPV for predicting doctor behavior by individual and combined criteria for non-stable patients

Gold Standard	Predictor	Predictor Statistics					
		Frequency	Prevalence, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Individual Criterion of Non-Stable Visits							
ARV Change	Detectable Viral Load	37,380	26.8 (26.5 – 27.0)	31.1 (30.0 – 32.1)	73.5 (73.2 – 73.7)	6 (5.8 – 6.3)	95.1 (95 – 95.3)
ARV Change	Weight change > 5% from previous visit	25,914	18.6 (18.3 – 18.8)	22.8 (21.8 – 23.8)	81.7 (81.5 – 81.9)	6.4 (6.1 – 6.7)	95.1 (95 – 95.2)
ARV Change	Declining CD4+ count or low CD4+ count combined with undetectable viral load	18,061	12.9 (12.8 – 13.1)	13.3 (12.5 – 14.1)	87.1 (86.9 – 87.3)	5.3 (5 – 5.6)	94.8 (94.7 – 95)
ARV Change	Comorbid Condition	15,831	11.3 (11.2 – 11.5)	73.9 (72.9 – 74.9)	92.1 (91.9 – 92.2)	33.7 (33 – 34.5)	98.5 (98.4 – 98.5)
ARV Change	Recent Regimen Change (< 3 months)	12,939	9.3 (9.1 – 9.4)	4.4 (3.9 – 4.9)	90.5 (90.3 – 90.6)	2.4 (2.2 – 2.7)	94.5 (94.4 – 94.7)
ARV Change	Currently Pregnant	3,003	2.1 (2.1 – 2.2)	4.0 (3.6 – 4.5)	98.0(97.9 – 98.0)	9.7 (8.7 – 10.8)	94.9 (94.8 – 95)
ARV Change	ART Problem	167	0.1 (0.1 - 0.1)	0.7 (0.5 – 0.9)	99.9 (99.9 - 99.9)	29.9 (23.1 – 37.5)	94.9 (94.7 – 95)
Combined Criteria of Non-Stable Visits							
ARV Change	Patient Not Stable	79,540	56.9 (56.7 – 57.2)	88.9 (88.2 – 89.7)	44.8 (44.5 – 45.1)	8.1 (7.9 – 8.3)	98.7 (98.6 – 98.8)
Visit Less than 28 days	Patient Not Stable	71,104	56.6 (56.3 – 56.9)	72.6 (71.8 – 73.4)	45.1 (44.8 – 45.4)	12.1 (11.9 – 12.3)	94.0 (93.8 – 94.2)
Visit Less than 14 days	Patient Not Stable	71,104	56.6 (56.3 – 56.9)	75.6 (74.0– 77.1)	43.9 (43.6– 44.2)	3.3 (3.2 – 3.4)	98.6 (98.5 – 98.7)
ARV Change or Visit Less than 28 days	Patient Not Stable	79,540	56.9 (56.7 – 57.2)	77.6 (77 – 78.2)	46.1 (45.8 – 46.4)	17.4 (17.1 – 17.6)	93.4 (93.2 – 93.6)
ARV Change or Visit Less than 14 days	Patient Not Stable	79,540	56.9 (56.7 – 57.2)	84.6 (83.9 – 85.3)	45.2 (44.9 – 45.5)	10.7 (10.5 – 10.9)	97.4 (97.3 – 97.6)