The Journal of Mental Health Policy and Economics
J Ment Health Policy Econ **12**, 33-46 (2009)

Cost-effectiveness Analysis of Integrated Care for People with HIV, Chronic Mental Illness and Substance Abuse Disorders

Marcia R. Weaver,[1] Christopher J. Conover,[2] Rae Jean Proescholdbell,[3] Peter S. Arno,[4] Alfonso Ang,[5] Karina K. Uldall,[6] Susan L. Ettner[7]

[1]*PhD, Research Associate Professor, Department of Health Services and International Training and Education Center on Health, University of Washington, Seattle, WA, USA*
[2]*PhD, Research Scholar, Center for Health Policy, Durham NC, USA*
[3]*PhD, Research Scholar, Center for Health Policy and Global Health Institute, Durham NC, USA*
[4]*PhD, Professor, Department of Health Policy and Management, New York Medical College, New York, NY, USA*
[5]*PhD, Principal Statistician, Department of Family Medicine, University of California, Los Angeles, CA, USA.*
[6]*MD, MPH, Associate Professor, Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, USA*
[7]*PhD, Professor, Departments of Medicine and Health Services, University of California, Los Angeles, CA, USA*

Abstract

Background: Triply diagnosed patients, who live with HIV and diagnosed mental health and substance abuse disorders, account for at least 13% of all HIV patients. This vulnerable population has substantial gaps in their care, attributable in part to the need for treatment for three illnesses from three types of providers.

Aims of the study: The HIV/AIDS Treatment Adherence, Health Outcomes and Cost study (HIV Cost Study) sought to evaluate the cost-effectiveness of integrated HIV primary care, mental health, and substance abuse services among triply diagnosed patients. The analysis was conducted from a health sector budget perspective.

Methods: Patients from four sites were randomly assigned to intervention group or (n=232) or control group (n=199) that received care-as-usual. Health service costs were measured at baseline and three, six, nine and 12 months and included hospital stays, emergency room visits, outpatient visits, residential treatment, formal long-term care, case management, and both prescribed and over-the-counter medications. Costs for each service were the product of self-reported data on utilization and unit costs based on national data (2002 dollars). Quality of life was measured at baseline and six and 12 months using the SF-6D, as well as the SF-36 physical composite score (PCS) and mental composite score (MCS).

Results: During the 12 months of the trial, total average monthly cost of health services for the intervention group decreased from $3235 to $3052 and for the control group decreased from $3556 to $3271, but the decreases were not significant. For both groups, the percentage attributable to hospital care decreased significantly. There were no significant differences in annual cost of health services, SF-6D, PCS or MCS between the intervention and control group.

Implications for Health Care Provision and Use: The results of this randomized controlled trial did not demonstrate that the integrated interventions significantly affected the health service costs or quality of life of triply diagnosed patients. Professionals could pursue coordination or integration of care guided by the evidence that it does not increase the cost of care. The results do not however, provide an imperative to introduce multi-disciplinary care teams, adherence counseling, or personalized nursing services as implemented in this study.

Implications for Health Policies: There is not enough evidence to either limit continued exploration of integration of care for triply diagnosed patients or adopt policies to encourage it, such as financial reimbursement, grants regulation or licensing.

Implications for Further Research: Future trials with interventions with lower baseline levels of integration, longer duration and larger sample sizes may show improvement or slow the decline in quality of life. Future researchers should collect comprehensive cost data, because significant decreases in the cost of hospital care did not necessarily lead to significant decreases in the total cost of health services.

Received 6 June 2008; accepted 24 November 2008

*** Correspondence to:** Marcia R. Weaver, PhD; 901 Boren, Suite 1100; Seattle, WA 98104, USA
Tel.: +1-206-616 9173
Fax: +1-206-221 4945
E-mail: mweaver@u.washington.edu

Source of Funding: This work was supported by a cooperative agreement for the ''HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study'' (HIV Cost Study), a collaboration of six Federal entities within the U.S. Department of Health and Human Services (DHHS): The Center for Mental health Services (CMHS), which had the lead administrative responsibility, and the Center for Substance Abuse Treatment (CSAT), both components of the Substance Abuse and Mental Health Services Administration (SAMHSA); the HIV/AIDS Bureau of the Health Resources and Services Administration (HRSA); the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), all parts of the National Institutes of Health (NIH).

Introduction

People who are triply diagnosed with HIV infection, mental illness (MI) and substance abuse (SA) are a sizable

proportion of people living with HIV/AIDS (PLWHA). Within clinics that specialize in treatment of PLWHA, estimates of the prevalence of triple diagnosis range from 8%[1] to 24%[2] to as high as 38%.[3] In a nationally representative sample of people receiving HIV-related medical care collected by the HIV Cost and Service Utilization Study (HCSUS), 13% screened positive for mood and/or anxiety disorders, as well as drug dependence symptoms and/or heavy drinking.[4] In a study at two infectious disease clinics in the southeastern United States, 23% of HIV patients met similar screening criteria.[5] A recent review summarizes evidence on the prevalence of triple diagnosis in mental health (MH) and SA service settings.[6]

This vulnerable population has substantial gaps in their care,[7] attributable in part to their need for treatment of three illnesses, often from three types of providers, each with their own theoretical background and policies. Several experts recommend integrated care at one agency[8-12] or coordinated care across agencies,[9,12] as well as communication among providers[12] to promote concurrent access. The merging of behavioral health services with medical services can be conceptualized on a continuum of care ranging from *coordinated,* meaning that care is delivered in different settings with information sharing among programs, to *co-located,* meaning that services are delivered at one location, to *integrated,* meaning that medical and behavioral health care components are merged in one treatment plan.[13]

Little is known about the effects of integration of care on the health outcomes of the triply-diagnosed population from randomized controlled studies. Soto *et al.* reviewed articles describing programs that integrated care for triply-diagnosed people and lessons learned during their implementation, but concluded that few data on health outcomes were available.[10] Since that time, two notable studies have been published. Winiarski *et al.* provided culturally responsive, co-located HIV and MH services, integrating care by holding monthly interdisciplinary patient case conferences and weekly meetings among social service staff.[14] Medical and MH providers were also able to see each other's notes and communicated with each other frequently. Using a comparison group design, more use of project services was related to experiencing fewer emotional/psychological difficulties, fewer HIV symptoms, decreased alcohol and cocaine use, and improved social functioning. Whetten *et al.* integrated care for triply-diagnosed people by providing weekly or bi-weekly sessions of MH and SA treatment on-site at an infectious disease clinic for 12 months.[15] Using a pre-post research design, they found decreases in drug and alcohol use and psychiatric symptomatology.

In addition to improving health outcomes, integration of care holds the promise of being cost effective or even cost-saving. For example, integration of care may improve access to combination antiretroviral therapy (ART) or adherence to it. There is substantial evidence that combination ART[16,17] and interventions that promote adherence to it[18] are cost-effective, as well as evidence that combination ART was associated with lower total cost of medical care.[19-21] Integration of care may also improve access to MH or SA services. There is evidence in samples of unknown HIV status that the total cost of health services decreased after initiation of MH[22] or SA services,[23,24] but recent reviews reported that the evidence was inconclusive.[25,26]

Little is known about the effects of integration of care on the cost of health services for the triply-diagnosed population. The total cost of their medical services may be higher than people with HIV only; Mijch *et al.* reported that triply diagnosed people were more likely to be hospitalized for both psychiatric and medical complications than people with HIV only.[27] Soto *et al.* summarized evidence from several programs showing that integrated MH and/or SA services for PLWHA were related to increased use of HIV primary care.[10] Comprehensive data on cost is needed to test whether or not these increases were associated with savings in inpatient, emergency room or other costs. In the study of integrated care for triply diagnosed patients cited above, Whetten *et al.* reported decreases in emergency room visits and inpatient hospital days and calculations that suggested the intervention was cost-saving.[15]

This study makes two major contributions to the literature on people who are triply diagnosed. (i) It is the first report on a randomized controlled trial of integration of care. (ii) It is also among the first reports on the cost-effectiveness of integration of care. One of the effectiveness measures is quality adjusted life years based on preference weights so that the results could include a cost-utility analysis.

