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The Association of Adherence to Antiretroviral Therapy with Healthcare Utilization and Costs for Medical Care

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Abstract

Background—The association between antiretroviral adherence, healthcare utilization and medical costs has not been well studied.

Objective—To examine the relationship of adherence to antiretroviral medications to healthcare utilization and healthcare costs.

Methods—A retrospective cohort study was conducted using data from 325 previously antiretroviral medication-naive HIV-infected individuals initiating first antiretroviral therapy from 1997 through 2003. The setting was an inner-city safety net hospital and HIV clinic in the US. Adherence was assessed using pharmacy refill data. The average wholesale price was used for prescription costs. Healthcare utilization data and medical costs were obtained from the hospital billing database, and differences according to quartile of adherence were compared using analysis of variance (ANOVA). Multivariate logistic regression was used to assess predictors of higher annual medical costs. Sensitivity analyses were used to examine alternative antiretroviral pricing schemes. The perspective was that of the healthcare provider, and costs were in year 2005 values.

Results—In 325 patients followed for a mean (± SD) 3.2 (1.9) years, better adherence was associated with lower healthcare utilization but higher total medical costs. Annual non-antiretroviral medical costs were $US7612 in the highest adherence quartile versus $US10 190 in the lowest adherence quartile. However, antiretroviral costs were significantly higher in the highest adherence quartile ($US17 513 vs $US8690), and therefore the total annual medical costs were also significantly higher in the highest versus lowest adherence quartile ($US25 125 vs $US18 880). In multivariate analysis, for every 10% increase in adherence, the odds of having annual medical costs in the highest versus lowest quartile increased by 87% (odds ratio 1.87; 95%

CI 1.45, 2.40). In sensitivity analyses, very low antiretroviral prices (as seen in resource-limited settings) inverted this relationship – excellent adherence was cost saving.

Conclusion—Better adherence to antiretroviral medication was associated with decreased healthcare utilization and associated costs; however, because of the high cost of antiretroviral therapy,

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total medical costs were increased. Combination antiretroviral therapy is known to be cost effective; lower antiretroviral costs may make it cost saving as well.

Background and Objective

The cost of healthcare for individuals with HIV infection has been estimated to be $US18 300–$US25 600 annually (values given are in 1996 $US,[1] 1998 €,[2] 2001 $US[3] and 2004 $US.[4])Prior to the introduction of potent combination antiretroviral therapy, most of the expenditures for HIV care were spent on hospitalizations and the treatment of opportunistic illnesses.[5] After the introduction of potent combination antiretroviral therapy, the need for hospitalization and the incidence of opportunistic illness decreased considerably.[6-8] It is now estimated that 54–64% of healthcare expenditures in HIV-infected populations in resource-rich settings are attributed to the cost of combination antiretroviral therapy.[1,4,8] Despite the expense, antiretroviral therapy is cost effective for HIV-infected individuals in resource-rich (and resource-limited) settings.[9-13]

Excellent adherence to antiretroviral therapy increases the likelihood of successful clinical outcomes and would thus be expected to decrease non-antiretroviral healthcare costs.[14-16] The association of level of adherence to antiretroviral therapy with medical expenditures has not been thoroughly evaluated. We sought to describe the competing costs attributable to antiretroviral medications and non-antiretroviral healthcare. In addition, we wanted to explore the effect that varying costs for antiretroviral therapy might have on this relationship in resource-rich settings. In previously antiretroviral medication-naive HIV-infected individuals initiating antiretroviral therapy, we quantified healthcare utilization and medical costs and assessed the association between level of adherence to antiretroviral therapy and these parameters.

Methods

Denver Health (Denver, CO, USA) is an integrated urban healthcare system providing primary medical care for approximately 1300 HIV-infected individuals each year.[17] Patients can access care at multiple sites, including an emergency department and 350-bed hospital, urgent-care centre, ten community health centres, 11 school-based clinics, multiple subspecialty clinics and the public health department. Primary HIV care is provided in an infectious diseases clinic and within dedicated HIV primary-care clinics.

