Published in final edited form as:

J Acquir Immune Defic Syndr. 2012 June 1; 60(2): 183–190. doi:10.1097/QAI.0b013e31824bd605.

Determination of Optimized Multidisciplinary Care Team for Maximal Antiretroviral Therapy Adherence

Michael Alan Horberg, MD MAS^{1,2}, Leo Bartemeier Hurley, MPH^{2,3}, William James Towner, MD⁴, Michael Warren Allerton, MS³, Beth Ting-Ting Tang, MS⁵, Sheryl Lynn Catz, PhD⁶, Michael Jonah Silverberg, PhD MPH^{2,3}, and Charles Price Quesenberry, PhD³

¹Mid-Atlantic Permanente Research Institute, Rockville, Maryland ²HIV Initiative, Kaiser Permanente, Oakland, California ³Kaiser Permanente Northern California, Oakland, California ⁴Kaiser Permanente Southern California, Los Angeles, California ⁵Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California ⁶Group Health Research Institute, Seattle, Washington

Abstract

Objective—We seek to determine the optimized multidisciplinary care team (MDCT) composition for antiretroviral therapy (ART) adherence.

Methods—We analyzed all new regimen starts (n=10,801; 7,071 ART naïve, 3,730 ART experienced) among HIV+ patients in Kaiser Permanente California from 1996–2006. We measured 12-month adherence to ART (pharmacy refill methodology) and medical center-specific patient exposure to HIV/ID specialist (reference group), non-HIV primary care provider (PC), clinical pharmacist, nurse case manager, non-nurse care coordinator, dietician, social worker/benefits coordinator, health educator, and mental health. We used recursive partitioning to ascertain potential MDCT compositions associated with maximal mean ART adherence. We then employed mixed linear regression with clustering by provider and medical center (adjusting for ART experience, age, gender, race/ethnicity, HIV risk, HCV+, ART regimen class and calendar year) to test which potential MDCT identified had statistically significant association with ART adherence.

Results—We found maximal increase in adherence with pharmacist +coordinator +PC (+8.1% ART adherence difference compared to reference; 95% CI: +2.7–+13.5%). Other MDCT teams with significant (p<0.05) improved adherence compared to specialist only were: nurse +social work +PC (+7.5%; +5.4–+9.7%); specialist +mental health (+6.5%; +2.6–+10.4%); pharmacist +social work +PC (+5.7%; +4.1–+7.4%); pharmacist +PC (+3.3%; +0.8–+5.8%). Among these MDCTs, there were no significant differences in mean adherence, odds maximal viral control, or change CD4+ at 12 months (except pharmacist +PC).

Corresponding Author (address and request for reprints): Michael Horberg, MD, MAS, Executive Director Research, Mid-Atlantic Permanente Research Institute, 2101 East Jefferson Street, 3 West, Rockville, MD 20852, (T)—301-816-6302, (F)—301-816-7115, (E)—michael.horberg@kp.org.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Disclosures:

The authors have no further disclosures relevant to this manuscript.

The data was presented in part at the IAPAC/NIMH 6th HIV Treatment Adherence Conference, May 23–25, 2011, Miami, FL.

Conclusions—Various MDCTs were associated with improved adherence, including ones that did not include HIV specialist but included primary care plus other health professionals. These findings have application to HIV care team design.

Keywords

Multidisciplinary Care Team; Antiretroviral Therapy Adherence; Clinical Pharmacist; Patient Centered Medical Home; HIV Specialist; Recursive Partitioning

INTRODUCTION

HIV/AIDS has progressed to a complex, chronic manageable disease in many nations.^{1, 2} However, estimates are that only 19% of all HIV+ patients in the US have maximal virologic control (HIV RNA level below limits of quantification of the assay, “BLQ”).³ While the exact level of antiretroviral therapy (ART) adherence necessary to achieve BLQ is debated, it is widely accepted that ART adherence can be influenced by factors at the patient, provider, and system levels.⁴ In the United States, HIV care is often provided by an HIV multidisciplinary care team (MDCT), comprised of varying professionals including nurses, pharmacists, case managers and social workers. The composition of these teams can vary greatly by clinical site, yet the impact of this varied composition on ART adherence has not been determined.^{5, 6}

Improved ecologic or system factors including access to optimized multidisciplinary care should improve the individual’s health care, thus improving their willingness to adhere to the treatment program.^{7, 8} The Department of Health and Human Services (DHHS) guidelines for use of anti-retroviral agents recommend a health care team approach with nurses, pharmacists, and peer counselors to improve adherence to anti-retroviral therapy, but provide no further specific recommendation.⁹ Recommendations for HIV MDCT have stemmed from studies that show MDCT are associated with increased receipt of ancillary services results and more HIV patients seeking and remaining in care.^{10, 11} In addition, US healthcare reform has given renewed emphasis on the “patient centered medical home”, of which HIV MDCT (as in Ryan White Part C clinics) can be a paradigm.^{12, 13} Typically, HIV MDCT is comprised at least of a physician, nurse and/or case manager, and often a clinical pharmacist.^{13, 14} Other personnel cited as beneficial are nurse practitioners¹⁵, mental health workers¹⁶, social workers^{17, 18}, dieticians¹⁹, health educators¹⁴, and transportation service consultants^{13, 20}. While some studies have shown benefit to MDCT,^{13, 14, 21, 22} studies did not measure ART adherence, nor account for the contribution of MDCT components in their analyses.

