Published in final edited form as:
*AIDS Behav*. 2013 July ; 17(6): 2253–2259. doi:10.1007/s10461-013-0436-x.

# Pharmacy and self-report adherence measures to predict virological outcomes for patients on free antiretroviral therapy in Tamil Nadu, India

**James H. McMahon**[1,2], **Anand Manoharan**[3], **Christine A. Wanke**[2], **Shoba Mammen**[4], **Hepsibah Jose**[3], **Thabeetha Malini**[3], **Tony Kadavanu**[3], **Michael R. Jordan**[2], **Julian H. Elliott**[1,5,6], **Sharon R. Lewin**[1,5,6], and **Dilip Mathai**[3]

[1]Infectious Diseases Unit, Alfred Hospital, Melbourne, Victoria, Australia

[2]Department of Public Health and Community Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA

[3]Department of Medicine and Infectious Diseases, Christian Medical College, Vellore, Tamil Nadu, India

[4]Clinical Virology, Christian Medical College, Vellore, Tamil Nadu, India

[5]Department of Medicine, Monash University, Melbourne, Victoria, Australia

[6]Burnet Institute, Melbourne, Victoria, Australia

## Abstract

Over 480,000 individuals receive free antiretroviral therapy (ART) in India yet data associating ART adherence with HIV viral load for populations exclusively receiving free ART are not available. Additionally estimates of adherence using pharmacy data on ART pick-up are not available for any population in India. After 12-months ART we found self-reported estimates of adherence were not associated with HIV viral load. Individuals with < 100% adherence using pharmacy data predicted HIV viral load, and estimates combining pharmacy data and self-report were also predictive. Pharmacy adherence measures proved a feasible method to estimate adherence in India and appear more predictive of virological outcomes than self-report. Predictive adherence measures identified in this study warrant further investigation in populations receiving free ART in India to allow for identification of individuals at risk of virological failure and in need of adherence support.

### Keywords

HIV; adherence; antiretroviral therapy; India; virological outcomes

## Background

It is estimated that 2.4 million people are living with HIV in India with over 480,000 people receiving free National AIDS Control Organization (NACO) funded antiretroviral therapy (ART) (1) However, ART coverage remains a challenge with somewhere between 23 – 55%

**Corresponding author:** James McMahon, Infectious Diseases Unit, Alfred Hospital, Level 2 Burnet Tower, 85 Commercial Road, Melbourne, Australia 3004. Ph: +61 3 9076 9026, Fax: +61 3 9076 2431; ja.mcmahon@alfred.org.au.

**Conflicts of Interest:** SRL receives payment for lectures (Viiv Healthcare and Janssen), payment for educational presentations (Janssen) and SRL's institution receives grant funding (Merck and Gilead). All other authors, no conflicts.

of eligible patients receiving ART during 2009 (2). Furthermore a smaller group of individuals estimated to be somewhere between 6 – 25% of the population receiving ART (3) pay for these medications in the private system. Rapid scale-up of free government funded ART has occurred since 2004 yet it is recognized that nearly 20% of patients are presenting at a very late stage (CD4 count < 50) with an increased risk of mortality. NACO has responded by decentralizing ART services to the district and sub-district level in an attempt to close gaps in public health infrastructure between HIV testing and treatment programs, and non-HIV related health services (4).

Achieving optimal adherence to ART is critical to prevent treatment failure, HIV related mortality, emergence of HIV drug resistance, and preserve the efficacy of available ART (5-8). High levels of adherence have been reported in meta-analyses of studies performed in sub-Saharan Africa and understanding this success has become a focus of investigation (9, 10). Maintaining maximal adherence is particularly important in countries such as India where switching to second line ART is more costly, complex, and restricts future treatment options (11). In addition patients in India suspected of treatment failure on first-line ART are only recommended to commence second-line ART once good adherence has been ensured (12).

