Study Protocol

ClinicalTrials.gov ID: NCT02929069
Study Title: A Unified Intervention for Young Gay and Bisexual Men's Minority Stress, Mental Health, and HIV Risk
Final Date: 8/5/2020

YALE UNIVERSITY IRBs
Application for Full or Expedited IRB Review of a Study
Involving Human Participants in
Social or Behavioral Science or Educational Research

100 FR 28 (2015-1)

NOTE: IF YOUR STUDY INVOLVES:

Genetic Testing
Blood Draws → ***Do not use this form. Use the biomedical HIC application***
MRI scans

Secondary analysis of data → ***Use the Request for Approval of Secondary Analysis of Data***

Activities that may qualify as exempt research → ***Use the Request for Exemption form (which includes a decision tree to determine whether or not your study qualifies as exempt).***

SECTION I: ADMINISTRATIVE INFORMATION

Title of Research Project: A unified intervention for young gay and bisexual men's minority stress, mental health, and HIV risk			
Principal Investigator: John Pachankis, Ph.D.		**Yale Academic Appointment: Associate Professor**	
Department: Chronic Disease Epidemiology, YSPH			
Campus Address: 60 College St., Ste. 316			
Campus Phone: 203-785-3710			**E-mail:** john.pachankis@yale.edu
Protocol Correspondent Name & Address (*if different than PI***): Roxanne Winston**			
Campus Phone:		**E-mail:** roxanne.winston@yale.edu	

Faculty Advisor: (required if PI is a student, resident, fellow or other trainee) ☐ **NA**		**Yale Academic Appointment:**	
Campus Address:			
Campus Phone:			**E-mail:**

Investigator Interests:

Does the principal investigator, or do any research personnel who are responsible for the design, conduct or reporting of this project or any of their family members (spouse or dependent child) have an incentive or interest, financial or otherwise, that may affect the protection of the human participants involved in this project, the scientific objectivity of the research or its integrity? Note: The Principal Investigator (Project Director), upon consideration of the individual's role and degree of independence in carrying out the work, will determine who is responsible for the design, conduct, or reporting of the research.
See Disclosures and Management of Personal Interests in Human Research
http://www.yale.edu/hrpp/policies/index.html#COI

❑ Yes **X No**

Do you or does anyone on the research team who is determined by you to be responsible for the design, conduct or reporting of this research have any patent (sole right to make, use or sell an invention) or copyright (exclusive rights to an original work) interests related to this research protocol?

❑ Yes X No

If yes to either question above, list names of the investigator or responsible person:

The Yale University Principal Investigator, all Yale University co-investigators, and all Yale University individuals who are responsible for the design, conduct or reporting of research must have a current financial disclosure form on file with the University's Conflict of Interest Office. Yale New Haven Hospital personnel who are listed as co-investigators on a protocol with a Yale University Principal Investigator must also have a current financial disclosure form on file with the University's Conflict of Interest Office. If this has not been done, the individual(s) should follow this link to the COI Office Website to complete the form: http://www.yale.edu/coi/

NOTE: The requirement for maintaining a current disclosure form on file with the University's Conflict of Interest Office extends primarily to Yale University and Yale-New Haven Hospital personnel. **Whether or not they are required to maintain a disclosure form with the University's Conflict of Interest Office, all investigators and individuals deemed otherwise responsible by the PI who are listed on the protocol are required to disclose to the PI any interests that are specific to this protocol.**

SECTION II: GENERAL INFORMATION

1. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.

November 1, 2015 to December 31, 2020

2. **Study location:** State where the study will take place and in what setting.

This study will primarily take place in two sites – one affiliated with the Yale School of Public Health, the other affiliated with the University of Miami Department of Psychology. The Yale-affiliated site, overseen by Dr. Pachankis, will be an off-campus research office in New York City (220 East 23rd St., Suite 405, New York, NY 10010). The Miami-affiliated site will be the University of Miami Medical School (1120 NW 14th St, Suite 787, Miami FL 33136).

Data collection will also take place in the offices of our community partners, the Institute for Human Identity (322 8th Ave, New York, NY, 10001) in New York City and Care Resources (3510 Biscayne Blvd., Miami, FL) in Miami.

Dr. Pachankis' office at the Yale School of Public Health (60 College St., Ste. 316) and Dr. Safren's office at the University of Miami Department of Psychology will serve as secondary locations limited to meetings with project staff and data analysis. Study participants will not be seen at these secondary sites.

3. **Help us categorize your research**! Are you using any of the following?

- ☐ Class Project
- ☐ Participant Observation
- ☒ Interviews
- ☒ Surveys
- ☐ Focus groups (study is not anonymous)
- ☐ Research in K-12 schools (submit a School Agreement form for the study)
- ☐ Deception (submit a Debriefing sheet)
- ☒ Audiotaping, videotaping or photography of individuals (study is not anonymous)
- ☒ Public viewing of videotapes or photographs
- ☐ Yale Psychology Pool (study does not qualify for exemption)
- ☐ International research sites (attach the International Checklist)
- ☒ Online (web-based) activities
- ☐ Social networks

SECTION III: FUNDING, RESEARCH TEAM AND TRAINING

Funding Source: Indicate all of the funding source(s) for this study. Check all boxes that apply. Provide information regarding the external funding source. This information should include identification of the PI ***on the award***, agency/sponsor, the funding mechanism (grant or contract), and whether the award is pending or has been awarded. Provide the Yale institutional proposal number and Agency name (if grant-funded). If the funding source associated with a protocol is "pending" at the time of the protocol submission to the IRB (as is the case for most NIH submissions), the PI should note "Pending" in the appropriate section of the protocol application, provide the Yale institutional proposal number and Agency name (if grant-funded) and further note that University (departmental) funds support the research (until such time that an award is made).

PI of grant (if applicable)	Title of Grant (if applicable)	Name of Funding Source (i.e. Dept name or Fellowship)	Funding type	Funding Mechanism
John Pachankis, Ph.D.	A unified intervention for young gay and bisexual men's minority stress, mental health, and HIV risk	National Institute of Mental Health	☐ Yale fellowship ☐ Yale department ☐ No funding (student projects, etc.) ☒ Federal ☐ State ☐ Non Profit ☐ Industry ☐ Other For Profit ☐ Other	☐ Grant: Yale Inst. # ☒ Contract# **1R01MH109413-01** ☐ Contract Pending ☐ Investigator/Department Initiated ☐ Sponsor Initiated ☐ Other, Specify: IRES #: **15-005155**

Note – IRB fees are charged for projects funded by Industry or Other For-Profit Sponsors. Provide the name and Address of the Sponsor Representatives to whom the invoice should be sent. *The PI's home department will be billed if this information is not provided.*

1. **Research Team:** List all members of the research team. Indicate under the affiliation column whether the investigators or study personnel are part of the Yale faculty or staff, or part of the faculty or staff from a collaborating institution, or are not formally affiliated with any institution. **ALL members of the research team MUST complete Human Subject Protection Training (HSPT) and Health Insurance Portability and Accountability Act (HIPAA) training (if applicable) before they may be listed on the protocol. See NOTE below.**

NOTE: The HSC will remove from the protocol any personnel who have not completed required training. A request to change study personnel will need to be submitted when training is completed.

	Name	Affiliation: Yale/Other Institution (Identify)	Net ID
Principal Investigator	John Pachankis, Ph.D.	Yale	jep69
Role: Co-Investigator	Steven Safren, Ph.D.	University of Miami	
Role: Co-Investigator	Mark Hatzenbuehler, Ph.D.	Columbia University	
Role: Co-Investigator	David Paltiel, Ph.D.	Yale	adp6
Role: Co-Investigator (biostatistician)	Denise Esserman, Ph.D.	Yale	dae6
Role: Senior Research Assistant	TJ Sullivan	Yale	tjs66
Role: Study Therapist	Ingrid Solano, MA	SUNY Stony Brook	ias26
Role: Study Therapist	Craig Rodriguez-Seijas, MA	SUNY Stony Brook	cr672
Role: Postdoctoral Fellow	Chuck Burton, Ph.D.	Yale	clb79
Role: Research Assistant	Richard Branstrom, Ph.D.	Yale	pb659
Role: Part-time Research Aide	Colin Kimberlin	Yale	ck624
Role: Research Assistant	Maxwell Richardson	Yale	Mbr42
Role: Study statistician	Jesse Reynolds, M.S.	Yale	Jsr67
Role: Project Coordinator	Roxanne Winston, MPH	Yale	Rw527
Role: Summer Research Assistant	Dominic Schnabel	Yale	Dds36
Role: Research Assistant	Erin McConocha	Yale	Em795
Role: Study Therapist	Tenille Taggart	SUNY Stony Brook	TT443
Role: Study Therapist	Alexander Belser, M.Phil.	New York University	AB2922
Role: Research Assistant	Meghan Michalski	Yale	MM3536
Role: Research Assistant	Arjan van der Star, M.Sc.	Yale	AV564
Role: Study Therapist	Nitzan Cohen	Fordham University	NC545
Role: Study Therapist	Zach Rawlings	Long Island University	ZR63