Kaiser Permanente (KP) is one of the largest providers of integrated HIV care in the United States. While KP endorses an HIV specialty and multidisciplinary model of HIV care, our clinic compositions are quite diverse, and include some clinics where an MDCT is not present. The primary goal of our study was to explore which combinations of MDCT components are most associated with maximal ART adherence, when compared to the HIV/ID specialist without a MDCT. We also sought to examine which MDCT combinations were associated with improvements in other HIV-related outcomes.

METHODS

Study Design

We performed a retrospective cohort analysis of all new ART regimen starts in KP California from 1996–2006 and followed through 12 months post-initiation. We determined which components of the MDCT (clinician, clinical pharmacist, nurse manager, non-nurse

care coordinator, dietician, social worker/benefits counselor, mental health worker, clinical health educator) were most influential on maximal ART adherence. We determined the optimized MDCT associated with maximal ART adherence. We also determined if the optimized MDCTs for adherence were associated with improvements in other HIV-related outcomes, including achieving HIV RNA BLQ, changes in CD4+ counts, and odds of new AIDS defining events.

Subjects

KP California is an integrated healthcare system serving 18.3% of the California population and 12.3% of its HIV-infected population. Patients in our system receive multidisciplinary health care, including HIV specialty care. The HIV+ population in KP is demographically representative of the state;²³ data indicates that members overall are very similar to the general population with regard to age, gender, and race/ ethnicity, with only slight underrepresentation of those in lower and higher income and education categories.²⁴

We identified all HIV+ patients at least 18 years old initiating a first or new ART regimen dispensed from a KP pharmacy in the years 1996–2006, where HIV RNA prior to starting the new regimen was above lower limits of quantification. We classified the patients associated with the ART regimen as antiretroviral naïve if they had no record of any prior antiretroviral regimen; otherwise new regimens were classified as among ART-experienced patients. We defined an ART regimen among ART naïve patients as 3 antiretroviral drugs used in combination as defined by DHHS guidelines,⁹ with ritonavir at doses 400mg/day not considered an active drug in the regimen. New regimens among ART-experienced patients were defined as 2 antiretroviral drugs not previously used. Eligible patients had 6 months KP membership prior to initiation of the first or new regimen in order for baseline values to be determined and presence of prior antiretroviral history to be established.

Measurements

We surveyed each medical center in KP California to determine the presence of MDCT components of interest at that medical center in each year 1996–2006. Components of interest were: HIV or ID Specialist (MD/DO, HIV Nurse Practitioner, HIV Physician Assistant), HIV nurse case manager, non-nurse care coordinator, clinical pharmacist, social worker (or benefits coordinator), dietician, health educator, or mental health worker. Components were counted as present if they had a formal assignment to the HIV clinic. We determined whether providers were an HIV Specialist according to either HIVMA or AAHIVM definitions.^{25, 26} Using the data collected in the survey, we identified the components of the MDCT available to a particular patient at the time of their ART regimen initiation.

KP pharmacy records provide details of the each antiretroviral dispensed to a patient which allowed us to assess date of first antiretroviral prescription fill and regimen composition, as well as identify refills for patients during study follow-up. Adherence to the ART regimen over the 12-month observation period was calculated using established methods developed for administrative pharmacy databases. These methods account for all of the component medicines of an individual patient's ART regimen.^{27–29} This measure of adherence is computed across all antiretroviral medications as the number of doses in an interval (bounded by a first and last fill date of drug, requiring at least 2 fills per drug) for which the patient has drug in possession as a percentage of total intended doses in the span between the first and last filling. The computation takes quantity supplied and frequency of dosing into account. Employing pharmacy records to ascertain ART adherence has been validated and widely used in previous studies at other institutions and KP.^{30–33} We classified ART regimens as NNRTI-based, NRTI only, PI-based, PI+NNRTI, or new class.

We measured HIV RNA closest and prior to regimen initiation and closest to 12 months post-initiation. We defined BLQ as <500 copies/mL through 2000 and <75 copies/mL subsequently. We also recorded all clinical AIDS defining events (1993 CDC Classification except CD4<200/ μ L)³⁴ and all CD4+ counts at regimen initiation and through 12 months post-initiation. In addition, we recorded gender, race/ethnicity, HIV risk behavior, co-infection with hepatitis C, and the year the first/new ART regimen was initiated.