A comprehensive retrospective adherence database including previously antiretroviral-naive patients who initiated therapy between 1997 and 2003 has been described previously.[18,19] The database contains demographics, baseline disease-specific data, longitudinal clinical information (CD4+ cell counts, HIV-RNA levels, opportunistic illnesses and mortality), dates and components of all antiretroviral regimens and a validated antiretroviral medication adherence assessment calculated using pharmacy refill data.[18]

Population

Previously antiretroviral-naive patients were included in this analysis if they received care within the Denver Health system for at least 6 months following the commencement of initial antiretroviral therapy. This duration of follow-up was deemed necessary because events that occur during short time periods have a disproportionately large impact on annualized medical costs. Furthermore, it is unknown whether short-term clinical events are associated with the degree of adherence to combination antiretroviral therapy. Patients were excluded if they received antiretroviral therapy through a clinical trial pharmacy or if their initial antiretroviral regimen contained less than three antiretroviral medications. Follow-up lasted until the patient no longer received medical care or prescriptions within Denver Health, until death or until June 2005, whichever came first.

Definitions and Data Sources

Adherence was calculated as the average of doses obtained divided by doses prescribed for each antiretroviral medication for the first 180 days after antiretroviral therapy initiation. Using 6-month adherence standardized the duration of assessment for each patient and reduced the potential reverse causation of poor adherence being caused by declining health status.[15,20] Over long periods of time, ‘adherence’ becomes a poor descriptor of drug-taking behaviour as individuals spend periods of time on and off therapy initiated by themselves or under the direction of their HIV care provider. We used cost data to approximate whether 6-month adherence was an adequate surrogate for drug exposure over the duration of this study.

Institutional financial information and health resource utilization were obtained from a hospital billing database that contains medical charges from 1997 to present. Billing and healthcare utilization data were available from all areas of the comprehensive Denver Health system including medical and psychiatric hospitalizations, outpatient HIV care, outpatient mental health services, emergency room visits, subspecialty and other clinic visits, ancillary services, radiology and laboratory charges. Since most antiretroviral drugs were supplied by the state AIDS Drug Assistance Program without cost to the patient, we used the 2005 *Red Book* average wholesale price (AWP) for antiretroviral drugs and other prescription medications in cost calculations.[21]

This analysis represents a healthcare provider economic perspective. Except for prescription medications, all financial data are presented as costs. Charges were converted to costs by applying 2005 Denver Health cost-to-charge ratios for inpatient services (including physician services, ratio = 0.57) and outpatient services (ratio = 0.54). Financial data were converted to $US, year 2005 values using the producer price index (PPI) published by the US Department of Labor, Bureau of Labor Statistics.[22] Total medical costs were determined for the entire duration of follow-up using the following formula: total medical costs = inpatient costs + outpatient costs + antiretroviral therapy costs + non-antiretroviral outpatient pharmacy costs. Inpatient costs included all of the costs (medical, administrative, ancillary services, etc.) associated with a defined inpatient admission. Outpatient costs included all other costs incurred, including those associated with emergency department visits. Annualized costs, overall and by cost component, were determined by dividing costs for care during follow-up by the duration of follow-up in years.

Statistical Analysis

Comparisons between included and excluded patients were performed using the Wilcoxon rank-sum test for continuous variables and the chi-square (χ^2) test for categorical variables. Baseline demographics, baseline clinical data, medical costs and healthcare utilization data were reported using basic descriptive statistics. Baseline CD4+ cell counts and HIV-RNA levels were those obtained prior to (and closest to) the antiretroviral medication initiation date. Four groups of patients were identified based on quartiles of antiretroviral adherence. Quartiles were used because there is no currently accepted cut-off defining adequate and inadequate antiretroviral adherence, and this relationship is probably drug-class specific.[23] Baseline demographic and clinical data in the four quartiles were compared using the Kruskal-Wallis test for continuous variables and the χ^2 test for categorical variables. In order to approximate whether 6-month adherence was an adequate surrogate for drug exposure over the duration of this study, we estimated the proportion of actual to potential (if adherence had been 100%) annualized antiretroviral medication costs by quartile of adherence. The highest adherence quartile served as the reference for these calculations as median adherence in this quartile was 100%.