SECTION IV: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

ESTEEM (Effective Skills to Empower Effective Men) is a 10-session skills-building intervention designed to reduce young gay and bisexual men's (YGBM) co-occurring health risks by reducing the underlying cognitive, affective, and behavioral pathways through which minority stress impairs YGBM's health.[33,34] ESTEEM is based on the Unified Protocol, a cognitive-behavioral therapy (CBT) approach with efficacy across mental health and risk behaviors.[35,36] The Unified Protocol changes underlying stress pathways using motivational interviewing, emotional and situational exposure, cognitive restructuring, mindfulness, and self-monitoring exercises.[35-37] To create ESTEEM, through an NIMH R34 award, our team adapted the Unified Protocol by conducting interviews with 21 YGBM-expert mental health providers and 20 depressed, anxious YGBM at high risk for HIV infection. These stakeholders helped our team infuse the Unified Protocol with minority stress coping content.[34] ESTEEM aims to normalize the adverse impact of minority stress, reduce internalized homophobia and rejection schemas, reduce YGBM's unhealthy avoidance tendencies (e.g., substance use during sex, condom use non-assertion), and validate YGBM's unique strengths. In a preliminary trial (*n*=63), ESTEEM significantly reduced YGBM's spectrum of interrelated health threats, making it the first evidence-based intervention to simultaneously improve mental health, substance use, and sexual health outcomes among YGBM.[33]

Important questions remain in order to validate the efficacy and potential cost-effectiveness of ESTEEM. Accordingly, we propose a 3-arm RCT that would examine (1) whether ESTEEM (arm 1) demonstrates significant improvements compared to existing LGBT-affirmative community mental health treatment (CMHT; arm 2) or standard HIV/STD voluntary counseling and testing (VCT; arm 3) for high-risk depressed and anxious YGBM and (2) whether it improves outcomes through reducing hypothesized cognitive, affective, and behavioral minority stress processes. A transdiagnostic treatment like ESTEEM capable of simultaneously improving mental, behavioral, and sexual outcomes in a relatively short amount of time maximizes treatment resources in constrained economic contexts because it reduces the need for training in multiple interventions for multiple problems. Yet, as the field has been re-examining the potential utility of individual interventions to affect the HIV epidemic, ESTEEM's potential cost-effectiveness in terms of averted mental disorders and HIV infections represents an essential public health question. These unanswered questions will be addressed:

Aim 1: Test the efficacy of ESTEEM against (1) community mental health treatment (CMHT) and (2) HIV/STD voluntary counseling and testing (VCT). Our primary outcome is condomless anal sex in the absence of PrEP, with any HIV+ partner (except primary partners with a known undetectable viral load), casual partner, or status-unknown partner. Knowing whether ESTEEM yields greater improvement than time-matched CMHT will establish the benefit of our *transdiagnostic* approach. Comparing ESTEEM to VCT offers a strong test of ESTEEM's incremental cost-effectiveness.

Aim 2: Determine whether ESTEEM works through its hypothesized cognitive, affective, and behavioral minority stress processes. 4-, 8-, and 12-month follow-ups will determine if improvements in minority stress processes precede and statistically mediate outcome

improvements. Mediation will validate the minority stress theory of ESTEEM and provide transdiagnostic targets for future YGBM health interventions.

Aim 3: Estimate ESTEEM's incremental cost-effectiveness compared to VCT in terms of HIV infections averted and improved mental health. ESTEEM shows preliminary efficacy for improving the full spectrum of YGBM health. We will collect resource use and cost data to estimate return on investment of this transdiagnostic health approach compared to standard single outcome/stand-alone treatment approaches.

2. **Background:** Describe the background information that led to the plan for this project. **Provide references** to support the expectation of obtaining useful scientific data.

Clear and consistent evidence now suggests that young gay and bisexual men (YGBM) disproportionately experience depression, anxiety, and substance use problems compared to heterosexual men.[1-6] Diverse methods locate the source of these disparities in YGBM's exposure to minority stress—the stress associated with stigma-related social disadvantage.[7-10] Minority stress also drives YGBM's HIV risk[11-14] contributing to the reemerging epidemic in this group.[15,16] In fact, minority stress, mental health and substance use disparities, and HIV risk fuel each other, forming a synergistic threat to YGBM's health.[17-20] Yet, no existing evidenced-based intervention addresses minority stress and its impact on HIV risk in HIV-uninfected YGBM.

Minority stress theory suggests that stigma compromises YGBM's health through several cognitive, affective, and behavioral pathways.[10,21] These pathways emerge early in development and include negative thinking styles, unhealthy emotion regulation habits, low behavioral self-efficacy, and behavioral avoidance. Some of these processes are YGBM-specific, such as internalized homophobia and expectations of gay-related rejection;[22,23] others are universal but elevated among YGBM, such as low self-worth and unassertiveness.[24,25] All are related to poor mental health, substance use problems, and HIV risk.[12,23,25-31] Our conceptual model suggests that an intervention that reduces these minority stress processes could simultaneously improve the full spectrum of YGBM's mental, behavioral, and sexual health risks.[32]

3. **Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. If working with a Non-Government Organization (NGO) or other organization, be sure to highlight which are research-only activities and which activities would occur regardless of the research.

We propose to test the efficacy of a principle-based, transdiagnostic (cross-cutting) CBT intervention (ESTEEM) that addresses the pathways through which minority stress compromises YGBM's co-occurring mental (e.g., depression), behavioral (e.g., substance use), and sexual (e.g., condomless anal sex) health problems. In this RCT, we expand upon the initial success of our R34 pilot to examine stronger control conditions (Aim 1), test intervention mechanisms (Aim 2), and estimate cost-effectiveness (Aim 3).

Aim 1: We will utilize two comparison conditions—LGB-affirmative community mental health treatment (CMHT) and brief voluntary HIV testing and counseling (VCT). VCT offers a strong control, as it has been shown to reduce condomless anal sex, but not mental disorders or substance abuse, in a brief risk-reduction session.[104] Standard, non-protocoled LGB-affirmative community mental health treatment (CMHT) represents another important test. The efficacy of CMHT for YGBM has never been tested. This represents a startling gap given the significant male sexual orientation mental health disparities[1-4] and YGBM's disproportionate treatment use.[59] In our R34 pilot, we only compared ESTEEM to waitlist. Thus, comparing ESTEEM against two interventions—one brief (VCT), both widespread—represents an essential next step in determining ESTEEM's efficacy and cost-effectiveness.

Aim 2: Follow-up assessments at 4, 8, and 12 months will allow us to test whether changes in minority stress and mental health precede and statistically mediate the efficacy of ESTEEM. Our pilot's small sample size and lack of follow-up precluded us from testing mediation, but provides path estimates necessary to determine sample size and power in full prospective mediation, as proposed here.

Aim 3: CBT-based interventions, such as ESTEEM, are as effective as medication for depression and anxiety, effects last longer with fewer side effects, and recipients are typically satisfied.[119] However, CBT is costlier than one-session VCT interventions, which have been shown to avert HIV infection but not co-occurring mental health problems. Because of additional time requirements for CBT (e.g., training), CBT is also costlier than CMHT. While the current approach of delivering stand-alone interventions for isolated health risks is inefficient, the cost-effectiveness of multisession skills-based interventions for simultaneously addressing co-occurring health risks among the most vulnerable YGBM remains unknown. Two control groups will allow us to determine whether ESTEEM yields greater return on investment across the spectrum of YGBM's mental, behavioral, and sexual health than current single-outcome interventions. Collecting cost and resource utilization data for all intervention conditions will allow us to determine if the relatively costlier ESTEEM yields greater cost effectiveness and quality-adjusted life years across the spectrum of YGBM's mental, behavioral, and sexual health than common single-outcome interventions, namely CMHT and VCT.

Participants will be randomly assigned to receive one of the following three conditions (ESTEEM, CMHT, VCT only). We will use a 2:2:1 randomization scheme such that for every two participants randomized to ESTEEM, two participants will be randomized to CMHT and one participant will be randomized to VCT only.

Components of all assessments (baseline 1, baseline 2, 4-month, 8-month, 12-month) will take place in our research offices. In the event that a participant moves out of the New York City area or is no longer able to come in to our offices for their follow-up assessessments, we will conduct remote assessments via phone or video conference. The entire baseline 1 assessment will be done in office. Self-report online surveys will be sent to participants via email to complete prior to the in-office components of the baseline 2 and all follow up assessments. Allowing participants to do the online surveys in a location of their choice reduces the concentrated time burden of

each appointment and allows them to answer the questions where they feel most comfortable. Survey questions assessing suicidality will be completed in office under the supervision of a clinical staff member for the baseline 2 and follow up assessment visits. When scheduling any 4-month, 8-month, and 12-month remote follow-up assessment, prior to the appointment a trained study staff member will request participant address via email and locate the nearest emergency services. While assessing suicidality, if there is a concern for safety, just as with any participant seen in the offices, the study staff will contact the nearest emergency services and adhere to the remainder of the established clinical protocol.