Multiple methods to estimate adherence to ART are available and they include: self report, pharmacy adherence measures, electronic pill container caps (MEMS caps), measuring antiretroviral drug concentrations and web-enabled pill boxes (13) MEMS caps are considered the gold standard for estimating adherence by many authors but their use is largely confined to research settings in a similar manner to measuring drug levels or web based systems that record the opening of pill boxes (13, 14). Pharmacy adherence measures (PAMs) estimate ART adherence using pill pick-up data that is routinely recorded at pharmacies dispensing ART according to the prescription of a medical practitioner. This contrasts with the most widely utilized “over the counter” practice for delivering medication in India where pick-up data is often not available. PAMs predict virological and other clinical outcomes in high and low-middle income countries (15) (LMICs) and have been adopted by the World Health Organisation (WHO) as a standard for estimating population level adherence (16, 17). Interestingly most LMIC data originates from sub-Saharan Africa (15), with many prominent studies performed in the private health sector (7, 18, 19). Until now, no studies from India have reported PAMs and their association with virological outcomes which is notable considering the potential advantages of PAMs over self-report adherence measures (13, 15). Furthermore, only 2 cohorts in India have documented adherence to ART in association with virological outcomes with both cohorts assessing adherence by self-report. Importantly neither cohort reported on populations exclusively receiving free ART (20-23). Shah reports on patients in the private system who paid out-of-pocket for ART (21), while a Bangalore cohort document self-reported adherence predicting virological outcomes for individuals receiving free ART, or paying for ART in the private system (20, 22-24). The Bangalore cohort also documented more treatment interruptions (23) and virological failures (22) in patients paying for ART but did not document associations between adherence and virological outcomes for individuals only receiving free ART. This is an important distinction as at least 75% of individuals now receive free NACO funded ART (1, 3, 25) and ART cost has been repeatedly reported as a barrier to ART adherence in India (22, 23, 26, 27). Therefore relationships between adherence and viral load may be different from what is currently reported for most individuals receiving ART in India. In addition to ART cost other barriers to adherence have also been reported in India including: stigma, ART side effects, depression and co-morbid medical conditions (21-23, 26-29).

Therefore, our objective was to determine associations between ART adherence and HIV viral load for individuals receiving free ART within the public sector in India using both self-reported and pharmacy measures of adherence.

## Methods

### Population

The study was conducted at a NACO sponsored ART Clinic at Christian Medical College (ACTFID), Vellore, Tamil Nadu and is one of 5 sites providing free government sponsored ART in the Vellore district (population 3.5 million) The clinic is one of many public-private partnership sites in India where non-governmental and private organizations collaborate with NACO to provide free clinical care and ART services via the NACO program (12). Patients attended monthly for medical review and picked-up ART from a pharmacy staffed by a dedicated pharmacist within the clinic.. Patients did not require specific appointment times to attend the clinic which was open 6 days a week and all routine pathology including testing for CD4 T-cell counts was performed at a laboratory approximately 10 minutes walk from the clinic. At the time of the study 500 people were receiving ART and the clinic was staffed by two doctors, a social worker, pharmacist and clerical staff. The clinic was also able to manage some other medical conditions such as intercurrent respiratory or skin infections. Patients requiring hospital admission or other specialist medical care were referred to inpatient services or other outpatient clinics within Christian Medical College.

### Design

The study was a retrospective cohort of consecutive adults initiating ART and followed for 12-months. Patients were recruited from October 26, 2009, until October 10, 2010 and eligible for inclusion if initiating first line ART (12). Patients transferred in from other sites or re-initiating ART after a treatment interruption were excluded. Self-reported adherence (30, 31) and HIV viral load were determined for patients remaining in care 12-months after ART start.

### Procedures

230 consecutive initiators of ART were identified during a routine clinic visit after 11-15 months of ART. Patients were considered lost to follow-up (LTFU) at 12-months if they had not attended or picked up ART within 90 days of their last missed appointment. All baseline clinical and demographic data was abstracted from clinical records and ART dispensing data from pharmacy records.

Standardized self-report adherence measures asked about adherence since; initiating ART, or the preceding 30-days.(30) An additional 30-day self-report measure was the visual analog scale (VAS) where patients indicated on a line marked from 0% to 100% the point that best corresponded to the percentage of pills taken (31). Adherence questions were originally written in English, translated into Tamil or Telugu and independently back-translated. Questionnaires were administered in local languages by trained staff experienced in HIV counseling and treatment. ART adherence was also estimated using the medication possession ratio (MPR). This was calculated by dividing the days of ART dispensed by the period of time from ART start to the day of recruitment.. All patients completing 12-months ART provided written informed consent and the study was approved by the institutional review boards of Christian Medical College, Tufts University Health Sciences and Monash University.

