HIV/STD SAFER SEX SKILLS GROUPS FOR MEN IN METHADONE MAINTENANCE OR DRUG-FREE OUTPATIENT TREATMENT PROGRAMS
(A companion protocol to: HIV/STD Safer Sex Skills Groups For Women In Methadone Maintenance Or Drug-Free Outpatient Treatment Programs)

National Institute on Drug Abuse

Clinical Trials Network

NIDA-CTN-0018 Version 10 (3/5/04)

Lead Investigator:	Donald Calsyn, Ph.D., Washington Node, Puget Sound Health Care System, Department of Veteran Affairs, Seattle, WA.
Co-Lead Investigator:	Susan Tross, Ph.D., Long Island Node, N.Y. State Psychiatric Institute, N.Y., N.Y.
Project Manager:	Sara Berns, Ph.D. – Washington Node
CTP Collaborators:	Peter Benson, Psy.D. – Washington Node Al Cohen, M.A., M.F.T.- Pacific Node Janet Lerner, D.S.W. – Long Island Node Paul McLaughlin – New England Node Deborah Orr, Ph.D. – Florida Node
Scientific Collaborators:	Rob Malow, Ph.D. – Florida Node Edward Nunes, M.D. - Long Island Node Steve Shoptaw, Ph.D. – Pacific Node Paul Crits-Cristoph, Ph.D. – Delaware Valley Node Nabila el-Bassel, Ph.D. – HIV/STD Safer Skills Group Intervention Expert, Columbia University School of Social Work Norma Bartholomew, M.A., Institute for Behavioral Research, Texas Christian University Jennifer Potter, Ph.D., M.P.H. - Northern New England Node
Data Management:	Molly Carney, Ph.D. (Washington Node), James Robinson, Ed.D. (New York, Long Island, Rocky Mountain Nodes)
Design and Analysis:	Xiao-Hua (Andrew) Zhou, Ph.D. (Washington Node)
Quality Assurance:	Sherryl Baker, Ph.D. (New York Node), Anthony Floyd, Ph.D. – Washington Node
Training:	John Baer, Ph.D. – Washington Node, Gloria Miele, Ph.D. – Long Island Node
Dissemination:	Elizabeth Wells, Ph.D. (Washington Node)
Regulatory Affairs:	Jen Lima, M.P.H. (Long Island Node)
NIDA:	Ming Shih, Ph.D.

TABLE OF CONTENTS

TITLE PAGE 1
TABLE OF CONTENTS 2
LIST OF ABBREVIATIONS 5
SYNOPSIS and SCHEMA 6
STUDY FLOW CHART 8
1.0 INTRODUCTION 9
1.1. Background 9
1.1.1. CTN CTP HIV Snapshot 9
1.1.2. Evidence for Efficacy of HIV Focused Interventions in Drug Abuse Treatment 10
2.0 STUDY RATIONALE 11
2.1. Justification for Gender Specific Interventions 11
2.2. Rationale for Components Included in the Intervention 13
3.0 OBJECTIVES 14
3.1 Primary Objective 14
3.2 Secondary Objectives 14
4.0 STUDY DESIGN 14
5.0 STUDY POPULATION 15
5.1 Number of Sites and Subjects 15
5.2 Duration of Study and Visit Schedule 16
5.3 Informed Consent 16
5.4 Inclusion Criteria 16
5.5 Exclusion Criteria 16
5.6 Subject Discontinuation Criteria 17
5.6.1 Consideration of Early Termination 17
5.6.2 Procedures for Discontinuation 17
5.7 Replacement of Subjects 17
6.0 STUDY TREATMENTS 18
6.1 Study Therapies 18
6.1.1 HIV/AIDS Education 18
6.1.2 A Communications Skills and Sexuality Workshop (REMAS) 18
Table 1: Standard of Care HIV/AIDS Education: Intervention Outline 20
Table 2: A Communications Skills and Sexuality Workshop (REMAS): Intervention Outline 20
6.2 Selection and Training of Therapists 22
6.3 Administration of Study Therapies 22
6.3.1 Randomization 22
6.3.2 Blinding 23
6.3.3 Quality Control of Therapies Administered 24
7.0. COMITANT THERAPY 24
7.1 General Considerations 24

7.2 Therapies Prohibited During the Trial....25
8.0 MEASUREMENTS, EVALUATIONS, AND ANALYTICAL METHODS....25
8.1 Informed Consent....25
8.2 Inclusion/Exclusion Criteria Review....25
8.2.1. Screening Assessment 26
Demographic 26
Mental Status 26
Risk Behavior Survey 26
8.3 Baseline and Follow UP Assessments....26
8.3.1. Compositie International Diagnostic Interview 27
8.3.2. Addiction Severity Index-Lite 27
8.3.3. Drug Use and Drug Injection Risk Assessment 27
8.3.4. Sexual Risk Assessment 27
8.3.5. Condom Use Skill Behavioral Assessment 28
8.3.6. Condom Barriers Scale 28
8.3.7. Bem Sex Role Inventory 28
8.3.8 Biologic Measures 29
8.4 Adverse Event Evaluation....29
8.5 Treatment Compliance....29
Table 3: Schedule of Assessment Collection 30
9.0 Data and Safety Monitoring Plan....31
9.1 Safety....31
9.1.1. Definition of Adverse and Serious Adverse Events 31
9.1.2 Assessment, Reporting and Monitoring of Adverse and Serious Adverse Events 31
Figure 3: Adverse Events Reporting Flow Chart 33
9.1.2 Human Subjects Safety 34
9.2 Trial Performance 34
9.2.1. Treatment Intervention Integrity 35
9.2.2. Data Integrity 35
9.3 Trial Efficacy 35
10.0 DEPARTURES FROM PROTOCOL....36
11.0 STATISTICAL ANALYSIS....36
11.1 Objectives of Analysis....36
11.2 Primary Outcome Measure and Statistical Hypotheses....36
11.3 Sample Size and Statistical Power....36
11.4 Study Population....38
11.5 Demographic Profile....38
11.6 Analysis of Primary Outcome....38
11.7 Analysis of Secondary Outcomes....40
11.8 Secondary Analysis of Compliance on the Outcome Effects....40
11.9 Interim Analyses....41
12.0 STUDY TIMETABLE....41

13.0 DISCLOSURE OF DATA 41
14.0 ADHERENCE TO ETHICAL, REGULATORY AND ADMINISTRATIVE CONSIDERATIONS 41
14.1 IRB Approval 42
14.2 Informed Consent 42
14.3 Health Insurance Portability and Accountability Act (HIPAA) 42
14.4 Investigator Assurances 42
14.5 Outside Monitoring 42
14.6 Clinical Monitoring 42
15.0 DISPOSITION OF DATA 43
15.1 Lead Node Responsibilities 43
15.2 Data Collection 44
15.3 Data Submission, Editing and Monitoring 44
15.4 Automated Acquisition and Management System 44
15.5 Central Data Repository 44
16.0 REFERENCES 46
Protocol Signature Page 49
Consent Forms 50

LIST OF ABBREVIATIONS

Abbreviation	Definition
ACASI	Audio Computer-Assisted Self-Interviewing
AE	Adverse Event
AIDS	Acquired Immuno-deficiency Syndrome
ASI	Addiction Severity Index
CIDI	Composite International Diagnostic Interview
CRF	Case Report Form
CTN	Clinical Trials Network
CTP	Community Treatment Program
DATAR	Drug Abuse Treatment and AIDS Research
DSMB	Data and Safety Monitoring Board
DMAS	Data Management and Analysis Subcommittee
HIV	Human Immuno-deficiency Virus
DMC	Data Management Center
GEE	Generalized Estimated Equations
HIV-ED	Approaches To HIV/AIDS Education in Drug Treatment
IBR	Institute for Behavioral Research
IRB	Institutional Review Board
ITT	Intent to Treat
IWGEE	Inversely Weighted Generalized Estimated Equations
MAR	Missing At Random
MMTP	Methadone maintenance treatment program
NIDA	National Institute on Drug Abuse
NIMH	National Institute of Mental Health
NMHPTG	NIMH Multisite HIV Prevention Trial Group
ODF	Outpatient Drug Free Treatment
PL	Project Light
PLHPM	Project Light HIV Prevention Manual
RBS	Risk Behavior Survey
REMAS	Real Men Are Safe
SADAR	Sex and Drug Abuse Relationship Questionnaire
SERBAS	Sexual Experiences and Risk Behaviors Assessment Schedule
SC	Steering Committee
SOP	Standard Operating Procedure.
STI	Sexually Transmitted Infections
TCU	Texas Christian University
TOMe	Time Out! For Me
TOMen	Time Out! For Men

SYNOPSIS

Study Objectives: To compare the effectiveness of an intensive gender specific HIV/AIDS group intervention for men in drug abuse treatment to a standard single session group HIV/AIDS education. It is hypothesized that men provided the gender specific intervention will engage in less unprotected vaginal and anal intercourse than will men provided the standard intervention. In addition men in the gender specific intervention will during follow up have had fewer sexual partners, engage in more "outer course," demonstrate a more positive attitude toward condom use, be more likely to possess condoms, be more likely to have taken condoms from clinic supplies, report less frequent use of drugs in combination with sexual acts, and endorse a more egalitarian gender role.

Study Design: Men enrolled in either methadone or LAAM maintenance (MMTP) or outpatient drug free treatment (ODF) will be invited to participate. Eligible participants will complete an assessment battery at baseline, immediately post intervention, three months post intervention, and six months post intervention. Following the initial assessment participants will be randomly assigned to attend a one-session group standard HIV education intervention or a five-session gender specific group intervention.

Subject Population: Participants will be approximately 560 men in either MMTP (N = 280) or ODF (N=280) who have engaged in unprotected vaginal or anal intercourse in the past 6 months. Inclusion of patients from both MMTP and ODF will provide the opportunity to reach two important subgroups of male drug users: those whose primary substance of abuse is heroin (MMTP); and those who use stimulants or multiple other drugs (ODF).

Eligibility Criteria: Adult drug dependent males in treatment at participating CTPs will be invited to participate. An additional inclusion criterion includes having engaged in unprotected vaginal or anal intercourse during the prior six months. Exclusion criteria include: observable, gross mental status impairment – including severe distractibility, incoherence or retardation, having a primary partner who is trying to get pregnant, and being on methadone maitenance for less than 30 days (if applicable).

Study Interventions: There are two intervention conditions proposed: 1) a five-session HIV prevention and sexuality group workshop ("Real Men are Safe" (REMAS)); and 2) a single session HIV/AIDS education serving as a control condition. The HIV/AIDS education condition will be comprised of educational materials from REMAS. Male CTP drug treatment counselors will provide both interventions. Both interventions are manual-driven. These two features will make technology transfer to the CTPs highly likely.

Outcome Measurements: The primary outcome variable is number of unprotected vaginal and anal intercourse acts during the 3 and 6 month follow up periods. Secondary variables of interest include number of sexual partners, frequency of "outer course," possessing condoms, taking condoms from clinic supplies, attitudes toward condoms, frequency of combining drug use and sexual behavior, and gender role beliefs. Generalized Linear models will be used for statistical analyses, and parameter estimation will be done using the method of generalized estimating equation (GEE) combined with the multiple imputation technique for possible missing data (Xie and Paik, 1997; Rubin, 1987).

Protocol Schema

Figure 1

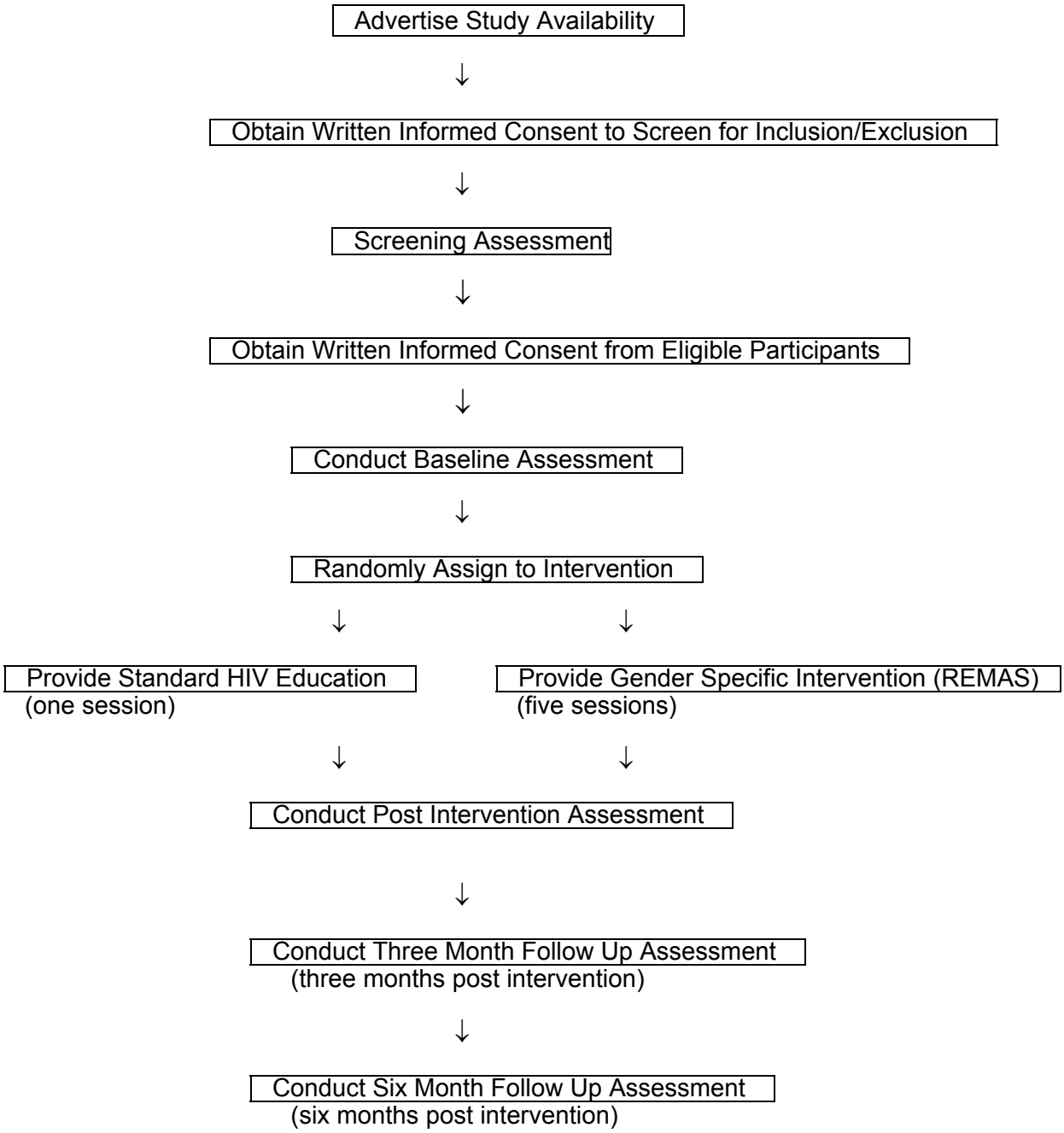


Figure 2: STUDY FLOW CHART

Protocol Number 0018						
Study Activity	Visit 0	Visit 1	Treatment Sessions (1 or 5)	Visit 2	Visit 3	Visit 4
	Day #	Day #	Day #			
Consent for screening assessment	1					
Screening assessment	1					
Obtain written informed consent	1					
Conduct baseline assessment		1-30				
Randomization of cohort			When 3 participants (but no more than 8) are in the cohort			
Attend intervention			Start approx day 8-26, attend over 1-3 weeks.			
Conduct post intervention assessment				21 days after first treatment session		
Conduct 3 mo. Follow up assessment					15 weeks after 1st session	
Conduct 6 mo. Follow up assessment						27 weeks after 1st session

1.0 INTRODUCTION

1.1. Background

The Clinical Trials Network (CTN) Steering Committee (SC) approved the third wave of CTN concepts at its Summer 2001 meeting. One concept approved for further development was Susan Tross's proposed "HIV/STD Safer Sex Skills Groups For Women In Methadone Maintenance Or Drug-Free Outpatient Treatment Programs." During the concept review process it had been strongly recommended by several reviewers that a "men's arm" be added. In consultation with Dr. Tross, the CTN SC selected Dr. Calsyn to adapt the intervention and develop a parallel protocol for men. One protocol development team was formed for both protocols, and Dr. Tross and Dr. Calsyn have worked closely together as Co-LI's. Unlike gender specific interventions for women, preliminary efficacy data from randomized clinical trials of interventions with men in substance abuse treatment are not yet available. However, observational and quasi-experimental studies with men in substance abuse treatment and a multisite randomized clinical trial of men attending STD clinics provide encouraging results that are consistent with the preliminary data for women, and warrant this parallel approach to investigating the effectiveness of gender-specific interventions to address this important clinical issue.

