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Evaluating the Effects of an Interdisciplinary Practice Model with Pharmacist Collaboration on HIV Patient Co-Morbidities

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Title: EVALUATING THE EFFECTS OF AN INTERDISCIPLINARY PRACTICE MODEL WITH PHARMACIST COLLABORATION ON HIV PATIENT CO-MORBIDITIES

Running Head: Pharmacist Impact on HIV Co-Morbidities

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ABSTRACT

Treatment of HIV now occurs largely within the primary care setting, and the principal focus of most visits has become the management of chronic disease states. The clinical pharmacist's potential role in improving chronic disease outcomes for HIV patients is unknown. A retrospective cohort study was performed for HIV-positive patients also diagnosed with diabetes, hypertension, or hyperlipidemia. Characteristics and outcomes in 96 patients treated by an interdisciplinary team which included a clinical pharmacist (i.e., the intervention group) were compared to those in 50 patients treated by an individual healthcare provider (i.e., the control group). Primary outcomes were changes from baseline over 18 month period of HbA1c, low density lipoprotein (LDL), and blood pressure, respectively. Secondary outcomes included number of drug-drug interactions, HIV viral load, CD4 count, percent change in smoking status, and percent of patients treated to cardiovascular guideline recommendations. The interdisciplinary team had a significant improvement in lipid management over the control group (LDL: -8.8 vs. +8.4 mg/dL; $p=0.014$), and the smoking cessation rate over the study period was doubled in the interdisciplinary group (20.4% vs. 11.8%). Among those with an indication for aspirin, a significantly higher percentage of patients were prescribed the medication in the interdisciplinary group compared to the control group (85.5% v. 64.9%; $p=0.014$). An informal cost analysis estimated savings of more than \$3000 per patient treated by the interdisciplinary team. Based on these results, pharmacist involvement in an HIV primary care clinic appears to lead to more appropriate management of chronic co-morbidities in a cost-effective manner.

Key Words: HIV, Pharmacist, Primary Care, Drug interaction, Interdisciplinary

INTRODUCTION

At the beginning of the human immunodeficiency virus (HIV) epidemic, diagnosis with an HIV positive status warranted a medical response focused on treating opportunistic infections and providing palliative care. Today, medical management of HIV includes co-morbidities, drug interactions, and other non-AIDS related complications typical of the aging process. Due to the increase in options and quality of treatments, patients with HIV can now have the same life expectancy as a person from the general population provided that adherence to antiretroviral medications is maintained.¹⁻³ It was estimated over 1.2 million people live with HIV infection in the United States today.⁴ The percentage of persons living with HIV who are 55 years of age or more increased from 13.2% in 2006 to 17.1% in 2009.⁵ By the year of 2015, it has previously been extrapolated that half of those living with HIV infection will be 50 years of age or older.⁶⁻⁷

It has even been noted that people with HIV may live longer than those without it because of closer follow-up as they age.⁸ With this increase in longevity, the paradigm of managing patients with HIV has shifted. Opportunistic infections are far less prevalent than they once were. Effective antiretroviral therapy, even for resistant patients, is readily available. Many patients are now cared for by HIV primary care clinics, with the challenge of most visits primarily being treatment of other chronic disease states such as diabetes, hypertension, and hyperlipidemia.

Appropriate management of such non-infectious co-morbidities is a challenge in any population, but may correlate to a higher burden of disease for individuals infected

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with HIV. Growing evidence suggests that HIV may accelerate inflammatory processes which promote atherosclerosis, and an increased risk of cardiovascular disease (CVD) in this population has been well established.⁹⁻¹⁰ Certain antiretroviral drugs are also known to induce metabolic changes such as dyslipidemia, lipodystrophy, and insulin resistance.¹¹⁻¹³ The most common medical co-morbidities for HIV-infected veterans 60 years of age or older were previously defined as hypertension (45%), diabetes (21%), and vascular disease (23%).¹⁴ Additionally, HIV-infected individuals may have a higher prevalence of co-morbidities than uninfected individuals of the same age.¹⁵ The AGEHIV study specifically showed higher rates of hypertension, myocardial infarction, peripheral arterial disease, and renal disease in those with HIV as compared to the general population.¹⁶ In the New York metropolitan area, where this study was performed, there are an estimated 140,000 people living with HIV.¹⁷ Prevalence rates of hypertension, hyperlipidemia, and diabetes have been identified as 26%, 48%, and 13% in a Bronx institution serving an urban, low-income, HIV-positive population similar to ours.¹⁸