### Laboratory testing

The HIV viral load test was performed at the same time as the routine assessment of CD4 T-cell counts (FACSCount) after 12-months of ART. HIV viral load was assessed by the Artus HIV-1 RT-PCR (Qiagen) with a detectable viral load defined as greater than 200 copies/mL based on viral load blips rarely being above 200 copies/mL (32)

### Analysis

Baseline characteristics and dichotomous adherence estimates after 12-months ART were compared to 12-month viral load using $\chi^2$, Fisher's exact, Student's t-test, and Wilcoxon rank-sum tests as appropriate. Odds ratios of a detectable viral load after 12-months ART were also calculated for the estimates of adherence. The 30-day self-report question was dichotomized around excellent (highest adherence category) versus less than excellent adherence, the self-report question for the entire period receiving ART was dichotomized around those reporting never having missed versus ever having missed ART and the VAS was dichotomized around 95% adherence. Dichotomous MPR estimates were created with different thresholds to define low adherence (<95%, <100%). To establish if MPR accuracy could be improved we combined the most predictive MPR measure with the 30-day and 12-month self-report questions. Individuals with low pharmacy adherence and less than excellent adherence in last 30-days, or ever reported missing ART were considered to have low adherence for this variable. Overall accuracy of adherence estimates was also assessed by calculating the area under receiver operating characteristic curves (AUROCs) and 95% confidence intervals (CIs) for continuous (MPR) or ordinal variables (self-report). 95% CIs of the AUROC that did not cross 0.5 indicated a statistically significant association. All analyses were conducted using SAS v9.2 (SAS Institute, Cary, NC).

## Results

### Baseline demographics

Baseline characteristics of 230 patients included: 65% male, 41% WHO clinical stage IV, active tuberculosis in 27%, and median CD4 141 T-cells micro/L (Table 1). After 12-months: 77% (n=177) were on ART of which 98% (n=174) undertook HIV viral load testing, 10% died, 8% transferred out, 5% were LTFU and no patients switched to second line therapy. Median CD4 T-cell count after 6 months was 309 cells/microL and after 12 months was 410 cells/microL which were both significant increases from baseline (p<.001) and 80% (n=140) of patients on treatment at 12-months had HIV viral load <200 copies/mL. There were no significant differences in baseline characteristics when stratified by viral load although a trend (p=0.08) for virological suppression was present in married individuals (Table 1).

### Adherence measures

Table 2 demonstrates associations between adherence estimates after 12-months ART and HIV viral load. All estimates of adherence solely using self-report were not associated with the virological outcome (p>.4). Furthermore AUROCs for self-report estimates demonstrated no association including: 30-day self-report 0.52 (95% CI: 0.42 – 0.61), last time missed ART 0.55 (95% CI: 0.45 – 0.65) and 30-day VAS 0.54 (95% CI: 0.44 – 0.63). The 12-month MPR with a 95% threshold was not associated with the virological outcome (OR 1.7, p=.2) but there was a significant association with the 100% threshold (OR 2.6, p=.01), although a greater number of individuals were considered to have low adherence with the 100% threshold (48.9%) compared to the 95% adherence threshold (16.7%). The MPR AUROC was 0.61 (95% CI: 0.50 – 0.72) demonstrating a statistical association albeit on the borderline of significance The variable that combined the 12-month MPR of 100% threshold

with the 2 self-report questions was associated with HIV viral load (OR 2.1, p=.05) and less patients were considered to have low adherence (35.6%) compared to the MPR with 100% threshold not combined with self-report.

## Discussion

This is the first report from India describing pharmacy adherence measures for individuals receiving ART and the first report from India documenting associations between any measure of adherence and HIV viral load for a population that has exclusively received free ART.

Importantly, and different from studies including patients who paid for ART (20, 21), we did not observe self-reported adherence predicting virological outcomes. A potential explanation is the increased likelihood of a social desirability bias (33, 34) leading to underreporting of missed doses in programs where patients receive free care compared to patients who pay for ART. Inaccurate and more socially desirable responses by individuals receiving free care may fail to detect associations between ART adherence and virological outcomes. Furthermore, objective assessments of adherence using pharmacy data were more closely associated with virological outcomes, with the 100% threshold variable significantly associated with viral load. This is notable as the 100% threshold establishes if individuals were in possession of ART for the entire 12-month period since initiation. By definition individuals with less than 100% pharmacy adherence did not have enough ART to take medication as prescribed for these first 12-months.

