YALE UNIVERSITY
HUMAN INVESTIGATION COMMITTEE

Application to Involve Human Subjects in Biomedical Research
100 FR1 (2011-6)

Please refer to the HIC website for application instructions and information required to complete this application. The Instructions are available at http://www.yale.edu/hrpp/forms-templates/biomedical.html Submit the original application and two (2) copies of all materials including relevant sections of the grant which funds this project (if applicable) to the HIC.	**HIC OFFICE USE ONLY**	
		1205010234

SECTION I: ADMINISTRATIVE INFORMATION

Title of Research Project: Three Strategies for Implementing Motivational Interviewing on Medical Inpatient Units: See One, Do One, Order One			
Principal Investigator: Steve Martino PhD		**Yale Academic Appointment:** Professor	
Campus Address: 142 Temple St, Suite 301, New Haven, CT 06510			
Campus Phone: 46621	**Fax:** 46766	**Pager:**	**E-mail:** steve.martino@yale.edu
Protocol Correspondent Name & Address (*if different than PI*)**:** Monica Canning-Ball			
Campus Phone: 203-812-0126	**Fax:** 203-764-6766	**E-mail:** monica.canning-ball@yale.edu	
Yale Cancer Center CTO Protocol Correspondent Name & Address (*if applicable*)**:**			
Campus Phone:	**Fax:**	**E-mail:**	

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

Investigator Interests:
Does the principal investigator, co-investigator, or any other responsible research team member, or any of their family members (spouse, child, domestic partner) have an incentive or interest, financial or otherwise, that may be viewed as affecting the protection of the human subjects involved in this project, the scientific objectivity of the research or its integrity? See Disclosures and Management of Personal Interests in Human Research http://www.yale.edu/hrpp/policies/index.html#COI

o Yes o No

If yes, list names of the investigator or responsible person:

The Yale University Principal Investigator and all Yale University and Yale New Haven Hospital individuals who are listed as co-investigators on a protocol with a Yale University Principal Investigator must 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. **Performing Organizations:** Identify the hospital, in-patient or outpatient facility, school or other agency that will serve as the location of the research. Choose all that apply:

a. Internal Location[s] of the Study:

- ☐ Magnetic Resonance Research Center (MR-TAC)
- ☐ Yale Cancer Center/Clinical Trials Office (CTO)
- ☐ Yale Cancer Center/Smilow
- ☒ Yale-New Haven Hospital
- ☐ Specify Other Yale Location:
- ☐ Yale University PET Center
- ☐ YCCI/Church Street Research Unit (CSRU)
- ☐ YCCI/Hospital Research Unit (HRU)
  - ☐ YCCI/Keck Laboratories
- ☐ Cancer Data Repository/Tumor Registry

b. External Location[s]:

- ☐ APT Foundation, Inc.
- ☐ Connecticut Mental Health Center
- ☐ Clinical Neuroscience Research Unit (CNRU)
- ☐ Other Locations, Specify:
- ☐ Haskins Laboratories
- ☐ John B. Pierce Laboratory, Inc.
- ☐ Veterans Affairs Hospital, West Haven
- ☐ International Research Site (Specify location(s)):

c. Additional Required Documents *(check all that apply)*:

- ☐ *YCCI-Scientific and Safety Committee (YCCI-SSC)

☒ N/A
Approval Date:

☐ *Pediatric Protocol Review Committee (PPRC) Approval Date:
☐ *YCC Protocol Review Committee (YRC-PRC) Approval Date:
☐ *Dept. of Veterans Affairs, West Haven VA HSS Approval Date:
☐ *Radioactive Drug Research Committee (RDRC) Approval Date:
☐ YNHH-Radiation Safety Committee (YNHH-RSC) Approval Date:
☐ Magnetic Resonance Research Center PRC (MRRC-PRC) Approval Date:
☐ YSM/YNHH Cancer Data Repository (CaDR) Approval Date:
☐ Dept. of Lab Medicine request for services or specimens form

Approval from these committees is required before final HIC approval is granted. See instructions for documents required for initial submission and approval of the protocol. Allow sufficient time for these requests. Check with the oversight body for their time requirements.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities. 9/1/2012-8/31/2017

3. **Research Type/Phase: (Check all that apply)**
   a. **Study Type**
   ☒ Single Center Study
   ☐ Multi-Center Study
   Does the Yale PI serve as the PI of the multi-site study? Yes ☐ No ☐
   ☐ Coordinating Center/Data Management
   ☐ Other:

   b. **Study Phase** ☐ **N/A**
   ☐ Pilot ☐ Phase I ☐ Phase II ☐ Phase III ☐ Phase IV
   ☐ Other (*Specify)*

4. **Area of Research: (Check all that apply)** Note that these are overlapping definitions and more than one category may apply to your research protocol. Definitions for the following can be found in the instructions section 4c:
   ☐ Clinical Research: Patient-Oriented
   ☐ Clinical Research: Epidemiologic and Behavioral
   ☒ Translational Research #1 ("Bench-to-Bedside")
   ☐ Translational Research #2 ("Bedside-to-Community")
   ☒ Clinical Research: Outcomes and Health Services
   ☐ Interdisciplinary Research
   ☐ Community-Based Research

5. Is this study a clinical trial? Yes ☒ No ☐

NOTE the current ICMJE (International Committee of Medical Journal Editors) definition of a clinical trial: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events"

If yes, where is it registered?

Clinical Trials.gov registry ☒ Will be registered promptly upon HIC approval and receipt of funding.

Other (*Specify*)

*Registration of clinical trials **at their initiation** is required by the FDA, NIH and by the ICMJE.*

If this study is registered on clinicaltrials.gov, there is new language in the consent form and compound authorization that should be used.

For more information on registering clinical trials, including whether your trial must be registered, see the YCCI webpage, http://ycci.yale.edu/researchers/ors/registerstudy.aspx or contact YCCI at 203.785.3482)

6. Will this study have a billable service as defined by the Billable Service Definition?

Yes ☐ No☐

If you answered "yes", this study will need to be set up in Patient Protocol Manager (PPM) http://medicine.yale.edu/ymg/systems/ppm/index.aspx

7. Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? Yes _X__ No ___ *If Yes, please answer questions a through c and note instructions below. If No, proceed to Section III.*

a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform?

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure?

c. Will a novel approach using existing equipment be applied?

If you answered "no" to question 7a, or "yes" to question 7b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

SECTION III: FUNDING, RESEARCH TEAM AND TRAINING

1. **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 agency/sponsor, the funding mechanism (grant or contract), and whether the award is pending or has been awarded. Provide the M/C# 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 HIC (as is the case for most NIH submissions), the PI should note "Pending" in the appropriate section of the protocol application, provide the M/C# 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	Title of Grant	Name of Funding Source	Funding	Funding Mechanism
Martino	Three Strategies for Implementing Motivational Interviewing on Medical Inpatient Units: See One, Do One, Order One	NIDA - 1R01DA034243	☒ Federal ☐ State ☐ Non Profit ☐ Industry ☐ Other For Profit ☐ Other	☒ Grant-M# 150452 ☐ Contract# ☐ Contract Pending ☐ Investigator/Department Initiated ☐ Sponsor Initiated ☐ Other, Specify:
			☐ Federal ☐ State ☐ Non Profit ☐ Industry ☐ Other For Profit ☐ Other	☐ Grant-M# ☐ Contract# ☐ Contract Pending ☐ Investigator/Department Initiated ☐ Sponsor Initiated ☐ Other, Specify:
			☐ Federal ☐ State ☐ Non Profit ☐ Industry ☐ Other For Profit ☐ Other	☐ Grant-M# ☐ Contract# ☐ Contract Pending ☐ Investigator/Department Initiated ☐ Sponsor Initiated ☐ Other, Specify:

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

Send IRB Review Fee Invoice To:

Name:
Company:
Address:

2. **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 before they may be listed on the protocol. See NOTE below.**

NOTE: The HIC will remove from the protocol any personnel who have not completed required training.

	Name	**Affiliation: Yale/Other Institution (Identify)**	**NetID**
Principal Investigator	Steve Martino, PhD	Yale	sm25
Role: Co-Investigator	Kimberly A Yonkers, MD	Yale	kay5
Role: Co-Investigator	Paul Desan, MD	Yale	Phd6
Role: Biostatistician	Ralitza Gueorguieva	Yale	Rg268
Role: Psychologist	Joy Kaufman	Yale	Jk26
Role: Psychiatrist	Paula Zimbrean	Yale	Pz36
Role: Co-Investigator	William Cushing	Yale	Wlc22
Role: Social Worker	Heather Howell	Yale	Hbh9
Role: Project Director	Ashley McCaherty	Yale	Ar578
Role: Research Assistant	Monica Canning-Ball	Yale	Mac6
Role: Co-Investigator	Ariadna Forray	Yale	Af343
Role: Research Assistant	Jessica Katon	Yale	Jk954
Role: Biostatistician	Brian Merry	Yale	Bcm6
Role: Other personnel	Junemarie Rosner	Yale	Jr662
Role: Other personnel	Steven L Bernstein	Yale	Slb4
Role: Other personnel	Teresa Kenyon	Yale	Tk378
Role: Other personnel	Timothy Pham	Yale	Tlp24
Role: Other personnel	Rachel Ramirez	Yale	Rr497
Role: Student	Isabella Hermantin	Yale	Ih77
Role: Student	Mollie Rich	Yale	Mr2243
Role: Research Assistant	Rebecca Aldi	Yale	Ra497
Role: Other personnel	Jose Salvana	Yale	Jas343
Role: Student	Sahar Amjad	Yale	Sa829
Role: Student	Tulasikrishna Kadiyla	Yale	Tk534
Role: Research Assistant	Jonathan Ryan	Yale	Jr963
Role: Data Manager	Kate Gilstad-Hayden	Yale	Krg24
Role: Study personnel	Virginia Otero-Santos	Yale	Vo48
Role: Study personnel	Rebecca Tutino	Yale	Rt466
Role: Study personnel	Lilit Kazazian	Yale	Lk527
Role: Study personnel	Eva Jones	Yale	Emj28

A personnel protocol amendment will need to be submitted when training is completed.

