Spring 5-2018

Evidence-Based Study of Medication Compliance Project in Hiv Prevention Using Pre-Exposure Prophylaxis (Prep) Antivirals for HIV-Negative Males

Ming-Chun Ho
California State University, Northern California Consortium Doctor of Nursing Practice

ABSTRACT

EVIDENCE-BASED STUDY OF MEDICATION COMPLIANCE PROJECT IN HIV PREVENTION USING PRE-EXPOSURE PROPHYLAXIS (PREP) ANTIVIRALS FOR HIV-NEGATIVE MALES

In 2012, emtricitabine/tenofovir was the only Food and Drug Administration-approved medication for pre-exposure prophylaxis (PrEP) used in human immunodeficiency virus (HIV) prevention. To date, there is little research on open-label and mixed-payer characteristics supporting medication compliance of men who have sex with men (MSM). The purpose of this research was to describe individual demographic variables associated with PrEP medication adherence and to examine the effect of a follow-up phone call from a nurse once a month for 3 months. A total of 30 MSM were recruited and data were collected using a demographic questionnaire, medication adherence tool and follow-up phone calls. Data were analyzed using a statistical package. Spearman's rho correlations demonstrated high medication adherence in single men (r_s (28) = −.375, p < .05) with no mental health issues (r_s (28) = .426, p < .05) and a higher educational level (r_s (28) = −.431, p < .05). A between group Chi-square demonstrated men with high medication adherence and medium medication adherence did not statistically differ over 3 months ($\chi 2$ (2, N = 28) = .668, p = .71). Individuals who exhibited higher PrEP use in an open-label and mixed-payer structure appeared to be young, single, well educated, and employed Caucasian gay males with multiple partners. More information will be needed from ethnically diverse populations, especially non-Caucasians. Finally, clinical nurses, by supplying accountability by phone calls, could improve PrEP compliance by providing planned monthly reminders.

Ming-Chun Ho
May 2018

EVIDENCE-BASED STUDY OF MEDICATION COMPLIANCE PROJECT IN HIV PREVENTION USING PRE-EXPOSURE PROPHYLAXIS (PREP) ANTIVIRALS FOR HIV-NEGATIVE MALES

by

Ming-Chun Ho

A project

submitted in partial

fulfillment of the requirements for the degree of

Doctor of Nursing Practice

California State University, Northern Consortium

Doctor of Nursing Practice

May 2018

APPROVED

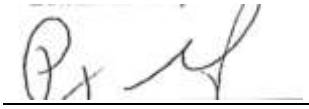
For the California State University, Northern Consortium
Doctor of Nursing Practice:

We, the undersigned, certify that the project of the following student meets the required standards of scholarship, format, and style of the university and the student's graduate degree program for the awarding of the Doctor of Nursing Practice degree.

Ming-Chun Ho
Project Author

Alice Butzlaff (Chair) Nursing

Edward Brooks, MD Stanford Health Care/Positive Care Clinic



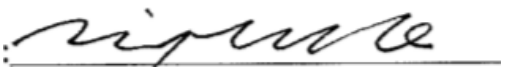
Philip Grant, MD Stanford Health Care/Positive Care Clinic

AUTHORIZATION FOR REPRODUCTION

OF DOCTORAL PROJECT

x I grant permission for the reproduction of this project in part or in its entirety without further authorization from me, on the condition that the person or agency requesting reproduction absorbs the cost and provides proper acknowledgment of authorship.

_____ Permission to reproduce this project in part or in its entirety must be obtained from me.

Signature of project author : 

ACKNOWLEDGMENTS

I would like to acknowledge a few important people who have supported me through the doctor of nursing practice program. Dr. Nair, project advisor, encouraged and inspired me to reveal my potential skills in nursing research. Dr. Butzlaff, project chair, guided and assisted me through the research design and analysis to publishing. And I am grateful for my work family at Stanford Health Care Positive Care Clinic. Especially, I would like to thank Dr. Brooks, Dr. Grant, and Sandra Valle, PA, for providing me extra help in Stanford IRB protocols and patient recruiting. Also, I would like to acknowledge Drea W of the Fresno Graduate Statistics Studio, who assisted me through data analysis with SPSS. Lastly, I would like to thank my family; they allowed me to dedicate myself to pursuing my personal goal of achieving my dream to become a doctoral nurse.

TABLE OF CONTENTS

LIST OF TABLES

Page

CHAPTER 1: INTRODUCTION

Since the 1980s, the human immunodeficiency virus (HIV) infection, which causes acquired immunodeficiency syndrome (AIDS), has been a global epidemic. The Centers for Disease Control (CDC) estimates the number of people living with HIV in the United States at approximately 1.2 million, and roughly 44,000 individuals are newly diagnosed with HIV each year (CDC, 2015). HIV is a costly disease; the on-going cost to manage HIV is estimated at $379,668 per person annually (in 2010 USD; CDC, 2015). Men who have sex with men (MSM) continue to be a more vulnerable to contracting HIV than men who have heterosexual sex. MSM may have recurrent exposure to HIV that is compounded by high-risk sexual behavior (e.g., multiple partners, unprotected sex, or drug abuse). Lelutiu-Weinberger et al. (2013) estimated that gay men represent 54% of HIV infections in the United States. Even though eradication of HIV remains elusive, highly active antiretroviral therapy has been promising for suppressing the virus and reducing HIV transmission. Treatment as prevention has been highly adapted to current HIV medical care. In addition, scientific clinical research has proven the effectiveness of using antiretroviral therapy in conjunction with condom us as prophylaxis for lowering the risk of contracting HIV infection (CDC, 2018).