Drug treatment, itself, has been a powerful deterrent to HIV drug use risk behavior, especially needle use behaviors (Metzger, Navaline & Woody, 1998, Sorenson & Copeland, 2000). However, sexual risk behavior has received less attention and has been slower to change (Coyle, Needle & Normand, 1998; Sorenson & Copeland, 2000). The proposed study will bring parts of the NIMH Multisite HIV Prevention Trial Group's (1998) Project Light: HIV Prevention Manual (PL-HPM), and parts of Bartholomew and Simpson's (1996), manual driven, gender-specific communication skills and sexuality workshop for men, *Time Out! For Men* to frontline drug abuse treatment counselors in MMTP or ODF. It will thereby attempt to bridge an important gap between HIV/AIDS intervention research and real world practice. A 5-session skills building group intervention was developed for this protocol taking the bulk of its material from PL-HPM and TOMen. In addition, material from Bartholomew et al's *Approaches to HIV/AIDS Education in Drug Treatment* (HIV-ED) was utilized, and new material was developed for this protocol that focuses on the problem of combining drug use and sexual behavior. In this protocol we are proposing to provide and evaluate this HIV prevention intervention that is specific to the needs of men. In this section we will: 1) describe the HIV prevention interventions currently being provided in CTN CTPs; 2) review the scientific literature that demonstrates HIV interventions provided in substance abuse treatment programs are efficacious. In the Rationale section we will; 1) provide a justification for conducting gender specific interventions; and 2) provide a rationale for the components that make up the proposed intervention.

1.1.1. CTN HIV Snapshot:

The CTN HIV Workgroup conducted a "snapshot" survey of CTN CTPs' HIV assessment and prevention practices in the spring of 2001. Most programs (80.4%) provide some type of HIV education to all clients. Of those that did not provide HIV education to all clients, most provided HIV education to clients deemed to be at high risk for HIV. For most programs (85.4%) the amount of education provided ranged from 30 to 90 minutes (mode=60 minutes [53.3% of clinics]) delivered in a single group or individual session. The bulk of the education

delivered was limited to providing basic information about HIV and risk behaviors associated with its transmission. Skill training interventions, using tools such as role-plays and practice of putting condoms on models, were infrequent.

1.1.2. Evidence for Efficacy of HIV Focused Interventions in Drug Abuse Treatment:

Prendergast, Urada and Podus (2001) conducted a meta-analysis of studies evaluating HIV risk reduction interventions conducted within drug abuse treatment programs. The intensity of intervention in the 18 studies ranged from one-hour interventions, similar to those provided in CTN CTPs, up to 24 total hours. However, only one study provided more than 9 contact hours of intervention. More intensive interventions often included a focus on skill building. Role-plays and peer group discussions were included along with lecture and video presentations. Distribution of bleach and condoms was also common. Prendergast et al. found that overall the interventions were effective and had a reliable effect size of 0.31. A few examples of the studies follow. St. Lawrence, Jefferson, Alleyne and Brashfield (1995) compared a six session informational package with a six session skill training package that included "hands on" practice of condom use, partner negotiation and communication skills with practice role-plays, problem solving and self management skills. Participants were adolescents in a residential drug treatment program. Adolescents in the skills training group exhibited increased knowledge about HIV/AIDS, more favorable attitudes toward condom use, more internal locus of control, increased self efficacy, increased recognition of HIV risks, and decreases in high risk sexual activity compared to adolescents in the informational group at post intervention follow up. Records of STIs post intervention corroborated self-reported sexual risk reductions. The St. Lawrence et al intervention was provided separately to young men and women. Schilling, el-Bassell, Schinke, Gordon and Nichols (1991) developed a five-session behavioral skills-building HIV prevention intervention especially for women in methadone treatment. The intervention contained basic information about HIV/AIDS, condom demonstration and practice, partner negotiation, assertiveness training, problem solving and communication skills. Role-plays were routinely used in the skills building sessions. Schilling et al. randomly assigned 91 women in methadone treatment to attend the women's skill building intervention or a one session HIV/AIDS education routinely provided to all clients in the clinic. At two weeks post intervention women in the skill building group reported that they initiated discussion of sexual issues with their partners more often, felt more comfortable talking with them about sex and reported using and carrying condoms more frequently than women in the educational group.

The NIMH Multisite HIV Prevention Trial Group (NMHPTG) conducted the Project Light (PL) HIV prevention intervention in 37 community based STD clinics or health services organizations in five metropolitan areas between 1994 and 1996. The PL study compared the effectiveness of a one-hour HIV education intervention to a seven session (90-120 minutes per session) experimental intervention. The interventions were provided separately to men and women. Assessments were conducted at baseline and at 3, 6, and 12 months following the completion of the intervention. Men in the experimental condition (n=684) had significantly decreased their frequency of unprotected anal and vaginal intercourse acts more than men in the control group (n=657) at each follow up time point compared to baseline (NMHPTG, 1998). The PL experimental intervention is manual driven (available at hivinsite.ucsf.edu/InSite.jsp?page=pr-02-07&doc=2098.461d) and is comprised of basic information about HIV/AIDS, HIV risk assessment, condom demonstration and practice,

partner negotiation, problem solving and communication skills.

2.0. Study Rationale

2.1. Justification for Gender Specific Interventions

Prendergast et al. (2001) found that the effect size of behavior change related to risk reduction interventions was positively correlated with a number of moderator variables. Of specific interest to the current protocol were positive correlations reported for intensity of the intervention, use of peer group discussion, and use of separate sex sessions. The St. Lawrence et al. (1995), the Schilling et al. (1991) and PL (NMHPTG, 1998) studies are good examples of the latter. The St. Lawrence et al. intervention was provided to males and females separately, but the content was not specifically differentially formulated for one sex. The Schilling et al. intervention was specifically developed for women with the content chosen appropriate to the needs of women. Although the PL-HPM materials were the same for men and women, the groups became gender focused because the participants brought into the role play, brainstorming and discussion activities material that was of more specific interest to each gender (Willo Peguegnat, NIMH, personal communication 10/7/2002).

The call to provide specialized programs for women substance abusers transcends the HIV prevention literature. See Straussner (1997) for a brief review of the calls for gender relevant treatment of substance abusers. The Institute for Behavioral Research at Texas Christian University developed a specialized psychoeducational workshop for women in substance abuse treatment programs entitled “Time Out! For Me “(TOMe) (Bartholomew, Chatham & Simpson, 1991). TOMe was developed under the auspices of the Improving Drug Abuse Treatment for AIDS Risk Reduction (DATAR) project (Simpson, 1993). TOMe consists of six weekly two-hour sessions. The module uses lectures, peer discussion/brainstorming, video and visual presentations, anatomically correct models for breast self examination and condom application, and role-plays. The primary purpose was to teach basic communication skills, improve health awareness and enhance self-esteem so that women would become more comfortable discussing sexual issues with their partners. TOMe has been evaluated in two treatment settings, methadone maintenance (Bartholomew, Rowan-Szal, Chatham & Simpson, 1994) and residential therapeutic community (Hiller, Rowan-Szal, Bartholomew & Simpson, 1996). Participants in the methadone clinic who attended most of the sessions demonstrated increased knowledge and self-esteem compared to clients attending less than 3 sessions. In the residential program, workshop participants demonstrated increased knowledge, assertiveness and communications skills, more positive attitudes towards being assertive and practicing safer sex, and increased self-esteem compared to a wait list control. The DATAR staff found the TOMe materials to be well received in the treatment programs in which they were conducting their research investigations. They quickly found themselves being requested to develop a gender specific module for men that would focus on communication skills, developing healthy relationships and sexual health. The DATAR staff developed the “Time Out! For Men” (TOMen) module (Bartholomew and Simpson, 1996). The module consists of eight two-hour sessions. The materials address communication skills, assertiveness, expressing feelings and conflict resolution. Men are provided a discussion/brainstorming forum for examining gender roles, socialization, stereotyping, and sexual myths. Bartholomew, Hiller, Knight, Nucatola and Simpson (2000) provided the TOMen module to 122 men court referred for residential treatment. Participants from one

dormitory (experimental) were provided the workshop immediately after the pre-intervention assessment, while participants from the other dormitory (control) attended the workshop after the post-intervention assessment during the aftercare phase of treatment. The experimental group increased its performance on the knowledge test whereas controls remained the same. The experimental group increased its scores more on measures of social conformity than did the controls. Men in the experimental group increased their endorsement of more egalitarian attitudes about gender roles and sexual beliefs. Post intervention interviews with participants supported the concept of men only groups. Most men felt they would not have discussed sexual issues in mixed gender groups. Also most men felt it was important for at least one of the therapists to be a man.

One of the most rigorous evaluations of an intensive HIV prevention intervention was conducted outside the drug abuse field by NMHPTG in PL (1998). Besides the significant decrease in frequency of unprotected vaginal and anal intercourse noted above, men in the experimental condition increased the proportion of condom use for these sexual acts, were more likely to be consistent condom users at follow up and reported fewer STD symptoms (based on chart review) than men in the control condition

The DATAR staff also developed an HIV/AIDS education module that utilizes the same style and format of the TOMe and TOMen modules (Bartholomew & Simpson, 1992). This four-session module focuses on general information about HIV/AIDS, safe needle use, safe sexual behaviors, “hands on” practice of bleaching, and condom application. Visual aides in the form of “informational maps” are heavily used. Peer group discussions cover topics such as: “Which Behaviors Are Risky” and “Developing a Risk Reduction Plan.” Assertive communication skills are taught with HIV risk focused role-play. Although this intervention has not been rigorously evaluated using an appropriate control group, Boatler, Knight & Simpson (1994) did demonstrate that clients attending 4 sessions early in methadone treatment (first 4 months) performed better on an HIV technical knowledge test than did clients attending fewer than 4 sessions.

A topic not covered in most HIV prevention interventions is the interplay between drug use and sexual behavior. Wells, Calsyn, Saxon and Greenberg (1993) found that 51% of men and 28% of women in treatment who participated in an AIDS prevention project reported that they had used drugs to enhance their sexual experience in the prior 5 years. In a subsequent methadone maintenance treatment outcome study, participants were asked at the 24-month follow-up the percentage of time they combined various sexual behaviors and drug use during the prior six months (Calsyn et al. 1996). Data were reported for heterosexually active males (n=106) and females (n=62) who had been monogamous for a minimum of two years. In this analysis we focused on the monogamous participants so as to eliminate the role drugs may have in meeting a new partner. Using illicit drugs shortly before or during vaginal intercourse more than 25% of the time was reported by 41.5% of the males and 40.3% of the females. Those combining sex and drug use reported more frequent use of heroin and cocaine. Even when individuals who reported very high frequency of drug use or no drug use were eliminated from the analyses, higher heroin use levels were reported by both males and females who combine sex and drug use. Females combining sex and drug use were more likely to identify sex as being more pleasurable under the influence of drugs. A similar association was not observed for males. Males and females who believe sex is more pleasurable under the influence of drugs reported higher levels of heroin use in the prior six months. More recently we developed a structured questionnaire to evaluate the interplay

between sexual behavior and drug use based on a series of elicitation interviews (Calsyn, Wells, Saxon & Jackson, 1999). Eighteen male and 13 female IDU in methadone maintenance for over 12 months were administered the newly developed structured interview (Calsyn, Wells, Saxon, Jackson & Heiman, 2000). For 14 (77.8%) men and 10 (76.9%) women their most recent sexual experience included substance use by them or their partner. Only 8 (44.4%) men and 3 (23.1%) women indicated they had had at least one sexual experience in the past year without being under the influence of drugs. Three (16.7%) men and 2 (15.4%) women indicated that the combining of sex and drugs during their most recent sexual experience represented a relapse to drug use. Participants rated the most recent sexual experiences with and without drugs on a 0-10 pleasurable/ satisfaction scale. Three (60%) of the five men who had sexual experiences in the past year both under and not under the influence of drugs rated the experience under the influence of drugs as more pleasurable. In the prior six months 5 men (27.8%) and 4 (30.8%) women said they were tempted to use drugs either to enhance sexual experiences or increase the likelihood that a sexual encounter would happen. These findings suggest that even for opiate addicts maintained on methadone for over a year, sex and drug use are often still intertwined. It appears that for some this interconnection may contribute to relapses and urges to use drugs. Thus, for the treatment provider this is not just an HIV prevention issue, it is also a relapse prevention issue in need of attention.

Another topic, which has not received much attention in HIV prevention or drug abuse treatment arenas, is the problem of sexual dysfunction. Nowhere is this problem more evident than in orgasmic dysfunction in methadone maintenance clients. We found that 47% of the men on methadone in the structured interview development studies noted above report difficulty achieving orgasm (Calsyn, Wells, Saxon, Heiman and Jackson, 2001). In HIV prevention programs these men are then asked to use condoms, which will further make achieving orgasm difficult.

2.2. Rationale for Components Included in the Intervention Package

The development of the intervention package to be used in this protocol, “Real Men are Safe” (REMAS), was guided by the findings noted in the background and rationale sections above. The intervention is more intensive than is normally provided in CTN CTPs (5 sessions vs. 1 session). The intervention is delivered by male therapists to groups of all male clients. In addition to lecture material, there is liberal use of role-plays and peer group discussions. There is nearly an equal focus on information giving and skills building. Sessions 1, 2, 4 and 5 are all adapted from the PL, TOMen, and HIV-ED materials. An outline for the intervention is provided in Table 2 . Two sessions per week are provided in the first two weeks. The fifth session is delivered at the beginning of week 3. Post intervention assessment happens immediately following session 5. The two DATAR manuals provide a total of 12 sessions, while PL was seven sessions. The following principles were used for selecting material. All homework and review of homework were dropped. All duplication was dropped. Activities that focused on strengthening a current intimate relationship were dropped (e.g. conflict resolution and sharing feelings). Demonstration of cleaning injection equipment with bleach was dropped. Focus on sexual health was dropped. More technical aspects of HIV disease and focus on current HIV treatments were dropped. In addition a session targeting the interplay between drug use and sexual behavior (#3) was added for this protocol.

3.0 OBJECTIVES

3.1 Primary Objective and Hypothesis

The primary objective is to compare the effectiveness of an intensive, 5-session, gender-specific group HIV/AIDS intervention for men, REMAS, to a standard single session HIV/AIDS education group. It is hypothesized that men provided REMAS will engage in fewer risky sexual behaviors as measured by the primary outcome measure of the number of unprotected vaginal and anal intercourse acts during the 90 days prior to the 3 and 6 month follow up assessments than will men provided the standard intervention. The time frame over which to measure risk behavior has varied from a few weeks to one year in studies examining sexual risk behavior. A shorter, more recent time frame should increase the reliability of the self report. A longer time frame provides greater opportunity for risk behavior to occur. This latter issue is especially important in populations such as drug abusers where frequency of sexual behavior varies greatly across and within individuals. The choice of a 90 day time frame provides a balance between these two issues. In addition 90 days was the time frame used in Project Light from which much of the intervention material is derived. It is also hypothesized that being non-monogamous in the prior six months and years of stimulant use will be associated with the frequency of unprotected vaginal and anal intercourse and intervention condition. Specifically, the intervention will be more effective with stimulant users and those with multiple sexual partners. These two variables will be entered into the data analytic model described more fully in section 11.2.

3.2 Secondary Objectives

We will also compare the effectiveness of an intensive gender specific HIV/AIDS intervention for men to a standard HIV/AIDS education on several secondary measures of interest. These variables are of interest as they may be precursors to reducing involvement in sexual risk behavior. It is hypothesized that men provided the gender specific intervention will at follow up assessments be more likely to have engaged in “outer course” (sexual activity to the point of orgasm that does not include penetration of body cavities or exchange of body fluids), have fewer sexual partners, be more likely to possess condoms, be more likely to have taken condoms from clinic supplies, express a more positive attitude toward condom use, report less frequent use of drugs in combination with sexual events, and endorse more egalitarian gender role beliefs than will men in the control group.