The association between antiretroviral adherence and healthcare utilization was assessed by adherence quartile. Healthcare utilization comparisons included the annualized number of the following: outpatient visits, inpatient admissions, inpatient days and emergency room visits. Analysis of variance (ANOVA) was used for all comparisons. Duncan's multiple range test (MRT) was utilized for interquartile comparisons when the ANOVA comparison yielded a statistically significant result. Duncan's MRT is a multiple comparison procedure that compares sets of means.[24]

The association of antiretroviral adherence with medical costs was assessed by comparison of data across the four adherence quartiles. Comparisons included annualized total medical costs, annualized inpatient costs, annualized outpatient costs, annualized antiretroviral medication costs and annualized non-antiretroviral outpatient pharmacy costs. Because cost data were right-skewed, statistical comparisons between quartiles were performed using ANOVA of log-transformed data. For annualized inpatient costs, ANOVA was performed on the log of inpatient costs plus one because many values were zero. Duncan's MRT was utilized for interquartile comparisons when the ANOVA comparison yielded a statistically significant result. In order to assure that extreme values did not significantly influence the analysis of the association of adherence quartile with annualized total medical costs, this analysis was repeated after excluding data from individuals with annualized total medical costs greater than three standard deviations above the mean.

Bivariate logistic regression was performed to assess predictors of having annualized total medical costs in the first (highest) versus the fourth (lowest) quartile for the study population. A first versus fourth quartile comparison was selected because adherence in the third quartile was close to the upper two quartiles, which would have restricted our ability to find differences in this exploratory study. Multivariate logistic regression was performed on the 158 patients from the first and fourth cost quartiles with all of the following information available: age, sex (female vs male), race (non-White vs White), mode of HIV transmission (men who have sex with men vs other), baseline CD4+ cell count and 6-month level of antiretroviral adherence. In addition, the multivariate analysis was adjusted for the duration of follow-up and year of antiretroviral therapy initiation to adjust for potential confounding by period of treatment. Baseline HIV-RNA was not included because of a lack of association with total medical cost on bivariate analysis and because of missing values that would have excluded 19 patients.

AWP overestimates the cost of antiretroviral therapy.[25] In order to explore the effect that varying antiretroviral costs might have on the interaction between antiretroviral medication costs and non-antiretroviral healthcare costs in resource-rich settings, we performed two sensitivity analyses. These assessed the association between antiretroviral adherence quartile and annualized total medical costs using other potential medication pricing schemes. The first analysis used US Public Health Service Section 340B (PHS 340B) Drug Discount Program pricing.[26] Dollar values in this analysis were estimated to be 38% lower than AWP based on Denver Health contractual data. The second analysis used prices for first-line generic combination antiretroviral therapy in low- and middle-income countries from January to June of 2005.[27] In this analysis, $US372, the average of reported values, was used as the cost for a full year of first-line antiretroviral therapy in patients with 100% adherence.[27] Multivariate logistic regression analysis assessing factors associated with annualized total medical cost in the first (highest) versus the fourth (lowest) quartile (using generic antiretroviral prices) was carried out in the same manner as described above in our primary analysis. For these sensitivity analyses no adjustments were made for medical or non-antiretroviral medication costs because the goal was to assess the effect of varying antiretroviral medication prices in a resource-rich setting.

Data collected were maintained in password-protected spreadsheets and all statistical analyses were performed using SAS version 8.2 (SAS Institute Inc., Cary, NC, USA). Significance levels reported are two-sided, and p-values <0.05 were regarded as statistically significant. The Colorado Multiple Institutional Review Board approved this study.

Results

Between 1997 and 2003, 423 previously antiretroviral-naive patients initiated antiretroviral therapy within Denver Health. Of these patients, 325 (77%) were included in this study. Reasons for exclusion included the following: 49 (12%) did not have 6 months of follow-up, 30 (7%) received medications through a clinical trial pharmacy, 18 (4%) had an initial antiretroviral regimen containing less than three medications and 1 (0%) did not have financial data available. The included cohort was mostly male (89%), the median age was 37 years (interquartile range [IQR] 32–43 years) and most were men who have sex with men (65%). The cohort was racially diverse: 46% were White, 32% were Hispanic and 19% were Black. Median baseline CD4+ cell count and HIV-1 viral load were 168 cells/uL (IQR 52–283 cells/uL) and 5.0 log copies/mL (IQR 4.5–5.6 log copies/mL), respectively. There were no significant differences in demographic or baseline disease-specific factors between included and excluded patients except that excluded patients were more likely to report a history of injection drug use (34% vs 20%; $p = 0.007$). The baseline demographics of this cohort closely approximate the characteristics of HIV-infected patients at Denver Health.