Since 2012, when the Food and Drug Administration (FDA) approved pre-exposure prophylaxis (PrEP) for HIV prevention, the demand for PrEP utilization has increased; however, accessing PrEP has many challenges. Recent PrEP literature reviews, as applied to PrEP research projects, demonstrate that emtricitabine/tenofovir is an effective oral medication for hindering HIV transmission when used in a continuous daily regimen. However, in a real-world clinical practice, there are challenges for PrEP compliance in the MSM population. Patients encounter obstacles to complying with the daily regimen, fail to follow through with their quarterly medical visits, experience side effects to the medication, or find themselves with a financial burden if

their insurance does not cover the medication. Thus, evidence-based research was needed to address those issues. Throughout this research review, the correlation of PrEP compliance factors in an open-label and mixed-payer structure for the MSM HIV-negative population needed to be understood so the gap in research could be filled. This PrEP study seeks to understand the PrEP compliance proclivities of the MSM population. Moreover, this PrEP compliance study will analyze the evidence-based research of monthly follow-up phone calls to showcase that nursing intervention could improve medication compliance in HIV prevention.

Theoretical Framework

Jean Watson's human caring theory, which focuses on patient- and family-centered collaborated care, is applicable in all care settings. The medication adherence issue is a major obstacle crossing the spectrum of disease management and prevention. Behavior change theory, which explains patients' behavior in regard to their attitude toward medication adherence and their health outcome, is predominately used for medication adherence. This PrEP compliance project takes the nursing perspective for factors that support patients' medication adherence behavior. Thus, Watson's human caring theory has been implemented and applied as a theoretical framework for this PrEP compliance evidence-based study.

Stanford Health Care (SHC) defines the nurse's profession practice model as affecting the patient's health outcome by addressing the patient's mind, body, and soul (SHC, 2015). In addition, patient centered care affects families, communities, and populations as a whole. In human caring theory, Watson (1988) explains that the major conceptual elements are carative factors, transpersonal caring relationships, and caring moments/caring occasions. The 10 carative factors are the groundwork for developing the nurse-patient relationship for fostering the problem-solving caring process; this translates into HIV prevention by providing holistic care for individual patients, whether healthy or sick. Furthermore, nursing care for HIV prevention is

amplified to protect the partner, family, and then the community for achieving a zero HIV infection rate.

The assumption of the human caring theory is based on a nurse who commits to his or her practice and is consciously aware of the need for human dignity while providing healing in the care environment. This mindset allows patients to heal and reach their optimum healthcare outcomes. The PrEP compliance project is a patient-centered care approach to HIV prevention. The nurse takes the initiative and looks for ways to improve adherence to a daily medication regimen. Watson's human caring theory explains the patient-centered approach, combining spirit, body, and soul, for optimizing the patient's healthcare outcome as a whole entity; this puts the HIV prevention project in focus from individual health to community health.

CHAPTER 2: REVIEW OF THE LITERATURE

Several studies have examined the use of pre-exposure prophylaxis (PrEP) using antivirals emtricitabine/tenofovir in HIV-negative subjects. In what is known as the iPrEx study, Grant et al. (2010) used a randomized double-blind placebo-controlled study of emtricitabine/tenofovir by sampling 2,499 HIV-negative MSM and transgender women. One group received oral antiretroviral medications daily, while the other received a placebo. Using regression statistics to show the effectiveness of PrEP, Grant et al. found a 44% reduction rate of HIV infection in the target group over the control group. The reduction of the HIV infection risk was between 92% and 95% while blood medication concentration levels reached therapeutic range. This research was the first study to prove PrEP utilization for HIV prevention. The strength of the study was its large sample size and the high quality of data gathered, especially in medication monitoring. The quality of the research lay in its protocol. However, the limitation of the study was the investigators' failure to distinguish high-risk sexual behavior of those with multiple sex partners or those with single episodes of condomless sex with the same partner.

To challenge daily consumption of emtricitabine/tenofovir, Kibengo et al. (2013) conducted a double-blind randomized study, known as the intermittent PrEP study, to demonstrate the effectiveness of the drug. Kibengo et al. sampled 72 HIV serodiscordant (one partner HIV positive, the other HIV-negative) couples in two groups. One group using an oral regimen within 2 hours after sex, not to exceed one dose per day while the other group followed a daily oral regimen. Both regimens were equally effective, yet the adherence rates in the intermittent group were 91% compared to 98% in the daily regimen group. Kibengo et al. suggest that PrEP could be considered if accessing medication is an issue. One of the strengths of this study was that the data was collected in real time using a smartphone daily or within 24 hours of a sexual encounter. A limitation included false data regarding medication consumption

if someone opened the electronic calculated pillbox but did not take the medication. Further limitations included a small sample size (N = 72) that was not large enough to generalize. In a side note, the intermittent use of emtricitabine/tenofovir has not been FDA approved in the United States.

In the partners PrEP study, Murnane et al. (2015) used randomized double-blind placebo-controlled emtricitabine/tenofovir versus tenofovir only. Murnane et al. studied 4,747 HIV serodiscordant heterosexual couples and used stratification and inverse probability of censoring weights and per-protocol analysis to determine the efficacy and safety of emtricitabine/tenofovir and tenofovir. They found that daily emtricitabine/tenofovir or tenofovir intake each yielded an 80% reduction of HIV compared to the placebo group and suggested that consuming a daily regimen consistently yields the highest safety and effectiveness level of HIV prevention. One of the partners PrEP study strengths was the large sample size with a quality randomized and double-blind setup; however, the study's limitation was the pill count method, which may be inaccurate (e.g., pill dumping could yield false results). Overall, Murnane et al.'s (2015) research findings supported Grant et al.'s (2010) iPrEx study results for daily consumption of emtricitabine/tenofovir. Despite the large sample size, use of tenofovir alone has not been FDA approved in the United States.