4.0 STUDY DESIGN

The proposed study will use a randomized clinical trial to assess the relative efficacy of a five-session gender specific intervention, REMAS, as compared to a single HIV/AIDS education session, for current male patients in MMTP or in ODF. Participants will be a minimum of 560 men in MMTP (N = 280) or ODF (N=280) who have engaged in unprotected vaginal or anal intercourse within the past 6 months. Inclusion of men from both MMTP and ODF will ensure heterogeneity among participants in terms of treatment modalities and drugs of abuse. We do not hypothesize there will be a differential impact of the intervention related to treatment modality as Broome et al., 1998 found comparable effects on reducing sexual risk in MMTP and ODF. The schema for the study design is presented in Figure 1. Male clients in

treatment will be invited to complete the screening interview for the study. Individuals meeting the study inclusion criteria, and agreeing to participate will provide written informed consent and be administered the baseline assessment battery. After completing the baseline assessment participants admitted to the study will be placed into an open cohort of participants waiting for randomization. The cohort will close once there are 8 men in the cohort or four weeks has passed since the first subject was placed in the cohort. If less than 3 men are in a cohort after four weeks have passed, the cohort will remain open until a third participant has been found. Once closed the cohort will be randomly assigned to attend either the five-session REMAS intervention or the one session standard educational intervention. Participants who drop out of the study prior to notification of randomization will be replaced since it is assumed dropping out is not related to randomization outcome. The use of a single one-hour HIV/AIDS education session as a comparison is intended to serve as a standard-of-care condition reflecting the current day-to-day practice of most CTPs as captured in the CTN snapshot described in section 1.1.1. The proposed design does not control for possible attention effects that might be present because the gender specific group receives more attention (five vs one session) than the standard HIV/AIDS education group. The protocol development team did consider adding non-HIV related treatment time to the control group, but rejected that concept in favor of the proposed design because it more closely approximates what currently happens in CTPs. A repeated measures battery will be administered at four points: 1) baseline; 2) immediately post intervention; 3) at approximately three months post-skills building intervention, and 4) at approximately six months post-skills building intervention. Follow up data will be deemed to be collected on time if they are collected within fourteen days prior to or thirty days after the scheduled date for 3-month and 6-month follow-ups and within fourteen days after scheduled date for the immediate post-intervention assessment. The primary outcome measure will be the frequency of unprotected vaginal and anal intercourse in the prior 90 days. Secondary outcome measures include; 1) number of sexual partners; 2) frequency of “outer-course;” 3) attitude towards condoms, 4) possessing condoms, 5) having taken condoms from clinic supplies, 6) frequency of combining of sexual behavior with drug use, and 7) beliefs regarding gender roles.

5.0 STUDY POPULATION

5.1 Number of Sites and Subjects

Approximately 560 men being treated in either methadone maintenance or outpatient drug free treatment will be enrolled into the study (approximately 280 from each modality). Entry into the study is open to adult men of all racial and ethnic groups. Each of the participating CTPs will enroll approximately 40-48 patients. Each clinic’s Institutional Review Board will approve recruitment and informed consent procedure. Methadone maintenance clinics will recruit participants who have been enrolled in the clinic for at least 30 days. This will allow time for potential participants to have achieved a stable dose of methadone. For outpatient drug free treatment clinics, efforts should be made to recruit participants immediately upon enrollment in the clinic. This recruitment method will ideally decrease the probability of early drop-out at both types of clinics.

The study will be carried out at a maximum of 7 MMTPs and 7 ODFs, which can each provide approximately 40 men who meet criteria for the study, within a recruitment period of approximately 6-12 months. Final site selection will not occur until the protocol has been

certified and will be in accordance with the CTN CTP selection process for protocol involvement. In selecting CTPs there will be a concerted effort to select clinics that will provide a diverse subject population in terms of ethnic backgrounds, regions of the country and primary drug of abuse. Participants will be recruited through a number of vehicles, as appropriate at each site. Recruitment may include posters and fliers conspicuously placed in CTP waiting rooms, announcements about the study to clinic patients, and directly through a participant's individual counselor.

5.2 Duration of Study and Visit Schedule

Once the protocol has been certified in accordance with the CTN protocol development process, it is anticipated it will take approximately 3-6 months to enroll sites and prepare them for subject recruitment. Participants will be recruited over a 6-12 month period, approximately. It will take approximately 9 months after final subject enrollment to complete the follow up assessment. Data analyses and dissemination of findings will be completed over the following year. Based on this timetable it will take approximately 33 months to complete the study.

The visit schedule is presented in "Figure 2: Study Flow Chart" on page 8.

5.3. Informed Consent

At both screening and entry into the main intervention trial, study staff will obtain written informed consent for study participation. The staff member and the patient will discuss the basic features described in the informed consent form. These include: voluntary nature of participation and freedom to withdraw without consequences to clinic services received, purpose, procedures, randomization, confidentiality, risks, and benefits. It also notifies the participant that all study interviews and treatment sessions will be audiotaped for supervisory and quality assurance purposes. A copy of the proposed consent forms are provided in the appendix.

5.4. Inclusion Criteria

1. Adult males 18 years of age and older in drug abuse treatment at a participating CTP who self report engaging in unprotected vaginal or anal intercourse during the past 6 months. A decision was made by the protocol development committee to not include engaging in unprotected oral sex as an inclusion criteria, because recently published studies indicate it is now considered a low risk behavior for HIV transmission (Page-Shafer, Osmond, Ball et al., 2002; del Romero, Marincovich, Castilla, et al. 2002).
2. Agreeable to being randomly assigned to attend either a one-session standard HIV education session or to the five session REMAS workshop as their HIV education.
3. Agreeable to completing 2-3 hour assessment battery at baseline, 90 minute assessments at three and six months post intervention, and a shorter battery upon completing the intervention.
4. Be able to speak and understand English.

5.5. Exclusion Criteria

1. Observable, gross mental status impairment – including severe distractibility, incoherence or retardation as measured by the Mini Mental Status Exam (a score less than 25).
2. Having a primary sexual partner who is planning on attempting to get pregnant while the participant would be involved in the trial. This is necessary because attempting to become pregnant is incongruent with the primary outcome measure.
3. Current treatment episode of methadone maintenance is less than 30 days.

5.6. Subject Discontinuation Criteria

Participants are free to withdraw at anytime from the study without cause and without penalty from the CTP at which they are receiving their drug abuse treatment. In addition, participants may be withdrawn if it is deemed further participation is harmful to them

Although we anticipate it will be a rare event, a potential problem would arise if a participant drops out of substance abuse treatment (or is discharged from treatment), but wishes to continue attending the protocol intervention to which he is assigned. Since the intent of the study is to evaluate the interventions conducted within treatment programs these individuals will not be allowed to attend intervention sessions, but will be followed to complete follow up assessments. In addition these individuals will be referred to community resources for HIV prevention information if so desired.

5.6.1 Consideration of Early Termination

The Lead Investigators, the CTP Lead Investigator and clinical care providers of the CTP staff may decide to discontinue a subject's participation if it poses a significant risk to his well being. The possibility of partner dissatisfaction with the participant's involvement in the protocol and consequent disruption of the relationship is the only foreseen consequence.

5.6.2. Procedures for Discontinuation

Participants wishing to discontinue participation voluntarily need only to inform the study staff of their wishes and they will be discontinued. If a subject wishes to withdraw from the study, we will ask if he would be willing to participate in the follow-up assessments to prevent missing data where possible.

For participants whom the clinical or research staff feel further participation in the study is detrimental to them, the node project coordinator or designee for the study will meet with the subject in person or over the phone and discuss the pros and cons of his continuation. If the subject chooses to remain in the study, but the project coordinator feels attendance at the groups is detrimental to the subject, the subject will be withdrawn from the groups, but will be allowed to complete follow up assessments. The project coordinator or a clinical staff person identified by the project coordinator will offer up to three debriefing sessions to discuss the discontinuation. Although the investigators recognize the possibility that a subject may need to be discontinued because the intervention is detrimental to him, we judge this to be a very rare event if it happens at all.

5.7 Replacement of Subjects

Participants who discontinue after randomization will not be replaced and will be included in all statistical analyses according to the intent to treat (ITT) design.

6.0 STUDY TREATMENTS

6.1 Study Therapies

There are two intervention conditions in the proposed study: 1) a five-session HIV prevention, communication skills and sexuality workshop, Real Men Are Safe (REMAS); and 2) a single session standard-of-care HIV/AIDS education, serving as a comparison condition. Male CTP drug treatment counselors who receive approximately 20 hours of training will conduct both interventions. Bartholomew et al., (2000), provided 20 hours of training to staff delivering the TOMen program to patients in drug abuse treatment, and this was considered an adequate dose of training. Both interventions are manual-driven. These two features will make ongoing technology transfer to the CTPs highly likely. Both conditions will consist of groups of 3-8 men. Groups will be run by coleaders who will share responsibility for delivery of the treatment (except when only one counselor is available).

6.1.1. HIV/AIDS Education:

For this protocol session selected educational material from sessions # 1 & 2 of the REMAS workshop will serve as the standard-of-care HIV/AIDS education (See Table 1). This intervention will consist of one approximately 60-minute group session. Using flipchart visual materials, and informational and resource handout materials, the counselor will conduct an approximately 60 minute session covering: HIV/AIDS definitions, transmission, testing and counseling, treatment, and prevention. Certificates will be distributed at the end of the session. Participants will be paid for their attendance to the treatment groups. Reasonable and non-coercive reimbursement sums will be determined on a site-by-site basis. Men will be paid in cash or vouchers (individual participating CTPs will decide if cash or vouchers are to be used) for attending the standard-of-care HIV/AIDS education intervention. It is recommended that participants are paid only if they attend the majority of the session (40 minutes), although the decision to do this may vary based on local IRBs. Paying participants to attend treatment sessions calls into question the issue of sustainability. In the ”real world” patients are not paid to attend sessions. Since the current protocol is research, patient participation is completely voluntary. It is the investigators’ experience that it is difficult to get a wide representation of patients at voluntary sessions without monetary incentives. If the intervention proves effective then CTPs could make the interventions a mandated part of treatment thus making incentives unnecessary.

6.1.2. Communication Skills and Sexuality Workshop (REMAS)

The intervention is a five session, approximately 90-minutes/session workshop delivered by male therapists to groups of all male clients. In addition to lecture material, there is liberal use of role-plays and peer group discussions. There is nearly an equal focus on information giving and skills building. Sessions 1, 2, 4 and 5 are all adapted from the PL, TOMen, and HIV-ED materials. Some of the PL materials were revised to be more relevant to an in-treatment population. Session 3 was developed based on research indicating the combining

of sexual behavior and drug use is common among drug abusers and is associated with high risk HIV transmission behaviors and drug use relapse (Calsyn et, al, 1995; Calsyn et al, 1999; Calsyn et al 2000). An outline for the intervention is provided in Table 2. Participants will be paid for their attendance to the treatment groups in cash or vouchers. Reasonable and non-coercive reimbursement sums will be determined on a site-by-site basis. It is recommended that participants are paid only if they attend the majority of the session (60 minutes), although the decision to do this may vary based on local IRBs. In an further effort to minimize attrition, the group interventionists or site coordinators will telephone all participants who miss a group and encourage them to attend the next group. In addition they will troubleshoot with the participant to help overcome any barriers to attendance.

Table 1. Standard of care HIV/AIDS education: Intervention outline

Session activities for the Standard of care HIV/AIDS education borrows from the manual Approaches to HIV/AIDS Education Drug Treatment (HIV-ED) and from the Project Light (PL) manual. Pages from these manuals are identified when the activity originates from one of them. Times provided in the table are estimates of the length of time to complete each section.

HIV/AIDS Update: Identifying Risks

I. Group Introductions. Goals and Guidelines 5 Minutes
II. HIV/AIDS Update 10 minutes
- A. HIV-ED pp. 9-16
- B. Introduce HIV Info MAP, AIDS info MAP, HIV Timeline MAP, Body Fluids MAP

III. HIV Risky Behaviors, injection practices 5 minutes
- A. HIV-ED pp. 40-43
- B. Safe injection practices, stress use of new equipment each time over bleach. Do not practice cleaning

IV. HIV Risky Behaviors, sexual practices 10 minutes
- A. HIV ED pp. 33-37, PL Mod 4-X, p. 18

V. Condom demonstration 10 minutes
- A. HIV ED pp. 42-50.

VI. Barriers to Condom Use 10 minutes
VII. Healthy options 10 minutes
- A. HIV-ED pp. 37-39

Table 2. A Communication and Sexuality Workshop: Real Men Are Safe (REMAS): Intervention outline

Session activities borrow heavily from TCU-IBR DATAR manuals Time Out for Men (TOMen) and Approaches to HIV/AIDS Education Drug Treatment (HIV-ED), and from the Project Light (PL) manuals. Pages from these manuals are identified when the activity originates from one of them.

Session 1: HIV/AIDS Update: Identifying Risks

I. Group Introductions. Goals and Guidelines 10 Minutes
- A. TOMen pp. 6-7
- B. Use pre-group handouts to shorten time, revise purpose to include HIV prevention, interplay between sexual behavior and drug use

II. Getting Started 10 Minutes
- A. TOMen pp. 3-6
- B. Revise purpose to include HIV prevention, interplay between sexual behavior and drug use
- C. minimize focus on intimacy

III. HIV Risky Behaviors Exercise, 15 minutes
- A. HIV-ED pp. 33-37, 43-50
  Add personal assessment activity
  Safety of behaviors, use PL terminology

IV. HIV/AIDS Update 15 minutes
- A. HIV-ED pp. 9-16
- B. Introduce HIV Info MAP, AIDS info MAP, HIV Timeline MAP, Body Fluids MAP

V. HIV Risky Behaviors, injection practices 5 minutes
- A. HIV-ED pp. 40-43
- B. Safe injection practices, stress use of new equipment each time over bleach. Do not practice cleaning

VI. HIV Risky Behaviors, sexual practices 15 minutes
- A. HIV ED pp. 33-37, PL Mod 4-X, p. 18

VII. Condom demonstration 10 minutes
- A. HIV ED pp. 42-50.

VIII. Revisit Risky Behaviors Exercise 10 minutes

Session 2: HIV/AIDS Update: Planning Prevention

I. Welcome, redo introductions 5 minutes
II. Healthy options 15 minutes
- A. HIV-ED pp. 37-39

III. Barriers to Condom Use 10 minutes
IV. Condom Practice 15 minutes
- PL, MOD.4-III, p13-17

V. Personalizing commitment to sexual safety 15 minutes
V. Identifying Triggers 25 minutes
- PL, Mod. 2-III, p. 6-8
- PL, Mod. 3-III, p. 8

VI. Risk Reduction Problem Solving 20 minutes
- PL, Mod. 3-IV, p. 9-10

Session 3: Sex without drugs. Can it happen? Is it Pleasurable?

I. Welcome, redo introductions 5 minutes
II. Experience with combining sex & drugs 40 minutes
- Enhancements
- Impairments

III. Enhancing sex without drugs 25minutes
IV. Coping with sexual impairment without drugs 20 minutes

Session 4: Beyond the pick up line, communicating about sex

I. Welcome, redo introductions 5 minutes
II. Challenging Stereotypes 30 Minutes
- TOMen pp. 7-9

III. Unwritten rules 10 minutes
- PL, Mod. 5-III, p. 7-8.

IV. Responsibility in sexual relationships 15 minutes
- A. TOMen pp. 129-131
- B. HIV-ED pp. 70-72

V. Communicating about Safe Sex I 30 minutes
- A. Assertive TALK, PL Mod 5-IV, pp. 8-11
- B. TALK Tools, PL Mod 5-IV, pp. 11-14

Session 5: Communicating about Safe Sex II

I. Welcome, redo introductions	5 minutes
II. Practice TALK PL, Mod 5-IV (D-E), pp. 15-20	25 minutes
III. Turning Around Partner Objections PL, Mod. 6-II, pp. 7-10	25 minutes
IV. Creative Negotiation PL, Mod. 6-II, pp. 11-17	25 minutes
VI. Closing/Wrap-up	10 minutes

6.2 Selection and Training of Therapists

Therapists will be recruited initially from the counseling staff of the CTP sites. Priority will be given to those with group therapy and HIV prevention education experience. Two therapists will be trained for each site. Should there not be two counselors available or interested in conducting the interventions, the node project coordinator for the study will recruit and hire potential therapists from the community at large. Study counselors will receive approximately 20 hours of training in providing the interventions. The interventions are manual driven. The intervention expert and author of the TOMen and HIV-ED interventions, Norma Bartholomew, and the lead investigator will conduct training. In addition, Jennifer Potter, a trainer from PL and member of the Northern New England Node, has joined the Protocol Development team and will consult with the training team.