Statistical Analysis

We utilized recursive partitioning to determine potential MDCT combinations that had maximal ART adherence through 12 months, the *a priori* primary outcome for the study. We constructed a regression tree using standard classification and regression tree (CART) methodology, a commonly used tool for identifying interactions (in this case the different components of MDCT and their combined effects on ART adherence), providing clues to data structure that might not be apparent from linear regression analysis.^{35, 36} A regression tree is built through a process known as binary recursive partitioning, an iterative process of splitting groups of patients (parent node) into two groups (child nodes) on the basis of an independent variable (e.g. MDCT component X present vs. absent and its effect on percent 12 month adherence), and then further splitting each new node into two groups. For a given node, the tree algorithm considers every possible binary split on every variable under consideration, choosing the split that partitions the data into two parts such that it minimizes the sum of the squared deviations from the mean adherence in the separate parts. The partitioning is then applied to each of the new nodes, continuing until each node reaches a user-specified minimum node size (or if the sum of squared deviations from the mean within a node is zero), specified here as $n=5$, thus becoming a terminal node. Each terminal node will have a unique combination of MDCT components (see Figure 1). Generally this process results in very large trees suffering from over-fitting (i.e. it is "explaining" random elements of the data that are not likely to be features of the larger population). Using 10-fold cross-validation, the tree is "pruned" to obtain a set of mutually exclusive and exhaustive groups of patients characterized by different combinations of MDCT components, selected to minimize unexplained variance (sum of within-node variance across terminal nodes) and complexity (number of terminal nodes). In this analysis, for parsimony (i.e. fewest number of terminal nodes), we chose the smallest tree within one standard error of the best-performing tree.

Mixed effects linear regression was used to examine the association between ART adherence and the terminal node MDCT combinations identified in the CART analyses, with clustering by medical center and provider and adjusting for ART experience, age, gender, race/ethnicity, HIV risk behavior, hepatitis C status, ART regimen class, and year of regimen initiation, compared to the HIV specialist only. We further analyzed only the MDCT teams found most associated with improved ART adherence. We employed mixed effects logistic regression to assess odds BLQ and odds new AIDS defining events (compared to the HIV specialist only) among these more limited MDCT combinations. Change in CD4+ count in the twelve month follow-up period among these more limited MDCT combinations was examined employing mixed effects linear regression models, utilizing all available repeated measurements per patient during follow-up, again compared to specialist only. These analyses were adjusted for the same potential confounders as in the adherence analysis, with the addition of further clustering by patient in the longitudinal CD4+ count analyses. The CD4+ count analyses utilized linear splines, allowing for different slopes in the two periods of 0–90 days and the latter 270 days, in methodology previously employed by the authors.³² Analyses were conducted using CART Pro 6.0 (Salford Systems, San Diego, CA), and Stata10 (Stata Corporation, College Station, TX).

We obtained approval from Kaiser Permanente Institutional Review Boards, which waived the requirement for informed patient consent.

RESULTS

We analyzed data on 10,801 regimen starts among 9669 unique patients. Of those regimen starts, 7,071 were first regimen starts among ART naïve patients and 3730 were new regimen starts among ART experienced patients. 1,742 of the naïve patients also contributed data as experienced patients when they started a subsequent new regimen. Characteristics of the patients at regimen start are shown in Table 1. Patients contributing data were predominantly male, men having sex with men (MSM), and a majority was Caucasian. The vast majority of patients were started on NNRTI- or PI-based regimens. Consistent with KP practice, a large majority of patients were exposed to an HIV or ID specialist (Table 1). However, the HIV clinics were quite heterogeneous, with wide variation of exposure to individual components of the MDCT.

The recursive partitioning results are shown in Figure 1. The first splitting variable was the clinical pharmacist. The eventual potential combinations (twelve terminal nodes including HIV/ID specialist only) identified in the CART analysis are quite varied. For example, two of the potential MDCTs were clinical pharmacist or nurse case manager with primary care, and other combinations were a clinical pharmacist or nurse case manager along with a social worker or a non-nurse care coordinator and primary care.

Five MDCTs, when compared to the HIV specialist only, were found to have statistically significantly greater ART adherence with linear regression modeling (Table 2). The clinical pharmacist with primary care was associated with mean +3.3% improved adherence ($p=0.01$). In the modeling, the clinical pharmacist was the only single allied health professional with a physician found to have statistically significantly improved adherence. The highest mean improved adherence was with the pharmacist plus non-nurse care coordinator plus primary care (+8.1%, $p=0.003$). Three other MDCT combinations with significantly improved adherence were: nurse plus social worker/benefits coordinator plus primary care (+7.5%, $p<0.001$), pharmacist plus social worker/benefits coordinator plus primary care (+5.7%, $p<0.001$), and HIV/ID specialist plus mental health (+6.5%, $p=0.001$). Of note, these five combinations were not found to be statistically significantly different from each other (Wald test, $p=0.29$).

We analyzed these five MDCT combinations for increased odds of achieving BLQ or new AIDS events in the first 12 months of follow-up (Table 3). While three of the MDCT in unadjusted analyses had significantly increased odds BLQ compared to the specialist only, these results attenuated in adjusted analysis (Wald test: unadjusted $p<0.001$, $p=.08$, adjusted). We did not find any statistically significant association between these MDCTs and odds of new AIDS event in either unadjusted or adjusted analyses.