On average, patients were followed for a mean (SD) 3.2 (1.9) years. The median level of antiretroviral adherence over the initial 6 months of combination antiretroviral therapy was 94.2% (IQR 78.7–99.2%). Overall healthcare utilization (mean value per year) was as follows: hospitalizations, 0.3 (0.8); hospital days, 1.9 (6.0); outpatient visits, 16.6 (17.4); and emergency room visits, 0.5 (0.9). Annualized total medical costs averaged $US23 073 (12 545), and this was broken down into its components as follows: annualized inpatient costs, $US2388 (6615); annualized outpatient costs, $US4387 (3576); annualized costs for antiretroviral therapy, $US14 068 (6430); and annualized non-antiretroviral outpatient pharmacy costs, $US2230 (3338).

We divided the population into four groups based on quartiles of antiretroviral adherence and report the baseline characteristics of these groups in table I. No differences in demographics, HIV acquisition risk factor, baseline CD4+ cell count, baseline HIV-1 viral load or duration of follow-up were identified between the four groups. Median antiretroviral adherence was very high (>97%) in the first and second quartiles, moderate in the third quartile (86.3%) and low in the fourth quartile (47.3%).

We assessed whether our 6-month adherence measure was an adequate predictor of antiretroviral medication exposure over the duration of the study by using cost data as a surrogate for adherence. The proportion of actual to potential (if adherence had been 100%) annualized antiretroviral medication costs closely approximated the 6-month adherence level in each quartile. For example, the lowest adherence quartile had a median 6-month adherence level of 47.3% and the proportion of actual ($US8690) to potential ($US17 513) annualized antiretroviral medication charges was 49.6% (calculated from data in table II).

Healthcare utilization by adherence quartile is presented in table III. There was no difference in the annual number of outpatient visits per patient based on quartile of adherence ($p = 0.34$). In contrast, as adherence decreased, the number of inpatient admissions ($p < 0.01$), the number of hospital days ($p < 0.01$) and the number of emergency room visits ($p < 0.01$) significantly increased. Statistically significant interquartile comparisons (by Duncan's MRT) included the following: the number of hospital admissions and number of emergency room visits per year were significantly higher for patients in the lowest adherence quartile than the other three quartiles and the number of hospital days per year was significantly higher in the lowest adherence quartile than the first and second quartiles. There were no differences in mortality during follow-up for the four adherence quartiles ($p = 0.45$) or when comparing individuals with adherence above or below the median ($p = 0.11$).

Medical costs, by quartile of adherence, are presented in table II. There was a significant association between annualized total medical costs and quartile of adherence – total medical costs were significantly lower in the lowest adherence quartile than in the other adherence quartiles ($p < 0.001$). By component of total medical costs, the difference was due to a significantly lower annual cost for antiretroviral medications in the lowest adherence quartile that was greater in magnitude than the higher annual costs for inpatient care in that quartile. There were no significant differences in annualized outpatient costs or annualized non-antiretroviral outpatient pharmacy costs. In a separate analysis that excluded individuals with annualized total medical costs greater than three standard deviations above the mean ($n = 5$), no differences in these results were seen; annualized total medical costs remained significantly lower in the lowest adherence quartile than in the other adherence quartiles ($p < 0.001$). In both of these analyses, there were no significant differences in annualized total medical costs in the top three quartiles of adherence.

Bivariate logistic regression analysis showed that higher levels of antiretroviral medication adherence, older age and lower baseline CD4+ cell count were significantly associated with having annualized total medical costs in the highest versus lowest quartile. In multivariate analysis, all three of these factors retained an association with higher annualized total medical costs (figure 1). For every 10% increase in antiretroviral medication adherence, the odds of having annualized total medical costs in the highest versus lowest quartile increased by 87% (odds ratio [OR] 1.87; 95% CI 1.45, 2.40). For every 100 cell/uL decrease in CD4+ cell count, the odds of having annualized total medical costs in the highest versus lowest quartile doubled (OR 2.04; 95% CI 1.43, 2.92). For every 1-year increase in age, the odds of having annualized total medical costs in the highest versus lowest quartile increased by 10% (OR 1.10; 95% CI 1.04, 1.17). Inclusion of variables in this model without a significant association with annual cost above the median did not change the direction, magnitude or significance of any relationships reported.