The 95% threshold of adherence is the most widely cited threshold to maximise virological suppression based on data from Paterson in treatment experienced patients receiving unboosted protease inhibitor based ART (35). Furthermore, attaining individual adherence above 95% is cited by NACO as one of the key goals of the national ART program (12). Subsequent studies have reported higher and lower thresholds predicting virological outcomes for populations receiving non-nucleoside reverse transcriptase inhibitor (NNRTI) based regimens in high-income and LMICs (19, 36). Therefore alternative thresholds to identify groups at risk for poor virological outcomes warrant consideration. Findings in this study suggest an MPR threshold of 100% may be more useful for defining individuals at risk of poor virological outcomes in this population. However, this threshold classifies approximately half the study population as having low adherence. The ability to target this patient group for viral load testing or adherence intervention may depend on available resources. Therefore selection of optimal adherence measures for different settings may be influenced by costs of subsequent interventions for patients with low adherence.

Combining a PAM with questions measuring self-reported adherence to more accurately identify a subpopulation at risk of a detectable viral load, in this study was above 200 copies/mL, is an innovative technique. This resulted in approximately one third of individuals defined as having low adherence yet this group was still significantly associated with the virological outcome. This finding suggests that combining different adherence measures should be further examined in populations receiving free ART in India. Replicating this technique in different settings may reinforce findings from this study and potentially identify alternate methods to accurately identify sub-populations at risk for virological failure or that require adherence support. In addition further research is necessary to identify risk factors for low adherence and virological failure for people receiving free ART in India. Barriers such as the stigma of HIV, medication side effects and depression have already been identified in studies where patients paid for ART and cost was the most commonly reported barrier (21-23, 26-29). Identifying barriers to adherence and targeting interventions to these factors is an essential step to improve virological outcomes for

individuals receiving free ART in India, in addition to identifying the best methods to estimate adherence.

Finally, immunological criteria recommended to define treatment failure in India performed poorly for predicting viral load greater than 200 copies/mL with only 9% of subjects with detectable viral load satisfying CD4 change criteria. This is consistent with other LMIC data concerning the limited ability of CD4 criteria to detect virological failure (18, 37, 38) and supports efforts to identify non-virological factors that accurately identify individuals with virological failure, including assessments of ART adherence. Failure to correctly identify individuals failing virologically that continue NNRTI containing regimens, leads to accumulation of HIV drug resistance mutations, decreased efficacy of the current regimen, potential reduction in the activity of future regimens, immunological progression and increased risk of clinical deterioration. Furthermore, individuals who satisfy CD4 change criteria but remain virologically suppressed results in unnecessary switching to expensive second line ART. Despite the limited availability of testing for HIV drug resistance in India, surveys performed on patients initiating ART in 2007 and 2008 reported 8-9% of individuals initiating ART had drug resistance detected after 12-months ART (39). These data highlight the need for accurate measures to identify individuals at risk of failing ART that can limit the development of HIV drug resistance.

Pharmacy adherence measures were established using routinely collected data in the pharmacy register. This register is essential element to establish the volume of ART stock by documenting the amount of ART dispensed, hence there is an emphasis on accurate recording of data to ensure continuous antiretroviral supply. In practical terms estimating the MPR requires a clinic staff member to tally up the days of ART dispensed and divide that by the number of days since the patient initiated ART. This adherence estimate can be easily updated at subsequent ART pick-ups and integrated into the work flow of the clinic. Furthermore, if dispensing data is recorded electronically there is the potential for pharmacy databases to automatically generate the MPR based on the dates of ART pick-up and amount of ART dispensed.

Limitations of this study include the generalisability to other people in India receiving free antiretrovirals in different settings. However, considering the paucity of data examining adherence measures and virological outcomes for those on free ART in India the findings of this study still merit consideration in alternate settings. In addition MPR estimates in this study did not account for remnant pills which may have lead to estimates of adherence with different characteristics for predicting viral load. However a recent systematic review did not find evidence that adherence estimates that included counting remaining pills were superior to MPR for predicting virological outcomes (15).Finally the findings of this study were limited by a relatively low sample size to detect significant association between the measures of adherence and virological outcomes.