We performed a similar analysis for change in CD4+ count through 12 months (Table 4). There was no association between MDCT and change in CD4+ for either the 90 day period or the subsequent 270 day period ($p=0.19$ for the 90 day period and $p=0.07$ for the 270 day period). The clinical pharmacist plus primary care MDCT had statistically significant increases compared to specialist only in both time periods ($p<0.001$ and $p=0.02$, respectively). In adjusted analysis, statistically significant covariates associated with change in CD4+ count were younger age, later year, NNRTI class, and injection drug use (but IDU negatively associated).

DISCUSSION

This study utilizes a novel approach to analyzing the many components of the HIV MDCT on ART adherence. We determined that several MDCT combinations had a positive influence on adherence, compared to the HIV/ID specialist alone. Although we did not see a consistent improvement in odds BLQ or new AIDS events among the groups found significantly associated with improved adherence compared to the HIV specialist only, we did see with the clinical pharmacist plus non-HIV specialized primary care a significant increase in CD4+ counts through 360 days of follow-up.

Our finding that team members other than the HIV specialist would have a significant impact on ART adherence is supported by prior studies indicating that doctors do not necessarily emphasize adherence in their patient interactions, including HIV providers.³⁷ Clinical pharmacists are trained to help patients manage and adhere to complex medication regimens.^{38, 39} In an earlier study, we showed that clinical pharmacists improved adherence and decreased outpatient office visits among both antiretroviral naïve and experienced patients.^{32, 40} Our earlier research with HIV clinical pharmacists also indicated that there was an interaction with provider experience, prompting us to initiate this study.

The potential MDCT combinations shown here associated with improved adherence are consistent with the literature. Earlier studies indicate that nurses improve patient adherence knowledge.⁴¹ The nurse case manager and social worker have different scopes of practice, but each help address patient unmet needs, which should improve the likelihood of being adherent to medications. The same reasoning would apply to the clinical pharmacist plus the social worker or plus the non-nurse care coordinator. The HIV specialist and mental health worker could address different significant impacts on the patient's ability to adhere to treatment plans and regimens. Of course, another primary outcome (like care retention) may derive different results.

We did not specifically designate a case manager among our MDCT components of interest, as many different personnel in KP function in that role, including the nurse, non-nurse care coordinator, social worker, clinical pharmacist, or others, depending on the clinic's structure. The ability of many different personnel to have the case manager role has made prior research in this area problematic.^{13, 42–44} However, the activities of case management in a medical system, including improving access to and retention in care, treatment plan adherence, and meeting unmet patient needs,^{13, 45} are likely represented by the personnel found to be associated with improved adherence in this study—obviating the need for a specifically designated case manager in all clinics.

There is a lack of prior research on health educators, dieticians, and social work in the area of HIV MDCT and improved outcomes.^{13, 14, 18, 19} We found improved adherence with the social worker when combined with both the nurse and the clinical pharmacist, demonstrating a likely synergy of roles. Given the many tasks that social workers provide (including arranging housing, transportation, insurance benefits and medication availability), our results are not surprising. We were disappointed to find that neither dieticians nor health educators were specifically associated with improved adherence, but it is possible that their services could be associated with improving other HIV-related outcomes.

We acknowledge a few limitations to our study. A small percent of patients (< 5%) do not receive their medications through our pharmacies. It is possible that their adherence results could be quite different, but this is unlikely. It also is possible that some patients use outside case management services and the impact of those services are not considered adequately, but this likelihood is quite low with our total integrated care system. As with all observational studies, there could be residual confounding, but we have accounted for the

most significant factors in ART adherence and even account for provider and system level factors, the contributions and interactions of which are rarely considered. Also, some patients could have self-selected which clinic to attend based on the MDCT composition, but most patients in KP select their clinic based on geography.

We likely see some confounding by indication in our results. This is especially true for mental health, as patients with mental health issues were likely referred to the mental health specialist (and medical centers where they were located); patients with mental health issues have previously been shown to have lower adherence.⁴⁶ There are parts of the CART analysis where mental health was associated with reduced adherence, although it is unlikely that mental health providers would have such a negative impact on adherence. In fact, our prior research has shown that HIV+ patients with depression but on anti-depression (SSRI) medication had ART adherence similar to HIV+ patients without a depression diagnosis.⁴⁶ This will require further study, but should not take away from the key findings of the study.

We employed a retrospective observational cohort design. We believe that this is justified as patient-MDCT component interaction is likely more than just assigned visit times (phone calls, “curbside” interactions as examples of unrecorded “visits”). Further, it is likely (and probably desirable) that there is ongoing “inter-component” education, leading to improved practices by all team members, and not just that single component; this would not be captured if only designated visits were used in our analysis. Ideally, a prospective clinic-based trial, comparing the different MDCT found significantly associated with improved adherence, should be the next step.

We accounted for common patient-level and medication-level factors associated with ART adherence, including age, gender, HIV risk, race/ethnicity, regimen class, and temporal trend.⁴ We have previously shown that more recent ART regimens may have a greater impact on adherence than provider experience.^{47, 48} However, it is clear that these factors do not account for all of the impact on ART adherence. Our work demonstrates that there is a significant and measurable impact of ecologic (system of care) factors on patient-level HIV-related outcomes. There is little research in HIV or other chronic conditions in this area. Our results demonstrate that there is great opportunity for care and health outcome improvement with such exploration. With United States healthcare reform, improving patient outcomes is a necessity, and often that starts with improved treatment adherence. Further, healthcare reform places a strong emphasis on the patient centered medical home.⁴⁹ Optimized MDCT is a key element of the medical home model. We demonstrate options for such core parts of the medical home.