6.3 Administration of Study Therapies

The control condition intervention will be delivered in a single session of approximately 60 minutes (see table 1). The experimental intervention, REMAS will be delivered in five group sessions of approximately 90 minutes each spread out over three consecutive weeks. The intervention will be manual driven (see table 2).

6.3.1. Randomization

As stated in section 4.0, upon completing the baseline assessment participants admitted to the study will be placed into an open cohort of participants waiting for randomization. The cohort will close once there are 8 men in the cohort or four weeks has passed since the first subject was placed in the cohort, which ever comes first. Groups should contain a minimum of 3 participants. If fewer than 3 are recruited during the four weeks, the cohort will remain open until a third participant is recruited. Once closed the cohort will be randomly assigned to attend either the REMAS intervention or the one session standard educational intervention. Separate block randomization schedules will be developed for each CTP with the assumption that 6 cohorts will eventually be randomized. Thus if recruitment is brisk a CTP may end up overshooting their target of 40 participants and actually recruit up to 48 participants. If a CTP has not recruited 40 subjects after six cohorts have been randomized the following procedures will be implemented. If there are less than 29 participants recruited (thus groups are averaging less than 5 participants each) a new block randomization schedule for four cohorts independent from the block randomization for the initial six cohorts will be prepared.

Assuming recruitment rates do not change dramatically the CTP should end up recruiting between 40-48 participants. If between 29-35 participants have been recruited a new block randomization schedule for two cohorts independent from the block randomization for the initial six cohorts will be prepared. If 35 or more participants have been recruited the CTP will recruit one additional cohort which will be randomly assigned to one of the conditions independent of previous cohort assignments in that CTP. The above randomization scheme was chosen over randomizing individuals so that the time participants would need to wait before being provided the intervention would be a maximum of 4 weeks after baseline assessment. With randomizing individuals an extended period of time might pass before enough participants to conduct the intervention had been randomized to one of the conditions.

Randomization will be managed through an outside independent randomization service provided by the Perry Point Cooperative Studies Coordinating Center (PPCSPCC). The PPCSPCC has designed and developed a centralized, automated telephone system to randomize subjects into clinical trials. Study sites access the system using a pre-specified phone number and respond to a series of prompts regarding the subjects' eligibility. After the system verifies subject eligibility, it assigns each subject a treatment assignment. Randomizations can be done 24 hours a day, 7 days a week. Following each randomization, a fax notification is automatically sent to the site and others as needed. The system has also been programmed to send summary reports on a weekly basis.

This methodology does allow for the intervention groups to become slightly unbalanced during the trial within a CTP. With this methodology the group assignments may become predictable toward the end of recruitment to individuals familiar with the randomization scheme. This predictability could threaten the integrity of the randomization if potential participants could manipulate which condition they ended up in by when they enrolled in the study. We will minimize this potential problem by not informing participants of the total number being recruited, thus they will not know when recruiting is near its end when group assignment might be predictable if they knew the number of participants already recruited and to which conditions previous cohorts had been assigned. Another concern with predictability of assignment is with the research assistants as they are conducting initial baseline assessments. The research assistants will be instructed to not speculate/predict with the participants which condition a participant is likely to be assigned to prevent participant bias. In addition the research assistants will be kept blind to the blocked nature of the randomization. Thus from their perspective each cohort's randomization should be independent from previous condition assignments. Since the primary outcome measure is going to be obtained by the ACASI method, it is unlikely any bias the research assistant might have related to predictability of condition assignment would affect the collection of this crucial data.

6.3.2. Blinding

Due to the nature of the study it will be impossible to blind either participants or therapists to study condition. We will make every effort to keep research assistants (RA) completing the follow up assessments blinded to study condition. The RA will instruct participants at the start of follow up assessments they are not to know which groups the client attended and will

request they not divulge it during the assessment. In addition the counselor or site coordinator will complete the study assignment line on any AE/SAE form the RA is required to complete.

6.3.3. Quality Control of Therapies Administered

Since therapists will be trained to deliver both interventions there is a concern of contamination of the HIV Education control condition with material from the REMAS intervention. In addition there is the possibility REMAS material might be delivered to HIV Education participants by the therapists in individual counseling or other group therapy sessions. Finally REMAS participants may deliver the material indirectly to HIV Education participants in their contacts that are beyond the control of the investigators. Five procedures will be in place to maintain quality control of the therapies. 1) The design of the HIV Education session leaves little room to add additional information, and there is no time for role plays and brainstorming that characterizes the REMAS condition. 2) Both interventions will be manual driven, and the therapists will receive approximately 20 hours of training in conducting the interventions. 3) Therapists will complete an intervention checklist at the end of each session where they indicate whether each topic and activity for the session was covered. 4) All intervention sessions will be audio taped. 5) Participants will complete a fidelity questionnaire at each follow up assessment to determine if they have been exposed to elements of both the intervention to which they were assigned and not assigned.

One option the protocol development team considered to lessen the potential of contamination was to have separate therapists for each intervention condition. This option was rejected because it may introduce a larger problem of interventionists' effects. Najavits, Crits-Christoph and Dierberger (2000) provide an excellent review of this literature. The following quote highlights the potency of therapists' effects. "Ironically, however, clinicians typically account for *more* variance in patient outcomes than do differences between active treatments or patient baseline characteristics, a result which holds both in the substance abuse disorder field and psychotherapy research in general." In addition smaller CTPs may have difficulty identifying enough interventionists to be trained. Separate interventionists would not prevent the other types of contamination mentioned above, and the planned fidelity checks would still need to be implemented.

7.0 CONCOMITANT THERAPY

7.1 General Considerations

During part or all of the time participants are participating in the trial they will be engaged in their substance abuse treatment. As part of their treatment, there may be discussions about HIV risk behaviors that come up in groups or individual sessions. It would be unfeasible to prevent these from happening during the trial. Participants will be asked about exposure to such events on the fidelity measure. Also during the trial participants may have contact with other HIV prevention interventions such as media campaigns and street outreach efforts. Again it would be unfeasible and unethical to try and prevent these from happening during the trial, and we will be asking about these possibilities on the fidelity measure.

7.2 Therapies Prohibited During the Trial

No concomitant therapies are prohibited during the trial. Therapists providing the communication skills and sexuality workshop will be instructed not to bring the interventions unique to the workshop into individual sessions during the trial. Participants will be asked about such exposures on the fidelity measure.

8.0. MEASUREMENTS, EVALUATIONS, AND ANALYTICAL METHODS

Assessments are conducted at five time points: 1) screening for study enrollment, 2) baseline assessment, 3) post intervention assessment, 4) three month follow up, 5) six month follow up. Measurement tools are described in the section that follows. In Table 3, at the end of the section, the schedule for instrument administration is provided. The post intervention assessment is limited to the measures where it is hypothesized the intervention may have an immediate measurable effect. Participants will be informed and assured that data collected from research assessments will not be shared with treatment staff. Prior research has indicated substance abusers are more likely to self disclose substance use behaviors when there are not legal or clinical contingencies tied to their self report.

A major consideration in planning treatment outcome research involves formulation of an effective plan to ensure follow-up data are obtained. To encourage participation in follow-up, the length of each visit has been kept relatively short. Participants will be paid in cash or vouchers for completion of follow-up assessments. Reasonable and non-coercive reimbursement sums will be determined on a site-by-site basis. It is anticipated that follow up rates for participants while they are still in treatment will be extremely high. Participants who have left the area will be interviewed by phone. A paper/pencil version of the Sexual Behavior Inventory (usually administered via ACASI) will be created so that we can collect data on participants who have left the area or are otherwise unable to be interviewed in person. All participants will complete a locator sheet that identifies stable individuals who are likely to know of the participants' whereabouts in the future. In a previous treatment outcome study conducted in a methadone clinic by the lead investigator the six month follow up completion rate was 91% using similar methods (Calsyn et al. 1994). To obtain a follow up estimate for the ODF sample we turned to the NIDA Collaborative Cocaine Treatment Study where 85.2% of participants completed the 5 or 6 month follow up.

8.1 Informed Consent

Sample consent forms for obtaining written informed consent are provided in the appendix. Consent procedures are described in section 5.3.

8.2 Inclusion/Exclusion Criteria Review

8.2.1. Screening Assessment

Several assessment instruments from the Common Assessment Battery will be used in the screening phase of this protocol. Participants will be paid in cash or vouchers for completion of the screening assessment. Reasonable and non-coercive reimbursement sums will be determined on a site-by-site basis..The screening assessment will not be audiotaped.

CTN Demographic Form. Age, gender, ethnicity, and drug use history are collected.

Mini-Mental Status Exam (MMSE). The MMSE (Folstein, Folstein & McHugh, 1975; Cockrell & Folstein, 1988) will be used to identify potential participants who are too cognitively impaired to engage in the study. Individuals with scores less than 25 will be excluded from study (Crum, Anthony, Bassett & Folstein, 1993). MMSE has the advantage of: 1) being widely used in research protocols for this purpose, 2) is relatively easy to administer and score; 3) is relatively short; 4) and has a very low ceiling so that only the most grossly cognitively impaired individuals will be excluded. This instrument will only be administered at the time of screening.

Risk Behavior Survey. The RBS is part of the common assessment battery. It is a brief interview assessing involvement in HIV risk behaviors of injection drug use and sexual behavior. Most of the questions assess involvement in risk behaviors for the prior 30 days. Sexual behavior questions will be repeated for the prior six months. If the client indicates no unprotected vaginal or anal sex in the prior six months he will be ineligible to participate in the study.

Basic Data and Locator Questionnaire. Locator information, including home address and phone number, will be collected and kept confidential in the participant's record. Data collected on this form will be used to contact the participant for assessment and follow-up and in emergencies. Participants will be asked to provide locator information including their residential street address and a working telephone number, or an address ofa relative if they are homeless, as well as the address and telephone number of a non-drug abusing relative or friend who can reach the participant in emergencies.

Participants excluded from the study during the screening assessment will not be informed of the reason for exclusion, so as to not bias screening assessments of other potential participants with whom they may come in contact. Excluded participants will be told there are several subject characteristics criteria that need to be met before a subject can be enrolled into the study. Unfortunately they did not meet one of these criteria. We do not inform excluded participants of the criterion that was not met so as to limit other potential participants from being able to misrepresent themselves if they did not meet similar criteria. With the exception of the RBS injection risk questions, the screening instruments will only be administered at the time of screening.

8.3 Baseline and Follow up Assessments

Participants will be paid in cash or vouchers for completion of the baseline and follow-up assessments. Reasonable and non-coercive reimbursement sums will be determined on a site-by-site basis..Participants will be tracked for follow up interviews. To the degree that it is feasible at a particular site, participants who become incarcerated during the course of the study period will also be tracked and contacted for follow-up interviews. The protocol specific assessments within the Baseline Assessment (not the Common Assessment Battery or ACASI administered SERBAS) will be audiotaped. The following CAB instruments and protocol specific instruments will be used as part of the baseline and follow up assessments.

8.3.1. Composite International Diagnostic Interview (CIDI)

The substance abuse subsections from the Composite International Diagnostic Interview, version 2.1 (CIDI-2.1) will be used to determine whether potential participants meet DSM-IV criteria for substance abuse or dependence. The results of this interview are recorded on the Substance Use Diagnosis CRF. This is administered at the baseline only.

8.3.2. Addiction Severity Index-Lite

The ASI is a standardized, multidimensional, semi-structured, comprehensive clinical interview that provides clinical information important for formulating treatment plans as well as problem severity profiles in six domains commonly affected in substance abusers. The domains covered are chemical abuse (alcohol and drug), medical, psychiatric, legal, family/social and employment/support. Composite Scores for each problem domain are derived mathematically. A revised version of the ASI Fifth Edition, 1997 version (ASI-Lite), that includes only those questions used to derive the composite scores along with some demographic information will be administered by a research staff member. The full ASI-Lite will be administered at the baseline assessment. At the 3 and 6 month assessment only the Drug and Alcohol section will be administered.

8.3.3. Drug use and drug injection risk behavior assessment

Drug use and injection practices Items from the Risk Behavior Survey (RBS) will be repeated if the interval between screening and baseline assessment is longer than 30 days. The RBS drug use and injection practice items will be repeated at the 3 and 6 month follow-up visits.

In addition to the CAB measures listed above the following measures will be collected at the baseline and follow up assessments:

8.3.4. Sexual and sexual risk behavior assessment

Items were selected or adapted from the SADAR (Sex and Drug Abuse Relationship Interview; Calsyn et al 2000) and the SERBAS (Sexual Risk Behavior Assessment Schedule; Meyer-Bahlburg et al., 1991; Sohler et al., 2000). Behaviors include: 1) absolute frequency of vaginal intercourse and relative frequency of unprotected vaginal intercourse by (main versus casual) partner type; 2) number, gender, and HIV serostatus of partners; 3) relative frequency of drug (including alcohol) use with sex. The number of unprotected vaginal and anal intercourse acts, which serves as the primary outcome measure, will be derived from two items for the previous 90 days included in this instrument. This is the same primary outcome measure being used in CTN Protocol 0019 (Safe Sex for Women). The items from the SERBAS and the SADAR will be administered using the audio computer-assisted self-interviewing (ACASI) method. Metzger et al. (2000) and Gross et al. (2000) have shown respondents to be more self-disclosive regarding participation in high risk behaviors with ACASI compared to in person, face-to-face interviews. This method lessens the impact of possible social desirability distortions on the self reporting of involvement in risk behaviors.

At the post intervention assessment only the items related to the most recent sexual event will be asked since the time frame being covered is since the intervention started, and not the past 90 days as will be the case for baseline and the 3 and 6 month follow up assessments.

In addition to self report of risky sexual behavior, it would be possible, although difficult from a CTP feasibility standpoint, to obtain a biological marker of risky sex behavior such as evidence of a new sexually transmitted infection (STI). The protocol development team considered this methodology, but rejected it for the following reasons. In PL the self report of the frequency of unprotected vaginal and anal intercourse was consistent with STI rates in the sample and there was a significant difference in gonorrhea rates at follow up between men in the control and experimental intervention at $\underline{p}$=.03 (NMHPTG, 1998). The PL investigators were able to demonstrate this relationship because they powered the study to detect such finding by having a sample size three times as large as proposed in this protocol. In a subsequent analysis of PL data Pinkerton et al., (2002) demonstrated that the self-report of unprotected vaginal and anal sex was the best behavioral predictor of HIV infection. The six-month incidence rates of STI in this population are not high enough to be useful without a very large sample size, and they generate many false negatives. Most people engaging in risky behavior will not become infected during the six-month follow up period. Thus the data will only inform us about the few people who deny risky behavior, but then become infected. Although this information might be of some marginal use, it comes at too high a price. The most useful STI would probably be Chlamydia. However, in two studies with drug abusers the prevalence rates were only 6.8 and 3.7% (Lu-Yu Hwang et al. 2000; DeHovitz et al. 1994); incidence rates will be much lower. The feasibility difficulties arise because to get this information we would need to test everyone by collecting a UA sample (collection & testing costs). Participants would need to be given feedback on the results (counseling costs), and infected individuals would need to be treated and retested (treatment, additional collection and testing costs).

8.3.5. Condom use skill behavior assessment

Assessor ratings of a man's observed use of male and female condoms on male and female genital models will be made.

8.3.6. Condom Barriers Scale

The Condom Barriers Scale (St. Lawrence, Chapdelaine, Devieux et al., 1999) is a 29-item scale with demonstrated reliability and validity. Items are responded to on a 5 point Likert scale from strongly agree to strongly disagree. There are four scales derived from factor analysis; access/availability, partner barriers, effect on sexual experience, and motivational barriers.

8.3.7. Bem Sex Role Inventory

The Bem Sex Role Inventory-Short Form (BSRI; Bem, 1981) will be used to assess levels of adherence to masculine and feminine gender roles (sex roles) among participants. One focus of the intervention is to explore sex roles and sex role stereotyping. In addition

participants are encouraged to adopt an egalitarian approach to negotiating safe sex with their partners. The short form of the BSRI consists of 30 items, which are evaluated on a seven-point Likert scale according to how much the masculine, feminine, and neutral personality characteristics describe the subject. Mean scores ranging from one to seven for feminine, masculine, and neutral gender role orientation are obtained based upon the mean ratings for each category. In the interest of parsimony and reducing response burden, the ten items considered "filler" items, which do not load onto either the masculinity or the femininity scales were eliminated. These items were originally designed to be a measure of social desirability, but did not prove to be an adequate measure of such (Bem, 1981).