ESTEEM treatment will take place over 10 sessions delivered in our offices. All participants, including those randomized to receive VCT only, will receive VCT during the baseline 1 and 12 month follow up appointments, which will take place over one session in our offices. Participants assigned to receive CMHT will receive 10 sessions of CMHT at the Institute for Human Identity (NYC) or Care Resources (Miami). CMHT is not prescribed in our treatment manuals, but is instead delivered by community providers as they usually provide treatment. These two sites are known for providing LGBT-affirmative treatment in safe, supportive environments. ESTEEM and CMHT sessions will be videotaped in the settings where they are delivered [i.e., the Institute for Human Identity (NYC) or Care Resources (Miami)] and both therapists and participants will complete short surveys after each therapy session at the appointment site; all assessments will be completed in our research offices and at home for the baseline 1, baseline 2, 4-month, 8-month, and 12-month assessment visits. Tapes of CMHT sessions will be immediately retrieved from the video recording devices at the CMHT offices by study stuff and provided to PI Pachankis via secure server.

Condition 1: ESTEEM. ESTEEM is a 10-session intervention based on the Unified Protocol,[35,36,120,121] an individually-delivered CBT intervention with efficacy for reducing stress-sensitive mental health disorders (e.g., depression, anxiety) by enhancing emotion regulation skills; reducing avoidance patterns; and improving motivation and self-efficacy for behavior change.[35,122] The Unified Protocol employs modules for motivation enhancement, interoceptive and situational exposure, cognitive restructuring, mindfulness, and self-monitoring techniques. Through an extensive R34 adaptation process described above,[34] we adapted the Unified Protocol to enhance YGBM's stigma coping by reducing minority stress processes. For example, modules were adapted to help YGBM identify minority stress experiences; track unhealthy reactions to minority stress, focusing on avoidance reactions, like substance use and condomless anal sex; attribute distress to minority stress rather than to personal failure; and assert themselves against unjust minority stress in safe situations. Adaptations were infused throughout the Unified Protocol *Therapist Workbook*;[123] this adaptation served as the therapist manual. The full manual is attached. ESTEEM participants will complete 10 sessions of therapy, with one session per week. If participants miss sessions or need to reschedule, we will make every effort to reschedule sessions such that participants stay as close to a one session per week schedule. If participants miss a week, they may be rescheduled to do two sessions in one week, but they will be told the goal is once per week. All sessions must be completed within four months.

Condition 2: CMHT. The current standard of care for LGB individuals who seek mental, behavioral, or sexual health care is LGB-affirmative therapy.[124] The practice of LGB-affirmative therapy is outlined across 21 guidelines published by the American Psychological Association. However, the efficacy of LGB-affirmative psychotherapy has never been tested,[125] despite several promising case studies.[126-128] Following previous tests of innovative NIMH-funded interventions,[129] we will refer YGBM to community clinicians who provide this standard of care. In NYC, this community clinic will be the Institute for Human Identity (322 Eighth Ave., New York, NY 10001). In Miami, this community clinic will be Care Resources (3510 Biscayne Blvd., Miami, FL 33137). CMHT therapists and participants randomized to CMHT will complete short surveys after each CMHT therapy session. Similar to participants randomized to ESTEEM, CMHT participants will complete 10 sessions of therapy, with one session per week. If participants miss sessions or need to reschedule, we will make every effort to reschedule sessions such that participants stay as close to a one session per week schedule. If participants miss a week, they may be rescheduled to do two sessions in one week, but they will be told the goal is once per week. All sessions must be completed within four months.

Condition 3: VCT only. Participants in all arms will receive VCT at their first baseline visit, before being randomized to their respective arms—ESTEEM, CMHT, or VCT only and again at the 12 month follow-up visit. Participants randomized to the VCT only arm will not receive any further intervention. We base VCT on CDC guidelines and the control arms of large community-based RCTs (e.g., Projects RESPECT, EXPLORE, AWARE).[101-104] VCT will consist of one unique 45-minute session given that 1-session VCT is as effective as 2-session VCT for GBM.[103] At the beginning of the session, the counselor will explain the purpose of HIV and STD testing, and with the participant's consent, administer an OraQuick® Rapid HIV-1/2 antibody test. While waiting for test results, the participant will provide a urine sample and oral and rectal swabs for chlamydia and gonorrhea testing, and, when done, the counselor will review a handout containing facts about HIV/STD transmission risk and PrEP. Misconceptions will be clarified. This handout will contain provider referrals for participants interested in PrEP or other HIV/STD prevention services. The counselor will then engage in a person-centered discussion to elicit the participant's current risk behavior, the contextual drivers of the behavior, perceptions of the pros/cons of continuing the behavior, and self-efficacy for changing the behavior based on the participant's past success. A personalized risk-reduction plan will be created that includes specific, achievable goals the participant can implement to reduce risk.[103] These goals will be written on the pamphlet. Participants who receive a preliminary positive HIV test result will be referred to nearby community health centers (e.g., Care Resource, Gay Men's Health Crisis, Callen-Lorde Community Health Center, Mount Sinai Beth Israel) for confirmatory testing and appropriate care. Urine, oral, and rectal samples will be sent to a lab (Quest Diagnostics) for testing. We will notify participants who screen positive for chlamydia or gonorrhea immediately upon receiving the lab results and refer them to a nearby community health center or their own medical provider for treatment.

4. **Participant Population:** Provide a detailed description of the types of participants who will be recruited into this study.

Intervention Participants:

Inclusion criteria. Eligible participants will meet the following criteria: (1) aged 18-35, (2) identify as a gay or bisexual man, (3) HIV-negative status, (4) diagnosis of any *DSM* depressive, anxiety, or trauma- and stressor-related disorder; (5) HIV sexual risk (≥1 act of condomless anal with a male partner of unknown status or HIV+ status, unless with a HIV+ primary/main partner with known undetectable viral load); (6) not currently adherent to PrEP (defined as taking 4 or more days per week) (7) NYC or Miami residential stability and planned availability for 12 months; and (8) provision of informed consent.

Exclusion criteria. Participants will be excluded for any of the following: 1) current active suicidality or homicidality (defined as active intent or concrete plan, as opposed to passive suicidal ideation); 2) evidence of active untreated mania, psychosis, or gross cognitive impairment; 3) current enrollment in an intervention study; 4) current enrollment in intensive mental health treatment (receiving treatment more than once per month or 8 or more sessions of CBT within the past year); or 5) HIV-positive status.

CMHT Therapist Participants:

Therapists at our CMHT sites will be considered participants in the study, as they will be videotaped and will complete short assessments after each therapy session. We will also collect demographic information about each therapist, including race, sexual orientation, and years of work experience from the CMHT therapists prior to their meeting with therapy participants. To be included as participants in the study, CMHT therapists must be currently providing therapy on an ongoing basis at the CMHT sites (Institute for Human Identity in New York City and Care Resources in Miami).

5. **Describe** how access to the population will be gained in the study.

We will use active and passive recruitment strategies. Active approaches will involve conducting eligibility screening via electronic tablet at bars/clubs and support groups (e.g., coming out groups and 20-somethings group at the NYC LGBT Center). Passive approaches will involve advertising on YGBM-oriented mobile apps and websites (e.g., Grindr, Scruff, BGCLive, Growlr), clinic waiting rooms (e.g., Callen-Lorde Community Health Center, college counseling centers), YGBM-focused media (e.g., Craigslist, Facebook, Reddit, party listservs), and referrals from previous or current study participants. As part of passive recruitment we will also contact participants from previous research studies who consented to be contacted for future studies. Advertisements will engage help-seeking YGBM by emphasizing the study as a safe venue for discussing sex and HIV.

CMHT therapists will be identified by directors at our CMHT partner sites.

6. **Participant classification:** Check off all classifications of participants that will be <u>specifically recruited for enrollment</u> in the research project. Will participants who may require additional safeguards or

other considerations be enrolled in the study? If so, identify the population of participants requiring special safeguards and provide a justification for their involvement.

☐ Children ☒ Healthy ☐ Non-English Speaking ☐ Prisoners
☐ Economically disadvantaged
☐ Decisionally Impaired ☐ Employees ☐ Pregnant women
☐ Yale Students
☐ Other vulnerable population (who?):
☐ Psychology Pool

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential participants? ☐ Yes ☒ No (If yes, see HRPP Policy 310.4 for further requirements)

7. **Inclusion/Exclusion Criteria:** What are the criteria used to determine participant inclusion or exclusion?