Gamarel and Golub (2015) tried to determine the intention of 164 HIV-negative MSM to adopt PrEP. Researchers used regression models and ANOVA to compare the tendency to adopt a PrEP regimen by age, income, and education. They found that motivation for condomless sex is accompanied by adopting PrEP by MSMs despite their age, income, and education. One strength of Gamarel and Golub's research was the receipt of localized data from a metropolitan area, which allowed for a significant descriptive statistical analysis pertinent to the study of

metropolitan phenomena. One of this study's limitations was that several MSM participants answered the questions based on hypothetical situations rather than an actual situation.

Mathur et al. (2016) conducted interviews and group discussions to elucidate cultural barriers affecting HIV prevention. Researchers sampled 24 discussion groups and conducted 24 comprehensive interviews to identify the nature of HIV perception and sexual risk assessment of youth and adults in Uganda. The researchers used "systematic analysis of narrative data" to generate the major themes by "across-case analysis" (p. 1). Mathur et al. found that generational conceptual differences affect HIV prevention in Uganda. The major cultural themes are fear, skepticism, and misconceptions about the HIV prevention message. The researchers suggest focusing on "disseminating HIV prevention knowledge that is tailored to generational differences" (p. 9). One of the strengths of this research was the qualitative design with in-depth follow-up interviews for identifying major themes. One of the limitations was that the interviewers may have had biases concerning the interviewees' answers, and the responses could have been misinterpreted.

Marcus et al. (2016), in a study known as the Kaiser PrEP study, conducted a cohort study of 972 MSM members at Kaiser Permanente Northern California using electronic medical record chart review in an open-label use of emtricitabine/tenofovir. Marcus et al. tried to determine the level of medication adherence/discontinuation, renal safety, and incidence of sexually transmitted infection and HIV infection. Findings revealed no incidences of new HIV infection during the 2.5 years of investigation. Marcus et al. concluded that being an African American, smoking, and having a high copay Kaiser insurance plan was associated with a low adherence to PrEP compliance. Marcus et al. suggested quarterly screenings to provide a baseline for healthcare maintenance and to improve PrEP adherence. One of the strengths in the Kaiser PrEP study was that it was open label in a large cohort within different locations in

Northern California. However, one weakness in the Kaiser PrEP study was that the study cohort did not represent the mix of payers in a majority of healthcare settings because the study participants were all covered by Kaiser insurance.

A review of the literature was undertaken to examine PrEP utilization in HIV prevention. Multiple studies (Grant et al., 2010; Kibengo et al., 2013; Murnane et al., 2015) have shown that oral antiretroviral use reduces HIV transmission to sexual partners. Other studies (Gamarel & Golub, 2015; Mathur et al., 2016; Marcus et al., 2016) have discussed individual adoption (or nonadoption) of HIV transmission prevention measures. This review demonstrates the need to fill the research gaps to determine the factors associated with PrEP compliance in the individual.

CHAPTER 3: METHODS

Design

This evidence-based project was a descriptive, correlational, longitudinal study using a convenience sample of HIV-negative males. The purpose of this research was to describe individual demographic variables associated with PrEP medication adherence and to examine the effect of a follow-up phone call from a nurse once a month for 3 months. Participants were HIV-negative men who had sex with men (MSM) in a mixed-payer, open-label, and outpatient care structure. The hypothesis was to find a positive relationship between less medical issues, less mental health issues, higher socioeconomic status and high level of MSM medication adherence. In addition, another aim was to determine the effects of follow-up phone call on medication adherence if provided by a clinical nurse once a month for 3 months.

Setting

The PrEP evidence-based study was conducted at a large outpatient clinic in Northern California. The clinic provided comprehensive HIV and STD care to the lesbian, gay, bisexual, transgender, questioning (LGBTQ) populations from Santa Clara, Alameda and San Francisco Counties. The clinic emphasized HIV prevention and was a member of Santa Clara's "Getting to Zero" campaign, whose mission has been to increase HIV/AIDS awareness and to reach a zero HIV transmission rate in the local LGBTQ population. The clinic was staffed by three medical doctors, one physician assistant, two psychiatrists, one clinical nurse, and one medical assistant. All medical staff members were trained and educated regarding PrEP education.

Sample Population

The clinic had approximately 100 homosexual, heterosexual, or bisexual patients enrolled quarterly for PrEP. The ethnicity of patients was 47.1% Hispanic, 29.1% Caucasian, 14.5% African American, and 8.4% Asian. Males represent 82%, females represent 15.8%, and

transgender people represent 2% (E. Brooks, personal communication, November 1, 2016). The project focused on recruiting the gay HIV-negative MSM population who took daily HIV prevention oral antivirals.

Ethical Considerations

On August 1, 2017, the local hospital and clinic system Institutional Review Board (IRB) approved the project (see Appendix A). The study timeframe was from September 2017 to February 2018. Approval was also obtained from a university IRB. Consent was obtained by the clinical nurse (see Appendix B). Potential risks were addressed: participants could experience psychological stress while completing the survey questionnaire, to include emotional discomfort, embarrassment, and anxiety. To minimize psychological stress, the clinical nurse emphasized that the study was voluntary. Participants were free to decline to answer any questions that made them uncomfortable. Participants were informed that they could withdraw from the study at any time without penalty or prejudice and that they would not be asked why they were withdrawing.

Other potential risks included that participants could worry that the survey would negatively affect their insurance and medical benefits. The clinical nurse reassured participants that their anonymity would not be violated and the subject and data would be held in confidence and would not be used against the participants' rights. Participants were granted free access to the onsite library where medical and psychological resources were available for information prior to joining the study.