## Conclusions

Pharmacy adherence measures such as the medication possession ratio are a feasible method to assess adherence within the public health model of care in India and appear more predictive of virological outcomes that commonly employed self-reported assessments of adherence. Combining the MPR with self-reported adherence is an innovative technique to further define at risk populations in this setting and warrants further investigation. As viral load testing is not currently required for monitoring ART in India and immunological criteria performed poorly for predicting HIV viral load, adherence measures such as the ones identified in this study should be further investigated to identify individuals at risk of virological failure and in need of increased adherence support.

## Acknowledgments

We thank the study participants and all staff within the NACO sponsored ART Clinic at Christian Medical College (ACTFID).

**Funding Sources:** JM was supported by a fellowship from Tufts Medical Center Department of Geographic Medicine and Infectious Diseases, and an Australian National Health and Medical Research Council (NHMRC) Postgraduate Scholarship. The study was supported by a Lifespan/Tufts/Brown Center for AIDS Research NIH grant (1P30A142853-12). AM was supported by a Fogarty International Center training grant (5D43TW000237-15). MRJ was supported by an NIH Career Development Award (5K23AI074423-04). SRL is an NHMRC Practitioner Fellow.

## References

1. NACO. National Aids Control Organisation, India HIV data. National Aids Control Organisation, India; New Delhi: Jul 12. 2012 2012Available from:http://www.nacoonline.org/Quick_Links/HIV_Data/
2. WHO. Towards universal access : scaling up priority HIV/AIDS interventions in the health sector : progress report 2010. World Health Organization; Geneva: 2010.
3. USAID. Private Sector Utilization of HIV/AIDS Services & Health Expenditures by People Living with HIV/AIDS in India: Findings from Five High-Prevalence States. Nov. 2009 2009
4. NACO. Annual Report 2011-12. Department of AIDS Control. Ministry of Health & Family Welfare. Government of India; India: 2012.
5. Nieuwkerk PT, Oort FJ. Self-reported adherence to antiretroviral therapy for HIV-1 infection and virologic treatment response: a meta-analysis. J Acquir Immune Defic Syndr. 2005; 38(4):445–8. [PubMed: 15764962]
6. Harrigan PR, Hogg RS, Dong WW, Yip B, Wynhoven B, Woodward J, et al. Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. J Infect Dis. 2005; 191(3):339–47. Epub 2005/01/06. [PubMed: 15633092]
7. Nachega JB, Hislop M, Dowdy DW, Lo M, Omer SB, Regensberg L, et al. Adherence to highly active antiretroviral therapy assessed by pharmacy claims predicts survival in HIV-infected South African adults. Journal of acquired immune deficiency syndromes (1999). 2006; 43(1):78–84. [PubMed: 16878045]
8. Chi BH, Cantrell RA, Zulu I, Mulenga LB, Levy JW, Tambatamba BC, et al. Adherence to first-line antiretroviral therapy affects non-virologic outcomes among patients on treatment for more than 12 months in Lusaka, Zambia. International Journal of Epidemiology. 2009; 38(3):746–56. [PubMed: 19223334]
9. Ware NC, Idoko J, Kaaya S, Biraro IA, Wyatt MA, Agbaji O, et al. Explaining adherence success in sub-Saharan Africa: an ethnographic study. PLoS medicine. 2009; 6(1):e11. Epub 2009/01/30. [PubMed: 19175285]
10. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, et al. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. JAMA. 2006; 296(6):679–90. Epub 2006/08/10. [PubMed: 16896111]
11. Elliott JH, Lynen L, Calmy A, De Luca A, Shafer RW, Zolfo M, et al. Rational use of antiretroviral therapy in low-income and middle-income countries: optimizing regimen sequencing and switching. AIDS. 2008; 22(16):2053–67. Epub 2008/08/30. [PubMed: 18753937]
12. NACO. Antiretroviral Therapy Guidelines for HIV-Infected Adults and Adolescents Including Post-exposure Prophylaxis. National AIDS and Control Organisation, Ministry of Health & Family Welfare, Government of India; 2007.
13. Nachega JB, Mills EJ, Schechter M. Antiretroviral therapy adherence and retention in care in middle-income and low-income countries: current status of knowledge and research priorities. Curr Opin HIV AIDS. 2010; 5(1):70–7. Epub 2010/01/05. [PubMed: 20046150]
14. van den Boogaard J, Lyimo RA, Boeree MJ, Kibiki GS, Aarnoutse RE. Electronic monitoring of treatment adherence and validation of alternative adherence measures in tuberculosis patients: a pilot study. Bull World Health Organ. 2011; 89(9):632–9. Epub 2011/09/08. [PubMed: 21897483]