Inclusion criteria. Eligible study participants will meet the following criteria: (1) aged 18-35, (2) identify as a gay or bisexual man, (3) HIV-negative status, (4) diagnosis of any *DSM* depressive, anxiety, or trauma- and stressor-related disorder; (5) HIV sexual risk (≥1 act of condomless anal sex with a male partner of unknown status or HIV+ status, unless with a HIV+ primary/main partner with known undetectable viral load); (6) not currently adherent to PrEP (defined as taking 4 or more days per week); (7) NYC or Miami residential stability and planned availability for 12 months; and (8) provision of informed consent. Eligible CHMT therapists must be approved therapists at the CMHT sites.

Exclusion criteria. Intervention participants will be excluded for any of the following: 1) current active suicidality or homicidality (defined as active intent or concrete plan, as opposed to passive suicidal ideation); 2) evidence of active, untreated mania, psychosis or gross cognitive impairment; 3) current enrollment in an intervention study; 4) current enrollment in intensive mental health treatment (receiving treatment more than once per month or 8 or more sessions of CBT within the past year); or 5) HIV-positive status. There are no exclusion criteria for CMHT therapists other than refusal to provide consent to study procedures.

SECTION V: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. **Recruitment Procedures:**
    1. Describe how potential participants will be identified and contacted, and by whom.

We will employ a number of strategies to recruit intervention participants. These strategies are designed to recruit an ethnically diverse sample from multiple types of venues in which gay and bisexual men are likely to be accessed (e.g., online social networking apps and websites, social

venues, community based organizations, health care organizations, gay bars/clubs).

1) Online recruitment. Online recruitment for our existing studies has been successfully utilized. The proposed study's ads will target HIV-negative gay and bisexual men who are over 18 years old and who experience symptoms of depression or anxiety. We will advertise on Facebook, Craigslist, and other social networking sites for gay and bisexual men. Potential participants will link to our website, read about the study and undergo a screener.

2) Passive recruitment. Passive recruitment will be employed at different venues, including, for example, locations and events serving YGBM, such as bars and dance clubs, Pride events, street fairs, bookstores, community centers, and health care clinics. These venues will have given us permission to post recruitment materials. Our recruitment staff will provide venues with recruitment materials such as tear off flyers and recruitment cards containing information such as study name, goals, and contact information for those interested in screening for eligibility.

3) Recruitment of participants from past studies. At the end of one of our current studies (Urban Migration, Self-Regulation, and Drug Abuse and HIV Risk Among Young Men, Protocol #: 1405013946), we ask participants whether they would be willing to be contacted for future studies. Participants who consented to be contacted for future research will be contacted using contact information they provided. We will also recruit from a prior study called Gay Community Stressors Among Gay, Bisexual, and Queer Men (Protocol #:1512016893). Additionally, participants from a colleague's study (Intervention to Promote PrEP Awareness and Equitable Prescription among Providers, Protocol #: 1308012487) who consented to being contacted for future studies for which they may qualify may be contacted using the contact information they provided. As well as participants who consented to being contacted for future studies from the Center for Human Identity and Behavior Prevention studies lab.

4) Active recruitment. In active recruitment, our recruitment staff will approach potential participants in a wide range of venues frequented by gay and bisexual men and ask if they might be willing to speak with them for a couple of minutes about HIV prevention and psychosocial health research. If the individual is willing, the recruiter will briefly describe the study and ask if they would be willing to answer a few questions to see if they might be eligible. If the potential participant does not want to answer the questions right then, the recruiter will give the participant a recruitment card and ask them to call the study number should they decide they would like to participate at some point in the future.

If the potential participant agrees to answer the eligibility questions, the recruiter will give the participant a tablet device so that they may answer the screening questions in private. The field screening questions are designed to give a general sense of eligibility for the project (such as age, recent sex, and HIV status), but not to determine strict eligibility for the study. At the end of the screening questions, the participant will be prompted to provide their name and contact information for later follow up. The participant will have the opportunity to have his contact information deleted in the event he is not eligible nor interested in future studies. The recruiter will inform interested participants that they will receive a call to participate in a full study

screener if they are eligible for the study. If not, participants will not be follow up with.

Recruiters will visit bars/clubs to post study materials and hand out study contact information. Recruiters will also visit bars/clubs and other venues with tablets set up with screening questions for the potential participant to complete; this field screening survey is preliminary and if the potential participant screens eligible, he will provide contact information within the survey, after which the recruiter will inform him that he can expect a call/email from a research assistant to complete the full study screener. The tablet will be password protected. No data will be stored on the tablet. The survey will be hosted on Qualtrics and only accessed if wifi is available to complete it. Use of a tablet to complete a preliminary screening helps to maintain privacy, even in a crowded bar setting, given that the potential participant can read the survey to himself, rather than answering questions aloud to the recruiter; a privacy screen protector will also be used on the tablet so as to prevent outsiders from overseeing questions/responses on the tablet. As an additional measure of privacy, recruiters will locate the most private part of the bar/club to do these screenings.

Throughout the course of the study, we will periodically hold sweepstakes for people who complete our in-person screening survey. We will pool the contact information for all people who completed the survey during our event (noted by timestamp) and will use a random number generator to select people to win the prize. The sweepstakes prize will be a $25 gift card that will be emailed to them immediately after the selection of the winners.

5) Letters and postcards sent to community organizations. We will send a letter and postcards to community organizations, including community-based organizations supporting the LGBT community and local college counseling centers. The letter will ask these organizations to distribute the postcards in their waiting areas and to potentially eligibile individuals.

6) Peer-recruitment and referrals by previous and current study participants. Participants in the study will be asked to distribute study recruitment materials to peers who may be interested in participating in the study. Participants will be reminded that staff will never disclose any information about an individual's participantion in the study, but that participants are free to disclose information about their own participation to whomever they desire. Participants are not required to distribute recruitment materials as a condition of study participation and the strictly voluntary nature of this request will be emphasized by study staff.

Recruitment text and images are attached to this application.

Are you collecting any information about the individuals prior to their signing a consent form?
Yes ☐ No ☒
If yes, indicate what information you will be collecting and how it will be gathered *(phone screen, paper questionnaire, etc.)*

2. **Indicate recruitment methods below.** Attach copies of any recruitment materials that will be used.

☒ Flyers
☐ Posters
☐ Letter
☒ Newspaper
☒ Through local NGO or other local contact
☐ Classroom recruitment
☒ Table set-up / in-person recruitment of public
☒ Snowball sampling
☐ Other (describe):

☒ Internet/Web Postings
☒ Mass E-mail Solicitation
☐ Departmental/Center Website
☒ Social Media (Facebook, Twitter)

☐ Radio
☒ Telephone
☐ Television

3. **Targeted Enrollment: Give the number of participants:**
   1. Targeted for enrollment at Yale (site: New York) for this protocol: 150
   2. If this is a multi-site study, give the total number of participants targeted across all sites:

New York: 150 (60 ESTEEM, 60 CMHT, 30 VCT)
Miami: 100 (40 ESTEEM, 40 CMHT, 20 VCT)

4. **How was this estimate derived?**

Our primary goal is to demonstrate a greater reduction at 4, 8, and 12 months in "unprotected sex" as defined as past-90-day condomless anal sex without PrEP or with HIV+ or status-unknown casual partners or with HIV+ primary partners without known undetectable viral load, in the ESTEEM arm versus the CMHT and VCT arms. In our pilot study, we saw a 60% reduction in condomless anal sex at 6 months in the ESTEEM arm. Based on previous studies of VCT[104] and the fact that CMHT does not specifically focus on condomless anal sex, we expect that these arms will yield lower reductions compared to ESTEEM, but a slightly larger reduction in CMHT (20%) compared to VCT (15%). To achieve at least 90% power at a 5% type I error rate, accounting for an R-square of 0.1 between treatment arm and the covariates, we will need 80 individuals in the ESTEEM and CMHT arms, and 40 individuals in the VCT arm. Although we plan to take steps to increase our retention rate from our pilot study, we conservatively estimate the retention at 6 months to be 80%. Therefore, we plan to randomize 100 ESTEEM, 100 CMHT and 50 VCT YGBM. Sample size calculations were carried out using PASS 12 (Kaysville, Utah) for logistic regression. For secondary outcomes (e.g., mental health, substance use), we will have 80% power to detect an effect size of 0.55 and 0.70 for ESTEEM vs. CMHT and ESTEEM vs. VCT, respectively, at a type I error rate of 0.01 (conservative due to multiple testing). These effect sizes are smaller than those found in the pilot.

5. **Consent Personnel:** List the names of all members of the research team who will be obtaining consent/assent.