Costs for antiretroviral medications accounted for 61% of annualized total medical costs in this study. In order to estimate the effect of antiretroviral pricing on the association between adherence and medical costs in resource-rich settings, we conducted sensitivity analyses using alternative antiretroviral medication pricing schemes (figure 2). Using Denver Health negotiated PHS 340B pricing, there continued to be a significant positive association between quartile of antiretroviral adherence and medical costs − as adherence increased, annualized total medical costs increased ($p = 0.002$). In the most adherent patients (first adherence quartile), a 57% reduction in antiretroviral cost would make antiretroviral and non-antiretroviral costs approximately equivalent.

A second sensitivity analysis using an approximate cost for 1 year of first-line generic antiretroviral medications in low- and middle-income countries in the year 2005 ($US372) showed that quartile of antiretroviral medication adherence and annualized medical costs were no longer significantly associated ($p = 0.11$). However, multivariate logistic regression analyses using the cost of generic antiretroviral therapy showed a significant inverse association between adherence and annualized total medical cost in the highest versus lowest quartile. For every 10% increase in antiretroviral medication adherence, the odds of having annualized total medical costs in the highest versus the lowest quartile decreased by 20% (OR 0.80; 95% CI 0.68, 0.96).

Discussion

Excellent adherence to antiretroviral therapy is critical for successful HIV treatment outcomes, but the relationship of antiretroviral adherence with healthcare utilization and medical costs has not been well studied. We have shown that individuals with better antiretroviral adherence have lower healthcare utilization, but the association of antiretroviral adherence with total medical costs was more complex. The average annual medical cost for our antiretroviral-naive population initiating combination antiretroviral therapy between 1997 and 2003 was $US23 073. More than half (61%) of this figure was accounted for by antiretroviral therapy. Antiretroviral adherence was positively associated with total medical costs – patients with better adherence had higher total medical costs. This resulted from the high costs of the antiretroviral drugs, which outweighed the savings in inpatient costs that were made with higher adherence. Sensitivity analyses showed that, in resource-rich settings, substantially lower antiretroviral medication costs inverted the adherence-cost relationship – better adherence was cost saving.

Costs of care in this study were obtained from patient-level financial data within our comprehensive healthcare system. Annualized total medical cost in our population ($US, year 2005 values) were similar to those published previously.[1-4] The proportion of medical costs attributable to antiretroviral therapy in our study (61%) was also similar to that found in previous studies.[1,4,8] The association of baseline CD4+ cell count with cost of medical care has been previously demonstrated.[1] Age as a factor associated with increased total medical costs is not surprising as it likely acted as a surrogate for increased co-morbid illness. However, after adjusting for baseline CD4+ cell count and age, adherence retained a significant positive association with total medical costs in the primary analysis.

Two prior studies support that better adherence to antiretroviral therapy is associated with higher direct costs for medical care over shorter time periods (12–18 months).[28,29] However, another analysis from South Africa showed that excellent adherence was associated with lower overall non-antiretroviral-related expenditures, which is similar to the findings of our sensitivity analysis using generic drug pricing.[30] In the non-HIV literature, analyses of the association between disease-specific medication adherence and chronic disease medical costs have typically shown that adherence is cost saving.[31-33] Notably, medication costs accounted for 6–22% of total medical costs in these studies. The significantly higher proportion of total medical costs attributable to chronic disease (antiretroviral) medications in our HIV-infected population (61%) is likely responsible for the apparently discordant findings.

That excellent adherence to expensive medications is costly is not the message of this analysis. It is intuitive that the more of a medicine one uses, the higher the cost for that medicine. Instead we have assessed the competing costs of antiretroviral therapy and non-antiretroviral healthcare in a resource-rich setting. What we have demonstrated is that, despite lower healthcare utilization in more adherent patients (and thus lower non-antiretroviral costs), total costs were higher in this population. In addition, we have demonstrated that the expense of antiretroviral therapy (compared with therapy for other chronic diseases) was the primary determinant of this relationship. The sensitivity analyses assessing alternative antiretroviral medication pricing schemes are critical to this interpretation. Using generic drug pricing, antiretroviral therapy made up just 3% of total annual medical costs and better adherence was cost saving. This supports our hypothesis that better medication adherence in a system where antiretroviral costs make up a smaller proportion of overall costs would be cost saving. These results are likely generalizable to other resource-rich settings; however, further analyses in resource-limited settings, using appropriate non-antiretroviral costs, will be necessary to evaluate this relationship further.