15. McMahon J, Jordan M, Kelley K, Bertagnolio S, Hong S, Wanke C, et al. Pharmacy adherence measures to assess adherence to antiretroviral therapy: review of the literature and implications for treatment monitoring. Clinical Infectious Diseases. 2011; 52(4):493–506. [PubMed: 21245156]
16. Bennett DE, Bertagnolio S, Sutherland D, Gilks CF. The World Health Organization's global strategy for prevention and assessment of HIV drug resistance. Antivir Ther. 2008; 13(Suppl 2):1–13. Epub 2008/06/26. [PubMed: 18578063]
17. WHO. Meeting report on assessment of World Health Organization HIV drug resistance early warning indicators : report of the Early Advisory Indicator Panel meeting; Geneva, Switzerland. 11-12 August 2011; Aug 22. 2012 2012Available from:http://apps.who.int/iris/bitstream/10665/75186/1/9789241503945_eng.pdf
18. Bisson GP, Gross R, Bellamy S, Chittams J, Hislop M, Regensberg L, et al. Pharmacy refill adherence compared with CD4 count changes for monitoring HIV-infected adults on antiretroviral therapy. PLoS Med. 2008; 5(5):e109. Epub 2008/05/23. [PubMed: 18494555]
19. Nachega JB, Hislop M, Dowdy DW, Chaisson RE, Regensberg L, Maartens G. Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes. Annals of internal medicine. 2007; 146(8):564–73. Epub 2007/04/18. [PubMed: 17438315]
20. Ekstrand ML, Chandy S, Heylen E, Steward W, Singh G. Developing useful highly active antiretroviral therapy adherence measures for India: the Prerana study. Journal of acquired immune deficiency syndromes (1999). 2010; 53(3):415–6. Epub 2010/03/02. [PubMed: 20190588]
21. Shah B, Walshe L, Saple DG, Mehta SH, Ramnani JP, Kharkar RD, et al. Adherence to antiretroviral therapy and virologic suppression among HIV-infected persons receiving care in private clinics in Mumbai, India. Clin Infect Dis. 2007; 44(9):1235–44. [PubMed: 17407045]
22. Shet A, DeCosta A, Heylen E, Shastri S, Chandy S, Ekstrand M. High rates of adherence and treatment success in a public and public-private HIV clinic in India: potential benefits of standardized national care delivery systems. BMC Health Serv Res. 2011; 11:277. Epub 2011/10/19. [PubMed: 22004573]
23. Vallabhaneni S, Chandy S, Heylen E, Ekstrand M. Reasons for and correlates of antiretroviral treatment interruptions in a cohort of patients from public and private clinics in southern India. AIDS Care. 2011 Epub 2011/11/24.
24. Ekstrand ML, Shet A, Chandy S, Singh G, Shamsundar R, Madhavan V, et al. Suboptimal adherence associated with virological failure and resistance mutations to first-line highly active antiretroviral therapy (HAART) in Bangalore, India. International health. 2011; 3(1):27–34. Epub 2011/04/26. [PubMed: 21516199]
25. Private Healthcare in Developing Countries. Jul 31. 2012 2012Available from:http://ps4h.org/hiv_aids.html
26. Kumarasamy N, Safren SA, Raminani SR, Pickard R, James R, Krishnan AK, et al. Barriers and facilitators to antiretroviral medication adherence among patients with HIV in Chennai, India: a qualitative study. AIDS patient care and STDs. 2005; 19(8):526–37. [PubMed: 16124847]
27. Wanchu A, Kaur R, Bambery P, Singh S. Adherence to generic reverse transcriptase inhibitor-based antiretroviral medication at a Tertiary Center in North India. AIDS and behavior. 2007; 11(1):99–102. [PubMed: 16607479]
28. Sarna A, Pujari S, Sengar AK, Garg R, Gupta I, Dam J. Adherence to antiretroviral therapy & its determinants amongst HIV patients in India. The Indian journal of medical research. 2008; 127(1): 28–36. [PubMed: 18316850]
29. Anuradha S, Joshi A, Negi M, Nischal N, Rajeshwari K, Dewan R. Factors Influencing Adherence to ART: New Insights from a Center Providing Free ART under the National Program in Delhi, India. J Int Assoc Physicians AIDS Care (Chic). 2012 Epub 2012/01/17.
30. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, et al. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). AIDS Care. 2000; 12(3):255–66. Epub 2000/08/06.