The pharmacist's role in management of both HIV and chronic disease states has continued to expand over the years. In 2011, the American Academy of HIV Medicine developed a new program to certify pharmacists specializing in HIV management (AAHIVP).¹⁹ Additionally, the Department of Human & Health Services (DHHS) HIV/AIDS Guidelines recommend the use of multidisciplinary teams, including pharmacists, as the optimal practice model.²⁰ The advent of collaborative drug therapy management (CDTM) allowed pharmacists to further expand their role in patient care with New York State (NYS) becoming the 47th state to sign a CDTM bill into law on September 12, 2011. Pharmacists where CDTM has been made legal may perform patient

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assessments, order drug-related laboratory tests, administer drugs, and select, initiate, monitor, continue, or adjust drug regimens under a pharmacist-physician agreement.²¹

The use of CDTM to improve patient outcomes in chronic disease states has been extensively addressed and demonstrated in the literature.²²⁻²⁴ A meta-analysis on the role of team-based care involving pharmacists to improve cardiovascular and renal outcomes found patients in the team-based care group to have reduced blood pressure, LDL, HbA1c, and in heart failure patients, reduced all-cause mortality, heart failure events, and hospitalization rates as compared to the usual care group.²² The impact of CDTM on HIV treatment outcomes has also been studied, primarily in settings such as pharmacist-driven adherence clinics or outpatient pharmacies.²⁵ Relevant interventions have been classified as medication adherence counseling, patient education, increased rates of HIV testing, antiretroviral regimen selection/initiation/discontinuation, dose adjustment for renal/hepatic impairment, and monitoring for adverse effects and drug interactions.²⁵⁻²⁹

In an HIV-primary care clinic which utilizes an interdisciplinary model, such as the Program for AIDS Treatment & Health (PATH) Center of The Brooklyn Hospital Center located in Brooklyn, NY, the clinical pharmacist does the aforementioned and more. Along with the primary medical provider, the pharmacist is simultaneously involved with managing antiretroviral medications in addition to the patient's chronic disease states. A patient satisfaction study was conducted at our clinic and indicated that overall satisfaction scores for this interdisciplinary practice model were high and a positive perception was found among patients. Patients indicated a preference for this particular clinic owing to the interaction between physicians, pharmacists, nurses and social workers.³⁰ Despite this patient endorsement, there has been no published literature

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to date evaluating the impact of including a clinical pharmacist in the interdisciplinary team practice model of an HIV-primary care clinic on both chronic diseases and HIV outcomes. The objective of this study was to determine if the addition of a clinical pharmacist to the treatment of HIV patients improves outcomes for chronic disease states, in addition to HIV. If such a collaborative approach is shown to improve selected clinical values over a usual care group, the results could be applicable to HIV primary care clinics nationwide.

METHODS

This study was a retrospective cohort study of HIV-positive patients seen at the PATH Center from June 2012 through December 2013. The “interdisciplinary group” served as the intervention group, including a clinical pharmacist in addition to a medical provider. As our institution is a teaching hospital, this group may also include medical and pharmacy residents and students. Both medical and pharmacy disciplines collaborate to determine a final plan of care. Patients who prefer a more private treatment setting may opt out of the interdisciplinary group and be seen individually by a separate physician, nurse practitioner, or physician assistant. These providers do not participate in the interdisciplinary team model and patients under “solo provider” care served as the control group. This research study received Institutional Review Board (IRB) approval.

As the interdisciplinary group contains members from medical and pharmacy, it can be difficult to assign study outcomes to one specific member of the team. To eliminate measurement bias, potential study subjects from the interdisciplinary group were determined based on the presence of documented interventions by the pharmacy team during 2011-2012. All interventions made by a pharmacist are documented in the

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paper medical chart and electronic medical record. Only patients from the interdisciplinary group with documented pharmacist interventions were reviewed for inclusion to ensure the clinical pharmacist had played an integral role in the patient's care. Two hundred and twenty such patients were identified and further reviewed for inclusion.