Methods

Study Population and Data

The HIV/AIDS Treatment Adherence, Health Outcomes, and Cost Study (HIV/AIDS Cost Study) was a multi-year cooperative agreement involving eight study sites, one Coordinating Center and six separate Federal agencies.[28] The primary goal of the HIV/AIDS Cost study was to test promising interventions to integrate the care of triply-diagnosed people. The sample size was 431 people from four sites that used a randomized controlled research design: the CORE Center, Cook County Bureau of Health Services (Chicago, IL); University of Missouri-St. Louis (St Louis, MO); University of Washington (Seattle, WA); and The Well-Being Institute, Inc. (Detroit, MI). The sample included people who completed the interview 12 months after baseline and represented 77% of the 559 participants who enrolled in the four sites at baseline. In sensitivity analyses, the 25 people who died before the 12-month interview were included for a total response rate of 82%.

All participants met diagnostic criteria for MI and SA. To determine the presence of co-occurring MI and SA disorders, the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID)[29] was modified for the HIV/AIDS Cost Study[30] and administered to potential participants by interviewers who were trained and certified in SCID administration. All interviewers had at least a bachelor's degree and many had master's degrees in psychology or social work.[31]

Intervention

Although all sites sought to integrate care, there were differences in interventions across sites. At the CORE Center, multi-disciplinary medical care, MH, SA and case management teams collaborated on diagnosis, treatment planning, service delivery and coordination of care. At the University of Missouri-St. Louis, a multi-disciplinary team provided MH, SA and case management services and coordinated care with an offsite medical provider. At the University of Washington, an adherence counselor coordinated care with on-site medical providers and on or off-site MH and SA services. At the Well-Being Institute, a nurse provided case management and coordinated care across medical, MH and SA services. More information on the treatment setting, target population, integrated service model, and care-as-usual condition at each site is reported in **Table 1**, which was originally published in[28] and has been updated and reprinted by permission of the publisher (Taylor & Francis Ltd, http://www.tandf.co.uk/journals). The duration of the intervention was 12 months in every site except Seattle, where it was six months.

Health Service Costs

The cost analysis was conducted from a health sector budget perspective that focused on health services.[32] Although the United States Panel on Cost-Effectiveness in Health and Medicine[33] recommended that all cost-effectiveness analyses include a reference case from the social perspective, the most important difference between the health sector budget and social perspectives for this trial was the omission of patient and family costs, such as informal home care, patient time when using health services, and transportation costs. Data were not collected on patient time and transportation costs. Some experts have advised that including informal home care and patient time in cost analysis adds measurement error.[34]

Information about the patient's health services utilization during the previous three months was collected at baseline through in-person interviews. Similar information was collected at three, six, nine and 12 months after baseline. Self-reported data are the most comprehensive source of information on utilization, because PLWHA use services from a broad range of providers.[35] Participants reported on utilization by both setting and type of service. They reported on all medical, MH and SA visits in three types of settings: inpatient (hospital, nursing home, day hospital and residential treatment facilities), outpatient (emergency room, hospital outpatient, community clinic, private medical office, mental health provider, substance abuse provider), and correctional facilities (jail, prison). In addition to visits, they reported on eight types of services: (i) surgical procedures, (ii) major procedures, (iii) methadone maintenance, (iv) case management; (v) formal home health care; (vi) alternative medicine; (vii) other services; and (viii) medications (prescription pharmaceuticals, alternative medications and over-the-counter medications).

The total number of units of each service was multiplied by a unit cost (2002 dollars) for each service. Where feasible, the unit costs were based on Medicare payments (for example average Medicare payments per diem for different types of inpatient stays) or fee schedule amounts (physician services), weighting the numerous codes within a particular procedure type (for example, eye surgery) by empirical frequencies observed in administrative data for all HIV/AIDS patients (including study non-participants) available from selected HIV/AIDS Cost Study sites. Medicare payments to hospitals closely approximate average costs[36] and may reflect the opportunity costs of resources more accurately than private insurance fees.[33]

To account for the ancillary services in a typical outpatient encounter, we used administrative data for all HIV/AIDS patients at selected HIV/AIDS Cost Study sites to calculate the ratio of ancillary services to professional fees for outpatient services. This ratio was used to estimate the cost per outpatient visit, using the Medicare fee schedule to monetize the professional component of costs. A similar procedure was used to calculate the ratio of professional fees to inpatient costs and estimate inpatient cost based on per diem Medicare hospital expenditures. Services for which no Medicare data were available were assigned costs from nationally representative data reported in the literature or by trade organizations. For a few services for which nationally representative data were not available, unit costs were estimated from one or more HIV/AIDS Cost Study sites.

We estimated pharmaceutical use based on participants' responses and expert judgment on dosages. Information on dosages and prices from the Red Book were used to estimate average wholesale price (AWP) per day; costs were estimated to be 21% below AWP.[37] We estimated separate unit costs for all medications reported by patients in the following categories: HIV/AIDS, HIV/AIDS-related illnesses, psychiatric, and selected expensive medications within the ''herbal supplement and other'' category. A standardized unit cost was imputed for all remaining medications.

Annual costs were calculated using the sum of the units of each service from four interviews. In accordance with the recommendations of the U.S. Panel on Cost-Effectiveness in Health and Medicine, neither costs nor quality of life were discounted because they occurred within the first year of the trial.[33] Thirty-four percent of the sample missed at least one of the four follow-up interviews, but completed the interview 12 months after baseline. When someone missed an interview, they reported their utilization since the last interview and their responses were based on recall of longer than three months.

Considering the cost of integration, if it involved additional services such as case management or counseling visits, the cost was reflected in the analysis. If it involved professional time outside of patient visits such as cross-disciplinary treatment planning or nurse-to-nurse coordination of care, the baseline cost was reflected in the unit cost assigned. For example, the time that a case manager spent outside of patient visits was allocated to the unit cost of each visit. However, the same unit costs were applied at baseline and during the intervention, so any change in the amount of time spent outside of patient care was not included in the analysis.