SECTION IV:
PRINCIPAL INVESTIGATOR/FACULTY ADVISOR/ DEPARTMENT CHAIR AGREEMENT

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

- The information provided in this application is complete and accurate.
- I assume full responsibility for the protection of human subjects and the proper conduct of the research.
- Subject safety will be of paramount concern, and every effort will be made to protect subjects' rights and welfare.
- 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.
- All members of the research team will be kept apprised of research goals.
- 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.
- I will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set by the University and qualify to serve as the principal investigator of this project or have acquired the appropriate approval from the Dean's Office or Office of the Provost, or the Human Subject Protection Administrator at Yale-New Haven Hospital, or have a faculty advisor.
- I will identify a qualified successor should I cease my role as principal investigator and facilitate a smooth transfer of investigator responsibilities.

PI Name (PRINT) and Signature

11/16/15
Date

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

- The information provided in this application is complete and accurate.
- 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.
- I will train the student investigator in matters of appropriate research compliance, protection of human subjects and proper conduct of research.
- 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.
- 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.
- The student investigator will report to the HIC any serious injuries and/or other unanticipated problems involving risk to participants.
- I am in compliance with the requirements set forth by the University and qualify to serve as the faculty advisor of this project.

_____ _____

Advisor Name (PRINT) and Signature Date

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

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:

- I have read a copy of the protocol and approve it being conducted at YNHH.
- I agree to notify the IRB if I am aware of any real or apparent institutional conflict of interest.
- 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 _____

SECTION V: RESEARCH PLAN

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

General medical hospitals provide care for a disproportionate share of patients who abuse or are dependent upon substances.[1,2] This group is among the most costly to treat and has the poorest medical and substance use outcomes.[3,4] Motivational interviewing[5] (MI) is a well-recognized, evidenced-based substance abuse treatment that has been adapted for use as a brief intervention in health care settings.[6] MI is applicable to many health-related behavioral problems, and can be taught to a broad range of health care clinicians.[7] However, it is unclear which implementation strategies will lead to the efficient and proficient uptake of MI in general medical settings, such as medical inpatient units.

Primary care clinicians have multiple practice demands and time constraints. New practices have the greatest chance of being implemented if they are simple and compatible with existing workflows and systems.[8-12] Two widely used strategies to bring specialized practices into use within general hospital settings are the "see one, do one" apprenticeship model of training[13-16] and use of consultation-liaison (CL) services.[17] "See one, do one" has been a *modus operandi* in medical education for centuries and relies upon a competency-based supervision training approach. While it has been empirically validated in the specialty addiction field, less controlled testing of this implementation strategy is available in general medical settings. The apprenticeship approach requires that appropriate patients and trainers are available with high flexibility for teaching and supervision; when applied to behavioral counseling approaches, this may be seen as incompatible with the medical role and time constraints of clinicians.[6] In contrast,

ordering MI through CL is a relatively simple, minimally burdensome process and highly compatible with the way clinicians secure other specialist services for their patients in the hospital.

We propose to conduct a randomized controlled trial using mixed quantitative and qualitative methods to examine the effectiveness of three different strategies for integrating MI into the practice of healthcare providers working within Yale New Haven Hospital's internal medicine hospitalist service and other general medical inpatient units. Specifically, we will randomize 30 healthcare providers to one of three conditions: (1) a continuing medical education workshop that provides background and "shows" healthcare providers how to conduct MI (the control condition, called SEE ONE); (2) a "see one, do one" apprenticeship model involving workshop training plus live supervision of bedside practice (DO ONE); and (3) ordering MI from CL after learning about it in a workshop (ORDER ONE). Following the respective MI trainings, each healthcare provider will be assessed for the provision of MI to 40 study-eligible inpatients, recruited by the research team after admission to our general medical units.

Our Primary Aims are:

1. To assess the uptake of MI by Healthcare providers on the medical units.
   H1a. The percentage of MI interviews in the first 40 consecutive, study-eligible inpatients identified by the research team will be higher in the "DO ONE" than "SEE ONE" group;
   H1b. The percentage of MI interviews in the first 40 consecutive, study-eligible inpatients identified by the research team will be higher in the "ORDER ONE" than "SEE ONE" group.
2. To assess the integrity of MI when Healthcare providers use it on the medical units.
   H2a. DO ONE will result in more proficiently conducted MI sessions than SEE ONE;
   H2b. ORDER ONE will result in more proficiently conducted MI sessions than SEE ONE.
3. To assess the cost-effectiveness of the three strategies.
   H3a. SEE ONE will be the most cost-effective implementation strategy when the threshold value to decision makers of inpatients receiving an additional MI session to a criterion level of adequate performance is relatively low;
   H3b. DO ONE and ORDER ONE will be more cost-effective than SEE ONE when the threshold value is relatively high.

The primary outcome for MI *uptake* will be the percentage of MI sessions conducted for study-eligible inpatients as verified by audio recordings. For MI *proficiency*, primary outcomes will be 1) independently rated MI adherence and competence ratings of the sessions, and 2) the percentage of sessions achieving a criterion level of adequate MI performance used in MI effectiveness[18-20] and clinician training trials.[21,22] In addition, we will calculate the relative costs and cost-effectiveness of the three MI implementation strategies. Secondary outcomes across the three conditions will be 1) independently rated strength and frequency of patient statements that favor change in the sessions (called change talk) as a proxy for patient outcomes,[23,24] and 2) themes related to implementation facilitators and barriers identified through qualitative assessment.

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.

Substance abuse and dependence are among the most prevalent and costly health problems in the United States. Individuals who abuse substances are seven times more likely than non-substance using individuals to be admitted to a hospital for medical care secondary to complications that are caused by their substance use. Hence, inpatient hospitals provide care for a disproportionate share of patients who abuse or are dependent on substances- patients who are disproportionately costly to treat and at risk for poor health outcomes.[3,4] On the other hand, hospitalization provides a unique opportunity to identify and motivate patients to address their substance use problems in that patients are: 1) accessible; 2) have time

for an intervention; and 3) are often admitted for complications related to substance use that renders hospitalization a "teachable moment".[43,44]

MI has a strong evidence-base in the treatment of substance abuse (alcohol, drugs, smoking), reducing risky behaviors (e.g., unsafe sex or needle sharing), increasing healthy behaviors (e.g., improved diet, increased exercise), and engaging patients in treatment; it consistently demonstrates small to moderate and clinically significant effects across targeted behaviors.[45-47] As a brief intervention for primary care patients, MI has its most consistent support with non-dependent unhealthy alcohol use,[48-52] though recent studies suggest that MI is more effective than expected with dependent drinkers in hospitals and other primary care settings.[53-55] MI also has promise for addressing medical patients' illicit drug use.[56,57] The strength and frequency of in-session patient change talk is highly correlated with improved substance use outcomes post-treatment and at follow-up points.[58-63] Moreover, clinicians who use MI proficiently (i.e., adhere to MI-consistent strategies and use them competently) are significantly more likely to elicit patient change talk in their sessions.[23,58,62,64] These findings have led Miller and colleagues[23,24] to recommend client change talk as a good proxy for patient outcomes in clinician training studies. Thus, the evaluation of successful MI implementation should include the clinicians' adherence and competence in using the newly introduced practice, with the frequency and strength of change talk within sessions as a proxy for the effectiveness of the practice as delivered.

Importantly, MI can be taught to a broad range of health care providers via a one-time workshop training, especially in health care where formal continuing medical education or CME events such as one-day workshops are common and acceptable venues.[7,70,71] MI workshop training alone consistently produces small increases in MI integrity immediately following training; however, without subsequent training, these gains diminish in as little as 2-3 months.[23,59,72,73] In contrast, numerous studies in the mental health and addiction fields show significantly increased competency when a workshop is followed by direct observation and supervision coupled with formal treatment integrity ratings.[21,23,64,72,74] The purpose of this research is to subject this training approach to a randomized controlled trial for implementation of a substance abuse intervention into primary care settings.

Integration of substance abuse interventions into primary care could improve health outcomes and reduce health care costs.[51,52,57,75,76] However, this is contingent upon effective implementation strategies. Implementation theories identify two important components for consideration when crafting strategies: complexity and compatibility. The more complex a strategy, the greater the difficulty in implementation.[8-10,12] Similarly, if a strategy is not compatible with the existing workflows and systems of the setting, implementation is likely to fail.[8,9,11,12] In short, implementation strategies that are straightforward and fit into existing practices of primary care clinicians and their workplaces are most likely to succeed.[77] This principle of "keeping it simple" is particularly salient for primary care clinicians who would require between 3.5 – 10.6 hours per day if they were to follow all recommended guidelines for screening and behavioral management of the top 10 chronic diseases.[78]

Traditionally, an apprenticeship model has been used to instruct inpatient medical clinicians in bedside procedures,[13-16] but this model has not been applied to promoting the use of behavioral counseling techniques in primary care. Commonly referred to as "see one, do one", the instructor explains the theory and techniques of a practice and demonstrates it in a simulated scenario (e.g., manikin) or directly with patients. Subsequently, trainees practice the approach under the supervision of an expert clinician who provides live performance feedback and coaching to improve the technique. Eventually, these clinicians will "teach one" to others when they have mastered the practice. This form of learning on the job has been a *modus operandi* in medical education for centuries[16,79] and is analogous to the competency-based supervision approach noted above. The ultimate aim of "see one, do one" is to have *clinicians implement the procedure proficiently with their patients*. While incorporating familiar and efficacious teaching methods (direct observation, feedback, coaching), a potential caveat is that "see one, do one" is somewhat

complex in that it requires appropriate patients and a trainer to be available for teaching. Moreover, when applied to behavioral counseling approaches like MI, it may be seen as potentially incompatible with the clinicians' medical role and time constraints.[6]