Other inclusion criteria consisted of age greater than or equal to 18 years, diagnosis of HIV or AIDS (defined as CD4 <200 cells/mm³ at any point in patient's history), consistent follow-up with the PATH center from June 2012 through December 2013 (defined as at least 1 visit every 6 months), and past medical history including diabetes, hypertension, or hyperlipidemia. Patients were excluded from the study if they were lost to follow-up or did not have at least one of the co-morbidities. Ninety-six patients in the interdisciplinary group were found to meet inclusion criteria. The minimal required sample size (96:48= interdisciplinary:solo) was calculated based on 80% power at a two-tailed alpha of 0.05 using independent t-tests to detect a difference in two means of the primary outcomes (i.e., 10 mmHg in systolic blood pressure, 20 mg/dL in low density lipoprotein [LDL] cholesterol, and 1% in HbA1c). The comparator group of 50 solo-provider patients was selected using block randomization from a data query which identified patients seen over the 18-month study period and prescribed anti-hypertensives, lipid lowering agents, or anti-diabetics.

As it is plausible that either group could have seen more complicated patients, the Charlson Co-morbidity Index (CCI) Scoring System was applied to indicate each patient's severity level for use as a potential confounding variable. This system represents a 10-year mortality risk score and has been validated in both in-patient and out-patient settings.^{24,31} The CCI score was calculated based on patient diagnoses at the beginning of

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the study period. Although the CCI scoring system assigns a score of 6 points to patients with a diagnosis of AIDS, for our purposes only patients with actively uncontrolled disease and CD4 <200 mg/dL were assigned 6 points towards their total score, considering most of our patients with an AIDS diagnosis have recovered immune function.³²

Electronic medical records of eligible study subjects were retrospectively reviewed and the 18-month follow-up data were collected. The primary outcome was the change from patient's own baseline for systolic and diastolic blood pressure, LDL cholesterol, and HbA1c, which were chosen as surrogate markers for hypertension, hyperlipidemia, and diabetes due to the implications of disease control on risk of cardiovascular events. Secondary outcomes included differences between treatment groups in HIV-related outcomes such as number of drug-drug interactions, viral load, and CD4 counts. Other secondary outcomes were also chosen for their potential impact on cardiovascular disease (CVD) including appropriate use of low-dose aspirin, percent change in reported smoking status, and percent of patients treated according to guideline recommendations. This included appropriateness of cardiovascular medications per JNC 7 and ACC/AHA Joint Guidelines and medication therapy for stroke, coronary artery disease, and congestive heart failure as per most recent AHA guidelines.³³⁻³⁷

Smoking cessation is of particular concern for HIV-infected individuals as it is more prevalent in this population and has been shown to contribute to elevated CVD risk, increased rates of pulmonary diseases, and increased infections.³⁸⁻⁴⁰ During clinic visits, smoking cessation was addressed by all providers, however pharmacists were responsible for assessing readiness to quit and initiating smoking cessation agents such as nicotine

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replacement therapy, bupropion, or varenicline. Fagerstrom scores and motivational counseling were utilized and additional counseling or follow up was provided by pharmacists on subsequent visits.

All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS version 21, SPSS Inc., Chicago, Illinois) at the significance level of 0.05 (two-tails). Viral load was stratified into <200, 200-500, or >500 and CD4 into ≤ 500 cells/mm³ and >500 cells/mm³ before statistical analysis was performed. Independent t-test was used to compare normally distributed data and Mann-Whitney U test (a non-parametric test) was used to compare non-normally distributed data in baseline characteristics and outcome measures between two groups. Fisher-exact test and chi-square test were used to compare percentages between two study groups. When $p < 0.10$ was found in comparison of subject characteristics between two groups, this characteristic was treated as a potential confounding factor and included as an independent variable in the regression models. Linear regression analyses with the forward stepwise method were performed to identify potential covariates. General linear model was used to adjust final measures of primary outcomes for the covariate(s).

RESULTS

Baseline characteristics and distribution of co-morbidities is reported in Table 1. Although the interdisciplinary group had significantly lower rates of co-morbid hypertension ($p=0.043$), higher baseline values for systolic BP ($p=0.042$), diastolic blood pressure ($p=0.005$), and LDL ($p=0.003$) were found. The interdisciplinary group had more medications (10.6 vs. 8.8; $p=0.005$), but fewer drug-drug interactions than the solo provider group (0.14 vs. 0.38; $p=0.008$) when considering combinations which are

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contraindicated or recommended to consider avoiding. More patients were reported as smokers in the interdisciplinary group, however this number did not achieve statistical significance ($p=0.050$). Other baseline measures and characteristics were comparable between groups, including CCI score and HIV-related measures.