Table 1. Description of Four Sites of the HIV/AIDS Cost Study

Study site	Integration	Treatment setting	Target population	Integrated service model	Care-as-usual	Study design
CORE Center, Chicago IL	Multidisciplinary MH, SA, case management, and HIV/AIDS medical care provider teams	State-of-the-art urban HIV/AIDS clinic with co-located MH, SA, and case management services	Multiply diagnosed individuals receiving medical care at the CORE Center	Formation of integrated medical care, MH, SA, and case management treatment teams that feature collaborative cross-disciplinary diagnosis and treatment planning, service delivery, and care co-ordination	HIV/AIDS medical care with referral to on-site MH, SA, and case management services	Serial assignment to integrated treatment team clinics or care-as-usual clinics dependent on slot availability at time of admission
University of Missouri, St Louis MO	Multidisciplinary MH, SA, and case management services co-ordinated with off-site HIV/AIDS medical care	Community-based integrated MH, SA, and case management services provider	Multiply diagnosed individuals recruited from Ryan White-funded case management providers and HIV/AIDS medical care providers	Multidisciplinary treatment team providing MH, SA, and case management services, including street outreach; ongoing coordination with HIV/AIDS medical providers	Referral by Ryan White case manager or medical provider to MH or SA treatment, with limited availability to multiply diagnosed individuals	Random assignment to multidisciplinary treatment team or care-as-usual
University of Washington, Seattle WA	Individual and group adherence counseling co-ordinated with on-site HIV/AIDS medical care and on- or off-site MH and SA services	Two settings: Multi-service agency at urban medical center providing HIV/AIDS clinical care, case management, and limited MH and SA counseling to women and families, 2) university-based infectious disease outpatient clinic with limited MH services and referral to off-site SA services	Multiply diagnosed women recruited from the multiservice agency and men recruited from an infectious diseases outpatient clinic	Six-month individualized adherence counseling combined with 3-month group adherence counseling	HIV/AIDS clinical care and case management with referral to on- or off-site MH and SA treatment services	Random assignment to adherence counseling plus care-as-usual or care-as-usual
Well-Being Institute, Detroit MI	Nursing co-ordination of care across medical care, MH, and SA services	Urban nursing provider partnering with HIV/AIDS medical clinics, a community MH center, and a private SA treatment programme	Multiply diagnosed women who were lost to follow-up at partner HIV/AIDS clinics	Intensive personalized nursing services, including transportation, case management to facilitate engagement in care, and nurse-to-nurse co-ordination of HIV/AIDS medical care, MH, and SA services	Referral to off-site MH and SA services by HIV/AIDS medical providers	Random assignment to intensive personalized nursing services or to care-as-usual

Quality of Life

Respondents' answers to the Short Form-36 (SF-36)[38] were used to construct the SF-6D,[39] which is a well-established measure of quality adjusted life years. The SF-6D mapped responses to 10 items on the SF-36 into a preference-based single index of a quality adjusted life-year. Brazier *et al.* originally estimated the preference weights using a Standard Gamble technique with a representative sample of the general population of United Kingdom.[39] Our estimates were calculated using the preference weights for the United States (Brazier, personal communication July 19, 2004) rather than the United Kingdom, because the study was conducted in the United States.

To facilitate comparisons with other studies, two additional measures of quality of life were constructed based on the SF-36: (i) mental composite score (MCS),[40,41] and (ii) physical composite score (PCS).[40,41] The MCS and PCS are more widely used, even though quality adjusted life years based on expected utility theory are preferred by many economists.

Participants completed baseline interviews asking SF-36 items based on the preceding six months, and again at six and 12 months after baseline. Annual quality of life was calculated with the sum of two numbers: (i) average of baseline and six month score weighted by number of days between the two interviews, and (ii) average of six-month and 12-month score weighted by number of days between the two interviews. The sum was divided by number of days between the baseline and 12 month interviews. Sixteen percent of the sample missed the six-month interview. Their responses at the 12-month interview were about the 12 months prior and the calculation of their annual quality of life was adjusted accordingly.

As noted above, 25 people died within 12 months of baseline. An analysis of complete cases that discards data on the deceased may be biased. As Diehr *et al.* explained, ''The group with more deaths has the advantage because more of the sickest cases are removed from the analysis.''[42] Previous research about PLWHA found that the SF-36 was less sensitive than a preference-based measure of quality of life, primarily because people who died were excluded from analysis of the SF-36 and included in analysis of the preference-based measure.[43] The preference-weights of the SF-6D addressed this limitation of the SF-36 by combining mortality and morbidity on a single scale. In one set of estimates, the people who died during the trial were included in the analysis. Their quality of life during the six-month interval when they died was calculated as the sum of two numbers: (i) one-half the value at the previous interview until date of death, and (ii) zero after death, weighted by number of days in each period.

Independent Variables

The estimates controlled for the demographic, socio-economic and health variables in **Table 2**. To facilitate interpretation of results, income was converted to a categorical variable based on each family's percentage of the Federal poverty level given its number of members (e.g., $18,100 for a family of four). Racial/ethnic and insurance variables were based on the hierarchies shown in **Table 2**. Some people without insurance received drug benefits through AIDS Drug Assistance Programs (ADAP).

Among health variables, the SA diagnoses based on the SCID were represented by four mutually exclusive variables; drug and alcohol dependent represented the most severe category. Estimates of the PCS also included the MCS as an independent variable and vice versa. The quartile indicator of values was used instead of the continuous measures; the lowest quartile (0-25%) corresponded to the sickest participants.

Data on participants' HIV viral load were collected from two sources: (i) abstracted from medical records from six months prior to one month following baseline and (ii) self-reported at baseline interview. The highest values represented the sickest participants. Due to missing data, primarily for HIV viral load, we performed multiple imputation using five datasets created using the Markov Chain Monte Carlo approach.[44,45] The HIV viral load variable was based on medical records for 60% of the sample, self report for 2%, and multiple imputation for 38%.

Data Analytic Methods

The comparison of intervention and control group characteristics at baseline used two independent sample tests: (i) t-test for quality of life variables and (ii) chi-square for categorical variables. Two comparisons of average monthly health service cost were performed with two statistical tests. The test for differences between the intervention and control group at baseline was performed with the Wilcoxon-Mann-Whitney test, which is the non-parametric analog to the independent samples t-test. The test for change between the average monthly cost during the three months prior to baseline and average monthly cost during the 12 months of the trial was performed with the Wilcoxon signed rank sum test, which is the non-parametric version of a paired samples t-test.

Annual total cost of health services was analyzed with a regression of the square root of the cumulative total cost of health services during the 12 months of the trial. The results were retransformed using the smearing estimate;[46] residuals were homoskedastic. Significance of the intervention effect was determined based on 95% empirical confidence intervals derived from standard bootstrapping methods with replacement,[47] using 1000 replicate samples. Annual quality of life was analyzed as the untransformed annual scores.

Significance of comparisons between intervention and control groups was based on the regression coefficient of the binary variable for treatment group. The estimates for each dependent variable controlled for baseline values of the dependent variables, and year of the baseline interview to adjust for secular decreases in the cost of health services. Even if the randomization process and retention were flawless this simple model would yield consistent but potentially inefficient estimates, so the estimates also controlled for demographic, socio-economic and health variables. All estimates used a ''fixed effects'' approach to

Table 2. Baseline Comparison of HIV/AIDS Cost Study Participants

	Intervention	Control	Total	(p-values)
SF-6D -mean (standard deviation)	.617 (0.12)	.623 (0.12)	.620 (0.12)	0.57
MSC - mean (standard deviation)	35.1 (12.4)	35.3 (11.8)	35.20(12.0)	0.83
PCS - mean (standard deviation)	43.5 (11.1)	43.6 (10.7)	43.57 (10.9)	0.89
Gender				
Male	43%	39%	41%	0.41
Female	57%	61%	59%	0.41
Age				
18-34	26%	22%	24%	0.36
35-49	64%	67%	66%	0.49
50+	10%	11%	10%	0.83
Race/ethnicity				
Latino	3%	4%	3%	0.57
Black, non-Latino	68%	71%	70%	0.60
Other, non-Latino	7%	6%	7%	0.88
White	22%	19%	20%	0.45
Marital status				
Married or cohabiting	7%	9%	8%	0.19
Divorces, separated, widowed	27%	32%	29%	0.31
Never married	66%	60%	63%	0.47
Education				
< 12 years	44%	42%	43%	0.64
12 years	22%	25%	24%	0.51
13-15 years	27%	29%	28%	0.64
16+years	6%	4%	5%	0.26
Income (as % poverty level)				
le 50%	38%	33%	36%	0.15
50 < income le 75%	21%	18%	19%	0.49
75< income le 100%	17%	24%	20%	0.08
>100%	24%	25%	24%	0.73
Insurance				
Private	7%	7%	7%	0.91
Medicaid and Medicare	7%	11%	9%	0.51
Medicaid only	32%	36%	34%	0.41
Medicare only	3%	3%	3%	0.77
Other public	31%	30%	30%	0.91
None, no ADAP meds	7%	5%	6%	0.32
None with ADAP meds	11%	9%	10%	0.43
Prescription drug coverage from at least one insurer	22%	26%	24%	0.43
SCID				
Alcohol & drug dependent	41%	46%	44%	0.31
Drug dependent only	40%	30%	35%	0.04
Alcohol dependent only	14%	19%	16%	0.21
Alcohol &/or drug abuse only	5%	5%	5%	0.95
Viral Load				
0 – 999	31%	42%	36%	0.07
1,000-9,999	34%	27%	31%	0.15
10,000-100,000	25%	26%	26%	0.87
=100,000	9%	5%	7%	0.08
Sample size	232	199	431	