Our results have implications for the United States National HIV/AIDS Strategy (NHAS), released in 2010.⁵⁰ A goal of NHAS is to increase the number of HIV+ Americans on ART and increase the percent with maximal viral control. While clinicians always will be the MDCT member who ultimately determines which patients should be on medications and which ART regimen to use, our results indicate that other team members have integral roles in ensuring that treatment’s success, including adherence and improved outcomes. However, in times of constrained revenues and expensive care (total HIV care costs can be over \$24,000 per year),⁵¹ it is tempting to think that the solo practitioner or specialist is all that is needed. Our results would indicate otherwise. Further, some of the MDCT combinations discovered here may be less costly per year than just the specialist alone who might experience a higher rate of failed regimens due to poor ART adherence.⁵²

CART analysis can be successfully employed to help discover potential optimal care teams for adherence-related outcomes. We believe that the methodology applied here should be investigated for other HIV-related outcomes; especially those found in NHAS and improved

healthcare quality. For example, NHAS calls for increased accessing care at time of HIV diagnosis and increased retention in care. The HIV MDCT could be optimized through this methodology for such desirable outcomes.

Acknowledgments

The authors wish to thank Courtney Ellis for her assistance with manuscript preparation. This study was funded by NIMH grant 1R21MH085553-01A1. MJS was supported by grant number K01AI071725 from the NIAID.

REFERENCES

1. Press N, Tyndall MW, Wood E, Hogg RS, Montaner JS. Virologic and immunologic response, clinical progression, and highly active antiretroviral therapy adherence. *J Acquir Immune Defic Syndr*. 2002 Dec 15; 31(Suppl 3):S112–S117. [PubMed: 12562032]
2. Simoni JM, Frick PA, Pantalone DW, Turner BJ. Antiretroviral adherence interventions: a review of current literature and ongoing studies. *Top HIV Med*. 2003 Nov-Dec;11(6):185–198. [PubMed: 14724327]
3. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis*. 2010 Mar 15; 52(6):793–800. [PubMed: 21367734]
4. Chesney MA. Factors affecting adherence to antiretroviral therapy. *Clin Infect Dis*. 2000 Jun; 30(Suppl 2):S171–S176. [PubMed: 10860902]
5. Grzywacz JG, Fuqua J. The social ecology of health: leverage points and linkages. *Behav Med*. 2000 Fall;26(3):101–115. [PubMed: 11209591]
6. Chesney MA, Morin M, Sherr L. Adherence to HIV combination therapy. *Soc Sci Med*. 2000 Jun; 50(11):1599–1605. [PubMed: 10795966]
7. Green LW, Richard L, Potvin L. Ecological foundations of health promotion. *Am J Health Promot*. 1996 Mar-Apr;10(4):270–281. [PubMed: 10159708]
8. Richard L, Potvin L, Kishchuk N, Pric H, Green LW. Assessment of the integration of the ecological approach in health promotion programs. *Am J Health Promot*. 1996 Mar-Apr;10(4):318–328. [PubMed: 10159711]
9. Department of Health and Human Services: Panel on Antiretroviral Guidelines for Adult and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. 2011:1–128. ed.
10. Ashman JJ, Conviser R, Pounds MB. Associations between HIV-positive individuals' receipt of ancillary services and medical care receipt and retention. *AIDS Care*. 2002 Aug; 14(Suppl 1):S109–S118. [PubMed: 12204145]
11. Messeri PA, Abramson DM, Aidala AA, Lee F, Lee G. The impact of ancillary HIV services on engagement in medical care in New York City. *AIDS Care*. 2002 Aug; 14(Suppl 1):S15–S29. [PubMed: 12204139]
12. Hoang T, Goetz MB, Yano EM, et al. The impact of integrated HIV care on patient health outcomes. *Med Care*. 2009 May; 47(5):560–567. [PubMed: 19318998]
13. Sherer R, Stieglitz K, Narra J, et al. HIV multidisciplinary teams work: support services improve access to and retention in HIV primary care. *AIDS Care*. 2002 Aug; 14(Suppl 1):S31–S44. [PubMed: 12204140]
14. Le CT, Winter TD, Boyd KJ, Ackerson L, Hurley LB. Experience with a managed care approach to HIV infection: effectiveness of an interdisciplinary team. *Am J Manag Care*. 1998 May; 4(5): 647–657. [PubMed: 10179919]
15. Wilson IB, Landon BE, Hirschhorn LR, et al. Quality of HIV care provided by nurse practitioners, physician assistants, and physicians. *Ann Intern Med*. 2005 Nov 15; 143(10):729–736. [PubMed: 16287794]
16. Berg MB, Mimiaga MJ, Safren SA. Mental health concerns of HIV-infected gay and bisexual men seeking mental health services: an observational study. *AIDS Patient Care STDS*. 2004 Nov; 18(11):635–643. [PubMed: 15633261]