Primary outcomes are reported as either final measures or the difference from baseline to final value (Table 2). There was no significant difference between groups for change in systolic BP ($p=0.619$), diastolic BP ($p=0.366$) or HbA1c ($p=0.190$). A significant change in LDL was found with the interdisciplinary group over the solo provider group (-8.8 vs. +8.4 mg/dL; $p=0.014$).

The two groups had similar results in terms of achieving “goal” BP, LDL, and HbA1c at final visit. Results of secondary outcomes are shown in Table 3. More patients in the interdisciplinary group as compared to the solo provider group had appropriate therapy prescribed for compelling cardiovascular indications (71.6% vs. 60%), but the difference was not statistically significant. Among those with an indication for aspirin, a significantly higher percent of patients (85.5%) were prescribed the medication in the interdisciplinary group, compared to only 64.9% in the solo provider group ($p=0.014$). Among smokers at baseline, the smoking cessation rate over the study time period was doubled in the interdisciplinary group (20.4%) compared to that in the control (11.8%); however, no significant statistical difference was found ($p=0.714$). There continued to be significantly fewer drug-drug interactions identified in the interdisciplinary group at the end of follow-up ($p=0.023$); however, the significance disappears when baseline measure was considered ($p=0.432$). Regarding HIV-related outcomes, no statistically significant difference was identified for either baseline or final value for CD4 and viral load.

DISCUSSION

This is the first piece of literature describing an interdisciplinary team model with such close collaboration between medical and pharmacy providers in an HIV primary care setting. Although many studies have reported the benefit of clinical pharmacist involvement for improvement of HIV outcomes²⁵⁻²⁹, none have yet evaluated the benefit of such collaborative practice on outcomes for chronic co-morbidities. In this study, patients seen by the interdisciplinary group tended to be more complicated, with statistically higher baseline values for blood pressure and LDL cholesterol, although CCI was not significantly different between groups.

While the most recently updated cholesterol guidelines published in late 2013 have represented a controversial shift away from numerical LDL goals in favor of appropriate prescribing⁴¹, it is still important to note the significant reduction in cholesterol lowering seen with the interdisciplinary group as patients with HIV are at a higher risk for developing coronary artery disease.⁹⁻¹⁰ The reduction in LDL cholesterol were reflective of pharmacist recommendations of using more appropriate intensity statins. Additionally, although there was no statistical difference between groups regarding blood pressure control, these results are likely no longer relevant as blood pressure goals for primary prevention have become more lenient with the updated hypertension guidelines published in late 2013.⁴²

Although no statistically significant difference was seen between groups in regards to better blood pressure or diabetes control, the HbA1c reduction of 1.3% seen in the interdisciplinary group may still be interpreted as clinically significant. In addition to the clinical pharmacist involvement in routine clinic visits, patients may also be referred

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for individual appointments with the pharmacist if further counseling or education is requested. Uncontrolled diabetes represents a significant portion of these one-on-one referrals and such positive diabetes outcomes may be a reflection of this individual attention. As only 17 patients from the solo provider group and 29 patients from the interdisciplinary group were included in this part of the analysis, it is likely that the study was underpowered to detect a significant difference between groups.

The PATH Center serves a primarily Medicaid population with approximately 99% of patients living below the federal poverty level. The care of such patients is often complicated by psychiatric and socioeconomic issues such as drug abuse, depression, and unemployment.⁴³ Due to such confounding factors, it was suspected that many patients may not achieve therapy goals due to issues with medication access and adherence, rather than inappropriate prescribing habits. This seemed to be true for the interdisciplinary group as only 53.3% of patients achieved adequate blood pressure control over the study time period despite 71.6% being prescribed appropriate therapy. Our interdisciplinary group overall was shown to be more thorough in their prescribing habits, specifically for compelling cardiovascular medications and aspirin for primary or secondary prevention as per JNC, NCEP, AHA, ASA, ACCF, and the U.S. Preventative Services Task Force (USPSTF) recommendations.^{33-37,44}

Smoking cessation can also be more difficult to address in an urban population, particularly in HIV patients who have a high rate of tobacco use. Traditional therapies, such as nicotine replacement therapy, varenicline, and bupropion have been shown to facilitate abstinence in HIV-positive smokers.⁴⁵ Unique interventions to address smoking cessation in this population have included nurse-driven interventions, culturally tailored

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group-based sessions for African-American MSM, and cell-phone delivered intensive counseling sessions, all combined with nicotine replacement therapy (NRT).⁴⁶⁻⁴⁸ Studies have suggested that helping HIV-positive smokers develop adaptive strategies to cope with HIV symptom distress may be an effective approach to cessation.⁴⁹ It is hypothesized that the heightened awareness and willingness to prescribe pharmacologic interventions by the pharmacy team is behind the doubled rate of smoking cessation in the interdisciplinary group.