control for unobservable site-specific heterogeneity that may have been correlated with participant-level characteristics. We also tested for interactions between treatment and site effects. As the interaction terms were not significant, we do not present these estimates as part of our main analysis but they are available upon request from the authors.

As described above, each annual quality of life variable was the weighted sum of two averages, one of which included the baseline value of the dependent variable. The statistical analysis controlled for baseline value of the dependent variable, which potentially introduced a conservative bias to the estimates, i.e., the effect of the baseline variable could potentially be over-estimated, leaving less variation to be explained by the binary variable for treatment group. To explore this possibility, alternate models were estimated with the first difference as the dependent variable instead of controlling for baseline values of the dependent variable in the regression.

Results

Baseline Characteristics of Sample

The participants were demographically diverse, economically disadvantaged, and in poor health. At baseline, the mean SF-6D score was .620 on a scale where 0 was death and 1 was optimal health. The mean MCS score was 35.20 and PCS score was 43.57, where 50 out of 100 was calibrated to be the average score for the population of the United States.

As shown in **Table 2**, at baseline there were no significant differences between the intervention and control group across demographic, socio-economic or health characteristics. The exception was that a higher percentage of participants in the intervention group had drug dependence only compared to the control group (40% vs. 30%, p=0.04).

There were no significant differences in the response rates between intervention and control groups. Seventy-nine percent of the intervention group participants completed the 12-month interview compared to 73% of control group (p=0.093). When participants who died were included, the response rates were 83% and 78%, respectively (p=0.164).

Average Monthly Health Service Cost

The total average monthly cost of health services during the three months prior to baseline was $3,235 for the intervention group and $3,556 for the control group, as shown in columns 2 and 3, respectively, of **Table 3**. There was no significant difference in the total average monthly cost between groups, nor was there a significant difference in the average monthly cost of any of the services.

The total average monthly cost during the 12 months of the trial decreased to $3,052 (6%) for the intervention group, and $3,271 (8%) for the control group. To aid comparisons, the average monthly costs during the 12 months of the trial in columns 5 and 7 of **Table 3** are presented as a ratio with the average monthly cost during the 12 months of the trial as the numerator and the average monthly cost during the three months prior to baseline as the denominator. (To obtain the dollar amount of the average monthly cost during the 12 months of the trial, simply multiply columns 2 and 5 for the intervention group or columns 3 and 7 for the control group.)

Although the change in total average monthly cost was not significant for either group, the percentage of total average monthly cost attributable to hospital services decreased significantly from 37% at baseline to 28% (p<0.001) for the intervention group, and from 32% to 29% (p<0.001) for the control group.

The percentage attributable to outpatient services did not change significantly for either group, but within the category of outpatient services, the cost of major procedures, emergency room, and visits to community clinics or private doctors' offices decreased significantly for both groups. The unit costs were the same at baseline and during the intervention, so changes in costs also reflected changes in utilization. The cost of outpatient MH and SA visits, methadone maintenance, and alternative health care increased significantly for the intervention group and decreased significantly for the control group. The cost of case management visits increased significantly for the intervention group, but not the control group. The cost of outpatient clinic visits decreased significantly for the intervention group, but not the control group. The cost of surgical procedures decreased significantly for the control group, but not the intervention group.

Effect of the Integration of Services on Annual Cost of Health Services

The total annual cost of health services during the 12 months of the trial was not significantly different between intervention and control groups (p=0.980), as summarized in **Table 4**. When results were retransformed, the effect was an insignificant increase of $290 (CI -$4,343, $4,922), which was less than one percent of the total annual cost. Retransformed effects of the other co-variates are presented in **Appendix**, **Table A1**.

Effect of Integration of Services on Quality of Life

The predicted mean of the SF-6D, MCS and PCS during the 12 months of the trial for the sample under care as usual is presented in **Table 4**. Column 2 presents the results for the participants who completed the 12-month interview. For the sample as a whole, the SF-6D decreased from 0.620 at baseline to 0.606, the PCS decreased from 43.57 to 40.76, and the MCS increased from 35.20 to 36.39. The effect of the intervention was not significant however, for any of the three measures of quality of life.

Among the 25 deaths in the sample, 11(4.5%) were treatment and 14 (6.6%) were control group participants (p=0.338.) Column 3 presents the results when they were included in the analysis. None of the three measures of quality of life were significantly different between

Table 3. Monthly Average Cost by Service at Baseline and During the Intervention

Type of Service	Baseline (3-month average)			Intervention (12-month average) presented as a ratio with baseline (3-month average) as the denominator			
	Intervention (2)	Control (3)	Test of difference between intevention vs control at baseline (4)	Intervention (5)	Test change in intervention group over time (6)	Control (7)	Test change in control group over time (8)
Inpatient Services	$1,205	$1,152	p=0.12	0.70	p<0.001	0.82	p<0.001
Hospital inpatient	$860	$786	p=0.20	0.67	p<0.001	0.61	p<0.001
Day hospitalization program	$77	$85	p=0.52	0.41	p<0.001	0.46	p<0.001
Nursing home/hospice facility	$48	$76	p=0.44	0.71	p<0.001	1.25	p<0.001
Residential treatment facility	$220	$205	p=0.27	0.90	p=0.46	1.61	p=0.09
Outpatient Services	$984	$1,024	p=0.66	0.95	p=0.83	0.85	p=0.29
Surgical procedures (e.g., appendectomy*)**	$14	$19	p=0.43	1.06	p=0.57	0.65	p<0.001
Major procedures (MRI, CT, lumbar puncture)**	$63	$49	p=0.25	0.48	p<0.001	0.66	p<0.001
Emergency room	$118	$110	p=0.76	0.69	p=0.003	0.72	p=0.02
Outpatient clinic (medical)	$194	$167	p=0.13	0.60	p=0.01	0.66	p=0.63
Community or private MD office (medical)	$27	$25	p=0.37	0.40	p<0.001	0.43	p<0.001
Outpatient MH/SA	$125	$136	p=0.79	1.07	p<0.001	0.84	p<0.001
Methadone maintenance	$61	$88	p=0.24	1.49	p<0.001	0.64	p=0.01
Case management (face-to-face & phone contact)***	$129	$123	p=0.99	1.49	p=0.01	1.18	p=0.77
Professional home care (visiting nurse, home health aide, therapist, social worker, babysitter)***	$85	$148	p=0.42	1.05	p=0.75	1.32	p=0.24
Alternative health care (includes chiropractic)	$67	$74	p=0.68	1.15	p=0.003	0.53	p<0.001
Other care (dental, foot, eye, nutritionist)***	$102	$85	p=0.78	1.03	p=0.92	0.79	p=0.59
Medications	$1,046	$1,380	p=0.26	1.21	p=0.09	1.06	p=0.36
Grand Total	$3,235	$3,556	p=0.71	0.94	p=0.41	0.92	p=0.81
Sample Size	232	199		232	199		