Another common practice in general hospitals is the use of psychiatry consultation-liaison (CL) services. The main function of CL is to provide assessment and specialty guidance on the management of patients with mental health and addiction problems.[17] Inpatient clinicians request a CL consult by ordering it through the electronic medical record. CL provides the relevant service on the same day or day thereafter, depending on the urgency of the request (e.g., concerns about risk for deliberate self-harm). About 20% of CL consultations typically involve the assessment, treatment recommendations and referrals for patients who have substance abuse/dependence problems.[80-85] The ultimate aim of CL is to have *highly trained specialists implement the procedure proficiently with patients, rather than having the referring clinicians conduct it themselves*. The use of CL as a vehicle for implementing specialized behavioral counseling approaches such as MI in primary care has never been tested. From the perspective of inpatient clinicians, using CL is a simple, minimally burdensome process (i.e., order one) and highly compatible with the way they secure other specialist services (e.g., neurology consult) for their patients. The provision of MI by CL clinicians upon request is a very promising implementation strategy for integrating substance abuse treatment into inpatient medical care. The potential problems with this approach are: 1) it requires clinicians to recognize and order the service, 2) patients must accede to a consultation with a substance abuse expert, 3) it may be more expensive since it requires additional staff time from individuals who have expert training and work on a specialty service, and 4) the treatment would be delivered by providers who are not central to the overall care of the patient, thus potentially reducing the potency of the intervention Given the possible pros and cons of these approaches, we currently lack information about the most effective and cost effective strategies by which to implement MI into a general inpatient medical setting.

3. **Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths.

The proposed project will evaluate the effectiveness of three different implementation strategies for integrating MI into the YNHH's internal medicine hospitalist service and other general medical inpatient units. Specifically, we will randomize 30 Healthcare providers to one of three conditions: (1) a continuing medical education workshop that "shows" the healthcare providers MI (the control condition, referred to as SEE ONE); (2) a 'see one, do one" apprenticeship model involving workshop training plus live supervision of bedside practice (DO ONE); and (3) ordering MI from CL after learning about it in a workshop (ORDER ONE). After receiving the respective MI training, each Healthcare provider will be followed for provision of MI to study-eligible/consented patients. In ORDER ONE, healthcare providers may elect to conduct MI themselves or order it to be conducted by Psychiatrists from the CL service.

After the Healthcare providers have attended their respective workshops, research staff will identify substance using patients in need of a MI intervention. Research staff will independently screen, assess and obtain consent from eligible patients who are admitted to the internal medicine hospitalist service and other general medical inpatient units. Patients will be potentially included if they are assigned to a participating Healthcare provider according to the hospital's usual clinical administrative procedures. Thus, patients will follow the randomization condition of their Healthcare provider, though Healthcare provider will not know which patients on their caseloads have enrolled in the study. This approach will permit a naturalistic test of the Healthcare provider' ability to identify and intervene using MI with patients who have substance use problems. Each Healthcare provider will be followed until he or she has

cared for 40 study-enrolled patients, whether or not the Healthcare provider has recognized the patient as a substance user and/or provided a MI intervention. These patients will be the first 40 patients administratively assigned to the Healthcare provider who are screened, consented and enrolled into the study. Screening and consent of inpatients will be done in the "background" and Healthcare provider will not be told in advance that a patient has been enrolled since this may "cue" their behavior. We will not tell the Healthcare provider of our target enrollment but rather will tell them when they have reached our "target" number. In this way, we will enroll 1200 medical inpatients who may potentially receive a MI intervention.

After completion of their caseload, Healthcare provider will have a post-trial assessment to evaluate their reaction to their assigned condition, including a qualitative interview that will determine implementation facilitators and barriers. This post-trial conversation will also debrief Healthcare provider on the overall aims of the study, individual and group performance and success in administering motivational interviewing (both in terms of the quality of individual sessions, the use of MI in appropriate cases, as well as an overview of "missed opportunities" for pts who clinically warranted the MI services but were not provided with it by their healthcare provider). This debriefing will be provided in an MI-consistent manner, supporting strengths and successes of the providers while pushing them to improve technique and accuracy.

Primary outcomes will be 1) the percentage of MI sessions, as verified by audio recordings, conducted among each Healthcare provider 40 consecutively enrolled study patients, 2) independently rated MI adherence and competence ratings of the sessions, and 3) the percentage of sessions conducted that meet a criterion level of adequate MI performance used in MI effectiveness[18-20] and clinician training trials.[21,22] In addition, we will calculate the relative costs and cost effectiveness of the three conditions. Secondary outcomes will be 1) independently rated strength and frequency of patient statements that favor change in the sessions (called change talk) as a proxy for patient outcomes,[23,24] and 2) themes related to implementation facilitators and barriers identified through qualitative interviews. The YNHH hospitalist and the psychiatric CL services will work closely with research staff to implement all aspects of this project.

Initially our main unit of randomization was the PAs within the YNHH hospitalist service. The director of the hospitalist service, Dr. Victor Morris, and Will Cushing, Chief PA of the hospitalist service, both co-investigators on this proposal, have committed the participation of the PAs on the service to the protocol. The service includes 33 PAs who work during days Mon-Fri on non-critical care general medical units. There is a turnover rate of about 2 per year that nets 40 PAs during the 4-year data collection phase of the project. Prior to randomization, Dr. Morris, Will Cushing and other members of the study team will meet with the PAs during staff meetings, wherein we will describe the project and elicit interest. Thereafter, we will screen PAs for eligibility and obtain written consent for their participation. PAs will next complete baseline assessment, including an audio recorded sample of their usual manner of interviewing an inpatient with a substance use problem. Following baseline assessments, a restricted randomization procedure will be used to allocate an equal number of PAs to the three conditions (10 PAs per condition).

Originally this study focused on training PAs because they have become very prevalent and important midlevel providers in all practice settings in U.S. medicine. PAs have been used to address current health system and societal needs for primary care[105] and to reduce service costs[106] and house staff hours as mandated by the Accreditation Council of Graduate Medical Education.[107,108] Moreover, they spend more time interacting with their patients than physicians within the YNHH hospitalist system, and recent work has shown PAs have the interest and capacity to learn behavioral intervention strategies such as MI.[69]

While our initial goal was to randomize and enroll PAs only in this study, other healthcare providers have shown interest, ability to incorporate MI into their daily schedule and proven to be ideal candidates to include as a part of our cohort.

C. Study Setting

The study will take place on the general medical inpatient units of YNHH. The internal medicine hospitalist service (where we will be recruiting PA participants) consists of 8 teams, each comprised of an attending physician and 2-5 PAs. PAs typically see patients on more than one unit and see each assigned patient 1-2 times per day. Hospitalist patients are followed by one PA and one MD from the service. The hospitalist teams cover about 160 beds/day (range = 130-210) on 13 different units excluding intensive care units. In 2010, the service was responsible for approximately 9,900 discharges. The average length of stay for patients is 4 days. The psychiatric CL is available to all attending MDs and PAs for the assessment and initiation of treatment for mental health and addiction problems. Attendings and PAs order CL services via entry into the electronic medical record, which are viewed by a CL administrative assistant and CL staff throughout the day. Consultations are typically seen within 4-8 hours of placement, depending upon the acuity and time sensitivity of the requested consult. Non-urgent consults may be seen the next day if the caseload is high.

General medical inpatient units have a patient population characterized by very high rates of co-morbid substance use disorders typically in excess of rates found in other primary care settings.[1] Moreover, large numbers of hospitals have adopted the hospitalist model for inpatient care on medical units,[109] and almost all hospitals have psychiatric CL services for addressing mental health and addiction problems that fall outside the expertise of medical providers.[17,1110] This study has the potential to identify highly disseminative strategies for integrating substance abuse services into primary care in a major sector of the U.S. health care system.

The practice under study for implementation is a single 20-min MI session that we have used to train medical students and physicians[21,89] and are currently comparing to a computerized MI approach with substance using women in outpatient primary care treatment.[87] The MI session includes six steps: (1) understand patient's view of his/her substance use and motivations for change; (2) discuss reasons for using vs. not using/cutting down; (3) provide personalized feedback about patient's substance use; (4) continue handling resistance skillfully and draw out change talk; (5) develop a change plan or present change options for later consideration; and (6) summarize and support what the patient has decided to do. Clinicians ask key questions at the conclusion of steps 2-4 to ascertain the patient's commitment to change. If the patient endorses a goal of quitting or cutting back substance use, the clinician immediately proceeds to Step 5. Thus, clinicians adapt MI to their specific patient's readiness to change, giving the manualized treatment flexibility to avoid a rigid application of MI that might undermine its effectiveness and acceptability to clinicians.[24,46]

Healthcare providers will each receive the MI implementation strategy offered within their assigned condition. Separate workshop trainings will occur for Healthcare providers within conditions. Additional workshops will be conducted as needed if new Healthcare providers are recruited into the study. In each condition, all Healthcare provider as well as the Psychiatrists from CL in ORDER ONE will audio record their MI interviews to confirm the interviews have occurred and to permit MI integrity rating.

1. Workshop (See One)

Healthcare providers in this condition will participate in a 1-day skill-building workshop. Dr. Martino, a member of the Motivational Interviewing Network of Trainers (MINT) and a highly experienced MI workshop trainer, will conduct the workshop per MINT recommendations, giving the Healthcare providers an opportunity to "see" the MI intervention and learn how to conduct it through expert and

video demonstrations and experiential activities. He also will teach the Healthcare providers how to screen patients for risky substance use with NIAAA Guidelines, the CAGE Questionnaire and Heaviness of Smoking Index[114] (described below). A 2-hr "booster" session will be provided to Healthcare providers once they have reached their halfway point of the trial phase (20 eligible patients), consistent with the common practice of requiring annual refresher training for critical procedures used by staff in hospitals.