This study strictly complied with HIPAA and information security requirements. The participants' names and medical record numbers were not linked to the survey, instead subjects were randomly identified a number. The completed survey forms, the consent forms, and the medication compliance questionnaires were secured in a locked drawer in the unit office. The

access key could be obtained only from the clinical nurse or clinic manager. There were no personal computers, USB drives, external hard drives, tablets, or smartphones used in this study.

Procedure

The frontline providers identified the inclusion candidates after meeting the subjects in the clinic setting; the physician or physician assistant then notified the clinical nurse. The population of interest were male, men who have sex with men (MSM) who requested emtricitabine/tenofovir for HIV prevention. The inclusion criteria for participants included naïve or new patients who were seeking a PrEP regimen or current existing patients on a PrEP regimen without previous failure. The exclusion criteria were patients who had a failure history on PrEP or who had been consistently in and out of the PrEP program.

The clinical nurse initiated an individual 10-minute face-to-face study consultation with each MSM candidate and obtained written legal consent during that visit. The clinical nurse also informed participants of the research purpose, benefits, risks, and compensation. Candidates who agreed to participate in the study received a $5 gift card and a $1 scratch lottery ticket as compensation. The clinical nurse then explained and had the candidate take the survey.

The clinical nurse instructed participants about a medication-monitoring phone consult that would continue for 10-minutes via phone once a month for a 3-month period. The follow-up phone call would include questions about emtricitabine/tenofovir and 4-questions from the Morisky's Medication Adherence Scale. Participants would be discharged from the study after data collection was completed.

Instrument

The clinical nurse distributed a survey (see Appendix C). The survey consisted of nine demographic questions and the 4-item Morisky's Medication Adherence Scale (MMAS-4). The MMAS-4 instrument developed by Morisky et al. (1986) has been tested for predictive validity

of self-reporting measures (alpha reliability = 0.61). The MMAS-4 has been taken under a control group environment showing high adherence reliability (p <0.01).

The instrument was initially used with hypertensive patients for medical providers to follow-up on patients' behavior changes when self-scoring via MMAS-4. In addition, the validated MMAS-4 instrument has been cited by more than 300 articles in various settings, including diabetes, COPD, and hypertension. MMAS-4 was the first to be used in a HIV PrEP compliance study. The tool consists of the four questions listed below:

1. Do you ever forget to take your medicine?
2. Are you careless at times about taking your medicine?
3. Sometimes if you feel worse when you take the medicine, do you stop taking it?
4. When you feel better, do you sometimes stop taking your medicine?

The answer to each MMAS-4 question is either yes or no. Patients who answer yes receive one point. A total score of 3–4 indicates low adherence, 2–3 indicates medium adherence, and 0–1 indicates high adherence. The potential limitation of the instrument was that "the tool could not distinguish the trend of medium adherence" (Morisky et al., 1986, p. 72). Thus, the MMAS-4 results can be skewed if the subject is either high adherence or low adherence.

Data Analysis Plan

Data analysis were conducted with a statistical program for social sciences. Spearman's rho was used to test the correlation between categorical variables (i.e., age, marital status, sexual relationships, medical status, mental health status, ethnicity, education level, employment status, and income) and the MMAS-4 score. Correlations helped predict which variables were associated with compliance in the MSM population in an ambulatory setting. Furthermore, chi-square tests could demonstrate medication adherence within groups.

CHAPTER 4: RESULTS

A total of 30 HIV-negative MSMs were recruited for the PrEP compliance study. One participant dropped out of the study, and another was instructed to stop the regimen because of an increase of liver and kidney enzymes. In total, N = 28 HIV-negative MSMs participated in the study.

The demographics of age, marital status, relationship status, mental health status, education level, employment status, and annual income were analyzed (see Table 1). Study participants were males under 40 years of age (*n* = 20, 71.4%). Most participants reported that they were single (*n* = 19, 67.9%) and had more than two sexual partners or were in open relationships (*n* = 19, 67.9%). Most participants had few medical issues or no mental health issues (*n* = 23, 82.1%). Participants self-reported their ethnic backgrounds as Caucasian (*n* = 14, 50%), Hispanic (*n* = 9, 32.1%), and Asian (*n* = 5, 17.9%). The majority of study participants were employed (*n* = 25, 89.3%) with college or postgraduate degrees (*n* = 24, 85.7%) and an annual household income of over $75,000 per year (*n* = 15, 53.6%).

Table 1

Sample Demographics

Age in Category	Frequency *n* =	Percent %
18–39 years old	20	71.4
40–49 years old	6	21.4
50–59 years old	2	7.1
Marital Status		
Single	19	67.9
Married	4	14.3
Partnered, Not Married	3	10.7
Divorced or Separated	2	7.1

Relationships		
1 Sex Partner	4	14.3
>2 Sex Partners	15	53.6
Open Relationship	4	14.3
Other	5	17.9
Medical Status		
No Medical Issue	13	46.4
1 Acute Medical Issue	6	21.4
1 Chronic Medical Issue	8	28.6
>2 Acute Medical Issues	1	3.6
Mental Health Status		
No Mental Health Issue	23	82.1
1 Medication for Mental Issue	4	14.3
>2 Medications for Mental Issue	1	3.6
Ethnic Background		
Asian	5	17.9
Hispanic	9	32.1
White	14	50.0
Education Level		
Some College	4	14.3
College or Post-Grad	24	85.7
Employment Status		
Employed	25	89.3
Unemployed	2	7.1
Student	1	3.6
Annual Household Income		
<$20,000	1	3.6
$40,001~$75,000	12	42.9
>$75,001	15	53.6
Time 1 Month MMAS-4		
High Adherence	13	46.4
Medium Adherence	15	53.6
Time 2 Months MMAS-4		
High Adherence	16	57.1
Medium Adherence	12	42.9
Time 3 Months MMAS-4		
High Adherence	15	53.6
Medium Adherence	13	46.4