Even though there are significant differences in total number of medications ($p=0.0014$) and drug-drug interactions ($p=0.008$) between two groups at baseline, both groups had a similar pattern of reduction in drug-drug interactions during the entire study time period ($p=$ NS after adjusting final values for baseline). Certain interactions, such as acid-suppressant medications and rilpivirine or atazanavir, can compromise the efficacy of a patient's antiretroviral regimen. In addition, ritonavir or cobicistat based regimens often result in drug interactions concerning patient safety. Therefore, recognition of interactions is a tremendously important part of any HIV patient's care.⁵⁰

We did not expect to find any difference between groups for CD4 counts and viral loads as successful management of these outcomes has become routine since the development of highly active antiretroviral therapy. All providers at the clinic are experienced and fully competent in choosing safe and effective regimens for their patients, with consideration always given to resistance and adherence. As long as patients are compliant with their medications, the CD4 and viral load are expected to respond appropriately. The study data supported our argument by showing no statistical difference between groups at either baseline or final visit for CD4 or viral load. While several

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studies have reported a significant reduction in viral load with pharmacist involvement⁵¹⁻⁵⁵, most of these studies were not performed in an HIV primary care clinic such as ours where addressing antiretroviral adherence and simplifying regimens is an integral part of each visit. The true impact of this study was shown in the patient's chronic co-morbidities which, as described in the introduction, are frequently now the focus of HIV primary care visits.

Possible limitations for the study include its retrospective design and small sample size for each disease state evaluated. Although the pre-specified number for inclusion was met, power may not have been achieved for disease state specific outcomes as not every patient reviewed had all three co-morbidities. While measures were taken to establish if one group of patients was more medically complicated than the other, differences in psychiatric capacity or socioeconomic status were not captured. These and other confounding variables could have represented significant barriers to medication access or adherence, which subsequently could have influenced outcomes. It is also important to note patient self-selection as a study bias. The intervention and control groups are not randomized as the patient chooses who they would like to receive care from. Personality traits and factors which influence this private decision are unaccounted for in our analysis. The interdisciplinary group also involves medical residents which may be cited as another difference between the intervention and control groups. However, all patients included in the interdisciplinary group were identified only from a pool of patients with documented pharmacist interventions, suggesting that the presence of a clinical pharmacist had significantly impacted the patient's care. Lastly, this study was based on the goals and therapy recommendations of previous disease state guidelines.

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Although aforementioned updated guidelines were recently released⁴¹⁻⁴², the guidelines used in the methodology of this study were considered the gold standard for the vast majority of the follow-up time period.

Despite being a small, single-center study, it is the first of its kind to address the benefit of HIV clinical pharmacist involvement in an HIV primary care clinic for disease state outcomes beyond just HIV. The results of this study showed pharmacist involvement to be beneficial for lipid management, as well as improvement in diabetes, smoking cessation rates, adherence to optimal prescribing recommendations, appropriate use of aspirin, and reduced drug-drug interactions. It is important to note that although this study primarily reported surrogate markers of cardiovascular disease, interventions by the pharmacist at this clinic were previously quantified in many additional disease states, such as asthma/COPD, chronic pain, Hepatitis C co-infection, and anticoagulation.⁵⁶

Although the benefits of incorporating a clinical pharmacist into the HIV primary care setting are numerous, cost may be viewed as a significantly limiting factor. This study was not originally designed to compare costs between the two study groups. However, we may informally estimate potential cost savings based on values from the literature and databases of commercially available insurance claims in regards to our study outcomes (Table 4).⁵⁷⁻⁶¹ All values are converted to 2015 US dollars based on the Consumer Price Index⁶². As these cost estimates are synthesized from different sources, patient cohorts, settings, and study years, interpretations should be made cautiously. It was estimated that \$3329 per patient would be saved for the interdisciplinary group in terms of financial returns on smoking cessation and emergency department/hospital

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utilization due to hypertension, diabetes mellitus, hyperlipidemia, and drug-drug interactions. This value may be over-estimated when compared to our results, as not all of these outcomes achieved statistical significance. To our knowledge, there is no pharmaco-economic study evaluating the effects of a multidisciplinary team with pharmacist interventions for HIV-infected patients. Future research in this area is warranted to further justify our results.