John Pachankis, Ph.D.
Steven Safren, Ph.D
Richard Branstrom, Ph.D.
TJ Sullivan, BA
Craig Rodriguez-Seijas, MA
Ingrid Solano, MA
Chuck Burton, Ph.D.
Roxanne Winston, MPH
Dominic Schnabel
Erin McConocha
Tenille Taggart
Colin Kimberlin
Cal Brisbin
Meghan Michalski
Alexander Belser
Arjan van der Star, M.Sc.
Maxwell Richardson
Nitzan Cohen
Zach Rawlings

6. **Process of Consent/Assent** *(NOTE: When a study includes minors, parent provide permission [not consent] for the child's participation, and the child provides assent for participation)*

Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure participants' independent decision-making.

Informed consent will be obtained for all participants at two points – before completion of the phone screener and/or in-person screener and before completion of the first in-office baseline assessment. A small selection of participants previously randomized to ESTEEM will also be contacted an additional time by research staff to gain consent for our team to display short clips of their therapy sessions during training of community therapists in ESTEEM therapy techniques.

Before administering the phone screener, a project staff member will first assess participants' willingness and capacity to consent to completing the brief (15 min) screener to determine eligibility. Participants will provide their verbal consent for the phone screener. Participants' identifying information, including their name, will be kept in a separate database from the remainder of their study responses.

Before completing the in-person screener, participants will review an online consent form describing the screening purpose and risks/benefits and indicate their consent by selecting the

commensurate button. Participants' identifying information, including their name, will be kept in a separate database from the remainder of their study responses. Participants who are deemed preliminarily eligible based on the in-person screen will be contacted by our study staff to confirm eligibility by phone screen.

Participants who are deemed eligible based on the phone screener will then be invited to the office for a baseline 1 appointment. During this appointment, participants will complete a written consent. After the baseline 2 appointment, participants will be randomized to either the ESTEEM intervention, CMHT, or VCT.

During phone and in-office consent, a trained staff member will review the consent form in person, including details of the full study and study risks and precautions against risk. Participants who choose to participate in the remainder of the study will be asked to sign the consent form in the presence of the staff member (in-office) or provide verbal consent (phone screen).

We will select video clips from approximately 12 total sessions delivered to approximately five currently and formerly enrolled study participants. These videos do not contain participants' faces or identifiable information other than participants' voice and therapists' image and voice. Selected participants who have completed ESTEEM therapy will be contacted prior to completion of the study or after completion of the study in order for us to gain consent to present small portions of their therapy videos during future professional trainings at community-based clinics and agencies. Participant will be contacted by either an ESTEEM therapist or a research team member. The research team member or therapist will clearly explain that videos will only be used for instructional purpose to train community clinicians and future trainees on the ESTEEM therapy protocol. They will also be reminded in that videos do not include the participant's face or any identifiable information, only their voice and the therapist's face and voice. The therapist or research team member will explicitly state that the participant is free to decline or to ask any questions about the purpose of this request. Newly recruited participants will be able to note on the informed consent form whether or not they consent to have a small selection of their therapy recording used in the future for new therapist trainings.

CMHT therapists will provide written consent prior to providing therapy to their first participant.

7. **Evaluation of Participant(s) Capacity to Provide Informed Consent/Assent:** Indicate how the personnel obtaining consent will assess the potential participant's ability and capacity to consent to the research being proposed, if applicable

Prior to the in-office appointments, a trained Research Assistant (RA) will assess participants' consent in a private room. The RA will ensure that the participant understands the risks associated with the disclosure of information that could indicate imminent threat to self or others. Verification of comprehension of informed consent will be accomplished by asking participants to recall central points in the consent process; points of confusion will be clarified. Once participants have fully understood the consent, they will be asked to sign the consent form.

RAs will be instructed to contact the PI or project coordinator if he or she is unsure about any participant's capacity to consent.

For the phone screener, participants will be asked to provide verbal consent prior to answering the screener questions.

For the in-person screener, recruitment staff will assess willingness and capacity to consent to completing the brief (4 min) screener to determine eligibility (e.g., visible signs of substance intoxication). Those who are deemed capable of providing consent will be asked to review the consent form and indicate their consent on the consent form delivered via iPad / tablet. Participants who are deemed to be incapable of providing consent will be provided with a recruitment card with our contact information in order to contact our office for a phone screen once they are not incapacitated.

CMHT therapists will receive hard copies of consent forms and will sign the consent forms prior to providing therapy to their first participant.

8. **Documentation of Consent/Assent:** Specify the documents or verbal scripts that will be used during the consent/assent process. Copies of all documents should be appended to the protocol, in the same format that they will be given or spoken to participants.

Please find attached a copy of the: 1) phone screener consent text, 2) in-person consent, 3) in office consent, 4) therapy video viewing consent text, 5) consent form for CMHT therapists.

9. **Non-English Speaking Participants:** Explain provisions in place to ensure comprehension for research involving non-English speaking participants. Translated copies of all consent materials must be submitted for approval prior to use. **Do you speak the local language? Will you require a translator? (If so, please elaborate on how the translators will be trained).**

At this point, only English speakers will be enrolled in this study.

10. Are any of the study procedures likely to yield information subject to mandatory reporting requirements? (e.g. HIV testing – reporting of communicable diseases; parent interview -incidents of child abuse, elderly abuse, etc.). Please verify to whom such instances will need to be reported.

HIV and STI Testing
We will be conducting HIV testing using OraQuick® HIV-1/2 Antibody Test, an oral swab rapid test [sensitivity: 99.6% (98.5–99.9); specificity: 100% (99.7–100)] on all participants at two time points (in-office baseline and 12-month follow-up assessment appointments). All project staff will complete HIV/STI testing and counseling training.

Like conventional HIV enzyme immunoassays (EIAs), rapid HIV tests are *screening* (i.e., not diagnostic) tests that require diagnostic confirmation by Western Blots if reactive (positive).

Participants who test preliminarily positive will be immediately referred to local community HIV clinics (e.g., Callen-Lorde Community Health or Beth Israel in NYC, Care Resources in Miami) for confirmatory testing, care, and treatment. If a participant is unaware of his HIV status and tests positive for the first time in our study, he will be referred for immediate counseling and treatment. Appropriate risk-reduction counseling will be provided to all participants as part of their study participation as part of the VCT condition, which all participants will receive. Participants testing HIV positive will not be randomized into the study, as HIV negative status is one of the inclusion criteria, so they will receive immediate counseling by study staff. Study staff will provide all participants with lubricant and condoms. Study staff will seek HIV testing consent from the participants during the informed consent process. HIV test results will be returned to participants by trained study staff during the same day as testing. If the participant is preliminarily determined to be HIV-infected, study staff will direct the participant to established services for HIV-infected individuals in NYC or Miami; study staff will make an appointment for participants at the participant's desired confirmatory testing site (either our recommendation or their current provider). We will provide a staff escort to one of the recommended testing sites for participants who explicitly request such.

Participants will receive results of the HIV rapid testing in person from the VCT counselor, following the guidelines in the VCT manual. The rapid test results will be ready in 20 minutes. In the rare event that a participant needs to leave prior to receiving the results, the counselor will schedule a time to return to the study site to be retested so that he can receive results in person. If for some reason, the participant cannot return to be retested, we will provide results by phone with clear instructions regarding how to seek confirmatory testing if necessary. The clinical protocol will be followed.

STI testing (chlamydia and gonorrhea) will utilize the Quest Diagnostics collection kits for urine sample and rectal and oral swap collection. Participants will self-administer these sample collections following instructions of the trained research staff member. The counselor will follow Quest Diagnostics protocol for sending the samples to the assigned Quest laboratory location for assaying. Quest will send the test results to ESTEEM within one week, at which point ESTEEM staff will immediately notify participants of the results. A positive test is sufficient for diagnosis and participants will be directed to the respective partnering community clinic for treatment and follow up, unless participant prefers to access care at health clinic of his choice.

Sites that conduct screening tests such as our HIV screening test are required to connect participants to a site capable of providing confirmatory testing in the event of a preliminary positive. With regards to gonorrhea or chlamydia testing, participants who test positive for gonorrhea or chlamydia must be reported to the Department of Health. However, participants themselves will not be contacted if nucleic acid amplification testing is used to determine results, as planned for this study. Participants will be notified of this requirement in the written consent form given at the baseline assessment. In Florida law, there is a provision for identity protection of participants for "authorized medical or epidemiological researchers who may not further disclose any identifying characteristics or information;" participants are assured of their identity protection throughout the course of the study, and given the epidemiological nature of this

research, in accordance with Florida law, we will not be required to report individuals who screen as STI-positive during ESTEEM. Click here to access Florida reporting laws.

We will make every effort to ensure that participants with positive results are referred and have access to care at formal health clinics for confirmatory testing and follow-up care. These health facilities and healthcare providers will be subject to mandatory reporting laws governing their services, as any of the testing that takes place outside of ESTEEM will not be considered as testing for research purposes.