17. Olivier C, Dykeman M. Challenges to HIV service provision: the commonalities for nurses and social workers. *AIDS Care*. 2003 Oct; 15(5):649–663. [PubMed: 12959813]
18. Cox LE. Social support, medication compliance and HIV/AIDS. *Soc Work Health Care*. 2002; 35(1–2):425–460. [PubMed: 12365753]
19. Brunner RL, Larson TA, Scott BJ, Navarro S, Huba GJ, Melchior LA. Evaluation of the impact and acceptance of a nutrition program in an HIV community clinic. *AIDS Patient Care STDS*. 2001 Oct; 15(10):533–543. [PubMed: 11689141]
20. Johnson RL, Botwinick G, Sell RL, et al. The utilization of treatment and case management services by HIV-infected youth. *J Adolesc Health*. 2003 Aug; 33(2 Suppl):31–38. [PubMed: 12888285]
21. Levy RW, Rayner CR, Fairley CK, et al. Multidisciplinary HIV adherence intervention: a randomized study. *AIDS Patient Care STDS*. 2004 Dec; 18(12):728–735. [PubMed: 15659884]
22. Sorensen JL, Mascovich A, Wall TL, DePhilippis D, Batki SL, Chesney M. Medication adherence strategies for drug abusers with HIV/AIDS. *AIDS Care*. 1998 Jun; 10(3):297–312. [PubMed: 9828973]
23. California Department of Health Services: Office of AIDS. California AIDS Surveillance Report: Cumulative Cases as of December 31, 2005. 2006.
24. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. *Am J Public Health*. 1992 May; 82(5):703–710. [PubMed: 1566949]
25. HIV Medicine Association. [Accessed 10/30/2008] Qualifications for Physicians Who Care for Patients with HIV Infection. 2008. <http://www.hivma.org/Content.aspx?id=1782>
26. Grossman HA. Addressing the need for HIV specialists: the AAHIVM perspective. *AIDS Read*. 2006 Sep; 16(9):479–486. [PubMed: 17024767]
27. Sikka R, Xia F, Aubert RE. Estimating medication persistency using administrative claims data. *Am J Manag Care*. 2005 Jul; 11(7):449–457. [PubMed: 16044982]
28. Steiner JF, Koepsell TD, Fihn SD, Inui TS. A general method of compliance assessment using centralized pharmacy records. Description and validation. *Med Care*. 1988 Aug; 26(8):814–823. [PubMed: 3398608]
29. Kitahata MM, Reed SD, Dillingham PW, et al. Pharmacy-based assessment of adherence to HAART predicts virologic and immunologic treatment response and clinical progression to AIDS and death. *Int J STD AIDS*. 2004 Dec; 15(12):803–810. [PubMed: 15601486]
30. Fairley CK, Permana A, Read TR. Long-term utility of measuring adherence by self-report compared with pharmacy record in a routine clinic setting. *HIV Med*. 2005 Sep; 6(5):366–369. [PubMed: 16156886]
31. Seguy N, Diaz T, Campos DP, et al. Evaluation of the consistency of refills for antiretroviral medications in two hospitals in the state of Rio de Janeiro, Brazil. *AIDS Care*. 2007 May; 19(5):617–625. [PubMed: 17505922]
32. Horberg MA, Hurley LB, Silverberg MJ, Kinsman CJ, Quesenberry CP. Effect of clinical pharmacists on utilization of and clinical response to antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2007 Apr 15; 44(5):531–539. [PubMed: 17224844]
33. Silverberg MJ, Leyden W, Horberg MA, DeLorenze GN, Klein D, Quesenberry CP Jr. Older age and the response to and tolerability of antiretroviral therapy. *Arch Intern Med*. 2007 Apr 9; 167(7):684–691. [PubMed: 17420427]
34. Center for Disease Control and Prevention. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition of AIDS among Adolescents and Adults. Morbidity and Mortality Weekly Report. 1992; 41:1–19.
35. Breiman, L.; Friedman, JH.; Olshen, RA.; Stone, CJ. Classification and Regression Trees. Monterey: Wadsworth & Brooks/Cole Advanced Books & Software; 1984.
36. Zhang, H.; Singer, B. Recursive Partitioning in the Health Sciences. New York, NY: Springer Verlag; 1999.
37. Golin CE, Smith SR, Reif S. Adherence counseling practices of generalist and specialist physicians caring for people living with HIV/AIDS in North Carolina. *J Gen Intern Med*. 2004 Jan; 19(1):16–27. [PubMed: 14748856]