CONCLUSION

Pharmacist involvement in an HIV primary care clinic appears to result in more appropriate management of chronic co-morbidities in a cost-effective manner, although positive long-term outcomes may be difficult to establish in a complicated, urban population. We believe this data supports the expansion of clinical pharmacist involvement in HIV primary care centers to establish interdisciplinary team models as the standard for best practice.

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TABLE 1: BASELINE CHARACTERISTICS

Characteristic	Solo Provider (n=50)	Interdisciplinary (n=96)	p- value
Females [n(%)]	23 (46%)	46 (48%)	0.826
Age, years [mean (SD)]	54.5 (7.5)	54.0 (7.6)	0.500
Hypertension [n(%)]	39 (78%)	59 (62%)	0.043
Hyperlipidemia [n(%)]	39 (78%)	70 (73%)	0.503
Diabetes [n(%)]	17 (34%)	27 (28%)	0.463
Systolic blood pressure, mmHg [median (ICQ)]	132 (125, 142)	140 (130.5, 150.5)	0.042 ⁺
Diastolic blood pressure, mmHg [median (ICQ)]	82 (77, 89)	89 (81, 96)	0.005 ⁺
LDL cholesterol, mg/dL [mean (SD)]	97 (34)	120 (38)	0.003
HbA1c [mean (SD)]	7.99% (2.27%) n=17	8.27% (2.74%) n=29	0.726
No. of CHD risk factors [mean (SD)]	1.25 (0.99)	1.73 (1.07)	0.079
No. of medications [mean (SD)]	8.8 (3.19)	10.6 (4.59)	0.014
No. of drug-drug interactions			
0	33 (66%)	83 (87.4%)	0.009
1	15 (30%)	11 (11.6%)	
2	2 (4%)	1 (1.1%)	
mean (SD)	0.38 (0.57)	0.14 (0.38)	0.008
Smoking [n(%)]	17 (34%)	49 (51%)	0.050
Charlson Comorbidity Index [mean (SD)]	1.78 (1.88)	2.23 (1.98)	0.185
CD4 \geq 500 mmHg [n(%)]	29 (58%)	48 (50%)	0.358
Viral load [n(%)]			
<200 copies/mL	40 (80%)	78 (81%)	0.380
200-500 copies/mL	1 (2%)	0 (0%)	
>500 copies/mL	9 (18%)	18 (19%)	

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⁺Mann-Whitney U test was performed for non-normally distributed data

TABLE 2: PRIMARY OUTCOME RESULTS

Outcome	Solo Provider (n=50)	Interdisciplinary (n=96)	p-value
Systolic blood pressure, mmHg			
Final measure [median (ICQ)]	130.5 (122, 141.5)	134 (120, 149.5)	0.347 ¹
Final measure [mean (SD)]	132.3 (17.8)	137.6 (23.8)	0.964 ²
Change from baseline [median (ICQ)]	+2 (-12, +7.75)	-4 (-14, +8.5)	0.619 ¹
Diastolic blood pressure, mmHg			
Final measure [median (ICQ)]	80 (72, 89.5)	82 (75.5, 91)	0.222 ¹
Final measure [mean (SD)]	80.6 (10.2)	84.5 (12.8)	0.691 ³
Change from baseline [median (ICQ)]	-3.5 (-8, 4.75)	-7 (-12, +7)	0.366 ¹
LDL cholesterol, mg/dL			
Final measure [mean (SD)]	103 (34.7)	111 (35.3)	0.356 ⁴
Change from baseline [mean (SD)]	+8.4 (30.3)	-8.8 (35.6)	0.014 ⁵
HbA1c (%)	n=17	n=29	
Final measure [mean (SD)]	7.33% (1.78%)	6.97% (1.62%)	0.203 ⁶
Change from baseline [mean (SD)]	-0.44% (1.43%)	-1.30% (2.34%)	0.190 ⁵

¹Mann-Whitney U test was performed for non-normally distributed data

²General linear model was performed to adjust for covariates: baseline systolic blood pressure (p<0.001) and Charlson Comorbidity Index (p=0.007)