Suicidality, Homicidality, Severe Distress, Violence
Our ESTEEM clinical protocol successfully guided reporting of instances of suicidality, homicidality, severe emotional distress, and violence in our ESTEEM pilot trial. We will employ the same protocol in this study. The clinical protocol is attached. The protocol specifies that, in the event that a participant is at imminent risk of harming themselves or another person, as determined by a study staff member with mental health training, study staff will contact 911 to dispatch police or paramedics. Only the minimal necessary identifying information will be provided to these personnel. In less imminent instances of distress, we will refer distressed participants to local mental or behavioral health services. All self-report questionnaires assessing suicidality will be given in-office where participants can be monitored by a clinical staff member. Clinical staff members will receive an alert if the participant answers the online questionnaires in a manner that signals distress; such participants will be met by the clinical staff member on site to assess risk.

Participants will be notified of the reporting requirements under these circumstances during the consent process.

In the event that a participant is unable to complete the self-report questionnaires in the office, we will conduct remote assessments. Prior to these assesments, the Senior Research Assistant will contact the participant to locate their nearest emergency services. The session will be completed via video or phone call depending on participant preference. It will be conducted by a clinically trained research staff member who will administer the assessment and will follow the same in-office clinical protocol for expressed imminent participant distress, by contacting the participant's nearest emergency services only in the instance of imminent risk.

11. **Consent/Consent Waiver: In certain circumstances, the IRB may grant a waiver of documentation of consent, or a full waiver of consent, depending on the study.** If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

- ☐ **I plan to obtain signed consent**
- ☐ **I plan to obtain verbal or online consent**
- ☒ **I plan to obtain signed consent for part of the study, and verbal or online consent for another part of the study.**
- ☐ **I do not plan on obtaining consent due to the nature of the study (explain):**

☒ **Requesting a waiver of documentation of consent** (Note that an information sheet may be required.)

If requesting a waiver of documentation of consent, please address the following:
a. Would the signed consent form be the only record linking the participant and the research? ☐ Yes ☒ No
b. Does a breach of confidentiality constitute the principal risk to participants?
☒ Yes ☐ No

OR

a. Does the research pose greater than minimal risk? ☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** ☒ No

AND

b. Does the research include any activities that would require signed consent in a non-research context? ☐ Yes ☒ No

Consent will be obtained for all study components either verbally or signed or online as described above. However, we will not require participants to provide their name when consenting to completing the brief screen to be administered via electronic tablets at local venues (e.g., gay bars, clubs, parks). This brief (4 min) screen will assess age, HIV status, HIV and substance use risk behavior, and depression and anxiety symptoms to determine preliminary eligibility for this study. This brief screen does not pose greater than minimal risk. Before completing this screen, participants will be told via online text that this screen will ask several personal questions to determine eligibility for a larger study and that participants can choose to provide their name and contact information after they have found out if they are eligible via the electronic screen. Preliminarily eligible participants will be asked to provide their name and contact information in order to receive a call or email containing more information on how to complete a more comprehensive phone screen to verify study eligibility. Participants' identifying information, including their name, will be kept in a separate database from the remainder of their study responses. Participants will provide consent before completing this more comprehensive phone screen, as described above.

☐ **Requesting a full waiver of consent**

If requesting a full waiver of consent, please address the following:

a. Does the research pose greater than minimal risk to participants?
☐ Yes ***If you answered yes, stop. A waiver cannot be granted.***
☐ No
b. Will the waiver adversely affect participants' rights and welfare? ☐ Yes ☐ No
c. Why would the research be impracticable to conduct without the waiver?
d. Where appropriate, how will pertinent information be returned to, or shared with participants at a later date?

SECTION VI: PROTECTION OF RESEARCH PARTICIPANTS

Confidentiality & Security of Data:

1. What participant information will you be collecting?

The full packet of study measures and assessments is attached to this application. We propose to collect information about participants' general mental health status; HIV risk; demographics; HIV status; chlamydia and gonorrhea infection; experiences with stigma-related stress; depression and anxiety; cognitive, affective, and interpersonal functioning (e.g., rumination, social support, impulsivity, assertiveness); mental health treatment history and perspectives; substance use; sexual compulsivity; and perceptions of intervention helpfulness. We will also video tape-record all intervention sessions. Counselors will also complete session notes. Each participant will have a binder that contains all session notes. No name will be attached to the binder, only participant ID. The binders will be locked in a filing cabinet.

Participants will provide the following data at baseline and 4-, 8-, and 12-month follow-up appointments: (1) quantitative assessments, previously used with young gay and bisexual men, of mental health, substance use, and stigma-related stress, (2) interviewer-administered timeline follow-back of HIV risk behavior, including condomless anal, sex while under the influence of drugs or alcohol, PrEP use and adherence, and number of sexual partners, during the previous 3 months, (3) interviewer-administered mental health assessment with the Mini-International Neuropsychiatric Interview (MINI), (4) OraSure rapid HIV 1/2 antibody test (at baseline and 12-month follow-up), (5) urine sample and rectal and oral swabs for chlamydia and gonorrhea testing (at baseline and 12-month follow-up), and (6) engagement in the intervention.

Participants who complete remote assessments will be asked to provide their address to research staff to aide in establishing contact with the nearest emergencies services, if necessary. This information will be stored in a password protected contact database on secure Box only accessible to research staff. Once addresses are stored in the database, any emails containing identifiable participant information will immediately be hard deleted from study inboxes.

2. Will any of the following identifiers be collected?

☒ Names
☒ All geographic subdivisions smaller than a State, including: street address, city, county, precinct, zip codes
☒ Telephone numbers
☐ Fax numbers
☒ E-mail addresses
☐ Social Security numbers
☐ Medical record numbers
☐ Health plan beneficiary numbers
☐ Account numbers

☒ All elements of dates (except year) for dates related to an individual, including: birth date, admission date, discharge date, date of death, all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
☐ Certificate/license numbers
☐ Vehicle identifiers and serial numbers, including license plate numbers
☐ Device identifiers and serial numbers
☐ Web Universal Resource Locators (URLs)
☒ Internet Protocol (IP) address numbers
☐ Biometric identifiers, including finger and voiceprints
☐ Full face photographic images and any comparable images
☐ Any other unique identifying numbers, characteristics, or codes

Other potentially identifying information to be collected:
☐ Audiotapes
☒ Videotapes
☐ Faces (focus groups, photographs or other way that an individual would be physically recognized)
☐ Potential for identification from the bulk of the information, even if direct identifiers are not collected (deductive disclosure).

3. If applicable, what methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the participant's participation in the study?

Do all portable devices contain encryption software? ☐ Yes ☒ No

If no, seehttp://its.yale.edu/secure-computing/protecting-yales-data/data-encryption and http://hipaa.yale.edu/guidance/policy.html

The primary potential risk to participants is breach of confidentiality. Breaches of confidentiality will occur if a participant reports a clear intention to harm himself or another person. Additionally, health care professionals are required by state law to report suspected cases of abuse or neglect. The likelihood that any additional breaches of confidentiality would occur is minimal, as steps will be taken to guard against this risk. To protect participants' confidentiality, we will obtain a Federal Certificate of Confidentiality prior to enrolling participants. All counselors and research assistants (RAs) will undergo rigorous training in maintaining participants' privacy and confidentiality and will be in possession of valid Collaborative Institutional Training Initiative (CITI) certificates. Further, immediately upon providing consent, all participants will be assigned an identification number, which will only be kept on an electronic database that will be password protected and located on a designated study computer. This information will not be stored with any other data and no other identifying information will appear on any form. All contact with participants will be made by therapists and research staff under explicit guidelines to preserve confidentiality when telephoning, emailing, or mailing information to participants. All materials with identifying information will be kept in one password protected electronic file. Participants will provide the respective site, Yale or Miami, with alternative contact information (email, phone numbers, and mailing address) for compensation and study retention purposes. This information will be treated in the same confidential manner as all participant information, as described here. For participants

who consent to the presentation of small portions of their therapy videos to future trainees at community clinics and agencies, they will be reminded by the therapist or research team member acquiring this specific consent that all therapy video sessions only contain their voice and no images of their face or other identifying information.

Secure digital (SD) memory cards for the recording equipment will be stored at the research study site. When the video cameras are at community sites they will be retrieved weekly and brought back to the study site in a lock box. Data will immediately be uploaded to the Secure Box server on a Yale computer and the memory cards will be cleared.

4. How will the research data be collected, recorded and stored?

Research data will be collected via telephone, on electronic tablets, electronic databases, survey websites, paper-and-pencil, electronic documents, video recording, and specimen sample for HIV, chlamydia, and gonorrhea.