2. Workshop plus live supervision (Do One)

Healthcare providers will participate in a 1-day skill-building workshop conducted by Dr. Martino, including halfway point booster sessions, as outlined above. Following the workshop, the Healthcare providers will each "do one" MI intervention under the live supervision of a Psychiatrist from CL. Dr. Martino will have taught the CL psychiatrists to conduct MI and will have trained them in the supervisory practices developed in our prior MI training work (See Appendix B).[21,89,90] Healthcare providers can request additional live supervision at any point during the trial, consistent with the apprenticeship model.[13-16] Additionally, once the Healthcare provider in this condition reaches their halfway point of the trial phase (20 eligible patients), they will be offered another bedside supervision as a refresher of their MI skills.

3. Workshop plus consultation-liaison service (Order One)

Healthcare providers will participate in a 1-day skill-building workshop and annual booster sessions conducted by Dr. Martino. The Healthcare providers in this condition will be instructed that they may either administer MI or they may "order" a MI interview to be delivered by a Psychiatrist from CL with specialty MI training. This is the only group that may "order" a MI interview.

Before Healthcare providers can "order" MI from CL, Dr. Martino will train and supervise the CL Psychiatrists in MI, who will provide adequate coverage for administration of MI during the data collection period of the project. Training will follow a clinical trials training approach used in efficacy and effectiveness trials:[115,116] 1) a 2-day skill-building workshop; 2) three post-workshop supervised practice cases based on review of audio recorded sessions using the NIDA-SAMHSA MI supervision blending product, MIA: STEP,[86,94]; and 3) follow-up monthly individual supervision to maintain and monitor the CL experts' MI practice.

4. Rationale for implementation strategy choice and study design

Continuing medical education workshop/seminar training plus booster sessions is the usual approach for teaching medical professionals new or unfamiliar clinical practices[70,71] and will serve as our control condition. By holding this training constant across conditions, we can isolate the effects of live-supervision in DO ONE and ability to order MI from CL in ORDER ONE that exceed those which occur in primary care training-as-usual efforts. We considered a two cell design that would compared DO ONE and ORDER ONE. However, to our knowledge neither DO ONE or ORDER ONE have been tested in primary care settings. Given this, we felt that a true "control condition" by which to compare uptake, MI proficiency, and cost effectiveness is required.

5. Rationale for sample choice:

We are recruiting a heterogeneous sample of substance using patients to test the implementation strategies in clinical circumstances typically seen by Healthcare providers on general medical inpatient units. Finally, most Healthcare providers and all MI integrity raters are mono-lingual English speakers. We therefore do not have the capacity to include Spanish-only speaking patients in the study.

G. Procedures for monitoring Healthcare provider-patient assignments and audio recording MI interventions

Research assistants will be hired and will review a list of patients assigned to PA study providers who are part of the internal medicine hospitalist service. PA staff members from the Hospitalist Service at YNHH, will generate a daily list for review by research assistants/ study personnel. This list, will be furnished to the Project Director and research assistants via YNHH email to Yale University email accounts, for the sake of security and confidentiality. For other Healthcare providers working in general medical inpatient units and participating in the study, (i.e. RNs) patient lists will be obtained via the Project Director and/or research assistants logging into EPIC and sorting all the current YNHH patients

by Registered Nurse. The RAs also visit each applicable unit and asking an appropriate staff member or reviewing the patient list book to ensure EPIC was accurate. Permission to review books on the unit has been given by the Managers on each unit from which we are currently recruiting This list and corresponding admission notes will be preliminarily reviewed by the research assistant for the exclusive purpose of ruling OUT subjects 1) who do not speak English, 2) who have pre-existing diagnoses indicating cognitive impairment (ie dementia) such that consideration for enrollment in a research trial would be inappropriate, and 3) who have already been previously enrolled in this research protocol. Only relevant admission documents will be reviewed in the electronic record to determine these exclusionary criteria. We plan to do a brief review of admission notes because the project will entail screening thousands of individuals. Given the volume of inpatients at YNHH, it is impractical for research staff to approach every patient, nor is it an efficient use of their time. Review of the medical admission documents will guide research staff to offer study participation to those who are not obviously ineligible. It would enhance feasibility greatly to be able to know whether someone meets these basic potential exclusionary criteria. However, no data will be saved about the patient; instead the name of patients who are not eligible for screening will be removed from our list. The remaining individuals from the daily list will be approached by study personnel, namely Research Assistants, who will offer and administer written and verbal informed consent. After patients are consented, screened and assessed, the Research Assistant may collect data from the participant (see assessments outlined below) and the electronic medical record (concurrent medical conditions, number of previous admissions and admission medications). The Healthcare provider will not be informed by research staff about the use of substances by the patient but must rely on usual procedures and their workshop training to identify risky substance use and the need for a MI intervention. It should be noted that information about risky substance use is often noted in the patients' electronic medical records. However, lack of direct disclosure to the Healthcare provider allows us to assess the implementation of drug use detection strategies and maintains the confidentiality of information that we collect. Ideally, our training will augment information that ideally, is routinely collected. We will use the audio recording of the MI interview as evidence the intervention or referral occurred.

All Healthcare providers and Psychiatrists from CL will be issued a digital recording device. They will audio record their own MI sessions and personally consent patients for such recordings and give the recordings to the research assistant, along with identifying information that will enable the research assistant to check the patients' study enrollment status. If recordings are obtained from non-study participants (e.g., someone that was deemed ineligible or who did not provide consent), they will be immediately erased. Otherwise, they will be downloaded for storage on a secure server for later analysis.

As part of a research assistant's job, he or she will regularly send messages to all of the Healthcare providers reminding them to record any MI interventions (or CL referrals) they conduct with patients on the unit. As a back-up, additional recording devices will be conveniently placed on the units, and the administrative assistant on the CL service and research assistants will have additional recording devices that can be given to Healthcare providers and Psychiatrists from CL on demand. Dr. Morris and Mr. Cushing will be apprised of the overall success of obtaining audio recorded MI interviews, although they will not be told of the success for each of the Healthcare providers or their assigned conditions. They will assist with compliance for obtaining recorded sessions if there are problems.

H. Assessments:

Data will be collected by self-report, interview questionnaires and audio recordings. The Healthcare providers will complete structured questionnaires and qualitative interviews. All of this will be coded by a subject ID rather than the individual's name. Similarly, the audio recordings will be stored as computer files on a secure server and only include subject IDs to label the interview.

The proposed project will evaluate training effects using mixed methods to gather both quantitative and qualitative data[122,123] and be organized according to the basic structure of Kirkpatrick's widely applied four level training evaluation model.[124] Given space limitations, only instruments central to our primary and secondary outcomes or that are less familiar are described in more detail. Healthcare provider assessments will occur at baseline, during the trial, and post-trial (i.e., after their 40th assigned study-enrolled patient has been discharged from the unit). Patient assessments will occur only at baseline. Of importance, we will have several research staff trained in the ITRS and MISC 2.1 Client Language Coding System (both described below) rating MI proficiency throughout the trial to accommodate the large number of recorded sessions generated in this study.

1. Reaction level (reactions to the different implementation strategies)

- **Workshop Evaluation Form** and **Supervision Evaluation Forms**[21,22,91] will evaluate the Healthcare providers' satisfaction with the workshops and supervision provided in the study.
- **Facilitators and Barriers Qualitative Interview** will be used to assess the Healthcare provider and \ perception of the facilitators and barriers of their assigned implementation strategy post-trial. Focus groups consisting of approximately 8-12 Healthcare providers and that will target the five broad domains from the Consolidated Framework for Implementation Research:[8] (1) characteristics of the MI intervention; (2) external pressures to provide a substance abuse intervention, and specifically MI, to medical inpatients; (3) internal medical unit factors (e.g., fit within usual care, incentives, prioritization of tasks, leadership engagement, available resources); (4) characteristics of the patients; and (5) implementation processes used in the conditions including training, supervision, and availability of the CL service will be conducted immediately following their MI training. These focus groups will be audio-recorded for the purpose of utilizing information gathered for the qualitative data analysis of this study. In addition, we will assess characteristics of the health care professional (e.g., attitude, peer influence, openness to change) that have been found to impact implementation.[125-127] We will also conduct key informant focus groups and/or interviews throughout the study with the Chief PA, the Director of Hospitalist Services, Unit Chiefs, and hospital clinical staff to further assess organizational barriers and facilitators. These interviews will ask many of the same questions that facilitate and impede the use of Motivational Interviewing within the Hospitalist Service and other general medical inpatient units in the hospital. These interviews will also be audio-recorded for qualitative analysis purposes.
-

2. Learning level (changes in knowledge and attitudes)

- **Beliefs about MI**[128] will assess the Healthcare providers' personal experiences with and beliefs about MI and perceived barriers to implementing it.
- **Motivational Interviewing Questionnaire**[89,129] assesses Healthcare provider knowledge of MI principles.
- **Clinician Rulers**[89] assesses Healthcare provider interest, confidence, and commitment in using MI.

3. Behavior level (changes in behavior)

- **MI Uptake** will be based on the number of MI intervention sessions audio recorded by Healthcare providers and Psychiatrists from CL.
- **Independent Tape Rater Scale (ITRS)** will assess the integrity of MI delivery and the criterion level of adequate MI performance within each session collected at baseline and during the trial. The ITRS includes items that cover therapeutic strategies that are MI consistent (e.g. reflections) or inconsistent (e.g., unsolicited advice). It also has items detailing general counseling strategies (e.g., assessment of substance use) that are not unique to MI, nor antithetical to it, and interventions particular to other substance abuse treatment approaches (e.g., coping skill development). For each item, raters evaluate the practitioners for adherence (i.e., the extent of intervention delivery) and competence (i.e., the skill/quality of intervention delivery) along 7-

point Likert scales. For our primary outcomes, we will: 1) calculate mean adherence and competence scores for the two factors (fundamental and advanced MI strategies) identified in prior psychometric analyses;[91-93] and 2) determine if sessions achieve our criterion level for adequately performing MI,[18-22] namely, at least half the MI consistent items rated average or above for both adherence and competence. Descriptive analysis of other specific and general substance abuse interventions that do not involve MI will permit identification of how Healthcare providers and Psychiatrists from CL deviate from or modify the MI intervention for the inpatient setting, an important issue when studying the implementation of evidence-based treatments in real world settings.[125,126] We have extensive experience training ITRS raters to perform very reliable MI session process ratings.[21,22,91,93]

4. Results level (results that occurred from the application of the new practice)

- **Motivational Interviewing Skills Code 2.1 Client Language Coding System**[130] will obtain frequency counts and strength indices of positive (change talk) and negative (sustain talk) language categories in four categories: reason (includes desire, ability, and need statements as subcategories), other (hypothetical advice to others, if-then statements about the possibility of changing, foretelling of future problems if change does not occur, problem recognition), taking steps, and commitment.