* Separate unit costs were used for 16 different categories of surgical procedures. Results were weighted averages across all procedures.
** These may have been performed in either inpatient or outpatient settings.
*** Separate unit costs were developed for each service listed in parentheses. Figures shown represent weighted averages across all services.
Note: Excluded Items: self-help/support groups, informal home care, Meals on Wheels, shelter expenses for stays in jail, prison and homeless shelters.
The Wilcoxon signed rank sum test is the non-parametric version of a paired samples t-test (for test of change between baseline intervention to 12-month intervention)
The Wilcoxon-Mann-Whitney test is a non-parametric analog to the independent samples t-test (used for test of difference between intervention and control at baseline)

Table 4. Effect of the Intervention on Annual Expenditures and Quality of Life

	Participants who completed the 12-month interview* (2)	Participants who died or completed the 12-month interview* (3)
Annual health service expenditures		
Mean under care as usual	$31,447	
Effect of intervention	$290	
95% confidence interval	–$4,343, $4,922	
P-value	0.980	
SF-6D		
Mean under care as usual	0.606	0.630
Effect of intervention	0.005	–0.005
95% confidence interval	–0.011, 0.021	–0.027, 0.018
P-value	0.539	0.687
MCS		
Mean under care as usual	36.446	37.795
Effect of intervention	1.248	0.673
95% confidence interval	–0.342, 2.838	–1.068, 2.415
P-value	0.123	0.448
PCS		
Mean under care as usual	40.673	42.799
Effect of intervention	–0.901	–1.240
95% confidence interval	–2.113, 0.311	–2.681, 0.202
P-value	0.145	0.092
Sample size	431	456

*All estimates included the co-variates in **Table 2** and used a ''fixed effects'' approach to control for unobservable site-specific heterogeneity that may be correlated with participant-level characteristics.
Note: Estimates with the MCS and PCS as the dependent variable excluded the quartile indicators of values of the MCS and PCS, respectively, at baseline. Estimates with the SF-6D omitted the quartile indicator of values for both MCS and PCS at baseline.

intervention and control groups. Similarly, none of the measures of quality of life were significantly different between the intervention and control group in estimates with the first difference model (not shown).

Discussion

The randomized controlled trial at four sites of the HIV/AIDS Cost Study was an impressive and innovative attempt to improve treatment adherence and health outcomes of people who were triply diagnosed. The interventions represented changes within and across organizations. The participants' utilization of specific services changed significantly during the 12 months of the trial, and some of those changes were unique to the intervention group.

During the trial, the 6% and 8% percent decline in total average monthly cost of health services for the intervention and control groups respectively, was not significant. Several studies reported a decrease in the cost of health services for PLWHA after combination ART was introduced in 1996,[19-21] but continued decreases were not observed in 2001-2003 during the HIV/AIDS Cost Study.[48,49]

For the sample as a whole, two out of three measures of the quality of life decreased during the trial; the predicted mean of the SF-6D and PCS under care as usual were lower than the sample average during the three months prior to baseline. A recent longitudinal analysis of participants in the Multicenter AIDS Cohort Study also showed a decrease in quality of life, with the exceptions of slight increases in MCS and PCS two to four years after initiating combination ART.[50]

Unfortunately, the results failed to demonstrate that the interventions to integrate care significantly affected the cost of health services or quality of life. A recent review of randomized controlled trials of integration of MH and SA services among people with co-occurring MH and SA disorders (but unknown HIV status) also reported equivocal evidence of its effect on substance use and psychiatric symptoms.[51]

There were differences in the interventions across sites, but the heterogeneity would not necessarily explain the lack of effectiveness. Tests of the interaction between treatment and site effects did not show that the intervention at a specific site affected total cost or quality of life. Future trials are likely to encounter the same heterogeneity across sites. Any organization that moves incrementally along the continuum from sequential or parallel care to fully integrated services

does so within the context of a unique system of clinics and providers. Willenbring suggests that an appropriate integration strategy depends on system, patient and team factors and advocates that organizations adopt principles rather than models for integrating services.[12] The context of the clinics and providers may however, offer an explanation for the lack of effectiveness. Each of the sites in this study offered some coordination of care in the care-as-usual condition. It is possible that identical interventions would have been effective in sites with lower baseline levels of integration.

Coordination or integration of services might ultimately be beneficial even at the HIV Cost Study sites. A six or 12-month intervention may not have been long enough to observe changes in quality of life for this population. In an earlier analysis of the HIV/AIDS Cost Study participants at baseline, 33% received concurrent treatment for MH and SA; only this minority could have fully benefited from integration of care from the beginning of the interventions.[7] Donald et al. noted the lengthy and difficult process for recovery for dually diagnosed people, as well as heterogeneity among dually diagnosed people and small sample sizes.[51] In a review of randomized controlled trials for integration of primary care and SA services, Willenbring noted the potential for improvement over a one to two year period.[12]

Two additional analyses with the HIV/AIDS Cost Study data have been considered by other investigators on the multi-site study. First, the effects of integration on virologic outcomes could be assessed using the data on HIV viral load that were collected at baseline, six and 12 months. However, data from medical records on HIV viral load were incomplete particularly when examining longitudinal changes requiring multiple measurements (data were missing for 40% of the participants at baseline). So, any observed changes could not necessarily be generalized to the full sample considered in the present analysis. Second, the study compiled data on patient satisfaction data that could be used to assess differences in satisfaction between patients in the intervention group compared to the control group. Participants were asked to rate coordination of care as part of the service utilization questionnaire, as well as to respond to a single-item question about each of the settings and types of services. Single-item measures were however reported to have less score variability, and lower reliability and validity than multi-item scales.[52]

Limitations

There were at least five limitations to the study. First, the health sector budget perspective omitted patient and family costs. In future research, the cost analysis could be extended from the health sector budget perspective to include some patient and family costs, such as the cost of informal home care. Ettner *et al.* report that informal home care was 85% of the cost of home care at baseline for participants in the HIV/AIDS Cost Study.[53] The cost of formal home care did not change significantly in either the intervention or control groups, and that result may have extended to informal home care. Second, the unit costs were obtained in a heterogeneous fashion. These methods were necessary because of the broad range of services from which participants sought care and typical in multi-site studies. Third, the 25 participants who died were omitted from the cost analysis, because no cost data were available for them during the three-month interval when they died. This omission probably did not affect the results, because there was no significant difference in mortality rates between intervention and control groups. In future research, we would recommend proxy interviews on the cost of health services with someone who survived the deceased at an appropriate time.

Sherbourne *et al.* reported that preference weights for the SF-6D based on the Standard Gamble were less responsive than the MCS and other preference-weighted measures derived from the SF-36.[54] It is unknown however, whether this would apply to weights for the United States as well to weights for United Kingdom. Given that the effect of the intervention on the MCS was not significant, it is unlikely that other preference weights would alter the results.

Finally, there was potential for contamination to bias the trial against showing effects, because care-as-usual was offered at all four sites after randomization. At two of the sites (CORE Center and University of Missouri) the intervention was among the treatment team members, so intervention group participants could not chose to continue care-as-usual and control group participants did not have access to the intervention. At the other two sites (University of Washington and Well-Being Institute), intervention group participants could have chosen not to use the intervention as in any trial with an intention-to-treat design, but control group participants did not have access to the intervention.