Preliminary screening data will be collected in the field using online tablets. Screening data will also be collected on a secure survey website (Qualtrics.com) and via telephone, whereby a study staff member asks the potential participant a series of eligibility questions and enters this information into an electronic database at our research offices. Participants will complete surveys at our study sites/offices via yale.qualtrics.com. Participants themselves will enter most data into Qualtrics.com directly. However, study staff will enter interviewer-based data (e.g., clinical diagnostic assessment, timeline follow-back interview of risk behavior) into Qualtrics.com during the interview. Study sessions will be videotaped for quality control and will be downloaded to Yale's HIPAA-compliant Secure Box drive upon retrieval from study cameras. Participant session notes will be stored in a binder unique to each participant; these binders will be stored in a locked filing cabinet. Participant tracking and scheduling data will be recorded on a study database. One password-protected linking database containing participant names and ID codes will be kept at each of our offices and accessible only be study staff.

Participants will be identified with participant ID number, not with participant name. The diagnostic laboratory that will assay for chlamydia and gonorrhea will not have access to participants' names, only their ID number.

All study computers will be encrypted and password protected. All filing cabinets will be locked. Online surveys (yale.qualtrics.com) will use an encrypted web service (https) and will not ask participants' name or other identifying information, only participant ID number. The linking database will be kept separate from study data and will be password protected.

5. How will the digital data be stored? ☐ CD ☐ DVD ☒ Flash Drive ☐ Portable Hard Drive ☒ Secured Server ☒ Laptop Computer ☒ Desktop Computer ☐ Audiotaping ☒ Videotaping ☐ Handwritten notes ☐ Other

1. If applicable, how will transfer of data to Yale be completed? See http://its.yale.edu/secure-computing/protecting-yales-data/data-and-information-classification-yale-university

Data will be transferred from the University of Miami to Yale using the HIPAA compliant Yale Box. Videotape data from our CMHT sites will be retrieved in person by a study staff member transported via lock box to the research study office and downloaded to Yale Box upon arriving to our offices.

2. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data or the link to personal identifiers? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.

After study completion, data will be stored on an encrypted, password-protected server at the Yale School of Public Health. The identifiable data will remain separate from the remainder of participant data. After three years of study completion, the link to personal identifiers will be destroyed.

3. Will a Certificate of Confidentiality be needed? (*See also the NIH Certificate of Confidentiality Kiosk, http://grants.nih.gov/grants/policy/coc/index.htm)*

We have received an NIH Certificate of Confidentiality.

SECTION VII: POTENTIAL RISKS AND BENEFITS

1. **Risks:** Describe the reasonably foreseeable risks, including risks to participant privacy, discomforts, or inconveniences associated with participants participating in the research. *Note: <u>All</u> studies have the potential for risk, if not physical, there may be psychological, reputational, or financial risks or risks to breach of confidentiality*

The study participants are at minimal risk for harm as a result of participation in the proposed research study. Although unlikely, one risk of the proposed study is that participants will experience emotional discomfort as a result of completing the quantitative assessments or the intervention. Breach of participants' confidentiality presents another possible risk. The investigative team's strategies to protect against both risks are described below.

Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.

Recruitment and Informed Consent: The investigative team has conducted a number of studies involving young gay and bisexual men, which have involved asking participants to complete potentially sensitive interviews and self-report measures. Thus, we have extensive protocols in place for all aspects of the study. All staff complete IRB (re)certification as required. All new staff and research volunteers will receive local training in issues pertinent to research among young gay and bisexual men, and will sign a confidentiality pledge prior to any contact with participants or

data. No identifying information is collected prior to the moment at which a participant provides informed consent.

Participants will be actively recruited into the study by completing a brief screening instrument on a tablet device at the venue in which they were recruited or will be given an information card highlighting the goals of the project as well as a number to contact should they wish to participate. Passively recruited participants will be informed of the study through a posted flyer or website banner containing identical information as the information card used for active recruitment, including instructions to call the number should they wish to participate. Before completing phone screening questions, participants will be briefed on consent and asked to provide verbal consent specific to the screening.

Prior to the in-office appointments, a trained Research Assistant (RA) will assess participants' consent in a private room. The RA will ensure that the participant understands the risks associated with the disclosure of information that could indicate imminent threat to self or others. Verification of comprehension of informed consent will be accomplished by asking participants to recall central points in the consent process; points of confusion will be clarified. Once participants have fully understood the consent, they will be asked to sign the consent form. RAs will be instructed to contact the PI or project coordinator if he or she is unsure about any participant's capacity to consent.

Protection Against Emotional Discomfort. It is possible that participants may experience emotional discomfort in responding to assessments or receiving HIV/STD test results. While every possible step will be taken to minimize such risk, consent documentation will make it clear that if participants have any concerns about any aspect of the study they may refuse to continue with the study at any time, without penalty. In addition, we will remind participants during the course of their assessments that they can refuse to answer any questions and may discontinue participation at any time. Staff members at our Yale and Miami labs will be thoroughly trained in appropriate responses to participant distress through tri-annual trainings by a licensed clinical psychologist. This training will address the appropriate handling of imminent threats and provision of referrals to free counseling services in less imminent clinical situations. We have developed a protocol for immediately referring participants who learn that they are HIV-positive or infected with chlamydia or gonorrhea as a result of our study to a local LGBT-affirmative HIV care clinic (Callen-Lorde Community Health Center or Mount Sinai Beth Israel at the New York site; Care Resource at the Miami site).

Protection Against Breach of Confidentiality. The primary potential risk to participants is breach of confidentiality. Breaches of confidentiality will occur if a participant reports a clear intention to harm himself or another person. Additionally, health care professionals are required by state law to report suspected cases of abuse or neglect. The likelihood that any additional breaches of confidentiality would occur is minimal, as steps will be taken to guard against this risk. To protect participants' confidentiality, we will obtain a Federal Certificate of Confidentiality prior to enrolling participants. All counselors and research assistants (RAs) will undergo rigorous training in maintaining participants' privacy and confidentiality and will be in possession of valid Collaborative

Institutional Training Initiative (CITI) certificates. Further, immediately upon providing consent, all participants will be assigned an identification number, which will only be kept on an electronic database that will be password protected and located on a designated study computer. This information will not be stored with any other data and no other identifying information will appear on any form. All contact with participants will be made by counselors and research staff under explicit guidelines to preserve confidentiality when telephoning, emailing, or mailing information to participants. All materials with identifying information will be kept in one password protected electronic file. Participants will provide the respective site, Yale or Miami, with alternative contact information (email, phone numbers, and mailing address) for compensation and study retention purposes. This information will be treated in the same confidential manner as all participant information, as described here.

2. Data and Safety Monitoring Plan: *All studies require the inclusion of a Data and Safety Monitoring Plan (DSMP) with an explicit statement of overall risks (e.g., minimal, greater than minimal/moderate, or high), a means to address attribution and grading of adverse events and a description of procedures for monitoring the ongoing progress of the research and reporting adverse events. The Data and Safety Monitoring Plan should describe how the principal investigator intends to provide ongoing supervision and evaluation of the activities of the study including whether appropriate progress is being made. It should document the procedures and means to protect the welfare and safety of subjects and protect the integrity of the data.*

The plan must include provisions for data review and performance of safety reviews, at a specified frequency, as well as the plan for reporting to the HSC and/or other internal or external organizations. When participating in a multi-site study, the Yale principal investigator must indicate how safety reports and/or reporting of serious adverse events from other sites will be provided to the Yale HSC.

Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HSC will make the final determination of the risk to subjects.).

1. What is your assessment of the overall risk level for subjects participating in this study?

minimal

2. If children are involved, what is your assessment of the overall risk level for the children participating in this study?

N/A

c. **Copy, paste, and then tailor an appropriate Data and Safety Monitoring Plan from http://www.yale.edu/hrpp/forms-templates/biomedical.html** for

1. Minimal risk
2. Greater than minimal/moderate risk
3. High

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews quarterly. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The principal investigator, the Institutional Review Board (IRB) or the Data Safety Monitoring Board (DSMB) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project (e.g., through regular study meetings, via email as they are reviewed by the principal investigator.) The protocol's research monitor(s), e.g., the DSMBs, NIH, will be informed of serious or unanticipated adverse events within 5 days of the event becoming known to the principal investigator.

3. For multi-site studies for which the Yale PI serves as the lead investigator:
    1. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed?
    2. What provisions are in place for management of interim results?
    3. What will the multi-site process be for protocol modifications?

The Miami site-PI, Dr. Steven Safren, will notify PI Pachankis within one day of any adverse events and unanticipated problems involving risks to subjects or others. PI Pachankis and PI Safren will discuss any adverse events and unanticipated problems and PI Pachankis will be ultimately responsible for implementing the protocol described above for reporting these events to the IRB, the DSMB, and the NIH.