31. Giordano TP, Guzman D, Clark R, Charlebois ED, Bangsberg DR. Measuring adherence to antiretroviral therapy in a diverse population using a visual analogue scale. HIV clinical trials. 2004; 5(2):74–9. Epub 2004/04/30. [PubMed: 15116282]
32. Nettles RE, Kieffer TL, Kwon P, Monie D, Han Y, Parsons T, et al. Intermittent HIV-1 viremia (Blips) and drug resistance in patients receiving HAART. JAMA. 2005; 293(7):817–29. Epub 2005/02/17. [PubMed: 15713771]
33. Bangsberg DR. Preventing HIV antiretroviral resistance through better monitoring of treatment adherence. J Infect Dis. 2008; 197(Suppl 3):S272–8. Epub 2008/06/14. [PubMed: 18447613]
34. Nieuwkerk PT, de Boer-van der Kolk IM, Prins JM, Locadia M, Sprangers MA. Self-reported adherence is more predictive of virological treatment response among patients with a lower tendency towards socially desirable responding. Antivir Ther. 2010; 15(6):913–6. Epub 2010/09/14. [PubMed: 20834104]
35. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Annals of internal medicine. 2000; 133(1):21–30. Epub 2000/07/06. [PubMed: 10877736]
36. Bangsberg DR. Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. Clin Infect Dis. 2006; 43(7):939–41. Epub 2006/08/31. [PubMed: 16941380]
37. Mee P, Fielding KL, Charalambous S, Churchyard GJ, Grant AD. Evaluation of the WHO criteria for antiretroviral treatment failure among adults in South Africa. AIDS (London, England). 2008; 22(15):1971–7. Epub 2008/09/12.
38. Chaiwarith R, Wachirakaphan C, Kotarathititum W, Praparatanaphan J, Sirisanthana T, Supparatpinyo K. Sensitivity and specificity of using CD4+ measurement and clinical evaluation to determine antiretroviral treatment failure in Thailand. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2007; 11(5):413–6. Epub 2007/03/03. [PubMed: 17331776]
39. Hingankar NK, Thorat SR, Deshpande A, Rajasekaran S, Chandrasekar C, Kumar S, et al. Initial virologic response and HIV drug resistance among HIV-infected individuals initiating first-line antiretroviral therapy at 2 clinics in Chennai and Mumbai, India. Clin Infect Dis. 2012; 54(Suppl 4):S348–54. Epub 2012/05/11. [PubMed: 22544202]