Conclusion

The results of this randomized controlled trial did not demonstrate that interventions to integrate services significantly affected the health service costs or quality of life of triply diagnosed patients. Future trials with lower baseline levels of integration, longer duration and larger sample sizes may show improvement or slow the decline in quality of life. In the meantime, health service professionals could pursue coordination or integration of care guided by the evidence that they ''do no harm.''

Acknowledgments

We dedicate this manuscript to the patients and research staff that made the HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study possible.

This research was supported by a cooperative agreement for the ''HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study,'' a collaboration of six Federal entities within the U.S. Department of Health and Human Services (DHHS). The content of this publication does not

necessarily reflect the views or policies of DHHS, CSAT, SAMHSA, HRSA, or NIH.

In addition to the named authors, the members of the HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study were as follows (those in bold-face served as members of the Subcommittee on Costs that developed the utilization survey and unit costs used in this paper):

Steering Committee [Steering Committee Chair, CMHS Program Director, Consumer Liaison, Coordinating Center PI, and Study Site Principal Investigators]: Seth Kalichman, University of Connecticut; Storrs, CT; Mary C. Knipmeyer, Center for Mental Health Services, SAMHSA, Rockville, MD; Phil Meyer, Los Angeles, CA; James Bell, James Bell Associates, Arlington, VA; Marcia Andersen, Well-Being Institute, Detroit, MI; Robert Calsyn, University of Missouri, St. Louis, MO; Terence Keane, Boston University School of Medicine, Boston, MA; Stanley Sacks, National Development & Research Institutes, Inc., New York, NY; Tomas Soto, Cook County Bureau of Health Services/CORE Center, Chicago, IL; Karina Uldall, University of Washington, Seattle, WA; Mark Winiarski, Montefiore Medical Center, Bronx, NY; Kathryn Whetten, Duke University, Durham, NC.

Federal Collaborators: Health Resources and Services Administration (HRSA): Philomena Green-Morsell, Melinda Tinsley, HIV/AIDS Bureau, Rockville, MD; National Institutes of Health (NIH): Jerry Flanzer, National Institute on Drug Abuse, Bethesda, MD; David M. Stoff, National Institute of Mental Health, Bethesda, MD; and Kendall Bryant, Michael Hilton, National Institute on Alcohol and Alcoholism, Rockville, MD; Substance Abuse and Mental Health Services Administration (SAMHSA): Mary C. Knipmeyer, Center for Mental Health Services (Lead Agency), Rockville, MD; **David Thompson**, **Ali Manwar**, Center for Substance Abuse Treatment, Rockville, MD.

Collaborating Scientists – Co-Principal Investigators and Co-Investigators: Karen Bonuck, Montefiore Medical Center, Bronx, NY; Deborah Brief, Boston University School of Medicine, Boston, MA; **Lynn Dhanak**, University of Washington, Seattle, WA; **Patrick Flynn**, National Development & Research Institutes, Inc., Raleigh, NC; **Victoria Harris**, University of Washington, Seattle, WA; **Thomas W. Helminiak**, University of Missouri, St. Louis, MO; **Ann Hendricks**, Boston University School of Medicine, Boston, MA; W. Dean Klinkenberg, Missouri Institute of Mental Health, St. Louis, MO; Alec Miller, Montefiore Medical Center, Bronx, NY; Darlene Mood, Well-Being Institute, Detroit, MI; Gary A. Morse; Community Alternatives, St. Louis, MO; **Susan Pfoutz**, Well-Being Institute, Detroit, MI; **Jim Porto**, National Development & Research Institutes, Inc., Chapel Hill, NC; **Rebecca Roberts**, Cook County Hospital, Chicago, IL; Renslow Sherer, Cook County Bureau of Health Services/CORE Center, Chicago, IL; Laura Sadowski, Cook County Hospital; Chicago, IL; Geoffrey Smereck, Well-Being Institute, Detroit, MI; Marvin Swartz, Duke University Medical Center, Durham, NC; Glenn Trezza, Boston VA Medical Center, Boston, MA; Robert Weinstein, Cook County Hospital, Chicago, IL.

References

1. Pence BW, Miller WC, Whetten K, Eron JJ, Gaynes BN. Prevalence of DSM-IV-defined mood, anxiety, and substance use disorders at an HIV clinic in southeastern United States. *J Acquir Immune Defic Syndr* 2006; **42**: 298-306.
2. Lyketsos CG, Hanson A, Fishman M, McHugh PR, Treisman GJ. Screening for psychiatric morbidity in a medical outpatient clinic for HIV infection: the need for a psychiatric presence. *International J Psychiatry Med* 1994; **24**: 103-113.
3. Tegger MK, Crane HM, Tapia KA, Uldall KK, Holt SE, Kitahata MM. The effect of mental illness, substance use, and treatment for depression on the initiation of highly active antiretroviral therapy among HIV-infected individuals. *AIDS Patient Care STDs* 2008; **22**: 231-241.
4. Galvan F H, Burnam M A, Bing E G. Co-occurring psychiatric symptoms and drug dependence or heavy drinking among HIV-positive people. *J Psychoactive Drugs* 2003; **35**: 153-160.
5. Whetten K, Reif SS, Napravnik S, Swartz MS, Thielman NM, Eron JJ, Lowe K, Soto T et al. Substance abuse and symptoms of mental illness among HIV-positive persons in the Southeast. *South Med J* 2005; **98**: 9-14.
6. Douaihy AB, Jou RJ, Gorske T, Salloum IM. Triple diagnosis: Dual diagnosis and HIV disease, Part I. *AIDS Read* 2003; **13**: 331-341.
7. Weaver MR, Conover C, Proescholdbell RJ, Arno PS, Ang A, Arno P, Ettner SL for the Cost Subcommittee of the HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study. "Access to mental health and substance abuse care for people living with HIV/AIDS, chronic mental illness, and substance abuse disorders.'' *J Acquir Immune Defic Syndr* 2008; **47**: 449-458.
8. Douaihy AB, Jou RJ, Gorske T, Salloum IM. Triple diagnosis: dual diagnosis and HIV disease, part 2. *AIDS Read* 2003; **13**: 375-382.
9. Acuff C, Archambeault J, Greenberg B, Hoeltzel J, McDaniel J S, Meyer P, et al. *Mental Health Care for People Living with or Affected by HIV/AIDS: A Practical Guide*. Rockville, MD: United States Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, National Mental Health Information Center, 1999. Available online at: http://mentalhealth.samhsa.gov/publications/allpubs/KEN00-0081/default.asp Accessed on March 30, 2007.
10. Soto TA, Bell J, Pillen MB, et al. Literature on integrated HIV care: a review. *AIDS Care* 2004; **16**: S43-S55.
11. Klinkenberg WD, Sacks S et al. Mental disorders and drug abuse in persons living with HIV/AIDS. *AIDS Care* 2004; **16**: S22-S42.
12. Willenbring ML. Integrating care for patients with infectious, psychiatric, and substance use disorders: concepts and approaches. *AIDS* 2005; **19**: S227-S237.
13. Blount E. Integrated primary care: organizing the evidence. *Fam Syst Health* 2003; **21**: 121-133.
14. Winiarski MG, Beckett E, Salcedo J. Outcomes of an inner-city HIV mental health programme integrated with primary care and emphasizing cultural responsiveness. *AIDS Care* 2005; **17**: 747-756.
15. Whetten K, Seif S, Ostermann J, Pence BW, Swartz M, Whetten R, Conover C, Bois S, Thielman N, Eron J. Improving health outcomes among individuals with HIV, mental illness, and substance use disorders in the Southeast. *AIDS Care* 2006; **18**: S18-S26.
16. Freedberg KA, Losina E. Weinstein MC, Paltiel AD, Cohen CJ, Seage GR, Craven DE, Zhang H, Kimmel AD, Goldie SJ. The cost effectiveness of combination antiretroviral therapy for HIV disease. *N Engl J Med* 2001; **344**: 824-831.
17. Moore RD. Cost effectiveness of combination HIV therapy: 3 years later. *Pharmacoeconomics* 2000; **17**: 325-330.
18. Freedberg KA, Hirschhorn LR, Schackman BR, Wolf LL, Martin LA, Weinstein MC, Goldin S, Paltiel AD, Katz C, Goldie SJ, Losina E. Cost-effectiveness of an intervention to improve adherence to antiretroviral therapy in HIV-infected patients. *J Acquir Immune Defic Syndr* 2006; **43**: S113-S118.
19. Bozzette SA, Joyce G, McCaffrey DF, Leibowitz AA, Morton SC, Berry SH, Rastegar A, Timberlake D, Shapiro MF, Goldman DP for the HIV Cost and Services Utilization Consortium. Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. *N Engl J Med* 2001; **344**: 817-823.
20. Gebo KA, Chaisson RE, Folkemer JG, Bartlett JG, Moore RD. Costs of