Spearman's rho correlations were conducted to determine whether any relationships existed between demographic variables and medication adherence at 1 month, 2 months and 3 months (see Table 2). A two-tailed test of significance indicated a significant negative relationship between marital status and medication adherence at 1 month, $r_s(28) = -.375$, $p < .05$. A single male had higher medication adherence. A two-tailed test of significance indicated a significant positive relationship between mental health status and medication compliance at 1 month, $r_s(28) = .426$, $p < .05$. Participants with no mental health issues had higher medication compliance. Finally, a two-tailed test of significance indicated a significant negative relationship between the participant's education level and medication compliance at 2 months, $r_s(28) = -.431$, $p < .05$. Participants with postgraduate degrees had higher medication compliance.

Spearman's rho correlations were also conducted to determine whether any relationships existed between medication adherence at 1 month, 2 months, and 3 months. A two-tailed test of significance indicated a highly significant positive relationship between medication adherence at 1 month and 2 months, $r_s(28) = .521$, $p < .01$; at 1 month and 3 months, $r_s(28) = .490$, $p < .01$; and at 2 months and 3 months, $r_s(28) = .806$, $p < .01$. Participants had a consistent level of medication adherence over 3 months. Participants who had moderate medication adherence tended to predict moderate medication adherence over 3 months. Participants who had high medication adherence tended to predict high medication compliance over 3 months.

Table 2

Spearman's rho Correlations

		Age	Marital Status	Relations	Medical Status	Mental Health	Ethnic	Ed Level	Employ Status	Annual Income	Time 1 mos. MMAS	Time 2 mos. MMAS	Time 3 mos. MMAS
Age	CC	1.000	.019	.113	-.464*	.290	.480**	-.065	.035	.124	.053	.145	-.055
	Sig.	.	.924	.568	.013	.135	.010	.744	.860	.531	.787	.462	.780
Marital Status	CC	.019	1.000	-.125	-.179	-.159	.071	.058	.208	.045	-.375*	-.304	-.338
	Sig.	.924	.	.527	.361	.420	.719	.769	.288	.819	.049	.116	.079
Relations	CC	.113	-.125	1.000	.128	.298	.033	.372	-.117	.063	-.116	-.267	-.285
	Sig.	.568	.527	.	.516	.124	.869	.051	.553	.748	.558	.170	.141
Medical Status	CC	-.464*	-.179	.128	1.000	.126	-.128	-.123	.106	.316	.062	.048	.068
	Sig.	.013	.361	.516	.	.522	.516	.534	.592	.102	.755	.810	.730
Mental Health	CC	.290	-.159	.298	.126	1.000	.440*	.063	.207	-.060	.426*	.253	.252
	Sig.	.135	.420	.124	.522	.	.019	.751	.291	.762	.024	.194	.196
Ethnic	CC	.480**	.071	.033	-.128	.440*	1.000	-.017	.049	.041	-.013	.168	-.018
	Sig.	.010	.719	.869	.516	.019	.	.933	.803	.837	.947	.393	.926
Ed Level	CC	-.065	.058	.372	-.123	.063	-.017	1.000	-.030	.119	-.116	-.431*	-.367
	Sig.	.744	.769	.051	.534	.751	.933	.	.879	.548	.555	.022	.055
Employ Status	CC	.035	.208	-.117	.106	.207	.049	-.030	1.000	.030	-.017	.021	.014
	Sig.	.860	.288	.553	.592	.291	.803	.879	.	.881	.932	.917	.945
Annual Income	CC	.124	.045	.063	.316	-.060	.041	.119	.030	1.000	-.014	-.234	-.306
	Sig.	.531	.819	.748	.102	.762	.837	.548	.881	.	.944	.232	.113
Time 1 mos. MMAS	CC	.053	-.375*	-.116	.062	.426*	-.013	-.116	-.017	-.014	1.000	.521**	.490**
	Sig.	.787	.049	.558	.755	.024	.947	.555	.932	.944	.	.005	.008
Time 2 mos. MMAS	CC	.145	-.304	-.267	.048	.253	.168	-.431*	.021	-.234	.521**	1.000	.806**
	Sig.	.462	.116	.170	.810	.194	.393	.022	.917	.232	.005	.	.000
Time 3 mos. MMAS	CC	-.055	-.338	-.285	.068	.252	-.018	-.367	.014	-.306	.490**	.806**	1.000
	Sig.	.780	.079	.141	.730	.196	.926	.055	.945	.113	.008	.000	.

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

In the first month of nursing follow-up phone calls, the results showed that single MSM participants correlated with high medication compliance, as did participants with no mental health issues. For the second and third month follow-ups, the data showed that a higher education level correlated with high medication compliance. The study results demonstrated that in an open-label and mixed-payer structure of compliance, being single, having a high education level, and not having a mental health diagnosis correlated with a high level of PrEP compliance. Even though the nurse's follow-up phone calls did not prove to be significant in increasing medication adherence, the nursing follow-up intervention demonstrated that the phone calls served as accountability for maintaining patients' adherence levels through the 3-month period.