5. Healthcare provider, patient, and work environment characteristics

- **Clinician Survey**[127] collects baseline Healthcare provider demographics and background.
- **Confusion Assessment Method (CAM)** will be used to assess patients' cognitive impairment (i.e. delirium).
- **Time Line Follow Back**[118,131] assesses patients' past month self-reported substance use.
- **Heaviness of Smoking Index**[114] assesses 2 items from the Fagerström Test for Nicotine Dependence questionnaire[133] regarding amount smoked and time-to-first-cigarette of the day as a means to screen patients for smoking and likely nicotine dependence.
- **Mini-International Neuropsychiatric Inventory 5.0.0 Clinician-Rated**[119] will be used only to generate patient drug or alcohol use diagnoses (abuse and dependence).
- **Addiction Severity Index Alcohol/Drug Section**[120] will assess the frequency, duration, and severity of alcohol and drug problems over the patients' lifetime and in the past 28 days.
- **Patient Health Questionnaire (PHQ-9)** will be used to measure patients' level of depression.
- **SF-12** will measure a patient's overall health and functioning both now and during the last 4 weeks.
- **Medical Chart Review** will be conducted to 1) obtain admission and discharge diagnoses, 2) confirm self -report of substance misuse (e.g., labs), and 3) identify possible barriers to receipt of MI that may occur after consent or assessment, e.g., onset of delirium, cardiac arrest, early release from hospital.
- **The Motivation for Change Scale**[135] uses 3 items (analogue scale coded from 1 to 100) tapping patient drug, alcohol or tobacco use likelihood problem recognition, and treatment motivation. These types of ruler-based assessments of motivation have performed as well or better than more elaborate readiness to change questionnaires in predicting behavioral intentions.[136]
- **Medical Inpatient Work Index-Revised**[137] is a 15-item scale that will be adapted for use by Healthcare providers and nursing staff to access their perception of the YNHH work environment in terms of: (1) autonomy in making patient care decisions; (2) control Healthcare providers and nursing staff have over others to promote high-quality patient care; (3) collegiality with other medical staff; and (4) administrative/managerial support. The scale has been found to be a reliable and valid index of organizational traits in U.S. general medical hospitals.[138,139]

6. Additional assessments

- For Healthcare providers, we will track time in hours to MI implementation per patient (starting from the patient's admission to the unit) and, for DO ONE, the number of live supervisions

received. For patients, we will track length of stay on unit and CL services received other than "ordered" MI.

- For CL experts we will track how sleepy a patient is that they need to conduct a Motivational Interview with as a result of an order placed in EPIC by a Healthcare provider in the Order One Condition. This will be done using the **Stanford Sleepiness Scale**. The Stanford Sleepiness Scale (SSS) is a widely used instrument to assess subjective sleepiness with good validity (1). Respondents select which of seven statements best reflects their level of sleepiness; higher scores indicate greater sleepiness. The SSS predicts performance decrements following acute sleep deprivation (2).

Table 1: Assessments for Healthcare provider and patient participants

Participant	Assessment Name	Data Type	Assessor	Baseline	Trial	Post-Trial
Healthcare provider	Clinician Survey	Self-report	Healthcare provider	x		x
	Medical Inpatient Work Index – Revised	Self-report	Healthcare provider / nursing staff	x		
	Workshop and Supervision Evaluation Form	Self-report	Healthcare provider		x	
	Beliefs about MI Survey	Self-report	Healthcare provider	x		x
	Motivational Interviewing Questionnaire	Self-report	Healthcare provider	x		x
	Clinician Rulers	Self-report	Healthcare provider	x		x
	MI Uptake	Audio recording	RA		x	
	Live Supervision Evaluation Form	Self-report	Healthcare provider (Do One)		x	
	ITRS	Independent rating	Raters	x	x	
	MISC 2.1 Client Language Coding System	Independent rating	Raters		x	
	Facilitators and Barriers Qualitative Interview	Interview	Raters			x
Patient	Cage Questionnaire	Interview	RA	x		
	NIAAA Guidelines	Interview	RA	x		
	Confusion Assessment Method	Interview	RA	x		
	Heaviness of Smoking Index	Interview	RA	x		
	Timeline Follow-back	Interview	RA	x		
	Mini-International Neuropsychiatric Inventory	Interview	RA	x		
	Addiction Severity Index	Interview	RA	x		

	Alcohol/Drug Section					
	Patient Health Questionnaire (PHQ-9)	Interview	RA	x		
	SF-12	Interview	RA	x		
	Medical Chart Review	Chart Abstraction	RA		x	
	Motivation for Change Scale	Self-report	RA	x		
CL Expert	Stanford Sleepiness Scale	Self-report	CL Expert		x	

7. Cost estimates

- As in previous economic studies conducted by Dr. Olmstead,[95,140-144] including the economic study of our three-arm clinician training trial describe above,[95] the methodology we will use to estimate the costs of the three MI implementation strategies will be from the perspective of the provider (i.e., hospital) to increase the real-world usefulness of the cost estimates outside of this research protocol.[145] We will not include research costs (e.g., participant reimbursements, assessment measurement) but rather restrict cost estimates to those associated with implementing the three MI implementation strategies. Our cost methodology will follow the micro-costing steps recommended by Yates [146] and Zarkin et al.[147] We will first delineate relevant non-research activities (e.g., MI workshop training, MI interventions, supervision (including expert review of audio recorded Psychiatrists from CL sessions)) and, for each identified activity, we will gather data on both the time spent by personnel in the activities and, as relevant, the space associated with each activity using a modified version of the Resource Allocation Worksheet (RAW) developed for Project COMBINE.[145] This form will collect data on the total labor hours spent on each activity by the trainer, Healthcare providers, and Psychiatrists from CL and the space used in conducting the activity. The labor costs of each activity will be equal to the product of the amount of time spent by each person on the activity and their fully-loaded wage (i.e., including fringe and overhead). To estimate space costs, the research assistant will measure in square feet the size of the rooms used for training, MI interventions, and supervision. We will calculate an average space estimate per medical unit for the main activity domains (workshop training, MI intervention, supervision) and multiply these domains by the annual rent per square foot for the hospital. We will obtain salary data (actual wage plus fringe rate for salary staff and hourly contract rate for contract staff) for Healthcare providers and Psychiatrists from CL and annual rent per square foot from YNHH administrators. We also will record all the direct material expenses (e.g., manuals, rating forms, recording devices, audiotapes) of conducting the MI training workshops and supervisions.

4. Genetic Testing N/A ☒

A. Describe

i. the types of future research to be conducted using the materials, specifying if immortalization of cell lines, whole exome or genome sequencing, genome wide association studies, or animal studies are planned

ii. the plan for the collection of material or the conditions under which material will be received

iii. the types of information about the donor/individual contributors that will be entered into a database

iv. the methods to uphold confidentiality

B. What are the conditions or procedures for sharing of materials and/or distributing for future research projects?

C. Is widespread sharing of materials planned?

D. When and under what conditions will materials be stripped of all identifiers?
E. Can donor-subjects withdraw their materials at any time, and/or withdraw the identifiers that connect them to their materials?
    i. How will requests to withdraw materials be handled (e.g., material no longer identified: that is, anonymized) or material destroyed)?

F. Describe the provisions for protection of participant privacy
G. Describe the methods for the security of storage and sharing of materials

5. **Subject Population:** Provide a detailed description of the types of human subjects who will be recruited into this study.

Eligible for study participation will be PA's working in the general hospitalist service, other Healthcare providers on general medical inpatient units of the hospital and patients with any drug, alcohol, or nicotine abuse or dependence disorders admitted to the general medical units at YNHH. Study staff will screen all patients admitted to the medical inpatient service of YNHH unless deemed otherwise ineligible for screening, as outlined in procedures section G above. Research staff will approach all admitted patients assigned to the hospitalist service study providers or providers on other general medical inpatient units who speak English, who do not immediately evidence cognitive limitations and who have not been previously enrolled in this study. Given the volume of inpatients at YNHH, it is impractical for research staff to approach every patient, nor is it an efficient use of their time. Review of the medical admission documents will guide research staff to offer study participation to those who are not obviously ineligible.

6. **Subject classification:** Check off all classifications of subjects that will be <u>specifically recruited for enrollment</u> in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☐ Children	☐ Healthy	☐ Fetal material, placenta, or dead fetus
☐ Non-English Speaking	☐ Prisoners	☐ Economically disadvantaged persons
☐ Decisionally Impaired	☐ Employees	☐ Pregnant women and/or fetuses
☐ Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects? ☐ Yes ☒ No (If yes, see Instructions section VII #4 for further requirements)

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

1. <u>Inclusion criteria for</u> Healthcare provider <u>participants</u> :
    - Assignment to one of the general medical inpatient units at YNHH during day-time shifts; intensive care units will be excluded given the morbidity of patients in this setting.
    - Volunteer to serve as study clinicians, attend a workshop about MI, and possibly receive live supervision.

- Agree to all procedures of this trial (randomization to training condition and of assigned patients, audio recording MI sessions, and completing assessments).