## Table I

Baseline characteristic stratified by detectable viral load

| Baseline characteristic | | Total (n=174) | Viral load < 200 copies/mL (n=140) | Viral load > 200 copies/mL (n=34) | p-value |
|---|---|---|---|---|---|
| **Age** | | 38.3 ± 8.7 | 38.5 ± 8.7 | 37.3 ± 9.3 | 0.5 |
| **Gender** | Male | 105 (60.7) | 84 (60.4) | 21 (61.8) | 0.9 |
| **Transmission Risk Factor** | Heterosexual | 136 (87.7) | 108 (87.1) | 28 (90.3) | 0.5 |
| | MSM | 2 (1.3) | 2 (1.6) | 0 | |
| | Other | 13 (8.4) | 10 (8.0) | 3 (9.7) | |
| **Education level** | Non-literate | 31 (19.4) | 25 (19.5) | 6 (18.8) | 0.8 |
| | Primary School | 43 (26.9) | 34 (26.6) | 9 (28.1) | |
| | Secondary School | 68 (42.5) | 56 (43.8) | 12 (37.5) | |
| | College | 18 (11.3) | 13 (10.2) | 5 (15.6) | |
| **Employed** | | 106 (66.7) | 84 (65.6) | 22 (71.0) | 0.5 |
| **Marital Status** | Single / Separated / Partner Died | 50 (29.0) | 36 (25.9) | 14 (41.2) | 0.08 |
| | Married | 123 (71.1) | 103 (74.1) | 20 (58.8) | |
| **Previous ARV exposure** | | 5 (3.0) | 3 (2.3) | 2 (6.3) | 0.2 |
| **Baseline WHO clinical stage** | I/II | 74 (42.5) | 58 (41.4) | 16 (47.1) | 0.7 |
| | III | 38 (21.8) | 30 (21.4) | 8 (23.5) | |
| | IV | 62 (35.6) | 52 (37.1) | 10 (29.4) | |
| **Receiving TB treatment** | | 40 (23.4) | 34 (24.6) | 6 (18.2) | 0.4 |
| **ART regimen** | D4T/3TC/NVP | 78 (44.8) | 59 (42.1) | 19 (55.9) | 0.5 |
| | AZT/3TC/NVP | 58 (33.3) | 49 (35.0) | 9 (26.5) | |
| | D4T/3TC + EFV | 27 (15.5) | 22 (15.7) | 5 (14.7) | |
| | AZT/3TC + EFV | 11 (6.3) | 10 (7.1) | 1 (2.9) | |
| **CD4 (cells/microL)** | | 146 (77-202) | 142 (73-201) | 159 (81-219) | 0.5 |
| **HepBsAg positive** | | 9 (6.0) | 6 (5.0) | 3 (10.0) | 0.4 |

NOTE: MSM, men who have sex with men; ARV, antiretroviral; PMTCT, prevention of mother to child transmission; ART, antiretroviral therapy; WHO, World Health Organization; TB, tuberculosis; D4T, stavudine; 3TC, lamivudine; NVP, nevirapine; AZT, zidovudine; EFV, efavirenz

## Table II

Adherence measures and CD4 change after 12-months ART predicting viral load (n=174)

| Adherence measure or CD4 criteria | | Total | Viral load > 200 copies | Viral load < 200 copies | Odds Ratio | P value |
|---|---|---|---|---|---|---|
| 30 day Self-report (5 point Likert item) | < Excellent | 130 (76.5) | 25 (73.5) | 105 (77.2) | 0.8 | 0.7 |
| | Excellent | 40 (23.5) | 9 (26.5) | 31 (22.8) | | |
| Self-report – Last time missed | > Never | 57 (33.5) | 13 (38.2) | 44 (32.3) | 1.3 | 0.5 |
| | Never | 113 (66.5) | 21 (61.8) | 92 (67.7) | | |
| 30 day Visual analog scale | ≤ 95% | 50 (29.4) | 12 (35.3) | 38 (27.9) | 1.4 | 0.4 |
| | > 95% | 120 (70.6) | 22 (64.7) | 98 (72.1) | | |
| 12 Month MPR (Days ART / Whole time receiving ART) | < 95% | 29 (16.7) | 8 (23.5) | 21 (15.0) | 1.7 | 0.2 |
| | ≥ 95% | 145 (83.3) | 26 (76.5) | 119 (85.0) | | |
| | < 100% | 85 (48.9) | 23 (67.7) | 62 (44.3) | 2.6 | 0.01 |
| | ≥ 100% | 89 (51.1) | 11 (32.3) | 78 (55.7) | | |
| Combined Self-report and MPR (12 Month MPR < 100% + suboptimal adherence on either of 2 self-report measures[a]) | Low adherence | 62 (35.6) | 17 (50.0) | 45 (32.1) | 2.1 | 0.05 |
| | High adherence | 112 (64.4) | 17 (50.0) | 95 (67.9) | | |
| NACO immunological criteria for treatment failure[b] | Positive | 18 (10.9) | 3 (8.8) | 15 (11.5) | 0.7 | 1.0 |
| | Negative | 147 (89.1) | 31 (91.2) | 116 (88.5) | | |

Values represent n (% with that characteristic)

Characteristics compared by Chi-squared test or Fisher's exact test if expected cell frequencies ≤ 5

[a] < Excellent adherence in last 30 days, or ever reported missing ART

[b] Minimum requirement baseline and 6 month CD4. Positive criteria; 6 or 12 month CD4 < 100, or 12 month CD4 50% lower than 6 month CD4, or 6 or 12 month CD4 < baseline CD4

NOTE: ART, antiretroviral therapy; MPR medication possession ratio; NACO, India national AIDS control organization