8.3.8 Biologic Measures

Urine and alcohol screens will be done at the Baseline assessment to substantiate self-report data. The urine drug screen will occur onsite and test for 10 illicit substances. A breathalyzer will be used to screen for blood alcohol concentration (BAC).

8.4. Adverse Event Evaluation

An adverse event is defined as any reaction, side effect, or untoward event that occurs during the course of the clinical trial. In this study, the only foreseeable intervention-related adverse events are an increase in psychological distress (defined as an increase in depression and/or anxiety symptoms) secondary to focusing on involvement in risk behaviors. Study staff will be trained to provide crisis intervention and referral for clinical emergency situations. The occurrence of AEs will be determined through the use of an AE Worksheet (consisting of one general AE question and a follow up question to gather more information) filled out by the RA at baseline, immediate post treatment, 3 and 6 month follow up assessments. All SAEs will be recorded, respectively, on the AE Case Report Form (CRF) and SAE Form and SAE Summary Report. All adverse events will be recorded on the Adverse Event Forms. See section 9.1.1 for a more through discussion of adverse events monitoring

8.5. Treatment Compliance

The intervention exposure checklist is designed to measure whether the participant has been exposed to the interventions provided in both the intensive gender specific workshop and the standard HIV/AIDS education group. The participant “checks” the interventions he has been exposed to during the assessment period. In addition the participant identifies the source of the exposure.

Table 3

Schedule of assessment collection

Assessment Measures	Screening Visit 0	Baseline Visit 1	Post Intervention Visit 2	3 month follow up Visit 3	6 month follow up Visit 4
Addiction Severity Index – Lite (CAB)		X			
Addiction Severity Index-Lite (drug/alcohol only)				X	X
Adverse Events		X	X	X	X
Alcohol Breathalyzer		X			
Bem Sex Role Inventory		X	X	X	X
CIDI		X			
Condom Barriers Scale		X	X	X	X
Condom use skills		X	X	X	X
Demographic	X				
Drug Use Screening (part 2 of Demographics questionnaire)	X				
Inclusion/Exclusion		X			
Injection Risk Assessment (from RBS)				X	X
Intervention Exposure Checklist			X	X	X
Mini-Mental Status Exam	X				
Randomization		X			
RBS (CAB)	X	X			
Sexual Behavior Inventory		X	Most recent sexual event only	X	X
Study Termination Treatment			X		
Study Termination Followup					X

Treatment Session Attendance			**X** (completed after each treatment session)		
Urine Drug Screen		**X**			

9.0 DATA AND SAFETY MONITORING PLAN

The DSMB convened by CCTN will provide independent oversight monitoring of the trial. SAEs from all the sites will be reviewed by this DSMB. A summary report from the DSMB safety review will be forwarded to the LI, who is responsible for distributing it to all other study investigators, who will in turn submit the summary report to their local IRBs.

THE CCTN DSMB will also periodically monitor the trial as it progresses. Trial performance will be monitored with regards to adequate recruitment and enrollment, integrity of the informed consent process, random assignment to treatment arms, as well as data integrity.

The data and safety monitoring plan consists of three broad components: safety, trial performance and efficacy. In this section we will attend to each of these domains and when appropriate will refer the reader to other sections of the protocol that address these issues in more detail.

9.1 Safety

9.1.1. Definition of Adverse and Serious Adverse Events

Adverse events will be categorized as serious or non-serious, as related or not related to the study, and as expected or unexpected. An adverse event is defined as any reaction, side effect, or untoward event that occurs during the course of the clinical trial. Stable chronic conditions, such as drug use, which are present prior to clinical trial entry and do not worsen, are not considered AEs. Common, minor ailments and complaints will be excluded from any type of documentation. These may include: colds, flu's, cuts, scrapes, coughs, headaches, stomach complaints, and general fatigue.

Serious adverse events (SAEs) are defined as any fatal event, any immediately life-threatening event, any permanent or substantially disabling event, any event that requires or prolongs inpatient hospitalization, congenital anomaly or birth defect, or any event requiring intervention to prevent any of the previously listed serious events. Hospital visits that do not result in admittance are not considered SAE's (e.g. emergency room visit for a non study-related injury that does not result in admittance). Normal childbirth and pre-planned elective procedures are not considered SAEs.

9.1.2. Assessment, Monitoring and Reporting of Adverse and Serious Adverse Events

AE/SAE's will be elicited by research assistants at each assessment visit by asking the participant if he has noticed any new problems or existing problems that have gotten worse

(using the Adverse Events Worksheet). Disclosure of an AE/SAE may also occur in an unsolicited manner to one of the therapists during the treatment. The RA should be focused on gathering data to aid the Study Clinician in determining study relatedness. Assessment of depression must include an assessment of suicidal ideation, as suicidal ideation may require immediate clinical assistance and qualify as an SAE. All clinically significant AEs will be captured on a standardized AE Log, with immediate assessment for whether or not the AE is serious, and whether or not the AE is study-related, in consultation with the site coordinator or Study Clinician (PhD, MD, PI). Study-relatedness will ultimately be determined by the Study Clinician following discussion with the staff member reporting the AE. AEs that are not serious or study related do not require any further paperwork documentation besides the AE Log. In this study, potential adverse events that may be related to the study would be an increase in emotional distress in relation to discussion of past or current HIV risk behaviors or as a result of relationship conflict (i.e. related to the implementation of safe sex practices).

In the case of clinical emergency, staff will be trained to refer participants in such situations to clinical staff in the CTP who will then follow the CTP's policy for managing their clients in crisis.

All study related AEs and SAEs will be followed until resolution. Monitoring and reporting of SAEs will be maintained by the: CTP staff members (e.g. research assistants, therapists, etc.); CTP Site Coordinator; Protocol PI; Study Project Manager; Lead Investigator; and NIDA Medical Monitor.

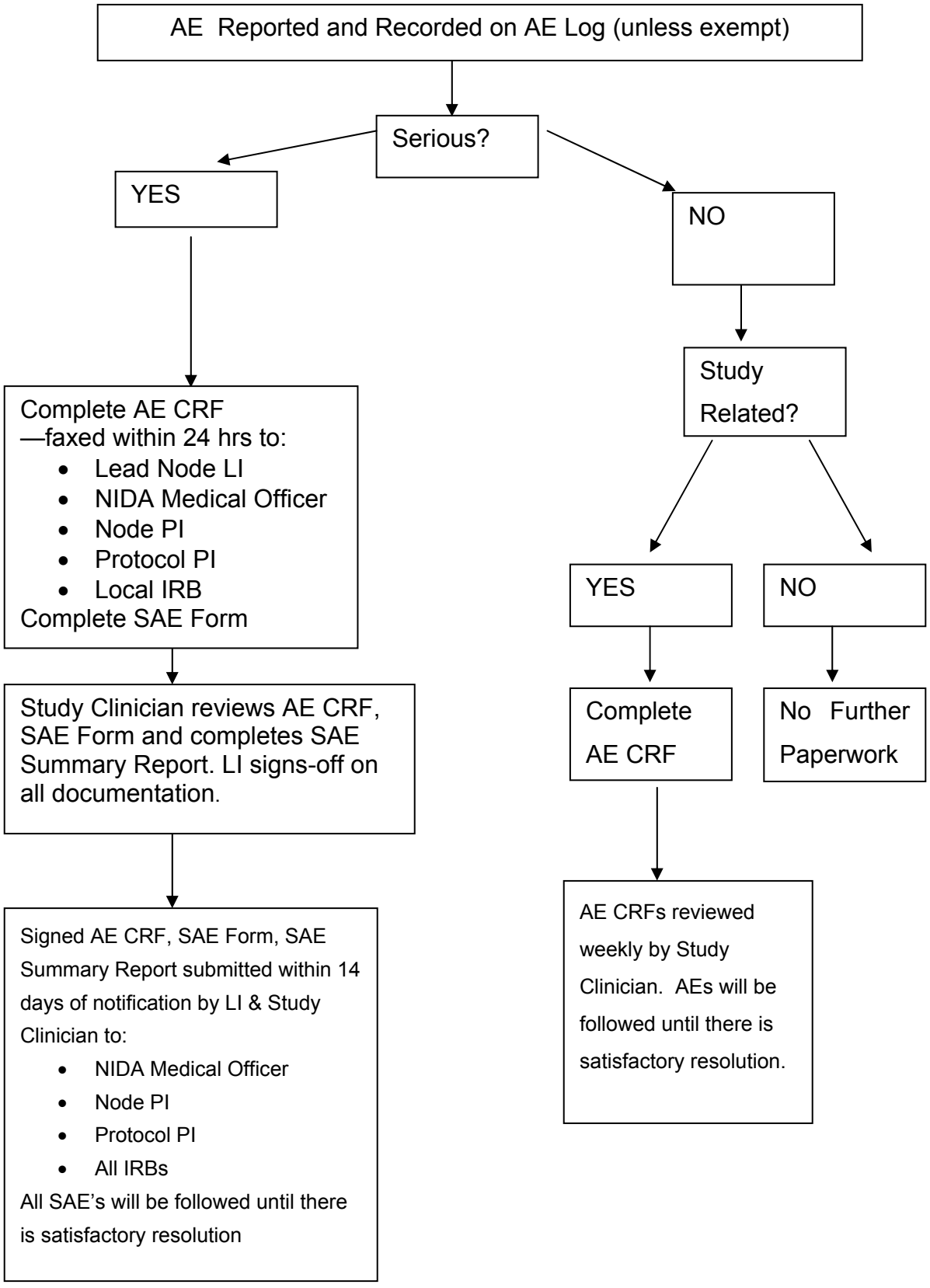
Only SAEs and related AEs will be recorded and entered into the study database (via the AE CRF). All SAEs will be recorded on the AE CRF, the SAE Form, and a summary narrative provided via the SAE Summary Report. The AE CRF is a form that will be used to document any adverse event that is thought to be serious or study related. The AE CRF is completed at each assessment point and on an as needed basis. If the adverse event is found to be serious, then a SAE Form and SAE Summary Report must be completed. The SAE Form should be completed by or in consultation with the Study Clinician. The SAE Summary Report contains demographic information and an event narrative and should be completed by the Study Clinician.

All SAEs must be reported by fax of the AE CRF, within 24 hours to the Lead Investigator, Protocol PI, Node PI, NIDA Medical Monitor, and to IRBs in accordance with their guidelines. The Study Clinician will be responsible for reviewing the AE CRF and SAE Form, querying the staff as needed, and completing an SAE Summary Report, to be co-signed by the Lead Investigator. Within 14 days the AE CRF and the SAE Form and the signed SAE Case Summary are forwarded to the NIDA Medical Monitor, Protocol PI, and Node PI. At the same time, reports will be submitted to all involved IRBs per reporting requirements.

All study staff – including research assistants, therapists, CTP Site Coordinator, Protocol PI, Lead Investigator, and Study Project Manager-will receive common training for AE and SAE detection, monitoring and reporting. Training will include: definition of AEs; definition and grading of SAEs; indications and procedures for completing the AE log; indications and procedures for completing AE CRFs; indications and procedures for completing SAE Forms and SAE Summary Reports; and procedures for reporting SAEs.

See Figure 3 for the AE/SAE reporting flow chart.

Figure 3: AE/SAE Reporting Flowchart



9.1.2 Human Subject Safety

Procedures for obtaining written informed consent from participants is provided in section 5.3. The study assessments and interventions consist of techniques that have been widely used in similar forms with comparable populations with minimal problems for the participants. Previous research experience suggests that participants generally perceive these discussions positively. There is, however, some risk that discussing sensitive topics, especially HIV risk behaviors, drug use, sexuality and intimate relationships, will cause distress in some participants. Men may become emotionally fatigued or stressed during the interviews. Yet these risks do not exceed those which are a normal part of any clinical interview or treatment session. The use of individual assessment procedures has not been shown to be either harmful or directly helpful to psychiatric/substance abusing patients. All clinical interviewers and research therapists will be trained to assess for level of distress and will be attentive to patient's needs. Appropriate breaks will be given, and if necessary, additional support at the end of the interview or session.

Participants who do become emotionally stressed will be encouraged to talk to their counselors and raters about their feelings. In the event that any subject is assessed to be in need of extra support, appropriate referrals will be given. At each site, there will be a well-established protocol for crisis intervention for acutely distressed patients. Participants may divulge engagement in HIV risk behaviors that do not generate emotional distress. Since each participant will soon be receiving an HIV prevention intervention as a component of study involvement no immediate intervention is planned unless the participant is continuously placing other identified or unidentified persons at risk for HIV infection. In such cases study staff will follow local reporting and or intervention required in the local community.

Prior to initiating the study, the Lead Investigator will obtain written IRB approval to conduct the study. Should changes to the study protocol become necessary, protocol amendments will be submitted in writing to the IRB by the Lead Investigator for IRB approval prior to implementation. The Washington Node Quality Assurance representatives and local IRB representatives will have access to facilities and records for review and verification of compliance with the IRB approved procedures.

For additional protection of confidentiality, the Washington Node will apply for a NIDA Certificate of Confidentiality once the protocol has received final approval.

All informed consent forms and inclusion/exclusion criteria will be reviewed for all protocol participants. In addition, all research records (case report forms, source documents, etc.) for participants experiencing serious adverse events will be reviewed. Per QAS policy, 100% of the research records for the first 10 participants and a random 10% of the remaining records will be reviewed. In addition, at each monitoring visit to a CTP, the randomization process will be reviewed to ensure that the randomization is occurring according to protocol procedures

9.2 Trial Performance

9.2.1. Treatment Intervention Integrity

There are two primary threats to the integrity of the interventions. First, the therapists may not deliver the interventions as intended. Important material may be left out or provided incorrectly. Two procedures will be employed to minimize this potential problem. Both interventions (HIV/AIDS Education and REMAS) will be manual driven, and the therapists will receive approximately 20 hours of training in conducting the interventions. All intervention sessions will be audio taped. The lead investigator, or the node investigator, or the node project coordinator for the protocol will review twenty percent of each therapist's tapes. Therapists will receive feedback on deviations from the manual. Section 6.3.3. provides additional details on maintaining treatment intervention integrity.

The second potential threat to intervention integrity is contamination between the interventions. Since the HIV/AIDS Education material is a subset of the REMAS intervention there is not a concern regarding HIV Education material contaminating the REMAS intervention. However there is a concern that HIV/AIDS Education participants may be exposed to REMAS intervention material in one of three ways. Since therapists will be trained to deliver both interventions there is a concern that the therapists will deliver REMAS unique materials when providing the HIV/AIDS Education intervention. Participants in the REMAS intervention group will share REMAS unique material to HIV/AIDS Education group participants. Finally HIV/AIDS Education participants may be provided REMAS unique material from sources the investigators will not be in a position to control. These include media, campaigns, street outreach workers and substance abuse counselors not associated with the study. Both of the procedures described above will help to lessen contamination problems (audio taping and supervision). Three additional procedures will be in place to maintain the integrity of the interventions. The design of the HIV/AIDS Education session leaves little room to add additional information, and there is no time for role plays and brainstorming that characterizes the REMAS condition. At the end of each session interventionists will complete a checklist of the topics and activities to be covered in the session. To further ensure integrity, however, study participants will be asked to complete an intervention fidelity questionnaire at post-intervention and at each follow up assessment to determine if they have been exposed to elements of both the intervention to which they were assigned and not assigned.

9.2.2. Data integrity

The Washington Node Data Management Center (DMC) will coordinate data management activities and be responsible for data integrity over-site. Please refer to sections 15.0 to 15.5 for more details of the data management plan. In addition the DMC will be responsible for ensuring the randomization procedures described in sections 6.3.1 and 4.0 are implemented and maintained correctly.

The CTN DSMB will review demographic characteristics of participants in each intervention condition to determine the efficacy of the randomization procedures. The CTN DSMB will review recruitment and retention data to determine the feasibility of the trial.

9.3 Trial Efficacy

Given the absence of strong evidence supporting the impact of this intervention within a drug abuse treatment setting, we will plan to conduct an interim analysis, primarily for utility. See section 11.9 starting on page 39 for details of the interim analysis plan.

10.0 DEPARTURES FROM PROTOCOL

All departures from protocol will be documented following appropriate CTN SOP forms, as well as Node-specific IRB reporting requirements.