This is not a cost-utility analysis; our primary conclusions are based on a healthcare provider economic perspective. This study does not take into account improved quality of life, increased life expectancy or other potential benefits of excellent antiretroviral adherence.[16,34,35] Because this study was retrospective, we were unable to assess health utility (i.e. quality of life). Therefore, in no way do these results support that lower levels of adherence are acceptable. Further research to define the cost-effectiveness relationships between adherence and medical costs when taking into account quality of life is needed. Nevertheless, our study is important in that it is one of the first to provide ‘real’ numbers (financial and healthcare utilization) to support the hypothesis that better antiretroviral adherence reduces non-antiretroviral healthcare expenditures. The cost of antiretroviral therapy may ultimately prove to be the most flexible of healthcare costs for HIV-infected patients in resource-rich settings. In low- and middle-income countries, generic antiretroviral medications are available at a fraction of the cost of combination antiretroviral therapy in the US.[27,36] Furthermore, generic antiretroviral medications are effective in these settings.[37,38]

This study is limited in several ways. First, it excluded individuals followed for less than 6 months, which may have excluded the least adherent patients. Second, we did not have access to costs incurred outside of our institution, making us underestimate total costs. This may have biased our results if there was a difference in utilization of outside services based on adherence level. However, we are confident that our patient population was well defined and received the overwhelming majority of their medical care primarily within Denver Health based on prescription refill and clinic attendance data. Third, pharmacy refill adherence may overestimate true adherence. However, compared with other adherence assessment tools, pharmacy refill adherence has the advantage of being non-interventional and, in our system, was available on a large proportion of patients. Fourth, this data reflects the relationship between adherence and medical costs in the setting of routine clinical care; whether this relationship is different in the setting of an active adherence intervention is unknown. Some data suggest that adherence interventions may decrease healthcare utilization outside of their effect on adherence itself.[39] Our data abstraction from the billing databases did not record the type of outpatient visit. It may be of interest in future studies to provide more indepth analysis of the patterns of outpatient healthcare utilization in such cohorts. Finally, although this study presents the longest follow-up to date of the association between antiretroviral adherence and healthcare costs, 3 years may not be long enough to capture clinical events in the modern treatment era.

Conclusion

Excellent adherence to antiretroviral therapy results in marked improvements in a variety of outcomes: better immunological response to therapy, decreases in hospitalizations and emergency room visits, and improved survival.[16,40] However, our analysis showed that better adherence resulted in higher overall healthcare costs in this previously antiretroviral-naive population, from the healthcare provider perspective. High antiretroviral costs compete with the savings in non-antiretroviral medical costs that are achieved with better adherence, resulting in higher total medical costs given current antiretroviral prices. Yet the dramatic clinical benefits of antiretroviral therapy suggest that interventions that promote adherence can be cost effective (i.e. the increased expense of better adherence will produce better health outcomes, at a price thought to be appropriate for the US).[41] We speculate that, as antiretroviral drugs become available as generic preparations in the US, excellent adherence will likely become cost saving, not just cost effective.

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Variable	OR	95% CI	p-Value
Age (per 1-year increase)	1.10	1.04, 1.17	0.001
Sex (female vs male)	4.52	0.66, 30.77	0.12
Race (non-White vs White)	0.86	0.32, 2.30	0.76
Mode of HIV transmission (MSM vs other)	0.91	0.30, 2.78	0.87
CD4+ cell count (per 100-cell decrease)	2.04	1.43, 2.92	<0.001
6-month adherence (per 10% increase)	1.87	1.45, 2.40	<0.001

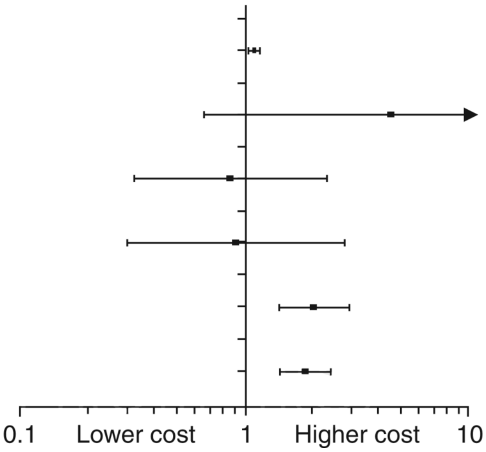

Fig. 1.
Multivariate associations of baseline factors and adherence with total annualized medical costs in the first (highest) vs fourth (lowest) adherence quartile for 158 previously antiretroviral medication-naive patients initiating first antiretroviral therapy within Denver Health, 1997−2003. **MSM** = men who have sex with men; **OR** = odds ratio.