2. Exclusion criteria for Healthcare provider participants:
   - Have been formally supervised to use MI with patients on the units.
   - Intend to give notice to YNHH that they plan to leave the hospital or are scheduled for medical or family leave such that they will not be able to interview 40 patients during the study period.

1. Inclusion criteria for patients are:
   - Are 18 years of age or older.
   - Acknowledge use of a substance within past 28 days and meets screening criteria consistent with substance (illicit drugs, licit drugs that are used in a non-medically indicated fashion, alcohol, or nicotine) use disorder.
   - Are willing to consent to audio recording of interview with the Healthcare provider or CL psychiatrist.
2. Exclusion criteria for patients
   - Have an altered mental status such as delirium, encephalopathy, dementia or mental retardation or a score on the Confusion Assessment Method > 0 since this would impair provision of consent and ability to participate
   - Inability to speak English. Most of the Healthcare providers are mono-lingual English speakers, and all MI integrity raters only speak English. We therefore do not have the capacity to include Spanish-only speaking patients in the study.
   - Stroke (that precludes participation)
   - Resides in a nursing home, skilled nursing facility or Hospice Care
   - Receiving palliative care
   - Deaf
   - Unable to speak lucidly
   - Previous participation in the protocol.

8. How will **eligibility** be determined, and by whom?

Research staff will need to review admission notes from hospital medical charts of patients admitted the previous day, as indicated from the admission list provided by PAs on the Hospitalist Service at YNHH . Given the volume of inpatients at YNHH, it is impractical for research staff to approach every patient, nor is it an efficient use of their time. Review of the medical admission documents will guide research staff to offer study participation to those who are not obviously ineligible Staff will be reviewing patients' electronic admission documents in a limited fashion to determine the purpose, length of stay, primary language and any indicator for delirium or dementia. Research staff will destroy names and any other identifying information on said list of patients who are deemed inappropriate to be screened for the study. After determining initial eligibility to be screened, research staff will explain the study procedures and obtain written consent. Individuals who provide consent, will be administered three items from the Confusion Assessment Method.[117] A score of 1 (yes) on any item will trigger an evaluation by a psychiatric investigator to determine if the patient has the capacity to provide consent. If they score 0 screening will continue. Next, researchers will collect the Heaviness of Smoking Index,[114] demographic information and will administered the Time Line Follow Back[118] for the past month. After these procedures are completed and eligibility is confirmed, patients will be informed that they are eligible to participate. They will then be asked to complete a computer intake that includes, questions about primary substance of misuse, the MINI International Diagnostic Interview,[119] a functional impairment measure (Short Form 12; SF 12) and sections of the Addiction Severity Index[120] that relate to medical complications of substance use. Research staff will also request permission to contact patients in the

future to clarify any unresolved data issues if needed. They will be told that a Healthcare provider may approach them on the unit to discuss their health habits, which might be audio recorded as part of the study.

9. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

The potential risks in this study are related to psychiatric interviewing and loss of confidentiality for medical inpatients and for Healthcare provider participants.

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

For the Healthcare provider participants, a Research Assistant, Project Director, or Investigator will obtain written consent from Healthcare providers. Medical information will not be collected from Healthcare providers but we will collect information on attitudes, experience and demographic background. This will all be coded under a subject ID and kept on password protected data bases and in double locked files in the offices of research staff. Any information that is collected from subjects who are not eligible to participate (including screening information from those who have not provided consent or audiotapes from those who have not consented to participate in the study), will be destroyed.

For potentially eligible medical inpatients, information will be kept in a research chart that is not available to non-research staff unless safety issues mandate disclosure (e.g., risk of self harm or harm to others). In this case, the subject will be apprised of safety concerns and the need to inform his or her primary clinician about psychiatric or behavioral health concerns. Only the minimal necessary information will be disclosed. We have obtained a Certificate of Confidentiality that will facilitate frank sharing of information between the researchers and the patients. However, the patient subjects will also be apprised of the limitations of the certificate which, as above, include risk of self harm or harm to others.

11. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.) For more information, see the Instructions, page 24.
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal
    b. If children are involved, what is the investigator's 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
        i. Minimal risk
        ii. Greater than minimal/moderate risk
        iii. High risk

The principal investigator, Dr. Yonkers is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews. She and Dr. Martino will review entrance criteria of all inpatient subjects at a weekly meeting.

The principal investigator, the Institutional Review Board (IRB) or NIDA 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. All serious adverse effects will be reported to the Yale IRB in compliance with University and Medical School research review boards' protocols. The protocol's research monitor(s), e.g., study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies will be informed of serious adverse events within 5 days of the event becoming known to the principal investigator.

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

12. **Statistical Considerations:** Describe the statistical analyses that support the study design.

I. Data Management and Analysis

1. Data management

Procedures for highly efficient, real-time managing, monitoring, and analysis of data have been developed and refined by our research group. We are using OnCore, Yale's new Clinical Trials Management System (CTMS), to track procedures and data entry for patient characteristics and outcomes. Participants enter data directly into the computer via CASI. All computers are encrypted and password protected. Identifying data are not kept on the computer. For office PCs where data that were collected on paper is entered, we use a double entry method (staff data) and regular data checks to assess the integrity of the data base and missing data. After data entry and cleaning, de-identified data are moved to SAS databases for analysis.

2. Data analysis for quantitative primary and secondary outcomes

Outlined below is the general strategy for data analyses which will address each of our specific aims: (1) assess the uptake of MI by Healthcare providers on the medical units; (2) assess the integrity of MI when Healthcare providers use it on the medical units; (3) assess the cost-effectiveness of the three strategies; (4) determine how long the initial training effects endure across the study period.

- *Data reduction:* Primary outcome variables have been defined *a priori* to reduce the risk of Type I error. Preparatory analyses will include evaluation of baseline equivalence of groups on demographic and comparability of rates of data availability across conditions. If imbalances exist we will enter the unbalanced variables as covariates in the models below. Descriptive statistics for all outcome variables will be calculated prior to statistical analysis. Continuous outcome

variables will be evaluated for normality and transformations will be applied as necessary. Two-sided tests and overall alpha level of 0.05 for all primary hypotheses will be used.

- S*trategies for management of differential attrition:* We do not expect differential attrition across conditions in that the rate of Healthcare provider job turnover is very low and their activities in the study overlap considerably with their normal duties. However, in the event of Healthcare provider discontinuation in the trial, we will recruit new Healthcare provider hires to maintain a balanced design.
- *Evaluation of effects at implementation strategies:* The principal strategy for assessing the effectiveness of the study implementation conditions on outcome will be mixed effects general linear models for continuously measured primary (e.g., MI integrity) and secondary (e.g., strength and frequency of patient change talk) outcomes variables, and generalized linear mixed models for binary outcomes (e.g. meets criterion MI performance threshold). In both types of models we will have training condition as the main predictor variable and will include random effects for Healthcare providers to account for clustering of observations within Healthcare providers. Our main hypotheses involve group comparisons with the SEE IT group as the reference condition. We will consider significant comparisons of the DO IT and ORDER IT conditions to the SEE IT condition as supportive of our hypotheses. Comparisons of DO IT with ORDER IT will be conducted for exploratory purposes only.
- *Adequacy of sample size for primary hypotheses:* Effect sizes for power estimation for the continuous outcomes were based on studies by Miller et al.[23] (d=0.4 to 0.8) and Martino et al.[21] (d=0.4 to 1.2). A review article by Apodaca and Longabaugh[148] also suggests that at least medium effect sizes are expected for the between-group comparisons. Martino et al. [21] observed large effect sizes for the binary outcome comparison (meets criterion MI performance threshold, 53% vs. 18%); however, we conservatively assume a medium effect size for this comparison as well. Intra-class correlations accounting for expected within clinician variance were estimated based on Imel et al[149] and are expected to be small (in the 0.05 to 0.10 range). Feasibility constraints (i.e., 10 Healthcare providers per condition) limited the number of clusters (Healthcare providers) that we could consider. Finally, because we do not expect all Healthcare providers to identify substance using patients and use MI with them (i.e., our 1st hypothesis about MI uptake), we will require a larger sample size of study-enrolled patients to reach our targeted number of audio recorded MI sessions for hypothesis testing purposes. We estimate 80% of patients across conditions will receive MI. Based on these estimates and constraints, alpha level of 0.05 and power of 80%, 30 Healthcare providers and 40 patients per Healthcare provider will be sufficient for testing the primary hypotheses of the study. Table 2 shows the actual total sample size for the cluster-randomized design for continuous and binary outcomes, adjusted for a conservative estimate of MI uptake.

Table 2: Sample size estimates for the primary aims of the study based on alpha=0.05 for the pairwise comparisons of each condition to the control condition and 80% power.

Effect size	Total sample size for an ordinary RCT (3 arms)	ICC	Number of Healthcare provider	Average number of patients per Healthcare provider	Total sample size for a cluster RCT unadjusted for estimated MI uptake	Total sample size for a cluster RCT adjusted for estimated MI uptake
d=0.4	300	0.07	31	31	930	1116
40% vs 18%	195	0.1	30	17	510	765

3. Incremental cost-effectiveness analyses

The relative cost-effectiveness of the three MI implementation strategies will be assessed using both incremental cost-effectiveness ratios (ICERs) and cost-effectiveness acceptability curves (CEACs).