A chi-square test of independence was performed to determine group adherence over time. The chi-square test aimed to determine whether the medication adherence level differed between 1 month, 2 months, and 3 months. The result of chi-square test showed that the percentage of patients with high adherence and the percentage of patients with medium adherence did not statistically differ between the three-time points, χ^2 (2, N = 28) = .668, p = .71 (see Table 3). The high adherence group, remained at high adherence with medication over 3 months. The medium adherence group, remained at medium adherence with medication over 3 months. There were no subjects with low adherence.

Table 3

Chi-square Tests

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	.668[a]	2	.716
Likelihood Ratio	.669	2	.716
Linear-by-Linear Association	.283	1	.595
N of Valid Cases	84		

There was no statistical significance to prove that a nurse's follow-up phone calls improved patient adherence from medium to high adherence. The adherence levels did not change over 3 months. As a result, the nurse's follow-up phone calls may have served to sustain medication compliance from changing throughout the 3-month period.

CHAPTER 5: DISCUSSION

Results described individual demographic variables associated with MSM and medication adherence. The first hypothesis was to find a positive relationship between MSM and less medical issues, less mental health issues, and higher socioeconomic status with a high level of medication adherence. Results demonstrated that there was a relationship between no mental health issues and a high level of medication adherence. However, there was not a relationship between no medical issues or higher socioeconomic status. Instead, findings suggested that a single male with no mental health issue and higher education had a strong relationship with high medication adherence in an open-label and mixed-payer structure of healthcare.

Previous studies (Grant et al., 2010; Kibengo et al., 2013; Murnane et al., 2015) have shown that HIV transmission was greatly reduced in HIV-negative partners on oral antiretrovirals. In comparison to these investigations, no HIV infection was reported by study subjects. During the short study timeframe, the effectiveness in HIV prevention associated with iPrEx (2010) and Partners PrEP (2015) was also seen in this investigation. Although, these previous studies (Grant et al., 2010; Kibengo et al., 2013; Murnane et al., 2015) supported the use of PrEP compliance, little information was given on the type of subject who would have medication compliance. Again, this research suggested that single males with no mental health issues and higher education levels had high medication compliance.

Other studies (Gamarel & Golub, 2015; Mathur et al., 2016; Marcus et al., 2016) have discussed individual adoption (or nonadoption) of HIV transmission prevention measures. Gamarel and Golub (2015) noted that regardless of age, income or education the motivation to adopt PrEP was related to condomless sex. In Uganda, Mathur et al. (2016) found that participants were less likely to adopt PrEP due to fear, skepticism and misconceptions. Marcus et al., found that being African American, smoking and having a higher insurance copay was a

deterrent to PrEP adoption. The participants in this study sample were primarily Caucasian MSM who were younger (18-39 years of age) single, in multiple relationships, without medical or mental issues, were employed with college or postgraduate degrees.

Limitations

Limitations included a small sample size, the setting, and the short length of the project. First, anecdotally, it appeared that participants did not show an interest in study participation and receiving follow-up phone calls, perhaps due to social stigma, resistance to being labeled, or disinterest toward phone calls about medication adherence. Second, the patient volume and traffic was insufficient to recruit a large sample size. A multi-site study involving different settings may have yielded a larger sample. The location of the study, in an area of high education and affluence did not necessarily represent typical healthcare settings across the United States. As a result, the study only represented the local population. Third, the study was of short duration and as a result recruitment discontinued in order to not exceed the project timeline. The study design of 3 months may not have been long enough to be demonstrating long-term PrEP compliance. Conceivably, 6 or 12 months of follow-up phone calls may have been ideal to provide stronger statistical evidence in support of PrEP compliance.

Conclusion

This descriptive study demonstrated higher PrEP compliance in young, single, educated, and employed Caucasian gay males with multiple partners. Study results represented an affluent urban metropolitan area in a care setting for an open-label and mixed-payer structure. The convenience population did not necessarily represent settings across the United States because of the specific location with higher levels of education and income. More information will be needed about the variables affecting PrEP compliance in other settings.

In addition, more studies need to look at human variables associated with clients that are of different race and ethnic backgrounds. Although, African Americans represent 14.5% of the clinic population, none were recruited into the convenience sample during the study timeframe. Further studies need to be conducted on HIV-negative issues, including sexual education, social stigma, gay culture, and sexual behaviors, especially concerning young MSMs of color.

It is important for clinical nurses to understand individual human variables related to HIV-negative antiviral medication compliance. Although no statistical significance was seen between groups with regards to medication adherence, findings suggest that clinical nurses may reinforce medication adherence by providing planned follow-up phone calls. Holistic care via the human caring theory seeks to achieve human wellbeing by nursing care support.

In conclusion, clinical nurses can support clients in achieving the highest level of HIV prevention and health outcomes. HIV prevention affects patients' partners, families, and communities. Finally, the goal of HIV prevention is to reach a zero-transmission rate in the community, and ultimately end the AIDS epidemic.

REFERENCES

REFERENCES

Centers for Disease Control and Prevention. (2015). *HIV Cost-effectiveness*. Retrieved from http://www.cdc.gov/hiv/programresources/guidance/costeffectiveness/index.html

Centers for Disease Control and Prevention. (2018). *Exposure Prophylaxis (PrEP).* Retrieved from https://www.cdc.gov/hiv/risk/prep/index.html

Gamarel, K., & Golub, S. (2015). Intimacy motivations and pre-exposure prophylaxis (PrEP) adoption intentions among HIV-negative men who have sex with men (MSM) in romantic relationships. *Annals of Behavioral Medicine*, *49*(2), 177–186.