³General linear model was performed to adjust for covariates: baseline systolic blood pressure (p<0.001) and Charlson Comorbidity Index (p=0.075)

⁴General linear model was performed to adjust for covariate: baseline LDL (p<0.001)

⁵Independent t-test was performed

⁶General linear model was performed to adjust for covariate: baseline HbA1c (p<0.001)

TABLE 3: SECONDARY OUTCOME RESULTS

Outcome [n(%)]	Solo Provider (n=50)	Interdisciplinary (n=96)	p-value
Final systolic blood pressure at goal	24/39 (61.5%)	32/60 (53.3%)	0.421
Final LDL at goal	24/36 (66.7%)	52/73 (71.2%)	0.626
Final HbA1c at goal	11/17 (64.7%)	21/29 (72.4%)	0.583
Appropriate cardiovascular therapy prescribed	21/35 (60%)	43/60 (71.6%)	0.242
Aspirin indicated	37/50 (74%)	69/96 (71.9%)	0.785
Aspirin prescribed	27/49 (55.1%)	64/96 (66.7%)	0.173
Aspirin prescribed among those with an indication for aspirin	24/37 (64.9%)	59/69 (85.5%)	0.014
Smoking	15/49 (30.6%)	42/96 (43.8%)	0.126
Smoking cessation rate among smokers at baseline	2/17 (11.8%)	10/49 (20.4%)	0.714
No. of drug-drug Interactions			
0	39 (78%)	88 (92.6%)	0.028
1	10 (20%)	7 (7.4%)	
2	1 (2%)	0 (0%)	
Mean (SD)	0.24 (0.48)	0.07 (0.26)	0.023 ¹
			0.432 ²
Change from baseline ³			
-2	1/17 (5.9%)	1/12 (8.3%)	0.931
-1	5/17 (29.4%)	4/12 (33.3%)	
0	11/17 (64.7%)	7/12 (58.3%)	
Mean (SD)	-0.35 (1.06)	-0.42 (1.08)	0.875
CD4 level ≥ 500	33 (66%)	58 (60.4%)	0.648
Viral load level >500 copies/mL	6 (12%)	13 (13.5%)	0.793
Cost estimates (USD)			

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¹Independent t-test

²General linear model was performed to adjust for covariate: baseline no. of drug-drug interactions ($p < 0.001$)

³Only for those who had drug-drug interactions at baseline

TABLE 4: Estimation of Cost-Savings (in 2015 US dollars)

	Solo Provider	Inter- disciplinary	Unit cost/patient (Reference Year)	Unit cost/ patient (2015)*
Estimates of Costs				
Salaries [†]	Ref.	\$55	---	\$55/hour
Total Costs	Ref.	\$55		
Estimates of Benefits				
Systolic blood pressure ⁵⁷				
Change from baseline	+2 mmHg [§]	-4 mmHg	\$166/mmHg	\$274/mmHg
Potential cost savings	-\$548 [§]	\$1096	(in 2001)	
Diastolic blood pressure ⁵⁷				
Change from baseline	-3.5 mmHg	-7 mmHg	\$103/mmHg	\$169/mmHg
Potential cost saving	\$592	\$1183	(in 2001)	
LDL cholesterol ⁵⁸ (mg/dL)				
Change from baseline	+8.7% [§]	-7.3%	\$35 per 1%	\$47 per 1%
Potential cost saving	-\$409 [§]	\$343	LDL-C decrease (in 2006)	LDL-C decrease
A1c ⁵⁹				
Change from baseline	-0.44%	-1.30%	\$1145 per 1%	\$1283 per 1%
Potential cost savings	\$565	\$1668	A1c lowering (in 2011)	A1c lowering
# Smoking cessation ⁶⁰	2/17	10/49		
Potential cost saving	\$365	\$634	\$3,105/quit (in 2015)	---
# Drug-drug interactions ⁶¹				
Change from baseline	7/50	6/96	\$910 (in 2013)	\$953
Potential cost saving	\$133	\$60		
Total potential cost savings	\$698	\$4984		
Potential Benefit[^]	Ref.	\$4286		

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Sensitivity Analysis^δ	\$1655	\$4984		
Total Benefit^δ	ref	\$3329		

*Cost conversions are based on Consumer Price Index (Medical Care component), Bureau of Labor Statistics; †Assumed 20 min/visit and 3 visits/patient; ^δ Negative outcomes ignored; ^ May be over-estimated