Incremental cost-effectiveness analysis is the appropriate approach to use in this study inasmuch as Do One and Order One both add clear and certain costs to See One.[150,151] ICERs and CEACs will be calculated from the provider (i.e., hospital) perspective. Using the cost estimates described in the Assessment subsection, we will calculate ICERs for multiple outcome measures, including (a) the number of MI sessions delivered (a measure of uptake of MI by Healthcare providers on the medical units), and (b) the number of MI sessions delivered to criterion (a measure of the integrity of MI delivered to patients on the medical units). The ICERs measure the incremental cost of using a given integration strategy, compared to the next-least-costly strategy, to produce an extra unit of effect for each of the outcomes. The most cost-effective integration strategy is then the strategy with the largest ICER that falls below the threshold value placed by decision makers on an additional unit of effect for a given outcome.[152] Because no threshold values exist for any outcomes used in the substance abuse treatment field, we will present ranges of values, defined by the ICERs for each patient outcome, over which each integration strategy would be considered cost-effective compared to the others. Decision makers can use these ranges in combination with their own evaluation of the value of outcomes to make policy decisions. By using multiple outcomes, we can determine the robustness of our cost-effectiveness findings and provide a more fine-grained cost-effectiveness analysis to address different priorities (e.g., uptake of MI by Healthcare providers on medical units, integrity of MI delivered to patients) that stakeholders may have.[153,154]

To illustrate the uncertainty associated with the ICER point estimates, costs and effects for each integration strategy will be bootstrapped (with 2,000 replicates) to produce confidence intervals around the ICERs and to produce CEACs for each of the outcome measures.[155] CEACs quantify the uncertainty in the cost-effectiveness analysis by showing the probability that each strategy is the most cost-effective for any given threshold value.[152,155,156] Intuitively, as the threshold value of an additional unit of a given outcome increases, the strategy that produces the **largest effect** becomes increasingly more likely to be the most cost effective, even though it adds incremental costs. Similarly, as the threshold value of an additional unit of a given outcome decreases, the strategy that has the **lowest cost** becomes increasingly more likely to be the most cost-effective. Finally, sensitivity analyses will be conducted to determine the robustness of the cost-effectiveness results to alternative assumptions about a wide variety of implementation parameters (e.g., cost of inputs). Dr. Todd Olmstead will conduct these cost-effectiveness analyses; he has extensive experience in this area. [95,140-144]

4. Qualitative data analyses

Each key informant interview will be will be audio recorded, transcribed, and independently coded by Dr. Kaufman *and* a member of her research team who will utilize debriefing to discuss and challenge findings.[157] Dr. Kaufman and her team will utilize grounded theory methods developed by Strauss and Corbin[158,159] to identify themes related to implementation facilitators and barriers across informants. The collection of data from multiple informants, iterative process of data collection and analysis, use of two researchers to code each transcript and work to consensus, keeping an audit trail of the data analysis process, and the theoretical sampling of themes and concepts will increase creditability, transferability, dependability, and confirmability of the findings.[157] We will identify the barriers and facilitators that are 1) unique to and 2) common across the conditions. Dr. Kaufman will oversee the qualitative analyses; she has extensive experience in this area.[96-100]

SECTION VI: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, state N/A and delete the rest of the section.

A. DRUGS, BIOLOGICS and RADIOTRACERS N/A

SECTION VII: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. Targeted Enrollment: Give the number of subjects:

a. targeted for enrollment at Yale for this protocol__see below_

b. If this is a multi-site study, give the total number of subjects targeted across all sites_n/a__

Participants will bePhysician Assistants (PAs) who work at the Yale New Haven Hospital (YNHH) Internal Medicine Hospitalist service and 1200-1600 inpatients who are being cared for by a PA from the Hospitalist Service. All PAs on the Internal Medicine Hospitalist service are eligible to participate. We will obtain written informed consent from all the PAs who express interest in participation and MI training. The PAs will be randomized to one of three conditions that are outlined below. The inpatients who may be eligible subjects will be followed for inpatient care by one of the Internal Medicine hospitalist service PAs. While they will not be randomized, they will follow the randomization condition of their PA. Additionally, we have expanded our target for enrollment to other Healthcare providers (i.e. nursing staff, physician, etc.) who work at Yale New Haven Hospital (YNHH) within general medical inpatient units. Between the PAs and other healthcare providers we intend to enroll 30-40 participants.

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

☐ Flyers	☐ Internet/Web Postings	☐ Radio
☐ Posters	☐ Mass E-mail Solicitation	☐ Telephone
☐ Letter	☐ Departmental/Center Website	☐ Television
☐ Medical Record Review	☐ Departmental/Center Research Boards	☐ Newspaper
☐ Departmental/Center Newsletters	☐ Web-Based Clinical Trial Registries	
☐ YCCI Recruitment database	☐ Clinicaltrials.gov Registry (do not send materials to HIC)	
☒ Other (describe): please see below		

3. Recruitment Procedures:

a. Describe how potential subjects will be identified.

b. Describe how potential subjects are contacted.

c. Who is recruiting potential subjects?

The PAs will be recruited from the Internal Medicine Hospitalist Service. All PAs will be encouraged to participate. Other Healthcare providers will be recruited from their general medical inpatient units.

The medical inpatients will be recruited from the inpatient Internal Medicine Internal medicine hospitalist service and other general medical inpatient units. The research assistant will review a list of patients either assigned to PAs working onthe internal medicine hospitalist service or those assigned to Healthcare providers working in other general medical inpatient units of the hospital. After patients are consented, screened and assessed, the research assistant will have access to the electronic medical chart and will identify which PA was assigned to a given patient.

4. Screening Procedures

a. Will email or telephone correspondence be used to screen potential subjects for eligibility prior to the potential subject coming to the research office? ☐ Yes ☒ No

b. If yes, identify below all health information to be collected as part of screening and check off any of the following HIPAA identifiers to be collected and retained by the research team during this screening process.

HEALTH INFORMATION TO BE COLLECTED:

Medical inpatients will undergo face-to face screening after providing consent. If eligible, they will undergo a comprehensive evaluation by computer and by Research Assistants, several of whom will be hired to work on this project. This will include medical, psychiatric and drug use histories. Standardized psychosocial assessments and self-report rating forms are administered via self-report on a computer or in limited instances (e.g., substance use calendar) on paper. All of this will be coded by a subject ID rather than the individual's name.

HIPAA identifiers:

☒ Names
☒ All geographic subdivisions smaller than a State, including: street address, city, county, precinct, zip codes and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly-available data from the Bureau of the Census: (1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people, and (2) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
☒ 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 voice prints (audio-recording of MI session)
☐ Full face photographic images and any comparable images

5. ☐ Any other unique identifying numbers, characteristics, or codes **Assessment of Current Health Provider Relationship for HIPAA Consideration:**

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

☐ Yes, all subjects
☐ Yes, some of the subjects
☒ No

If yes, describe the nature of this relationship.

6. **Request for waiver of HIPAA authorization:** (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

Choose one: For entire study: _____ For recruitment purposes only: _X_____

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data;

We request a waiver to conduct a brief and limited review of admission documents to determine patients who are not eligible for screening because they do not speak English, have an organic brain syndrome such as dementia or encephalopathy, or who have already been previously enrolled in this research protocol. Those who are not immediately excluded will be approached to request participation and informed consent will be obtained. Given the volume of inpatients at YNHH, it is impractical for research staff to approach every patient, nor is it an efficient use of their time. Review of the medical admission documents will guide research staff to offer study participation to those who are not obviously ineligible.

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data.

1. We estimate that we will have to screen over 5000 medical inpatients for participation. We further estimate that 20% will be ineligible for screening given the basic exclusion parameters outlined above. The cost and work will be substantially reduced by the initial waiver to determine preliminary ineligibility. Further, it reduces the risk of loss of confidentiality for data collected from subjects who have a planned short hospitalization or have a medical condition that would preclude participation (eg dementia). Information on patients who either are not eligible for screening or refuse participation is immediately destroyed.

By signing this protocol application, the investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

*Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered **entity** must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.*

7. **Required HIPAA Authorization:** If the research involves the creation, use or disclosure of protected health information (PHI), separate subject authorization is required under the HIPAA Privacy Rule. Indicate which of the following forms are being provided:
   - ☒ Compound Consent and Authorization form
   - ☐ HIPAA Research Authorization Form

8. **Consent Personnel:** List the names of all members of the research team who will be obtaining consent/assent.
   Research assistants will be hired to work on this project, and their names and copies of training certificated will be provided to the HRPP before study procedures begin.

9. **Process of Consent/Assent:** Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

   Consent of Healthcare providers: Healthcare providers will be consented primarily by study Principal Investigator and his Co-Investigator Kimberly Yonkers, MD, as part of outlining the MI Training offering. This will occur in a staff meeting group setting, with opportunity for individual questions in a one:one manner with the PI. The nature of randomization will be made clear to personnel, as well as the requirements of their participation (ie attending training and possible follow-up). Of particular importance to us is the risk for supervisory coercion to recruit PAs in particular into the study. Dr. Victor Morris, Director of the Hospitalist Services, and Will Cushing, Chief PA, have supervisory responsibility over the PAs. They are Co-Investigators for the proposed study and fully supportive of absolute voluntary PA consent for initial and ongoing study participation. They will provide research and supervisory support to the fact that the decision of any PAs to not participate in the study will not influence their job or performance appraisal. As an added protection, neither Dr. Morris nor Mr. Cushing will personally consent any PAs.

   Consent of hospital patient study subjects: The procedure for obtaining informed consent entails a face-to-face discussion between the potential subject and a trained research assistant who will attend HIC training specific to obtaining informed consent. For medical inpatients, we will consent preliminarily eligible inpatients, then verbally administer a de-identified screening battery. Those who are preliminarily eligible will be invited to complete a full intake. Medical inpatients are encouraged to ask questions about any confusing points, and to consider carefully their choice to participate in this, or any, research protocol. Significant conversation will cover the fact that the decision to decline study participation will in no way affect their medical care.
   All study data will be kept in a research chart. Medical inpatients will be told through the informed consent process that if they express suicidal or homicidal intent, this would incur assessment for voluntary or involuntary hospitalization, or a loss of some confidentiality. All subjects will be informed about the limits of confidentiality concerning suicidal intent and homicidal intent. Suicidal or homicidal attempts or completions, and hospitalizations, will be monitored as serious adverse events, and will be reported to the Human Research Protection Program (HRPP) at the Yale School of Medicine and other clinic research review boards.