Grant, R., Lama, J., Anderson, P., McMahan, V., Liu, A., Vargas, L., . . . Glidden, D. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *The New England Journal of Medicine*, *363*(27), 2587–2599. Retrieved from http://www.nejm.org.hmlproxy.lib.csufresno.edu/doi/full/10.1056/NEJMoa1011205

Kibengo, F., Ruzagira, E., Katende, D., Bwanika, A., Bahemuka, U., Haberer, J., . . . Priddy, F. (2013). Safety, adherence and acceptability of intermittent tenofovir/emtricitabine as HIV pre-exposure prophylaxis (PrEP) among HIV-uninfected Ugandan volunteers living in HIV-serodiscordant relationships: A randomized, clinical trial. *PLoS ONE*, 1–10.

Lelutiu-Weinberger, C., Pachankis, J., Golub, S., Walker, J., Bamonte, A., & Parsons, J. (2013). Age cohort differences in the effects of gay-related stigma: Anxiety and identification with the gay community on sexual risk and substance use. *AIDS & Behavior*, *17*(1), 340–349. doi:10.1007/s10461-011-0070-4.

Marcus, J., Hurley, L., Hare, C., Nguyen, D., Phengrasamy, T., Silverberg, M., . . . Volk, J. (2016). Preexposure prophylaxis for HIV prevention in a large integrated health care

system: Adherence, renal safety, and discontinuation. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *73*(5), 540–546.

Mathur, S., Romo, D., Rasmussen, M., Nakyanjo, N., Nalugoda, F., & Santelli, J. (2016). Re-focusing HIV prevention messages: A qualitative study in rural Uganda. *Journal of Adolescent Health*, *58*(2), 1–9.

Morisky, D., Green, L., & Levine, D. (1986). Concurrent and Predictive Validity of a Self-Reported Measure of Medication Adherence. *Medical Care*, 24(1), 67–74.

Murnane, P., Brown, E., Donnell, D., Coley, R., Mugo, N., Mujugira, A., Mugo, N. (2015). Estimating efficacy in a randomized trial with product nonadherence: Application of multiple methods to a trial of preexposure prophylaxis for HIV prevention. *American Journal of Epidemiology*, *182*(10), 848–856.

Stanford Health Care (2015). *Nursing: Team overview*. Retrieved from https://stanfordhealthcare.org/health-care-professionals/nursing/team.html

Watson, M. J. (1988). New dimensions of human caring theory. *Nursing Science Quarterly*, *1*(4), 175–181.

APPENDICES

APPENDIX A: IRB APPROVAL

STANFORD UNIVERSITY

Stanford, CA 94305 [Mail Code xxxx]

David D Oakes, M.D. (650) 723-5215
CHAIR, PANEL ON MEDICAL HUMAN SUBJECTS (650) 725-8013

Certification of Human Subjects Approvals

Date: August 1, 2017

To: Edward M Brooks, MD, Medicine - MedInfectious Diseases
Ming-Hsun Lin MSN, Laurie Anne S. va DNP, Sandra E. Valle VA

From: David D Oakes, M.D., Administrative Panel on Human Subjects in Medical Research

eProtocol Title: Evidence Based Study of Medication Compliance Project in HIV Prevention Using Pre Exposure Prophylaxis (PrEP) Antivirals for HIV-Negative Males

eProtocol #: 40293 **IRB 8 (Registration #:6708)**

The IRB approved human subjects involvement in your research project on 08/01/2017. **Prior to subject recruitment and enrollment, if this is: a Cancer-related study, you must obtain Cancer Center Scientific Review Committee (SRC) approval; a CTRU study, you must obtain CTRU approval; a VA study, you must obtain VA R and D Committee approval; and if a contract is involved, it must be signed.**

The expiration date of this approval is 07/31/2018 at Midnight. If the research is to continue beyond that date, it is your responsibility to submit a Continuing Review application in eProtocol. Research activities must be reviewed and re-approved on or before midnight of the expiration date. The approval period may be less than one year if so determined by the IRB. Proposed changes to approved research must be reviewed and approved prospectively by the IRB. No changes may be initiated without prior approval by the IRB, except where necessary to eliminate apparent immediate hazards to subjects. (Any such exceptions must be reported to the IRB within 10 working days.) Unanticipated problems involving risks to participants or others and other events or information, as defined and listed in the Report Form, must be submitted promptly to the IRB. (See Events and Information that Require Prompt Reporting to the IRB at http://humansubjects.stanford.edu.) Upon completion, you must report to the IRB within 30 days.

Please remember that all data, including all signed consent form documents, must be retained for a minimum of three years past the completion of the research. Additional requirements may be imposed by your funding agency, your department, HIPAA, or other entities. (See Policy 1.3.3.1 Retention of and Access to Research Data at http://doresearch.stanford.edu/policies/research-policy-handbook)

This institution is in compliance with requirements for protection of human subjects, including 45 CFR 46, 21 CFR 50 and 56, and 38 CFR 16.

Includes: STANFORD CONSENT_PCHIV
For MINIMAL RISK Medical Human Subject Research
Mod_survey_consent_rev02Y2016

David D Oakes, M.D., Chair

Approval Period: 08/01/2017 THROUGH 07/31/2018
Review Type: EXPEDITED - NEW
Funding: Edward Brooks discretionary account
Expedited Under Category: 7
Assurance #: FWA00003934 (SHC), FWA00000935 (SU)

APPENDIX B: CONSENT FORM

CONSENT FORM
For MINIMAL RISK Medical Human Subject Research

FOR QUESTIONS ABOUT THE STUDY, CONTACT: Edward Brooks, MD, Chief Medical Director and Ming-Chun Ho, MSN, RN. Address: 211 Quarry Road, Suite 202, Palo Alto, CA 94304. Phone number: 650-723-9001.