HIV medical care in the era of highly active antiretroviral therapy. *AIDS* 1999; **13**: 963-969.
21. Keiser P, Kvanti MB, Turner D, Reisch J, Smith JW, Nassar N, Gregg C, Skiest D. Protease inhibitor-based therapy is associated with decreased HIV-related health care costs in men treated at a Veterans Administration Hospital. *J Acquir Immune Defic Syndr* 1999; **20**: 28-33.
22. Simon GE, Katzelnick DJ. Depression, use of medical services and cost-offset effects. *J Psychosom Res* 1997; **42**: 333-334.
23. Armstrong MA, Midanik LT, Klatsky AL, Lazere A. Utilization of health services among patients referred to an alcohol treatment program. *Sub Use Misuse* 2001; **36**: 1781-1793.
24. Holder HD. Cost benefits of substance abuse treatment: an overview of results from alcohol and drug use. *J Ment Health Policy Econ* 1998; **1**: 23-29.
25. California Health Benefits Review Program (CHBRP). *Analysis of Assembly Bill 1887: Health Care Coverage: Mental Health Services* Oakland, CA: Report to California State Legislature, 2008. Available online at http://www.chbrp.org/documents/ab_1887_report.pdf Accessed on April 17, 2008.
26. Donohue JM, Pincus HA. Reducing the societal burden of depression: a review of economic costs, quality of care and effects of treatment. *Pharmacoeconomics* 2007; **25** (1): 7-24.
27. Mijch A, Burgess P, Judd F, Grech P, Komiti A, Hoy J, Lloyd JH. Gibbie,T, Street A. Increased health care utilization and increased antiretroviral use in HIV-infected individuals with mental health disorders. *HIV Med* 2006*;* **7**: 205-212.
28. The HIV/AIDS Treatment Adherence, Health Outcomes, and Cost Study Group. The HIV/AIDS Treatment Adherence, Health Outcomes, and Cost Study: conceptual foundations and overview. *AIDS Care* 2004; **16**: S6-S21.
29. First MB, Spitzer RL, Williams JBW, Gibbon M. *Structured Clinical Interview for DSM-IV (SCID)* Washington, DC: American Psychiatric Association, 1995.
30. Stoff, DM, Mitnick L, Kalichman S. Special Issue: HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study. *AIDS Care* 2004; **16**: S1-S5.
31. Palmer NB, Salcedo J, Miller AL, Winiarski M, Arno P. Psychiatric and social barriers to HIV medication adherence in a triply-diagnosed methadone population. *AIDS Patient Care STDs* 2003; **17**: 635-644.
32. Drummond MF, O'Brien B, Stoddart GL, Torrance, GW. *Methods for the economic evaluation of health care programmes (2nd edition)* Toronto: Oxford University Press, 1997.
33. Gold, MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-effectiveness in health and medicine* New York: Oxford University Press, 1996.
34. World Health Organization. *Generalized Cost-Effeciveness Analysis: A Guide* Geneva: World Health Organization, 2003. Available online at: http://www.who.int/choice/en/ Accessed on April 14, 2008.
35. Rabeneck L, Menke T, Wray NP. How good are U.S. Studies of HIV Costs of Care? *Med Care* 1999; **37**: 748-759
36. Medicare Payment Advisory Commission (MEDPAC). *Report To Congress: Medicare Payment Policy* Washington, DC: Medicare Payment Advisory Commission, 2004.
37. United States Department of Health and Human Services, Office of Inspector General. *Cost Containment of Medicaid HIV/AIDS Drug Expenditures* Washington, DC: Department of Health and Human Services, 2001.
38. Ware JE Jr, Sherbourne CD. The MOS 36-Item Short Form Health Survey (SF-36), I; conceptual framework and item selection. *Med Care* 1992; **30**: 473-483.
39. Brazier J, Roberts J, Deverill M. The estimation of a preference-based single index measure for health from the SF-36. *J Health Econ* 2002; **21**: 271-292.
40. Ware JE, Kolinski M, Keller SD. *How to score the SF-12 physical and mental health summaries: a user's manual.* Boston: The Health Institute, New England Medical Centre, 1995.
41. Ware JE Jr., Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; **34**: 220-233.
42. Diehr P, Patrick DL, Spertus J, Kiefe C, McDonell M, Fihn SD. Transforming self-rated health and the SF-36 scales to include death and improve interpretability. *Med Care* 2001; **39**: 670-680.
43. Anderson JP, Kaplan RM, Coons SJ, Schneiderman LJ. Comparison of the Qualify of Well-Being Scale and the SF-36 results among two samples of ill adults; AIDS and other illnesses. *J Clin Epidemiol* 1998; **51**: 755-762.
44. Rubin DB. *Multiple imputation for nonresponse in surveys*. New York: Wiley, 1987.
45. Schafer JL. *Analysis of incomplete multivariate data*. New York: Chapman & Hall, 1997.
46. Manning, WG. The logged dependent variable, heteroskedasticity and the retransformation problem. *J Health Econ* 1998; **17**: 283-295.
47. Mooney CZ, Duval RD. *Bootstrapping: A nonparametric approach to statistical inference.* Thousand Oaks, CA: Sage Publications, 1993.
48. Fleishman JA, Gebo KA, Reilly ED, Conviser R, Mathews C, Korthuis T, Hellinger J, Rutstein R, Keiser P, Rubin H, Moore RD, for the HIV Research Network. Hospital and outpatient health services utilization among HIV-infected adults in care 2000-2002. *Med Care* 2005; **43**: III-40 to III-52.
49. Duggan MG, Evans WN. Estimating the impact of medical innovation: a case study of HIV antiretroviral treatments. *Forum Health Econ Policy* 2008; **11**: 1-37.
50. Liu C, Ostrow D, Detels R, Hu Z, Johnson L, Kingsley L, Jacobson LP. Impacts of HIV infection and HAART on quality of life. *Qual Life Res* 2006; **15**: 941-949.
51. Donald M, Dower J, Kavanagh D. (2005). Integrated versus non-integrated management and care for clients with co-occurring mental health and substance use disorders: A qualitative systematic review of randomized controlled trials. *Soc Sci Med,* **60**: 1371-1383.
52. Ware JE Jr, Davies-Avery A, Steward AL. The measurement and meaning of patient satisfaction. *Health Med Care Serv Rev* 1970; **1**: 3-15.
53. Ettner S, Conover C, Proescholdbell RJ, Weaver MR, Ang A, Arno P for the Cost Subcommittee of the HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study. Triply-diagnosed patients in the HIV/AIDS Treatment Adherence, Health Outcomes and Cost Study: patterns of home care use. *AIDS Care* 2008; **20**: 1177-89.
54. Sherbourne CD, Unutzer J, Schoenbaum M, Duan N, Lenert LA, Sturm R, Wells KB. Can utility-weighted health-related quality-of-life estimates capture health effects of quality improvement or depression? *Med Care* 2001; **39**: 1246-1259.