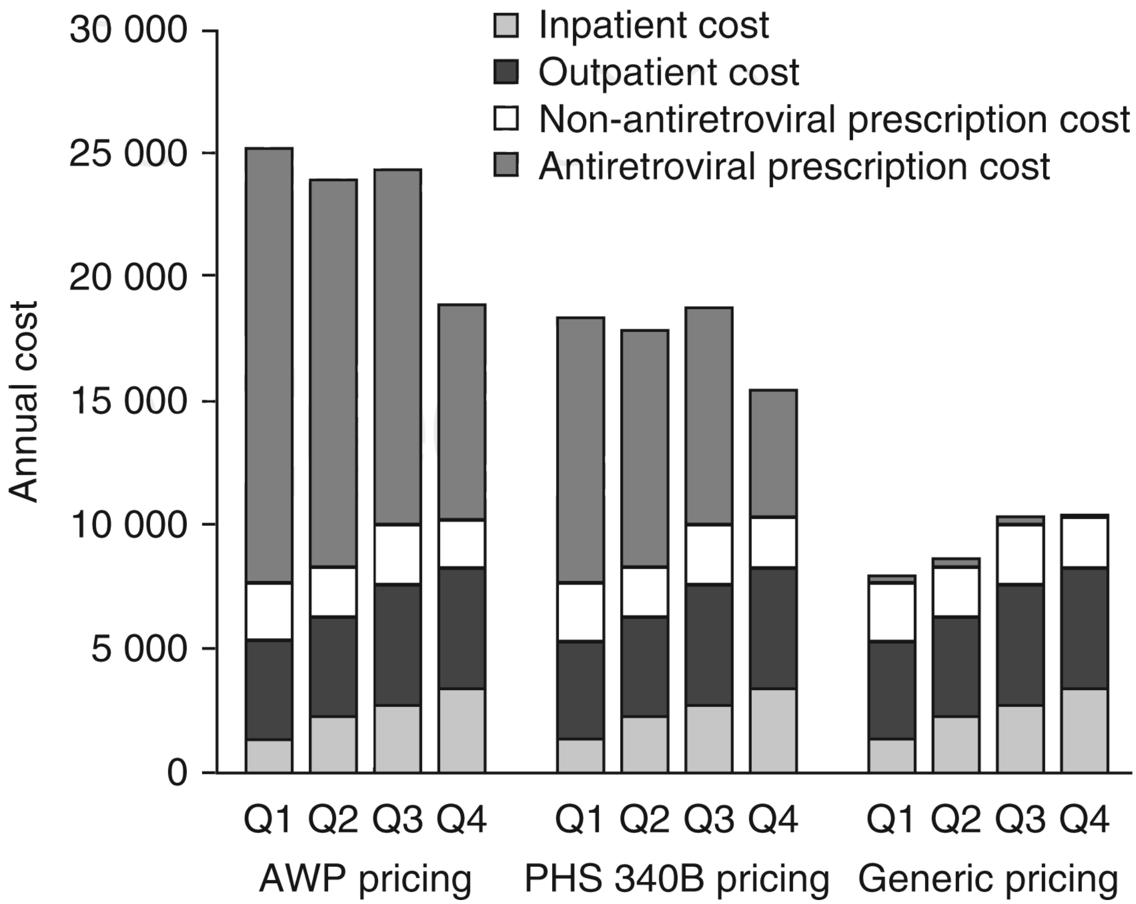

Fig. 2.
Annual medical costs ($US, year 2005 values) overall and by category using three different antiretroviral medication pricing schemes in 325 previously antiretroviral medication-naive patients initiating first antiretroviral therapy within Denver Health, 1997−2003. **AWP** = average wholesale price; **PHS 340B** = US Public Health Service Section 340B Prescription Discount Program; **Q** = quartile of antiretroviral adherence (Q1 = highest adherence, Q4 = lowest adherence).