DESCRIPTION: You are invited to participate in a research study on Pre-exposure Prophylaxis (PrEP) Antivirals for HIV Negative Males Medication Compliance study. The purpose of the study is to fill the gap in the research reviews and provide further evidence for institution to support PrEP adherence. You will be asked two pages of questionnaires about the medical, psychosocial, and financial status with basic demographic information. After complete the survey form, you will be asked to follow up the monthly self-report medication compliance questionnaires, which is 4 questions total, via a phone call from September 1st, 2017 through February 28th, 2018. These questionnaires should take about 10 minutes to complete.
The results of the study of your samples will be used for research purposes only and you will not be told the results of the tests.

_____ I consent to my samples being saved for future research
_____ I do not consent to my samples being saved for future research

RISKS AND BENEFITS: The risks associated with this study are none, and you are free to decline any questions, which make you feel uncomfortable**.** The benefits which may reasonably be expected from this study are none. However, by understanding the correlation factors associated with PrEP medication compliance via this study, the future patients will be benefit by standardized PrEP protocol to achieve higher medication adherence rate. We cannot and do not guarantee or promise that you will receive any benefits from this study. Your decision whether or not to participate in this study will not affect your employment/medical care.

TIME INVOLVEMENT: Your participation in this experiment will take approximately 10 minutes.

PAYMENTS: You will receive $5 Starbucks gift care and a $1 scratch-off ticket as payment for your participation. There is no cost for you to participate in this study.

PARTICIPANT'S RIGHTS: If you have read this form and have decided to participate in this project, please understand your participation is voluntary and you have the right to withdraw your consent or discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.
The results of this research study may be presented at scientific or professional meetings or published in scientific journals. However, your identity will not be disclosed**.** You have the right to refuse to answer particular questions.

Authorization to Use Your Health Information for Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

The purpose of the study is to fill the gap in the research reviews and provide further evidence for institution to conduct standardized PrEP protocols to support PrEP adherence. Your health information will be desensitized by randomly assigned two-digit number, which only Ming-Chun Ho, RN able to identify on a Stanford password protected computer via electronic medical record for HIV negative result. No health information will be linked to the paper questionnaires.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: Ming-Chun Ho, MSN, RN. Address: 211 Quarry Road, Suite 202, Palo Alto, CA 94304.

What Personal Information Will Be Obtained, Used or Disclosed?

Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to, age, marital status, sex relationship, medical and mental status, ethnic, employment status, household income, and HIV status. The protocol director: Edward Brooks, MD and admin contact: Ming-Chun Ho, MSN, RN will only use electronic medical records (EMRs) to identify and confirm your HIV-negative status for eligibility purposes. No specimens will be collected. In a paper format, your names and medication record numbers will be desensitized by randomly assigned two-digit numbers, which only the Ming-Chun Ho, MSN, RN will able to identify on a Stanford password protected and information secured computer via EMRs. No health information will be linked to the paper questionnaires.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director: Edward Brooks, MD, Chief Medical Director
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Admin Contact: Ming-Chun Ho, MSN, RN

Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your health information will end on February 28, 2018 or when the research project ends, whichever is earlier.

Will access to my medical record be limited during the study?

To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (e.g., if included in your official medical record).

_____ _____

Signature of Adult Participant Date

_____

Print Name of Adult Participant

WITHDRAWAL FROM STUDY

The Protocol Director may also withdraw you from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

CONTACT INFORMATION:

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Edward Brooks, MD, Chief Medical Director. You may contact him now or later at 650-723-9001.

If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Edward Brooks, MD, Chief Medical Director at 650-723-9001. You should also contact him at any time.

The extra copy of this signed and dated consent form is for you to keep.

_____ _____

Signature of Adult Participant Date

_____

Print Name of Adult Participant

Mark an X in the box that best describes **YOU**:

Your Age?

18-39	☐ 1
40-49	☐ 2
50-59	☐ 3
>60	☐ 4

Your marital status?

Single	☐ 1
Married	☐ 2
Partnered, Not Married	☐ 3
Divorced or Separated	☐ 4
Widowed	☐ 5

Your sex relationship status?

One sex partner	☐ 1
>2 sex partners	☐ 2
Open relationship	☐ 3
Other:_____	☐ 4

Your medical status?

One acute medical issue	☐ 1
One chronic medical issue	☐ 2
>2 acute medical issue	☐ 3
>2 chronic medical issue	☐ 4

Your mental health status?

No mental health issue	☐ 1
One medication for mental health	☐ 2
>2 medications for mental health	☐ 3

Your ethnic background?

Asian	☐ 1
Black	☐ 2
Filipino	☐ 3
Hispanic	☐ 4
Native American	☐ 5
Pacific Islander	☐ 6
White	☐ 7
Other	☐ 8

Check your highest level of education completed:

Elementary	☐ 1
Some High School	☐ 2
High School Diploma	☐ 3
Some College	☐ 4
College Degree	☐ 5
Post-Graduate Degree	☐ 6

Your employment status?

Employed	☐ 1
Unemployed	☐ 2
Homemaker	☐ 3
Retired	☐ 4
Student	☐ 5

Your gross annual (yearly) household income?

No income	☐ 1
< less than $20,000	☐ 2
$20,000 - $40,000	☐ 3
$40,001 - $75,000	☐ 4
$75,001 - $100,000	☐ 5
>$100,001	☐ 6

Thank you for your participation.
You will receive a monthly phone call for follow up your compliance.

Monthly self-report phone interview questions that best describes **YOU**:

Do you ever forget to take your medication? ☐ Yes ☐ No

Are you careless at times about taking your medication? ☐ Yes ☐ No

When you feel better do you sometimes stop taking your medicine? ☐ Yes ☐ No

Sometimes if you feel worse when you take the medicine, do you stop taking it? ☐ Yes ☐ No