11.0 STATISTICAL ANALYSIS

11.1 Objectives of Analysis

The proposed trial is intended to test the effectiveness of the REMAS intervention, as compared to that of a single HIV/AIDS education session, on the primary outcome, the number of unprotected vaginal and anal intercourse acts. Other secondary outcomes will include: frequency of "outer course," number of sexual partners, possessing condoms, taking (male and female) condoms from open clinic supplies, attitudes towards condoms, gender role beliefs, and frequency of using drugs with sex.

11.2 Primary Outcome and Statistical Hypotheses

There is one primary outcome measure, the number of unprotected vaginal and anal intercourse acts during the three month and six month follow up periods. This measure was used in Project Light (NIMH Multsite HIV Prevention Trial Group, 1998). The primary analyses will test the hypothesis that compared to single-session HIV/AIDS education participants, REMAS participants will significantly decrease their involvement in unprotected vaginal and anal intercourse from baseline assessment to follow up assessments. Intervention effects of secondary efficacy measures of interest will also be tested. We hypothesize that compared to the control group, the experimental group will have fewer sexual partners, engage in more "outer course," demonstrate an increase in frequency of possessing condoms, in the likelihood of taking condoms from clinic stocks, positive attitude toward condom use, and egalitarian sex role beliefs; and a decrease in the percentage of sexual events that include drug taking.

11.3 Sample Size and Statistical Power

The design of this study is a stratified cluster randomization trial (Donner & Klar, 2000). The randomization will be within strata (participating CTP site). A cluster is the cohort of 3-8 patients. Within each participating CTP site, cohorts of patients will be randomly assigned to the intervention or control conditions. Our sample size calculation is based on a comparison of outcomes between the intervention and control group measured at 6-month follow-up. This design has a two-level hierarchical structure, cohorts and CTP sites, resulting in two levels of correlation among subject's responses: correlation due to cohorts and correlation due to CTP sites. Since the planned analyses will be based on the method of generalized estimating equation (GEE), our sample size calculation will be based on the formula given by

Liu and Liang (1997). Since we do not have any information on the relative magnitude of the possible correlation due to cohorts within CTP sites and due to CTP sites, we assume an equal correlation structure.

We let Y_{ijk} be the frequency of unprotected vaginal and anal intercourse of the ith subject in the jth cohort of the kth CTP site measured at the 6 month follow-up time, where i =1,…,I, j=1,…,2m, and k=1,…,K. Let x_{ijk} be the treatment assignment indicator for the ith subject in the jth cohort of the kth CTP site. Here *m* is the number of cohorts per condition within the same CTP site.

We propose the following linear model for correlated data for our sample size calculation (Liu and Liang, 1997):

$Y_{ijk} = \beta_0 + \beta_1 x_{ijk} + \varepsilon_{ijk}$,

where $\varepsilon_k = (\varepsilon_{11k,}..., \varepsilon_{I(2m)K})'$ has a multivariate normal distribution with mean zero and covariance matrix $\sigma^2 R$. Here the correlation matrix *R* contains 1 for its diagonal entries and ρ for off-diagonal entries. Here σ^2 is the variance of ε_{ijk} and ρ represents the correlation between any two observations from the same cohort as well as the correlation between two observations from different cohorts within the same CTP site. Note that we assume that the correlation between two observations from the same cohort is the same as the one between two observations from different cohorts within the same CTP site. Under this linear model, to detect the effect size Δ in the average number of unprotected vaginal and anal intercourse between the intervention and control conditions at the type I error α with a power of 1-β, we need the following number of cohorts per condition in the study:

$$\mathrm{m} = 2(z_{1-\alpha/2} + z_{1-\beta})^2 \{1 + (I-1) * \rho\} / (I * (\Delta)^2),$$

where $z_{1-\beta}$ is the (1-β)th percentile of the standard normal distribution. This formula is the same as Formula (5.1) in Donner and Klar (2000).

From the above formula, we see that to calculate a required sample size we need to determine the standardized effect size Δ. We have estimated the effect size on the basis of clinically important intervention effects observed in prior studies. The NIMH Multisite HIV Prevention Trial Group (1998) used the number of unprotected vaginal and anal intercourse acts as a primary outcome measure in Project Light. They observed an effect size (Δ) of 0.29. Assuming that we have an intracluster correlation no greater than ρ of 0.01 and an average of 8 participants per cohort (I=8), using the above formula we find that the number of cohorts per condition required to detect the effect size of 0.29 with a type I error rate of 0.05 and a power of 80% is:

$$\mathrm{m} = 2 * (1.96 + 0.84)^2 * \{1 + (8-1) * 0.01\} / (I * (0.29)^2) = 25,$$

Therefore, we would require a total of 8*25=200 participants per condition, resulting in the total of 400 subjects in the study. Assuming each CTP site can contribute up to 40 subjects, the required number of CTP sites is 10. If each CTP site can only contribute an average of 32 subjects, we would require a total of 12 CTP sites. If each CPT can only contribute an average of 28, we would need a total of 14 CPT sites. Therefore, if we can recruit 14 good CTP sites, we would require each site to contribute a total of 28 subjects.

The following table provides estimates of the number of cohorts sites needed based on the above formula as should the average cohort size be less than 8.

I	# of the required cohorts per conditions
7	29
6	33
5	39
4	49

To allow a possible attrition rate of 10%, we would require a total of 440 participants for the estimate based on I=8. The investigators recognize that sample size calculations are best estimates based on previously obtained data when available. The effect size and intracluster correlation variation can result in significant variation in the sample sizes needed to obtain adequate power. For example if the intracluster correlation is twice what we are estimating (0.02) the total number of participants needed is 216 per condition or 476 total participants with 10% attrition rate. We propose to enroll 560 participants into the study. We feel this will provide some "cushion" for possible attrition, difficulty recruiting at any one site, or under estimation of the intracluster correlation.

11.4 Study Population

The study will be carried out at 7 MMTPs and 7 ODF who can each provide an average of 40 sexually active men within a recruitment period of approximately 6 - 12 months.

11.5 Demographic Profile

The demographic and screening or, if applicable, baseline characteristics of the (respective) total samples at each key point in the course of the study will be described using frequency distributions and measures of central tendency. These populations include: total population screened, total eligible population, total consenting population, total randomized population, and total completer populations. At each key point, frequencies and central tendencies of participating participants versus non-participating participants will be compared. At each key point, reasons for ineligibility, refusal, and/or dropping-out will be documented, and frequency of these reasons will be obtained. Within the randomized sample, the characteristics of participants in each intervention condition will be described.

11.6 Analysis of Primary Outcome

The primary objective is to compare the effectiveness of REMAS, an intensive, 5 session, male-specific group HIV/AIDS intervention, to a standard single session HIV/AIDS education group. It is hypothesized that men provided REMAS will engage in fewer risky sexual behaviors as measured by the number of unprotected vaginal and anal intercourse acts than will men provided the standard intervention. It is also hypothesized that being non-monogamous in the prior six months, years of stimulant use, and the baseline frequency of unprotected vaginal and anal intercourse will be associated with the number of unprotected

vaginal and anal intercourse acts at follow up. These three covariates will be entered into the data analytic model described more fully below. All analyses will be performed using an ITT strategy consisting of all randomized participants. Since our data have two levels of the hierarchical structure, we will apply a marginal semi-parametric regression model to analyze the primary outcome.

Hypothesis 1: REMAS will significantly reduce the number of unprotected vaginal and anal intercourse at both at the 3 and 6 month follow-up times in comparison with the standard single HIV/AIDS education session.

To test this hypothesis, we let Y_{ijkt} be the frequency of unprotected vaginal and anal intercourse of the ith subject in the jth cohort of the kth CTP site measured at the t[th] follow-up time. Let z_{1ijk} be the treatment assignment indicator for the ith subject in the jth cohort of the kth CTP site. Here *m* is the number of cohorts per condition within the CTP site. To adjust for the possible imbalance between conditions on the baseline value, we include the baseline value as a covariate; let z_{2ijk} be the baseline frequency of unprotected vaginal and anal intercourse of the ith subject in the jth cohort of the kth CTP site. The other two covariates we plan to include in the model are (1) z_{3ijk}, a binary indicator on whether the ith subject in the jth cohort of the kth CTP site is non-monogamous in the six months prior to the baseline and (2) z_{4ijk}, years of stimulant use for the ith subject in the jth cohort of the kth CTP site. As noted by Sen (1997), analyzing change from baseline does not remove the baseline imbalance. Hence, we propose to model the absolute frequency at a particular follow-up time and include the baseline frequency value as a covariate in regression.

The following marginal model for outcome of count will be used to test this hypothesis:

(1) $$\log E(Y_{ijkt}) = \beta_0 + \beta_1 z_{1ijk} + \beta_2 t + \beta_3 z_{1ijk} * t + \gamma_1 z_{2ijk} + \gamma_2 z_{3ijk} + \gamma_3 z_{4ijk}$$

where *t=0* for 3 months post intervention and *t=1* for 6 months post-intervention.

Based on the assumed model (1), our main null and alternative hypotheses are governed by the regression parameters β_1, β_2 and β_3. For example, $\beta_3 \neq 0$ indicates that over time the effects of the two study interventions are different; β_3=0 corresponds to no difference in the effectiveness of the interventions over time. If β_3=0, the parameter β_2 estimates the rate of change in the outcome measure from 3 to 6 months post-intervention in the two intervention groups, and the parameter β_1 estimates the difference between the experimental and control intervention, which is the same at the two follow-up assessment times.

Since all covariates used in the model are baseline covariates, we can assume we have complete information on the covariates. A patient who drops out during the study will result in missing outcomes. To be able to deal with possible missing-data, we will use the multiple imputation technique combined with the standard Generalized Estimating Equation (GEE) method for the parameters in model (1), $\beta = (\beta_0, \beta_1, \beta_2, \beta_3, \beta_4)$. A similar method for handling missing covariates has also been proposed by Xie and Paik (1997). In this multiple imputation approach, a missing value of the outcome will be imputed using a Bayesian bootstrap method (Rubin, 1987; Xie and Paik, 1997) to obtain 5 imputed values, resulting in 5 complete-data sets. We will use the following steps in this multiple imputation scheme: (1) we will build a logistic regression model to predict the missingness for the outcome; (2) based on this model we will assign a propensity score for missingness for each case; (3) for each patient with a missing outcome (Y), its donor pool of patients having observed outcomes will

be found such that their assigned propensity scores are close to the assigned propensity score for the patient with the missing outcome; (4) for the missing value of Y for the patient, we will generate 5 imputation values from its donor pool according to the Approximate Bayesian Method (Rubin, 1987).

This multiple imputation method has been implemented by Solas (Statistical Solutions Ltd, 2001). For each complete-data set, we will apply the standard GEE method to get a pair of GEE estimates for β and its variance, resulting in 5 pairs. Then, according to Rubin's formula (Rubin, 1987), we will obtain the multiple-imputation estimate for β and its variance with associated p-value and 95% confidence interval.

Although the above method can handle both missing at random (MAR) and non-MAR missing data patterns, the validity of the method requires appropriately modeling the missing-data mechanism. To assess sensitivity of the conclusions on the assumed missing-data mechanism we will use both a parametric model (Robins et al, 1994; Scharfstein et al, 1999) and a non-parametric model (Wang et al, 1997).

11.7 Analysis of Secondary Outcomes

There are seven secondary outcomes: number of sexual partners, frequency of "outer course," a dichotomous measure of whether or not the subject is possessing condoms; dichotomous measure of whether the subject reports to have taken or not taken (male and female) condoms from open clinic supplies; attitudes towards condom use as measured by the Condom Barriers Scale; frequency of combining sexual behavior and drug use; and gender role beliefs as measured by the BSRI. All analyses will be performed using an ITT consisting of all randomized participants.

For the continuous-scale outcomes, we will use the same models and estimation methods as used for the analysis of the primary outcome.

For the dichotomous outcomes, we will use marginal logistic regression models (Diggle et al., 1994, p. 147-153). Let W_{ijkt} be a dichotomous secondary outcome of the ith subject in the jth cohort of the kth participating CTP site at the t[th] follow-up time. Let z_{1ijk} z_{2ijk}, z_{3ijk} and z_{4ijk} be the same four covariates as defined previously. We will use the following marginal logistic regression for W_{ijkt}:

$$\log \frac{P(W_{ijklt}=1)}{P(W_{ijklt}=0)} = {}_0 + \beta_1 z_{1ijk} + \beta_2 t + \beta_3 z_{1ijk} * t + \gamma_1 z_{2ijk} + \gamma_2 z_{3ijk} + \gamma_3 z_{4ijk} \quad (1),$$

Similar to the estimation in the analysis of the primary outcome, we will use the multiple imputation GEE method to make inferences about the parameter of interest.

11.8 Secondary Analyses on compliance on the outcome effects

We anticipate that not all participants will attend all five intervention sessions. To assess whether participants who attend more intervention sessions exhibit greater magnitudes of

behavior changes, in addition to the binary treatment indicator (control vs. REMAS) we will create a three-level attendance covariate (attended no sessions, attended one, two, or three sessions, or attended four or more sessions), as done similarly in the NIMH Multisite HIV Prevention Trial Group (1998). We will then include this attendance covariate and its interaction with the treatment indicator to the regression models proposed above to see whether there is a significant intervention by dose (number of sessions attended) interaction for our outcome variables.

11.9 Interim Analyses

Given the absence of strong evidence supporting the impact of this intervention, as suggested by a reviewer we will plan to conduct an interim analysis, primarily for futility. We will use the method of stochastic curtailment using the conditional power method (Lan and Wittes, 1988; Jennison and Turnbull, 1999). This approach will provide the statistical rationale for consideration of early termination. We will briefly describe this interim analysis technique as follows.

Let T be the test statistics we will be using for testing the primary null hypothesis for our primary outcome H_0: $\beta_1=0$ versus H_1: $\beta_1 >0$. We will perform one interim analysis when 50% of the participants have finished the 3 month follow up. Let D(1) denote the data accumulated when we perform the interim analysis. The formal stopping rule at the interim analysis is given as follows. We will first compute the conditional power, which is defined as follows:

$$P(0)=P(T \text{ will reject } H_0 \text{ at the end of the study} \mid D(1), \beta_1 =0).$$

Then, if $1-P(0)\geq 0.8$ we will recommend to terminate the study early due to futility. If 1-P(0)<0.8, we will recommend the study be continued. For a detailed discussion of this approach, see Chapter 10 of Jennison and Turnbull (1999).

12.0 STUDY TIMETABLE

Estimated study start date	4/15/04
Estimated date when 50% of participants will be completed	4/15/05
Estimated study end date	7/15/06

13.0 DISCLOSURE OF DATA

It is understood by the investigator that the information and data included in this protocol may be disclosed to and used by the investigator's staff and associates as may be necessary to conduct this clinical study.

14.0 ADHERENCE TO ETHICAL, REGULATORY AND ADMINISTRATIVE CONSIDERATIONS

The ethical and regulatory requirements must be observed to comply with Principles of Good Clinical Practice for the conduct and monitoring of clinical investigations. By signing this protocol, the investigator agrees to adhere to these requirements. The study should be reviewed by the Institutional Review Board. Written informed consent is required for all participants. The ethical and regulatory requirements must be observed to comply with Principles of Good Clinical Practice for the conduct and monitoring of clinical investigations.

14.1 IRB Approval

Prior to initiating the study, the Principal Investigator at each study site will obtain written IRB approval to conduct the study. Should changes to the study protocol become necessary, protocol amendments will be submitted in writing to the IRB by the Principal Investigator for IRB approval prior to implementation. In addition, IRBs will approve all advertising materials used for subject recruitment and any educational materials given to the subject.

14.2 Informed Consent

The informed consent document provides a summary of the research study and the individual's rights as a research participant. The document acts as a starting point for the necessary exchange of information between the investigator and potential research participant.

14.3 Health Insurance Portability and Accountability Act (HIPAA)

Authorization for use of Protected Health Information (PHI) should be obtained at each site prior to initiating the study. Principal Investigators at study sites should ensure that the length of authorization extends throughout the study period. Study participants will need to sign an authorization agreement or a consent form with the appropriate authorization language, as specified by the local IRBs.

14.4 Investigator Assurances

Prior to initiating the study, the Principal Investigator at each study site will sign a protocol signature page, providing assurances that the study be performed according to the standards stipulated therein. The original signed copy of this document will be sent to the Lead Investigator site for record keeping and a copy will be maintained in the site's regulatory binder.