Table I

Baseline demographic and clinical data stratified by quartile of antiretroviral adherence in 325 antiretroviral-naive patients initiating first antiretroviral therapy within Denver Health, 1997−2003

Characteristic	1st quartile (n=82)	2nd quartile (n=81)	3rd quartile (n=81)	4th quartile (n=81)	p-Value
6-month adherence (%)[a]	100 (100−100)	97.4 (96.2−98.4)	86.3 (82.0−91.3)	47.3 (20.2−65.6)	
Duration of follow-up [y (mean ± SD)]	3.3 (2.0)	3.5 (2.0)	2.9 (1.9)	2.9 (1.8)	0.26
Age [y][a]	38 (30−44)	37 (32−44)	37 (33−42)	37 (32−43)	0.96
Sex: female [n (%)]	8 (10)	11 (14)	7 (9)	10 (12)	0.73
Race [n (%)]					
White	37 (45)	44 (54)	37 (46)	32 (40)	0.33
Black	17 (21)	10 (12)	16 (20)	19 (23)	
Hispanic	27 (33)	24 (30)	28 (35)	26 (32)	
other/unknown	1 (1)	3 (4)	0 (0)	4 (5)	
HIV acquisition risk [n (%)]					
MSM	46 (56)	46 (57)	49 (60)	38 (47)	0.57
IDU	2 (2)	4 (5)	8 (10)	6 (7)	
MSM/IDU	8 (10)	9 (11)	5 (6)	10 (12)	
heterosexual	9 (11)	6 (7)	9 (11)	10 (12)	
other/unknown	17 (21)	16 (20)	10 (12)	17 (21)	
Baseline CD4+ cell count [cells/uL][a]	188 (36−298)	183 (65−326)	133 (37−250)	164 (75−337)	0.14
Baseline HIV-RNA [log copies/mL][a]	5.0 (4.5−5.6)	5.2 (4.8−5.6)	5.0 (4.5−5.7)	4.9 (4.2−5.4)	0.09

IDU = injection drug users; **MSM** = men who have sex with men.

[a]Median (interquartile range).

Table II

Annualized medical costs ($US, year 2005 values), overall and by cost component, stratified by quartile of antiretroviral adherence in 325 antiretroviral-naive patients initiating first antiretroviral therapy within Denver Health, 1997–2003

Parameter	1st quartile (n=82)	2nd quartile (n=81)	3rd quartile (n=81)	4th quartile (n=81)	p-Value
6-month adherence [%][a]	100 (100–100)	97.4 (96.2–98.4)	86.3 (82.0–91.3)	47.3 (20.2–65.6)	
Total annual costs[b]	25 125	23 927	24 334	18 880	<0.001
annual antiretroviral AWP[b]	17 513	15 692	14 336	8 690	<0.001
annual non-antiretroviral costs[b]	7 612	8 235	9 997	10 190	0.06
annual inpatient costs[b]	1 384	2 212	2 667	3 301	<0.001
annual outpatient costs[b]	3 859	3 963	4 821	4 910	0.09
annual non-antiretroviral outpatient pharmacy AWP[b]	2 370	2 060	2 509	1 979	0.62

AWP = average wholesale price.

[a]Median (interquartile range).

[b]Mean.

Table III

Annualized healthcare utilization and overall mortality stratified by quartile of antiretroviral adherence in 325 antiretroviral-naive patients initiating first antiretroviral therapy within Denver Health, 1997–2003

Parameter	1st quartile (n=82)	2nd quartile (n=81)	3rd quartile (n=81)	4th quartile (n=81)	p-Value
6-month adherence [%][a]	100 (100–100)	97.4 (96.2–98.4)	86.3 (82.0–91.3)	47.3 (20.2–65.6)	
Annual outpatient visits [mean (SD)]	15.6 (15.1)	15.1 (12.5)	16.1 (15.2)	19.6 (24.4)	0.34
Annual number of hospitalizations [mean (SD)]	0.10 (0.29)	0.26 (0.62)	0.32 (0.63)	0.61 (1.21)	<0.001
Annual days of hospitalization [mean (SD)]	0.41 (1.26)	1.44 (5.36)	2.02 (5.81)	3.56 (8.60)	0.007
Annual emergency room visits [mean (SD)]	0.23 (0.44)	0.43 (0.91)	0.45 (0.79)	0.90 (1.23)	<0.001
Mortality [n (%)]	4 (5)	3 (4)	7 (9)	7 (9)	0.45

[a] Median (interquartile range).