38. Geletko SM, Poulakos MN. Pharmaceutical services in an HIV clinic. *Am J Health Syst Pharm*. 2002 Apr 15; 59(8):709–713. [PubMed: 11977854]
39. Rathbun RC, Farmer KC, Stephens JR, Lockhart SM. Impact of an adherence clinic on behavioral outcomes and virologic response in treatment of HIV infection: a prospective, randomized, controlled pilot study. *Clin Ther*. 2005 Feb; 27(2):199–209. [PubMed: 15811483]
40. Horberg, M.; Silverberg, MJ.; Hurley, LB.; Quesenberry, CP. Abstract TuPe0107, Impact of HIV Clinical Pharmacists on Antiretroviral Adherence and Clinical Outcomes in ARV Experienced Patients. Paper presented at: XVI International AIDS Conference; Toronto, Canada. 2006.
41. Holzemer WL. HIV and AIDS: the symptom experience. What cell counts and viral loads won't tell you. *Am J Nurs*. 2002 Apr; 102(4):48–52. [PubMed: 11943923]
42. Conover CJ, Whetten-Goldstein K. The impact of ancillary services on primary care use and outcomes for HIV/AIDS patients with public insurance coverage. *AIDS Care*. 2002 Aug; 14(Suppl 1):S59–S71. [PubMed: 12204142]
43. Lo W, MacGovern T, Bradford J. Association of ancillary services with primary care utilization and retention for patients with HIV/AIDS. *AIDS Care*. 2002 Aug; 14(Suppl 1):S45–S57. [PubMed: 12204141]
44. London AS, LeBlanc AJ, Aneshensel CS. The integration of informal care, case management and community-based services for persons with HIV/AIDS. *AIDS Care*. 1998 Aug; 10(4):481–503. [PubMed: 9828968]
45. Katz MH, Cunningham WE, Fleishman JA, et al. Effect of case management on unmet needs and utilization of medical care and medications among HIV-infected persons. *Ann Intern Med*. 2001 Oct 16; 135(8 Pt 1):557–565. [PubMed: 11601927]
46. Horberg MA, Silverberg MJ, Hurley LB, et al. Effects of depression and selective serotonin reuptake inhibitor use on adherence to highly active antiretroviral therapy and on clinical outcomes in HIV-infected patients. *J Acquir Immune Defic Syndr*. 2008 Mar 1; 47(3):384–390. [PubMed: 18091609]
47. Horberg, M.; Hurley, L.; Towner, W.; Allerton, M.; Tang, B.; Catz, S.; Silverberg, M.; Quesenberry, C. Abstract 1131, Impact of Provider Experience Characteristics on HIV-Related Outcomes among cART Naïve. Paper presented at: Infectious Disease Society of America 48th Annual Meeting; Vancouver, Canada. 2010.
48. Horberg, M.; Hurley, L.; Towner, W.; Allerton, M.; Tang, B.; Catz, S.; Silverberg, M.; Quesenberry, C. Abstract MOPE464, Impact of Provider Characteristics on HIV-related Outcomes among Antiretroviral Experienced Patients. Rome, Italy. The 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention; 2011 Jul.
49. Arvantes J. Health Care Reform Legislation Will Drive Adoption of Medical Home Projects, Officials Say. <http://www.aafp.org/online/en/home/publications/news/news-now/professional-issues/20100805pcpcstakeholders.html>.
50. The White House Office of National AIDS Policy. National HIV/AIDS Strategy for the United States. The White House Office of National AIDS Policy. 2010 ed.
51. Meenan, R.; O'Keeffe Rosetti, M.; Kimes, T.; Leyden, W.; Antoniskis, D.; Saget, R.; Young, T.; Horberg, M. Abstract TUPE0236; Excess Prevalence-Based Costs of Multiple HAART Switches among HIV+ Patients in a US Health Maintenance Organization; XVII International AIDS Conference; Mexico City, Mexico. 2006.
52. Salary.com. [Accessed July 30, 2011] National average salaries by profession. 2011. Available at: <http://www.salary.com/mysalary.asp>.

Figure 1. Recursive Partitioning Results

Regression tree of potential MDCT combinations that maximal ART adherence through twelve months post-regimen initiation. The tree was “pruned” to obtain a set of mutually exclusive groups of patients characterized by different MDCT components with minimized unexplained variance. For parsimony, we chose the smallest tree within one standard error of the best-performing tree.

Table 1

Characteristics of Patients at Regimen Start

Variable	Result (%)
Total Regimen Starts	10801 (100.0%)
ARV Naïve	7071 (65.5%)
ARV Experienced	3730 (34.5%)
Gender: Female	1070 (9.9%)
Race/Ethnicity:	
Black	2024 (18.7%)
Latino	2382 (22.1%)
White	5506 (51.0%)
Other/Unknown	889 (8.2%)
HIV Risk:	
MSM	6211 (57.5%)
IDU	525 (4.9%)
Heterosexual	1457 (13.5%)
Hepatitis C Co-infection	1100 (10.2%)
ART Regimen Class:	
NNRTI-based	3312 (30.7%)
NRTI only	414 (3.8%)
PI-based	5746 (53.2%)
PI+NNRTI	1310 (12.1%)
New Classes	19 (0.2%)
Year of Regimen Start	
1996–1999	4799 (44.4%)
2000–2002	2674 (24.8%)
2003–2006	3328 (30.8%)
Multidisciplinary Care Team Component Present at Regimen Start:	
HIV Specialist	8019 (74.2%)
Nurse Case Manager	6424 (59.5%)
Non-Nurse Care Coordinator	2562 (23.7%)
Clinical Pharmacist	6147 (56.9%)
Social Work/Benefits Coordinator	8761 (81.1%)
Dietician	3595 (33.3%)
Mental Health Worker	2897 (26.8%)
Health Educator	2347 (21.7%)