14.5 Outside Monitoring

The NIDA-CTN Data and Safety Monitoring Board, NIDA-CTN contracted Clinical Monitors, representatives from the Lead Investigators Node, and Quality Assurance representatives from the participating Node, will be given access to facilities and records to review and verify data pertinent to the study.

14.5.1. Clinical Monitoring

All informed consent forms and inclusion/exclusion criteria will be reviewed for all protocol participants. In addition, all research records (case report forms, source documents, etc.) for participants experiencing serious adverse events will be reviewed. Per QAS policy, 100% of the research records for the first 10 participants and a random 10% of the remaining participants will be reviewed. In addition, at each monitoring visit to a CTP, the randomization process will be reviewed to ensure that the randomization is occurring according to protocol procedures.

All investigators will allow representatives of the sponsor to periodically audit, at mutually convenient times during and after the study, all CRFs and corresponding source documents for each subject. These monitoring visits provide the sponsor with the opportunity to evaluate the progress of the study and to inform the sponsor of potential problems at the study sites. The monitors will assure that submitted data are accurate and in agreement with source documentation, verify that study medications are properly stored and accounted for, verify that participants' consent for study participation has been properly obtained and documented, confirm that research participants entered into the study meet inclusion and exclusion criteria, and assure that all essential documentation required by good clinical practices guidelines are appropriately filed.

Monitors will conduct a site initiation visit prior to the start of the study, either in person via conference call. At this visit, they will assure that proper study-related documentation exists, assist in training investigators and other site personnel in study procedures and good clinical practice's guidelines, confirm receipt of study supplies, and assure that acceptable facilities are available to conduct the study.

Routine monitoring visits by the sponsor's representatives will be scheduled at appropriate intervals, more frequently at the beginning of the study. At these visits, the monitors will verify that study procedures are being conducted according to the protocol guidelines. At the end of the study they will advise on storage of study records. All sites should anticipate visits by NIDA and the Lead Investigator's Protocol Team.

15.0 DISPOSITION OF DATA

The Washington Node Data Management Center (DMC) will coordinate data management activities and provide ongoing consultation and assistance to participating nodes throughout the study. All procedures will be in accordance with the Standard Operating Procedures (SOPs) developed by the CTN Data Management & Analysis Subcommittee (DMAS). The DMAS SOPs are in accordance with the Food & Drug Administration regulations, which NIDA has adopted as the data collection and management standards for all CTN studies.

15.1. Lead Node Responsibilities

The Washington Node Data Management Center will provide final Case Report Form (CRF) specifications for the collection of all data required by the study. While the study data content of the CRFs cannot be changed, it is understood that CRFs may be modified for incorporation into each participating node data management system as appropriate. The Washington Node DMC will also provide data dictionaries for each CRF that will comprehensively define each data element. The data dictionary will specify missing, illogical, out of range, and

inconsistent value checks for each data element as well as within-CRF logic checks and across-CRF logic checks. The data dictionaries provide the specifications necessary for each node to develop an automated data acquisition and management system that will be designed in accordance with standards established by DMAS. The Washington Node Data Management Center will also provide specifications necessary to conduct data monitoring activities and meet the requirements of all other DMAS SOPs.

15.2 Data Collection

Data will be collected at the study sites on either electronic (paperless) or paper case report forms (CRFs). Forms completion instructions will also be provided for each CRF.
Each participating node DMC will coordinate the preparation of paper CRFs and the distribution of these CRFs to participating Community Treatment Programs (CTPs) within their node. These forms are to be completed on an ongoing basis during the study. Forms should be completed according to the instructions provided. Each node is responsible for maintaining accurate, complete and up-to-date records and for tracking CRFs for each participant. Paper CRFs must be completed legibly with black ballpoint pen. Any corrections must be made by striking through the incorrect entry with a single line using a ballpoint pen and entering the correct information adjacent to the incorrect entry. Corrections to paper CRFs must be initialed and dated by the person making the correction.

15.3 Data Submission, Editing and Monitoring

Completed forms/electronic data will be submitted to each participating node DMC in accordance with Data Timeliness and Completeness SOP established by the DMAS. Only authorized individuals, in accordance with each participating node's DMC policies, shall perform data entry into electronic CRFs. Corrections to electronic CRFs must be tracked electronically with time, date, individual making the change, both the old data value and new data value, and the reason for the correction. Each node DMC will implement comprehensive error checking and data management procedures as per the Error Tracking SOP established the by DMAS. Data monitoring will be the responsibility of the DMC at each node. Data monitoring will be performed as specified in the Data Timeliness and Completeness SOP, Data Accuracy and Auditing SOP, Participant Recruitment Progress and Retention SOP, and other data monitoring SOPs as approved by DMAS.

15.4 Automated Data Acquisition and Management Systems

Each node is responsible for the development of a comprehensive automated data acquisition and management system in accordance with guidelines and SOPs published by NIDA and DMAS. The Washington node DMC is willing to discuss the use of the Washington automated data acquisition and management system if it is not desirable or cost effective for a node to develop its own independent data acquisition and management system for this protocol.

15.5 Central Data Repository

Data will be transmitted by the participating node DMC to the NIDA central data repository on the 10th of every month, in accordance with the DMAS Data Transmission SOP. The

Washington Node DMC will receive aggregated data from the NIDA central data repository on a monthly basis for data completeness, timeliness and accuracy quality assurance review. At the completion of the study, all data will be transmitted from the NIDA central data repository to the Washington Node DMC for data analysis and the development of the final study report. The Washington DMC will conduct final data quality assurance checks and “lock” the study database from further modification in accordance with the Database Lock SOP developed by the DMAS. The Washington DMC will send the final analysis dataset back to NIDA for storage and archive.

REFERENCES

Bartholomew, N.G., Hiller, M.L., Knight, K., Nucatola, D.C. & Simpson, D.D. (2000). Effectiveness of communication and relationship skills training for men in substance abuse treatment. Journal of Substance Abuse Treatment, 18, 217-225.

Bartholomew, N.G., Rowan-Szal, G., Chatham, L.C. & Simpson, D.D. (1994). Effectiveness of a specialized intervention for women in a methadone program. Journal of Psychoactive Drugs, 26, 249-255.

Bartholomew, N.G., Chatham, L.C. & Simpson, D.D. (1991). Time Out! For Me: An assertiveness/sexuality workshop specially designed for women. (Available from Lighthouse Institute Publishing, 720 W. Chestnut St. Bloomington, IL, 61701, or on the Internet at www.tcu.ibr)

Bartholomew, N.G., & Simpson, D.D. (1996). Time Out! For Men: A communication skills and sexuality workshop for men. (Available from Lighthouse Institute Publishing, 720 W. Chestnut St. Bloomington, IL, 61701, or on the Internet at www.tcu.ibr)

Bartholomew, N.G. & Simpson, D.D. (1992). Approaches to HIV/AIDS education in drug treatment. Institute for Behavioral Research, Texas Christian University, Fort Worth, TX.

Bem, S.L. (1981). Bem sex-role inventory: Professional manual. Palo Alto, CA. Consulting Psychologists Press.

Boatler, J.F., Knight, K. & Simpson, D.D. (1994). Assessment of an AIDS intervention program during drug abuse treatment. . Journal of Substance Abuse Treatment, 11, 367-372.

Booth, R. E., Crowley, T. J. & Zhang, Y. (1996). Substance abuse treatment entry, retention and effectiveness: out-of-treatment opiate injection drug users. Drug and Alcohol Dependence, 42, 11-20.

Broome, K.M., Joe, G.W. & Simpson, D.D. (1999). HIV risk reduction in outpatient drug abuse treatment: Individual and geographic differences. AIDS Education and Prevention, 11, 293-306.

Brown, H. and Prescott, R. (1999) Applied Mixed Models In Medicine: John Wiley & Sons; New York.

Bryk, A.S. and Raudenbush, S.W. (1992) Hierarchical Linear Models: Sage Publications: Newbury Park, Ca.

Calsyn, D.A., Wells, E.A., Saxon, A.J., & Jackson, T.R. (1996). Methadone clients combining drugs and sex use more drugs. In L.S. Harris (Ed.) Problems of Drug Dependence 1995 (p. 122). NIDA, Rockville, MD.

Calsyn, D.A., Wells, E.A., Saxon, A.J. & Jackson, R. (1999). Defining the relationship between sex and drugs. In Harris, L. (Ed). Problems of Drug Dependence 1998, National Institute on Drug Abuse, NIH Pub. No. 99-4395, 268.

Calsyn, D.A., Wells, E.A., Saxon, A.J., Jackson, R. & Heiman, J.R. (2000). Sexual activity under the influence of drugs is common among methadone clients. In Harris, L. (Ed). Problems of Drug Dependence 1999, National Institute on Drug Abuse, NIH Pub. No. 00-4773, 315.

Calsyn, D.A., Wells, E.A., Saxon, A.J., Heiman, J.R. & Jackson, R. (2001). Sexual desire and dysfunction among methadone maintenance clients. Drug and Alcohol Dependence, 63(S1), S23.

Calsyn, D.A., Wells, E.A., Saxon, A.J., Jackson, T.R., Wrede, A.F., Stanton, V. & Fleming, C. (1994). Contingency management of urinalysis results and intensity of treatment have an interactive impact on methadone maintenance treatment outcome. Journal of Addictive Diseases, 13, 47:63.

Cockrell, J.R. & Folstein, M.F. (1988). Mini-Mental State Examination. Psychopharmacology Bulletin, 24, 689-692.

Cohen, J. (1988) Statistical Power Analysis for the Behavioral Sciences, 2d. Ed. Lawrence Erlbaum Associates: Hillsdale, N.J.

Coyle, S.L., Needle, R.H. & Normand, J. (1998). Outreach-based HIV prevention for injecting drug users: A review of published outcome data. Public Health Reports, 113(S1), 19-30.

Crits-Christsoph, P, Siqueland, L., Blaine, J. et al. (1999). Psychosocial treatments for cocaine dependence: National Institute on Drug Abuse Collaborative Cocaine Treatment Study. Archives of General Psychiatry, 56, 493-502.

Crum, R., Anthony, J., Bassett, S., & Folstein, M. (1993). Population-based norms for the Mini-Mental State Examination by age and educational level. JAMA, 269, 2386-2391.

DeHovitz, J.A., Kelly, P., Feldman, J. et al. (1994). Sexually transmitted diseases, sexual behavior, and cocaine use in inner-city women. American Journal of Epidemiology, 140, 11251134.

del Romero, J., Marincovich, B., Castilla, J. et al. (2002). Evaluating the risk of HIV transmission through unprotected orogenital sex. AIDS, 16, 1296-1297.

Donner A and Klar N. (2000). Design and Analysis of Cluster Randomization Trials. Arnold, London.

Diggle, P.J., Liang, K.Y. and Zeger, S.L. (1994) Analysis of Longitudinal Data. Oxford University Press; Oxford, UK.

El-Bassel, N. and R. Schilling. (1992) 15-month follow-up of women methadone patients taught skills to reduce heterosexual HIV transmission. Public Health Reports, 107, 500-4.

Folstein, M.F., Folstein, S.E. & McHugh, P.R. (1975). "Mini-Mental State": a practical method for grading cognitive state of patients for the clinician. Journal Psychiatric Research, 12, 196-198.

Gross M, Holte SE, Marmor M., et al. (2000). Anal sex among HIV-seronegative women at high risk of HIV exposure. Abt Associates Inc., Cambridge, MA, and Bethesda, MD

Hiller, M.L., Rowan-Szal, G., Bartholomew, N.G., & Simpson, D.D. (1996). Effectiveness of a specialized intervention for women in a residential program. Substance Use and Misuse, 31, 771-783.

Joe, G.W., Menon, R., Copher, J.I & Simpson, D.D. (1990). Needle use and sex risk indicies: A methodological report. Research in Progress: Research summaries from the Southwest Regional Group. NOVA Research Co., Bethesda, MD.

Hwang, L., Ross, M.W., Zack, C., et al. (2000). Prevalence of sexually transmitted infections and associated risk factors among populations of drug abusers. Clinical Infectious Diseases, 31, 920-926.

Jennison C. and Turnbull B.W. (1999). Group Sequential Methods with Applications to Clinical Trials. Chapman & Hall/CRC, New York.

Lan K.K.G. and Wittes J. (1988). The B-value: a tool for monitoring data. Biometrics, 44, 579-585.

Liu G. and Liang K.Y. (1997). Sample size calculations for studies with correlated observations. Biometrics, 53, 937-947.

Metzger DS, Koblin B, Turner C, et al (2000). Randomized controlled trial of audio computer-assisted self-interviewing: Utility and acceptability in longitudinal studies. J Acquir Immune Defic Syndr, 24:393-8

Metzger, D.S., Navaline, H. & Woody, G.E. (1998). Drug abuse treatment is AIDS prevention. Public Health Reports, 113(S1), 97-106.

Meyer-Bahlburg, H, Ehrhardt, A., Exner, T.M., et al. (1991). Sexual Risk Behavior Assessment Schedule-Adult-Armory Interview. New York State Psychiatric Institute and Columbia University, New York, NY.

Najavtis, L. M., Crits-Christoph, P. & Dierberger, A. (2000). Clinicians' impact on the quality of substance abuse disorder treatment. Substance Use and Misuse, 35, 2161-2190.

The NIMH Multisite HIV Prevention Trial Group (1998). The NIMH Multisite HIV Prevention Trial: Reducing HIV Sexual Behavior Risk. Science, 280, 1889-1894.

Page-Shafer, K., Osmond, D., Ball, J., et al. (2002). Risk of HIV infection attributable to oral sex among MSM and in the MSM population: the HIV Oral Transmission (HOT) Study. Poster presented at the XIV International AIDS Conference 2002, Barcelona, Spain, July 7th, poster #TuPeC4872.

Pinkerton, S. D., Chesson, H. W., Layde, P.M., et al. (2002). Utility of behavioral changes as markers of sexually transmitted disease risk reduction in sexuaully transmitted disease/HIV prevention trials. Journal of Acquired Immune Deficiency Syndromes, 31, 71-79.

Prendergast, M.L., Urada, D. & Podus, D. (2001). Meta-analysis of HIV risk-reduction interventions within drug abuse treatment programs. Journal of Consulting and Clinical Psychology, 69, 389-405.

Robins, J.M., Rotnitzky, A., Zhao L.P. (1994). Estimation of regression coefficients when some regressors are not always observed. Journal of the American Statistical Association, 89, 846-866.

Rubin DB (1987). Multiple Imputation for Nonresponse in Surveys. Wiley & Sons, New York.

Scharfstein, D.O., Rotnitzky, A., and Robins, J.M. (1999). Adjusting for non-ignorable drop-out using semiparametric non-response models. Journal of the American Statistical Association, 94:1096-1120.

Schilling, R.F., El-Bassel, N, Schinke, S.P., Gordon, K. & Nichols, S. (1991). Building skills of recovering women drug users to reduce heterosexual HIV transmission. Public Health Reports, 106, 297-304.

Simpson, D.D., Camacho, L.M., Vogtsberger, K.N., et al. (1994). Reducing AIDS-risk through community outreach for drug injectors. Psychology of Addictive Behaviors, 8, 86-101.

Sohler, N., Colson, P. W., Meyer-Bahlberg, H. F. L., & Susser, E. (2000). Reliability of self reports about sexual risk behaviors for HIV among homeless men with severe mental illness. Psychiatric Services, 51, 814-816.

Sorenson, J.L. & Copeland, A.L. (2000). Drug abuse treatment as an AIDS prevention strategy: a review. Drug and Alcohol Dependence, 59, 17-31.

St. Lawrence, J.S., Jefferson, K.W., Alleyne, E. & Brasfield, T.L. (1995). Comparison of education versus skills training interventions in lowering sexual HIV-risk behavior of substance dependent adolescents. Journal of Consulting and Clinical Psychology, 63, 154-157.

St. Lawrence, J.S., Chapdelaine, A.P, Devieux, J.G. et al. (1999). Measuring perceived barriers to condom use: Psychometric evaluation of the Condom Barriers Scale. Assessment, 6, 391-400.

Statistical Solutions Ltd. (2001). SOLAS for missing data analysis 3.0, Crosses's Green, Cork, Ireland.

Straussner, S.L.A. (1997). Gender and substance abuse. In S.L.A. Straussner and E. Zelvin (eds), Gender and Addictions. Jason Aronson Inc, Northvale, NJ.