This behavioral/educational intervention trial is sufficiently powered to detect effects consistent with those found in our pilot trial of a highly similar intervention. We therefore do not expect that this trial will produce results that warrant early termination of this study or any of its components.

Protocol modification will be coordinated between the two sites in meetings between Dr. Pachankis (Yale) and Dr. Safren (Miami).

4. **Potential Benefits:** Identify any benefits that may be reasonably expected to result from the research, either to the participant(s) or to society at large. (*Payment of participants is not considered a benefit in this context of the risk benefit assessment.)*

Sexual risk behavior among young gay and bisexual men is a clear public health concern. All participants in the present study will be exposed to information about HIV transmission risks in relation to social stress and co-occurring mental health disorders. We anticipate that participants will acquire knowledge and skills and will receive support needed to improve their capacity for managing HIV risk. Benefits to society in general are anticipated through the dissemination of intervention findings and community trainings in the ESTEEM treatment approach. Results will better inform local and national public health agencies about potentially effective outreach and prevention strategies that can be delivered to YGBM who experience lifetime stress-sensitive mental health disorders, such as depression and anxiety, and HIV risk behavior. In sum, the potential benefits outweigh the potential risks to subjects, which are minimal.

We propose to further test a preliminarily efficacious intervention to better help YGBM manage their HIV risk. Findings from this study can be used to help guide prevention efforts for both YGBM and other socially disadvantaged groups who experience stress-sensitive mental health disorders and are at risk of HIV infection. Given the public health importance addressed by this project and the potential benefit of the information to be gained, we believe that the risk to subjects is reasonable. Further, the information from this intervention can serve to benefit more widespread sexual risk-reduction efforts. Specifically, information from this study will inform public health agencies regarding the effectiveness of an intervention that addresses co-occurring behavioral risk factors for HIV infection. This test will lay the groundwork for future studies examining the strategic implementation of this intervention alongside effective structural and biomedical approaches.

SECTION VIII: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives, if any, are available to the study participants outside of the research?

All participants and potential participants will be provided with a list of community referrals, including medical, HIV/STD testing, psychological, substance use, and housing supports.

2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to participants, if any, the amount and timing of payments and the conditions for receiving this compensation (if applicable). If you plan to hold a drawing, be sure to include the following on any consent or recruitment materials mentioning the sweepstakes: 1) the value of the prize; 2) the sponsor of the prize (this cannot be a federal funding source); 3) the odds of winning; 4) that there are no restrictions to winning.

Participants will receive $25 for completing each of the two baseline assessments (baseline 1 and baseline 2), $50 for completing the 4-month and 8-month follow-up assessments, and $75 for

completing the final 12-month follow-up assessment (total = $225). Participants randomized to the ESTEEM condition and CMHT condition will receive $10 per session for $10 sessions (total = $100). Therefore, depending on condition assignment, participants will receive between $225 and $325 for completing all aspects of the study. Payment will be prorated for partial study completion (i.e., participants will only be paid for the parts of the study that they completed).

Throughout the course of the study, we will hold a monthly sweepstakes at the New York site for participants who have completed their 4-month, 8-month, or 12-month follow-up appointments in the previous month. This sweepstakes winner will be selected using a random number generator. Winners will receive a $20 gift card which will be emailed to them directly after the selection of the sweepstakes winner. Participants will be notified about the sweepstakes prize, odds of winning, and prize sponsor in their monthly appointment reminder emails from the ESTEEM research team.

Annually, we will also hold a sweepstakes at the New York site for all randomized New York participants who successfully completed all of their follow up assessments (4, 8, and 12 month). This sweepstakes will occur every October beginning in 2018 and ending in 2021. Winners will be selected using a computer random number generators and receive a $200 gift card via email. The annual sweepstakes will be explained to participants during their first appointment and clearly explained during the consent process in the ICF.

The sweepstakes will only take place in New York due to the differential cost of living in New York city compared to that of Miami. According to the US Census cost of housing in Miami is 7.7% greater than the national average, where comparatively the cost of living in New York city is 286.7% the national average.[1] However, to maintain as much parity between sites we will account for the differential cost of living through the possibility to earn additional compensation through the sweepstakes.

Participants will also receive welcome bags with upon randomization into the study. The value of the welcome bags will be approximately $5.00-$10.00 and will include condoms, lubricant packets, a lanyard, candy, a welcome card, stickers, a pen, and a stress ball.

3. **Costs for Participation (Economic Considerations):** Clearly describe the participant's costs associated with participation in the research, if any, and the interventions or procedures of the study that will be provided at no cost to participants. If participants screen inconclusive or receive an HIV+ result during the rapid HIV testing, the testing site provides the confirmatory testing at no cost to the study and bills the participant directly if either the testing site or participant insurance is unable to cover the costs. Either way, it will be at no cost to the participant. Participants are welcome to use their private insurance for any confirmatory testing.

Study participation will generate no cost for participants. All study treatment (ESTEEM, CMHT, VCT) will be provided free of charge to all study participants.

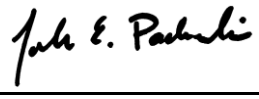
[1] C2ER, Arlington, VA, ACCRA Cost of Living Index, Annual Average 2010 (copyright).

SECTION IX:
PRINCIPAL INVESTIGATOR AGREEMENT

As the **principal investigator** of this research project, I certify that:

1. The information provided in this application is complete and accurate.
2. I assume full responsibility for the protection of human participants and the proper conduct of the research.
3. Subject safety will be of paramount concern, and every effort will be made to protect participants' rights and welfare.
4. The research will be performed according to ethical principles and in compliance with all federal, State and local laws, as well as institutional regulations and policies regarding the protection of human participants.
5. All members of the research team will be kept apprised of research goals.
6. I will obtain approval for this research study and any subsequent revisions prior to my initiating the study or any change and I will obtain continuing approval of this study prior to the expiration date of any approval period or submit a request to close the study prior to its expiration..
7. I will report to the HSC any unanticipated problems involving risk to participants.
8. I am in compliance with the requirements set by the University and qualify to serve as the principal investigator of this project or I have a faculty advisor.
9. I will identify a qualified successor should I cease my role as principal investigator and facilitate a smooth transfer of investigator responsibilities, if applicable

John Pachankis, Ph.D.
PI Name (PRINT)



Signature

May 23rd, 2017
Date

SECTION X
FACULTY ADVISOR AGREEMENT

As the **faculty advisor** of this research project, I certify that:

1. The information provided in this application is complete and accurate.

2. This project has scientific value and merit and that the student or trainee investigator has the necessary resources to complete the project and achieve the aims.
3. I will train the student investigator in matters of appropriate research compliance, protection of human subjects and proper conduct of research.
4. The research will be performed according to ethical principles and in compliance with all federal, state and local laws, as well as institutional regulations and policies regarding the protection of human subjects.
5. The student investigator will obtain approval for this research study and any subsequent revisions prior to initiating the study or revision and will obtain continuing approval prior to the expiration of any approval period.
6. The student investigator will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
7. I am in compliance with the requirements set forth by the University and qualify to serve as the faculty advisor of this project.
8. I assume all of the roles and responsibilities of a Principal Investigator even though the student may be called a PI.

_____ _____

Advisor Name (PRINT) Date

_____

Signature

For School of Medicine Applications only:

SECTION XI

DEPARTMENT CHAIR'S ASSURANCE STATEMENT

Do you know of any real or apparent institutional conflict of interest (e.g., Yale ownership of a sponsoring company, patents, licensure) associated with this research project?

☐ Yes (provide a description of that interest in a separate letter addressed to the HIC.)

☐ No

As Chair, do you have any real or apparent protocol-specific conflict of interest between yourself and the sponsor of the research project, or its competitor or any interest in any intervention and/or method tested in the project that might compromise this research project?

☐ Yes (provide a description of that interest in a separate letter addressed to the HIC)

☐ No

I assure the HIC that the principal investigator and all members of the research team are qualified by education, training, licensure and/or experience to assume participation in the conduct of this research trial. I also assure that the principal investigator has departmental support and sufficient resources to conduct this trial appropriately.

_____ _____

Chair Name (PRINT) and Signature Date

_____

Department

SECTION XII

YNHH HUMAN SUBJECTS PROTECTION ADMINISTRATOR ASSURANCE STATEMENT

Required when the study is conducted solely at YNHH by YNHH health care providers.

As Human Subject Protection Administrator (HSPA) for YNHH, I certify that:

1. I have read a copy of the protocol and approve it being conducted at YNHH.
2. I agree to notify the IRB if I am aware of any real or apparent institutional conflict of interest.
3. The principal investigator of this study is qualified to serve as P.I. and has the support of the hospital for this research project.

_____ _____

YNHH HSPA Name (PRINT) and Signature Date

For HIC Use Only

_____ _____

Date Approved **Human Investigation Committee Signature**

This protocol is valid through _____