Appendix

Table A1. Regression Results for Annual Expenditures and Quality of Life*

Baseline Variables	Annual Cost			SF-6D			MCS			PCS		
	Incremental effects	95% CI Lower Bound	95% CI Upper Bound	Coeffcient	95% CI Lower Bound	95% CI Upper Bound	Coeffcient	95% CI Lower Bound	95% CI Upper Bound	Coeffcient	95% CI Lower Bound	95% CI Upper Bound
Group (control omitted)												
Treatment	290	–4343	4922	0.005	–0.011	0.021	1.248	–0.342	2.838	–0.901	–2.113	0.311
Baseline dependent variable	**3497**	**2582**	**4411**	**0.639**	**0.571**	**0.706**	**0.601**	**0.534**	**0.668**	**0.664**	**0.606**	**0.722**
Gender (male omitted)												
Female	**6817**	**934**	**14568**	**–0.035**	**–0.057**	**–0.013**	–1.670	–3.884	0.545	**–2.447**	**–4.136**	**–0.759**
Age (18-34 omitted)												
35-49 years	**6588**	**877**	**12298**	–0.016	–0.037	0.004	–0.138	–2.203	1.927	**–1.681**	**–3.251**	**–0.111**
50 years or more	6580	–2063	15224	–0.010	–0.041	0.022	1.805	–1.386	4.997	–2.304	–4.727	0.120
Race/ethnicity (white, non-Latino omitted)												
Latino	–1576	–8360	5208	**0.026**	**0.004**	**0.048**	0.164	–2.107	2.435	**2.214**	**0.498**	**3.930**
Black, non-Latino	–3795	–14813	7223	–0.018	–0.066	0.029	–2.171	–6.970	2.627	–1.338	–4.982	2.306
Other, non-Latino	–6428	–15471	2615	0.005	–0.031	0.040	–1.103	–4.726	2.521	0.913	–1.836	3.662
Marital status (never married omitted)												
Married or cohabiting	–1499	–6586	3588	0.006	–0.024	0.037	1.939	–1.163	5.041	–1.246	–3.588	1.095
Divorces, separated, widowed	–2467	–7142	2208	–0.003	–0.021	0.016	–0.047	–1.943	1.849	–1.021	–2.459	0.418
Education (<12 years omitted)												
12 years	4472	–2297	11241	–0.011	–0.032	0.010	–1.109	–3.243	1.025	0.462	–1.159	2.083
13-15 years	4984	–106	10073	0.010	–0.010	0.030	0.142	–1.870	2.154	0.693	–0.838	2.223
16+years	–1996	–12549	8558	–0.010	–0.048	0.028	1.684	–2.115	5.483	–1.965	–4.840	0.909
Income (omit le 50% poverty level)												
50 < income le 75%	6378	–1159	13914	0.023	0.000	0.046	**2.419**	**0.096**	**4.742**	–0.150	–1.912	1.612
75< income le 100%	1225	–5782	8232	0.012	–0.011	0.036	1.047	–1.311	3.406	–0.267	–2.047	1.514
>100%	4019	–4982	13020	**0.032**	**0.010**	**0.055**	**2.609**	**0.347**	**4.871**	1.037	–0.681	2.755
Insurance (omit none, no ADAP meds)												
Private	–408	–9074	8259	–0.002	–0.046	0.041	–2.189	–6.591	2.214	0.551	–2.796	3.898
Medicaid and Medicare	1862	–8387	12112	**–0.044**	**–0.084**	**–0.003**	**–4.313**	**–8.402**	**–0.224**	0.569	–2.537	3.675
Medicaid only	–51	–7911	7810	–0.020	–0.052	0.012	–0.813	–4.010	2.385	0.110	–2.319	2.539
Medicare only	9054	–6715	24822	–0.006	–0.055	0.042	–1.830	–6.832	3.172	–0.263	–4.057	3.532
Other public	343	–6254	6940	–0.030	–0.065	0.004	–1.775	–5.288	1.738	–1.052	–3.720	1.615
None with ADAP	1369	–8432	11170	0.001	–0.037	0.039	2.032	–1.820	5.883	–1.394	–4.324	1.536

Note: All estimates used a ‘‘fixed effects’’ approach to control for unobservable site-specific heterogeneity that may be correlated with participant-level characteristics. Results in **bold** were significant at the 0.05 level.

Table A1. Regression Results for Annual Expenditures and Quality of Life*

Baseline Variables	Annual Cost			SF-6D			MCS			PCS		
	Incremental effects	95% CI Lower Bound	95% CI Upper Bound	Coeffcient	95% CI Lower Bound	95% CI Upper Bound	Coeffcient	95% CI Lower Bound	95% CI Upper Bound	Coeffcient	95% CI Lower Bound	95% CI Upper Bound
Baseline MSC (omitted < 25%)												
25% ≤ MCS ≤ 75	–1439	–6347	3469							–0.572	–1.931	0.787
MCS >75%	–5210	–11373	953							1.505	–0.158	3.168
Baseline PSC (omitted < 25%)												
25% ≤ PCS ≤ 75	**–6057**	**–11670**	**–444**				1.376	–0.597	3.350			
PCS >75%	**–10920**	**–17107**	**–4732**				**3.109**	**1.031**	**5.186**			
SCID (Alcohol &/or drug abuse only)												
Alcohol & drug dependent	–1837	–10867	7192	–0.010	–0.046	0.025	–0.215	–3.788	3.358	–2.022	–4.732	0.689
Drug dependent only	–3499	–12109	5111	–0.016	–0.051	0.019	–0.466	–4.008	3.076	–1.958	–4.652	0.736
Alcohol dependent only	–1082	–9915	7751	–0.016	–0.053	0.021	–0.021	–3.779	3.738	–0.891	–3.750	1.968
Viral Load (omit 0-999)												
1,000-9,999	–3052	–8756	2652	–0.019	–0.040	0.001	–0.800	–2.866	1.267	**–1.702**	**–3.272**	**–0.133**
10,000-100,000	2903	–3012	8819	–0.011	–0.031	0.010	0.027	–2.057	2.110	–0.739	–2.321	0.844
=100,000	**13396**	**1271**	**25520**	–0.025	–0.058	0.007	–0.890	–4.226	2.446	–1.245	–3.796	1.306
Year (omit 2000)												
’2001	–7621	–14071	–1171	0.009	–0.013	0.031	0.665	–1.581	2.911	0.386	–1.327	2.098
’2002	–7470	–14174	–767	0.011	–0.012	0.033	1.294	–0.990	3.578	–0.107	–1.847	1.634
Sample Size	431			431			431			431		

Note: All estimates used a ‘‘fixed effects’’ approach to control for unobservable site-specific heterogeneity that may be correlated with participant-level characteristics. Results in **bold** were significant at the 0.05 level.