Wang, C. Y., Wang, S., Zhao, L., Ou, S. T. (1997). Weighted semiparametric estimation in regression analysis with missing covariate data. Journal of the American Statistical Association, 92, 512-525.

Wells, E.A., Calsyn, D.A., Saxon, A.J., & Greenberg, D.M. (1993). Using drugs to facilitate sexual behavior is associated with sexual variety among injection drug users. Journal of Nervous and Mental Disease, 181, 626-631.

Xie F. and Paik M.C. (1997). Multiple Imputation Method for the Missing Covariates in Generalized Estimating Equation. Biometrics, 53, 1538-1546.

Protocol Signature Page

SPONSORS REPRESENTATIVE

Betty Tai, Ph. D._____ _____ _____
NIDA Representative Signature Date

INVESTIGATOR (S)

- I agree to conduct this clinical study in accordance with the design and specific provisions of this protocol and will only make changes in the protocol after notifying the sponsor except when necessary to protect the safety, rights, or welfare of participants.

- I will ensure that the requirements relating to obtaining informed consent and institutional review board (IRB) review and approval in 45 CFR 46 are met.

- I agree to report to the sponsor adverse experiences that occur in the course of the investigation, and to provide annual reports and a final report in accordance with 45 CFR 46.

- I agree to maintain adequate and accurate records and to make those records available for inspection in accordance with 45 CFR 46.

- I will ensure that an IRB that complies with the requirements of 45 CFR 46 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human participants or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human participants.

- I agree to personally conduct or supervise this investigation and to ensure that all associates, colleagues, and employees assisting in the conduct of this study are informed about their obligations in meeting these commitments.

Typed Name Signature Date

Donald Calsyn, Ph.D._____ _____ _____
Lead Investigator Signature Date

Susan Tross, Ph.D._____ _____ _____
Sub-Investigator Signature Date

_____ _____ _____
Sub-Investigator

UNIVERSITY OF WASHINGTON
CONSENT FORM
"HIV/STD Safer Sex Skills Groups For Men In Methadone Maintenance Or Drug-free Outpatient Treatment Programs"

Consent for Participant Screening

Donald Calsyn, Ph.D.
Professor
Department of Psychiatry and Behavioral Sciences
Alcohol and Drug Abuse Institute
1107 NE 45th St., Suite 120
University of Washington
Seattle, WA 98105
(206) 543-0937

Susan Tross, Ph.D.
Research Scientist
New York State Psychiatric Institute
New York, N.Y. 10032
(212) 420-4468

Ron Jackson, M.S.W.
Executive Director
Evergreen Treatment Services
Seattle, WA 98134
(206) 223-3644

Mary Hatch-Maillette, Ph.D.
Research Scientist
Alcohol and Drug Abuse Institute
1107 NE 45th St., Suite 120
University of Washington
Seattle, WA 98105
(206) 616-7730

Researchers' statement

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called 'informed consent.' We will give you a copy of this form for your

records.

PURPOSE AND BENEFITS

The purpose of the interview is to find out if you are able to take part in this research study. The research is about preventing and reducing HIV/AIDS and sexually transmitted diseases. This study will be conducted at many clinics across the country. Several hundred men will be in this study nationwide, including men at this clinic. You may not benefit from being in this interview.

PROCEDURES

The interview will take about 30-60 minutes. During this interview, we will ask you for information about your sexual experiences, and drug and alcohol use. We will also ask for some other information about you, including your age, race, income, and background. At the end of the interview, you may also be asked to be a part of the study. Not all men who do the interview will be asked to be in the study. If you are not invited to be a part of the study you will not be told the reason why.

The interview you will do today will be audio taped. Consenting to do the interview includes consenting to audiotaping. The purpose of audiotaping these interviews is 1) to make sure that the interviews are being conducted correctly and 2) to make sure study staff can review what was said at a later time.

Only the staff members involved in this research study will hear these audiotapes. Other staff members at this clinic will not have access to the audiotapes or be permitted to hear them. These audiotapes will be kept for up to 10 years in a locked file drawer in a secure office. Names of individual participants will not appear on the audiotapes. You have a right to listen to your tape and to have the interviewer delete any portion you wish to delete.

RISKS, STRESS, OR DISCOMFORT

Talking about sex, drug use, and relationships can make some people uncomfortable. You may feel embarrassed, or have other feelings. Our study staff is trained to help you deal with the feelings you may have. You can also talk about your feelings with other staff here at the clinic.

There is a risk that what you say to the interviewers or other study staff members could be told to others. You may also run into friends or associates while taking part in this study interview. However, we make every effort to protect the information you give us.

OTHER INFORMATION

<u>Compensation and Financial Obligations</u>
You will be paid for taking part in this interview. You will receive $10 for your time and effort. The interview is free of charge. Neither you nor your insurance company will be billed for it. However, you or your insurance company will have to pay for any other treatment you receive at this clinic that

is not part of the research.

Alternatives to Participation

Your participation in this study is VOLUNTARY. You do not have to take part in this study to receive drug and alcohol treatment at this clinic. The alternative to taking part in this screening interview would be to receive treatment without the additional interview. You will still receive treatment if you choose not to be in the study.

Confidentiality

Other researchers designated by the principle investigator who are working on this study may be able to see your study information. The other researchers include the sponsor, the Human Subjects Committee at the University of Washington, the VA Puget Sound Health Care System Research and Development Committee, and other federal and local agencies. To keep unauthorized people from being able to connect you with the information you provide, we will put a code number on the information instead of your name. You information will be stored in a locked cabinet or in a password protected computer. Your name and personal information will not be stored in the same place as your study or treatment information.

The National Institute on Drug Abuse pays for the study. Data collected for this study may be published in research journals. Data from this study may be compared in future to data from a similar study being conducted with women. Your name and personal information will not be shared with the other study. Any information published from these data will not include your name or any personal information. Data (including audiotapes) from individuals who are eligible from the study will be retained in an identifiable form for 10 years. Data (including audiotapes) from individuals who are not eligible for the study will be retained in an identifiable form for 5 years. After these time periods data in an identifiable form will be destroyed.

If you have any questions about your rights as a study participant, you may contact:
Human Subjects Division
University of Washington
3945 15th Avenue NE, Seattle, WA 98105-6607
(206) 543-0098
206-543-9218 (fax)

The Human Subject Division performs an independent review of this research.

Please do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

By signing this form you give permission for us to collect and use the health information described in this form. You do not have to give us permission. If you do not, you may not join the study. You may also take back your permission at any time. If you do, you may no longer be in the study. We will keep any information in the study record that we have already collected. To take back your permission, write to: Donald Calsyn Ph.D., Alcohol and Drug Abuse Institute, 1107 NE 45th St., Suite 120, University of Washington, Seattle, WA 98105.

_____ _____

Printed name of researcher Signature of researcher Date

Participant's statement

This study has been explained to me. I volunteer to take part in this research. I agree to the use, creation, and sharing of my health information for the purposes of this research study. I have had a chance to ask questions. If I have questions later about the research, I can ask one of the researchers listed above. If I have questions about my rights as a research subject, I can call the Human Subjects Division at (206) 543-0098. I will receive a copy of this consent form.

_____ _____

Printed name of research participant Signature of research participant Date

UNIVERSITY OF WASHINGTON
CONSENT FORM
"HIV/STD Safer Sex Skills Groups For Men In Methadone Maintenance Or Drug-free Outpatient Treatment Programs"

Consent for Main Study Participation

Donald Calsyn, Ph.D.
Professor
Department of Psychiatry and Behavioral Sciences
Alcohol and Drug Abuse Institute
1107 NE 45th St., Suite 120
University of Washington
Seattle, WA 98105
(206) 543-0937

Susan Tross, Ph.D.
Research Scientist
New York State Psychiatric Institute
New York, N.Y. 10032
(212) 420-4468

Ron Jackson, M.S.W.
Executive Director
Evergreen Treatment Services
Seattle, WA 98134
(206) 223-3644

Mary Hatch-Maillette, Ph.D.
Research Scientist
Alcohol and Drug Abuse Institute
1107 NE 45th St., Suite 120
University of Washington
Seattle, WA 98105
(206) 616-7730

In case of emergency, please call: (206) 223-3644

RESEARCHERS' STATEMENT
We are asking you to participate in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called 'informed consent.' We will give you a copy of this form for your records.

PURPOSE AND BENEFITS

You are being asked to be in this study because you are 18 years old or older and are trying to stop using drugs. The purpose of this study is to look at two programs that provide skills for reducing and preventing HIV/AIDS. One program is a standard HIV/AIDS education group used in drug abuse treatment clinics. The other program is a communication and sexuality group aimed specifically at men in drug abuse treatment. A total of 560 men will take part in the study across the country. Your participation is voluntary. If you participate in this study, you may not receive any direct benefit. You may benefit by learning skills that may help you reduce your chances of getting sexually transmitted diseases, like AIDS (Acquired Immune Deficiency Syndrome). You may also help benefit others by reducing the chances that sexually transmitted diseases are spread to others. You will be paid for your time involved in the study.

PROCEDURES

At the start of the study you will be interviewed to get information about your health, mental health, substance use, and sexual risk. You will also be asked to give a urine sample (for drug screening) and breathe into an alcohol breathalyzer (for alcohol screening) at the initial visit. This is the only time you will be asked to provide a urine sample and alcohol breathalyzer. Study staff will test your breath and urine and then discard the samples. This initial visit will last from 3-4 hours in total. After the interview is completed you will be placed in a study group. When the group has a certain number of men in it, the group will start and you will be placed in either a one-session HIV education group or a five-session communication and sexuality group aimed specifically at men.

The HIV education group will only meet one time. In the men's specific communication and sexuality program, each study visit will be about 90 minutes and will meet twice a week for the first 2 weeks and once in the final week for a total of five visits. These study visits will be in addition to your regular treatment. You must be enrolled at your treatment center in order to participate in the research groups. The first group would start within the next few weeks. At the first group you will be told whether you will be in the standard HIV/AIDS education or the communication skills and sexuality group specific for men.

Group Sessions:
If you take part in this study you will have an equal chance of being in one of two study groups. The first group is a single session of HIV education. The HIV education group will discuss the interplay between sexual behavior and drug use, HIV risky behaviors, HIV/AIDS, injection practices, sexual practices, and provide a condom demonstration.

The second group is a five-sessions communication skills and sexuality group. This group discusses all of the topics in the HIV education group and in addition discusses healthy options, identifying triggers and problem solving, having sex without drugs, and communicating about sex and safe sex.

Both groups will give you information on reducing the risk of getting and spreading sexually transmitted diseases including AIDS. Men in the gender specific HIV/AIDS prevention group will have 5 sessions over three weeks. Men in the standard HIV/AIDS education will have a single HIV/AIDS prevention group session over the next few weeks. There are four interview sessions that will take place over the next nine months as part of the study.

Audio Taping:
Group sessions and interviews will be audio taped. Consenting to be in the study includes consenting to audiotaping. The purpose of audio taping these interviews is 1) to make sure that the interviews are being conducted correctly and 2) to make sure study staff can review what was said at a later time.

Only the staff members involved in this research study will hear these audiotapes. Other staff members at this clinic will not have access to the audiotapes or be permitted to hear them. These audiotapes will be kept for up to 10 years in a locked file drawer in a secure office. Names of individual participants will not appear on the audiotapes. You have a right to listen to your tape and to have the interviewer delete any portion you wish to delete.

Interviews and Follow-up:
If you take part in this study we will interview you four times: 1) before starting any of the group sessions, 2) after the group sessions have ended, 3) at 3 months after the study sessions have ended, 4) at 6 months after the study sessions have ended. If you are discharged from your treatment center after completing the research groups, you may still participate in follow-up interviews. We will ask you to give us information so that we can find you for interviews after the study sessions have ended. To help with this process, you will be asked to name several people who might help us contact you if we are unable to find you. The contacts you name will not be asked to provide any information about your health, drug use, or any other personal information. The researcher that calls will only ask that you return a call to the number provided. At each of these interviews we will ask you about your health, sexual risk and drug use. We will ask if this information has changed since your last interview. Each follow-up interview will last 60-90 minutes. We will use the information you give us at the start of the study to contact you. One piece of information we will ask is your social security number. This number will go on your contact information sheet to help us get in touch with you if we have trouble finding you. You are not required to provide this information. Also, to help us know the whereabouts of participants we have trouble finding for interviews, we will be searching the public database of the regional correctional facility to see if any of our participants are housed there. If we find that you are there, we will not contact you until you have been released.

Study Participation and Payment:
Taking part in the study is voluntary. If you want to take part in the study you may stop at any time. You may decide not to answer any particular questions during the study interviews. You will still get treatment if you decide not to be in the study. If you agree to be in the study you will be paid for your time. We will give you $10 cash for each research group you go to up to a total of $50. You will also be paid $30 cash for the initial interview session, $20 for the end-of-treatment interview session, and $30 at 3-month and 6-month follow-up. Here is the total possible payment for being in the study:

Baseline Interview	$30
Study Sessions (up to 5)	$10-50
End of Study Interview	$20
3-month Follow-up Interview	$30
6-month Follow-up Interview	$30
Total	$120-160

RISKS, STRESS, OR DISCOMFORT

We will make every effort to protect your information, but we cannot be certain that all information will be kept private. The study groups will talk openly about sex and sexuality, which may be embarrassing. It may be possible for others to find out that you are getting drug treatment, which may be embarrassing, or cause problems with work, family or others. The study will use group treatment, and there is a risk that others in the group may share your information. If you share that you have a sexually transmitted disease there is a risk that others in the group may share that information.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, we cannot be forced to share information about you, even by a court order or subpoena. We will use the Certificate to refuse requests for information that would identify you. You or members of your family will not be prevented from voluntarily releasing information about yourself. For example, if someone obtains your written approval to receive information about you, then we would be able to provide it. The Certificate does not prevent the researchers from reporting, even without your consent, suspected or known sexual or physical abuse of a child, threatened violence to self or others, elder abuse, or having high-risk sex if you tell us that you are HIV positive. Such information must be reported to the appropriate authorities and may also be placed in your clinical record.

OTHER INFORMATION

Alternatives to Treatment and Financial Obligations:
You do not have to take part in this study to receive treatment. If you choose not to take part you may continue with regular clinic treatment. You will be responsible (or through insurance) for the cost of your regular treatment. If you are injured during treatment you will be referred to outside care. The study sponsor, NIDA, will not pay for emergency medical care. You will be responsible (or through insurance) for the cost of emergency or long-term medical care. You are not giving up any of your rights by being in this study.

Confidentiality:
Other researchers designated by the principle investigator who are working on this study may be able to see your study information. The other researchers include the sponsor, the Human Subjects Committee at the University of Washington, the VA Puget Sound Health Care System Research and Development Committee, and other federal and local agencies. After the study is completed, data from this study will be compared in to data from a similar study being conducted with women. Comparing these data will help us learn more about the differences between men and women in drug treatment. The study with women is being conducted by Susan Tross, Ph.D., whose contact information is on the first page of this form. Your name and personal information will not be shared with the other study. To keep unauthorized people from being able to connect you with the information you provide, we will put a code number on the information instead of your name. Your information will be stored in a locked cabinet or in a password protected computer. Your name and personal information will not be stored in the same place as your study or treatment information. Data will be retained in identifiable form for 10 years.

The National Institute on Drug Abuse pays for the study. Data collected for this study may be published in research journals. Any information published from these data will not include your name or any personal information. .

If you have any questions about your rights as a study participant, you may contact:
Human Subjects Division
University of Washington
3945 15th Avenue NE, Seattle, WA 98105-6607
(206) 543-0098
206-543-9218 (fax)

The Human Subject Division performs an independent review of this research.

Please do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

By signing this form you give permission for us to collect and use the health information described in this form. You do not have to give us permission. If you do not, you may not join the study. You may also take back your permission at any time. If you do, you may no longer be in the study. We will keep any information in the study record that we have already collected. To take back your permission, write to: Donald Calsyn Ph.D., Alcohol and Drug Abuse Institute, 1107 NE 45th St., Suite 120, University of Washington, Seattle, WA 98105.

_____	_____	
Printed name of researcher	Signature of researcher	Date

Subject's statement

This study has been explained to me. I volunteer to take part in this research. . I agree to the use, creation, and sharing of my health information for the purposes of this research study. I have had a chance to ask questions. If I have questions later about the research, I can ask one of the researchers listed above. If I have questions about my rights as a research subject, I can call the Human Subjects Division at (206) 543-0098. I will receive a copy of this consent form

_____	_____	
Printed name of research participant	Signature of research participant	Date