Table 2

Mixed Linear Regression Results Based on MDCT Determined by Recursive Partitioning

Team Composition	Mean Adjusted % Increase Adherence	95% Confidence Interval	p Value
a. HIV/ID Specialist Only	Reference[*]		
b. Pharmacist + non-HIV Primary Care	+3.3%	+0.1 to +5.8%	0.01
c. Pharmacist + non-nurse care coordinator+ non-HIV Primary Care	+8.1%	+2.7 to +13.4%	0.003
d. Nurse + Social Work/Benefits Coordinator+ non-HIV Primary Care	+7.5%	+5.4 to +9.7%	<0.001
e. HIV Specialist+ Mental Health	+6.5%	+2.6 to +10.4%	0.001
f. Pharmacist + Social Work/Benefits+ non-HIV Primary Care	+5.7%	+4.0 to +7.4%	<0.001
g. Primary Care Provider Only	+5.3%	+2.8 to +7.8%	<0.001
h. Nurse+ care coordinator+ non-HIV Primary Care	+5.6%	−0.4 to +11.6%	0.07
i. Nurse + non-HIV Primary Care	+1.0%	−2.0 to +3.9%	0.53
j. Nurse+ Mental Health+ non-HIV Primary Care	−0.5%	−3.0 to +2.0%	0.72
k. Mental Health+ non-HIV Primary Care	−3.9%	−10.0 to +2.2%	0.21

NOTE: Mixed linear regression with clustering by medical center and provider

Adjusted for ART experience, age, gender, race/ethnicity, HIV risk, HCV+, ART regimen class, temporal trend

^{*} HIV/ID Specialist Only 12 month antiretroviral adherence was 74.4% (95% Confidence Interval: 72.2 to 76.8%)

Table 3

Odds Maximal Viral Control and Odds New AIDS Defining Event among MDCT Found Significantly Associated with Improved Adherence Compared to HIV/ID Specialist Only

MDCT Team Composition	Odds BLQ at 365 Days [Mean (95% CI)]		Odds New AIDS Defining Event First 365 Days [Mean (95% CI)]	
	Unadjusted	Adjusted	Unadjusted	Adjusted
1. HIV/ID Specialist Only		Reference		
2. Pharmacist + non-HIV Primary Care	1.61 (1.10 to 2.36)	1.19 (0.81 to 1.74)	1.52 (0.90 to 2.58)	1.26 (0.76 to 2.10)
3. Pharmacist + non-nurse care coordinator+ non-HIV Primary Care	2.90 (1.39 to 6.02)	1.30 (0.64 to 2.67)	1.28 (0.48 to 3.41)	0.97 (0.36 to 2.58)
4. Nurse + Social Work/Benefits Coordinator+ non-HIV Primary Care	1.58 (1.07 to 2.36)	0.92 (0.62 to 1.37)	1.52 (0.88 to 2.63)	1.20 (0.72 to 2.02)
5. HIV Specialist+ Mental Health	0.63 (0.35 to 1.14)	0.69 (0.39 to 1.20)	0.50 (0.21 to 1.22)	0.56 (0.24 to 1.34)
6. Pharmacist + Social Work/Benefits+ non-HIV Primary Care	1.37 (0.97 to 1.93)	0.82 (0.58 to 1.18)	1.05 (0.66 to 1.67)	0.98 (0.63 to 1.51)

NOTE: Mixed logistic regression with clustering by medical center, patient and provider

Adjusted for ART experience, age, gender, race/ethnicity, HIV risk, HCV+, ART regimen class, temporal trend

Table 4

Change in CD4+ Count in 360 Days Post-Regimen Initiation among MDCT Found Significantly Associated with Improved Adherence Compared to HIV/ID Specialist Only

MDCT Team Composition	Change in CD4 First 90 Days [Mean (95% CI)]	Change in CD4 Latter 270 Days [Mean (95% CI)]
	Adjusted	Adjusted
1. HIV/ID Specialist Only	Reference	
2. Pharmacist + non-HIV Primary Care	+61/ μ L (+43 to +78)	+29/ μ L (+4 to +54)
3. Pharmacist + non-nurse care coordinator+ non-HIV Primary Care	+90/ μ L (+35 to +146)	-10/ μ L (-59 to +38)
4. Nurse + Social Work/Benefits Coordinator+ non-HIV Primary Care	+74/ μ L (+56 to +92)	+7/ μ L (-18 to +32)
5. HIV Specialist+ Mental Health	+28 (-12 to +69)	+21/ μ L (-20 to +61)
6. Pharmacist + Social Work/Benefits+ non-HIV Primary Care	+76/ μ L (+69 to +83)	+11/ μ L (-10 to +31)

For first 90 days, comparing these MDCT, $p=0.19$; for latter 270 days, $p=0.07$

Mixed linear regression with splines (0–90 days and 91–360) with clustering by medical center, patient, and provider

Adjusted for ART experience, age, gender, race/ethnicity, HIV risk, HCV+, ART regimen class, temporal trend