   Consent of Hospital Clinical Staff: Hospital Clinical Staff will be consented by study Principal Investigator, his Co-Investigator Kimberly Yonkers, MD and/or Project Director, Ashley McCaherty as part of describing the focus groups and/or interviews that will be conducted throughout the course of the study. This will take place in a scheduled meeting group setting, with opportunity for individual questions in a one:one manner with the PI, Co-Investigator and/or Project Director. All Hospital Clinical Staff will be given the choice to sign-up for these focus groups and /or interviews and will be fully informed that their participation is completely voluntary.

   Consent for audio recording: Healthcare provider's will independently consent their own patients throughout the course of their work day for the process of audio-recording MI sessions, being blind to

who is or is not a subject in the study and recognizing that the mere act of recording a clinical session requires patient permission. Such recordings will only be retained for patients who in fact are matched up with consented study subjects. In the event that a Healthcare provider records an MI session with a non-study subject, that recording will be immediately deleted from the digital recorder (ie never downloaded to the hard drive server). A de-identified copy of the consent for audio-recording will be maintained in research files for the sake of documentation.

10. E**valuation of Subject(s) Capacity to Provide Informed Consent/Assent:** Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

Healthcare providers will be able to provide consent, given the nature and sophistication of their employment and level of education. However, it is important to ensure that hospital patients possess the capacity to provide informed consent. Capacity to consent will be assessed in a systematic format. Immediately excluded from consideration will be new admissions of patients with obvious diagnoses indicating cognitive impairment, ie dementia. To ensure that the respondent has the capacity to provide consent, the study personnel will assess orientation to person, place and date. They will also be administered 3 questions for the Confusion Assessment Method. A positive score on any of these items will trigger an evaluation by an attending psychiatrist who is part of the study team. The evaluation will determine the patient's capacity to provide informed consent. Cases will be treated on a case-by-case basis, and at no point will research assistants make a final decision on cases of questionable capacity to consent. Patients that are determined by a study investigator to not possess the capacity to provide consent will be provided with information on community resources for support and treatment.

A waiver of signed consent will be needed for a subset of patient subjects. This is due to the study being conducted within an acute medical inpatient unit, where conditions that might limit a person's ability to sign the consent form may occasionally occur. This subset of patients will include: patients that are physically unable to write (i.e. hand tremors, spinal cord injury, broken hand, broken shoulder, muscular dystrophy and other physical ailments preventing a patient from physically signing), unable to see (i.e. legally blind, uncontrolled type 2 diabetes mellitus which led to blurred vision), unable to read (i.e. patient does not have their glasses on them).

11. Documentation of Consent/Assent: Specify the documents 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 to subjects.

Compound authorizations attached.

12. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. Translated copies of all consent materials must be submitted for approval prior to use. N/A. Only English-speaking subjects will be enrolled in this trial.

13. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed 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.

☐ **Not Requesting a consent waiver**

☐ **Requesting a waiver of signed consent**
☐ **Requesting a full waiver of consent**

A. Waiver of **signed** consent: (Verbal consent from subjects will be obtained. **If PHI is collected, information in this section must match Section VII, Question 6**)

☐ **Requesting a waiver of signed consent for Recruitment/Screening only**

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

a. Would the signed consent form be the only record linking the subject and the research?
☐ Yes ☐ No

b. Does a breach of confidentiality constitute the principal risk to subjects?
☐ Yes ☐ No

OR

c. Does the research activity pose greater than minimal risk?
☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** Please note: Recruitment/screening is generally a minimal risk research activity
☐ No

AND

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

☒ **Requesting a waiver of signed consent for the Entire Study (**Note that an information sheet may be required.)

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

a. Would the signed consent form be the only record linking the subject and the research?
☐ Yes ☐ No

b. Does a breach of confidentiality constitute the principal risk to subjects?
☐ Yes ☐ No

OR

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

AND

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

As mentioned in section 10, a waiver of signed consent will be needed for subjects that are physically unable to provide a signature (i.e. hand tremors, spinal cord injury, broken hand, broken shoulder, muscular dystrophy and other physical ailments preventing a patient from physically signing) or are unable to see (i.e. legally blind, uncontrolled type 2 diabetes mellitus which led to blurred vision), unable to read (i.e. patient does not have their glasses on them). We currently have an information sheet that is provided to this subset of patient subjects.

B. **Full waiver** of consent: (No consent from subjects will be obtained for the activity.)

☒ **Requesting a waiver of consent for Recruitment/Screening only**

a. Does the research activity pose greater than minimal risk to subjects?

☐ Yes ***If you answered yes, stop. A waiver cannot be granted.*** Please note: Recruitment/screening is generally a minimal risk research activity

☒ No

b. Will the waiver adversely affect subjects' rights and welfare? ☐ Yes ☒ No

c. Why would the research be impracticable to conduct without the waiver?

We estimate that we will have to screen over 5000 medical inpatients for participation. We further estimate that 20% will be ineligible for screening given the basic exclusion parameters outlined above. The cost and work will be substantially reduced by the initial waiver to determine preliminary ineligibility. Further, it reduces the risk of loss of confidentiality for data collected from subjects who have a planned short hospitalization or have a medical condition that would preclude participation (eg dementia). Information on patients who either are not eligible for screening or refuse participation is immediately destroyed.

d. Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

☐ **Requesting a full waiver of consent for the Entire Study (Note: If PHI is collected, information here must match Section VII, question 6.)**

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

a. Does the research pose greater than minimal risk to subjects?

☐ Yes ***If you answered yes, stop. A waiver cannot be granted.***

☐ No

b. Will the waiver adversely affect subjects' 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 subjects at a later date?

SECTION VIII: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

a. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research?

Interview dates, dates of birth, subject names & addresses & contact information, hospital Medical Record Numbers, voice recording.

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

All data obtained via paper and pencil, or by digital recordings, will be coded by a unique study number and will be stored in locked filing cabinets in locked research offices. For medical inpatients, all data entered via the computer will also be coded by a unique study identification number. In the event that Healthcare provider's ambitiously record a patient MI session with a non-study subject, the recording will be immediately destroyed from the digital recorded without ever being downloaded to our ITS server. However, this person's de-identified audio-recording consent will be maintained for paper files.

c. How will the digital data be stored? ☐ CD ☐ DVD ☐ Flash Drive ☐ Portable Hard Drive ☐ Secured Server ☐ Laptop Computer ☐ Desktop Computer ☐ Other

d. 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 subject's participation in the study?

Data stored on the computer will not contain any identifiable Personal Health Information (PHI). Interview dates, schedules, outcomes, and study progress will be stored in a de-identified tracking database stored on a secure server at Information Technology Services' Data Warehouse Center at Yale University. Contact information and other PHI will be kept in a separate database also located on the secure server at the Data Warehouse Center which is backed-up daily. Access to the server is double password-protected and limited to a select number of authorized Yale staff. All staff accessing the server must use a Yale-managed and owned administrative desktop computer located in the Department of Psychiatry. Similarly, authorized study personnel will be able to access the server via Virtual Private Networks (VPN) configured on Yale-managed and owned laptop computers. Yale VPN provides a method for using a public network (e.g. internet) to securely access a private network (e.g. server). Lastly, Yale University passwords must be changed at least once per calendar year to a different password. This includes primary and responsible Yale-issued NetIDs. Access to Yale's network and affiliated servers will be denied to any staff member who fails to change their password annually. Each year's password must be unique and cannot be similar to previous year's passwords or the new password will not be accepted. Yale's password must have 8-14 characters; must contain at least 2 letters; must contain at least 2 non-letters; must NOT contain Illegal characters < > & \ , ' " : (less than, greater than, ampersand, backslash, comma, apostrophe and quotation marks).

Do all portable devices contain encryption software? ☒ Yes ☐ No
If no, see http://hipaa.yale.edu/guidance/policy.html

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

Upon completion of the study, files will be destroyed in a manner consistent with HIC policy at that date.

f. Who will have access to the protected health information (such as the research sponsor, the investigator, the research staff, all research monitors, FDA, Yale Cancer Center Data and Safety Monitoring Committee (DSMC), SSC, etc.)? (please distinguish between PHI and de-identified data)

The databases are stored on an "exclusive" data drive that can only be accessed by authorized Yale-issued NetIDs who work on this study, including the PI, Project Director, and Research Assistants. As an extra safe guard, we will create a "strong" password on the Access study database which is at least 8 characters with at least one uppercase and lowercase letter and one number or symbol. Individual computers that have access to PHI have Pretty Good Privacy (PGP) whole disk encryption installed on them as well as

MXI Security. Therefore, at the time of initial login to the desktop you need to enter your Yale NetID and password and you also need to logon to MXI Security which also requires a password. Failure to logon to MXI Security will prohibit anyone from accessing any of the files on that desktop computer.

g. If appropriate, has a Certificate of Confidentiality been obtained?

A COC has been obtained and copy has been provided for the HIC.

h. 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. No.

SECTION IX: POTENTIAL BENEFITS

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

Integrating substance abuse interventions into primary care could improve health outcomes and reduce health care costs.[51,52,57,75,76] However, this is contingent upon effective implementation strategies. We will compare and estimate the cost effectiveness of three implementation strategies that have the ability to interdigitate well into a general medical inpatient setting.

This study proposes great value in service delivery and increased medical knowledge to individual patients and their healthcare providers. Substance use increases general medical and psychiatric morbidity. Knowledge about the best methods for implementing evidence-based practices such as motivational interviewing into general medical settings is sorely needed.

Medical inpatients who have a substance use problem may receive a motivational intervention that may enhance their interest in substance use treatment.

Healthcare providers who participate may benefit in the receipt of additional training for motivational interviewing. In addition, they will receive CMEs for didactic training.

SECTION X: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?

Participation in this study is voluntary for Healthcare providers, Hospital Clinical Staff, and hospital inpatients alike and the quality of or general provision of their healthcare is in no way related to their

choice to enroll or not enroll in this RCT. Treatment alternatives include receipt of usual services from hospital social work of CL services.

2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.

   Study subjects (patients) will be paid $30 for their full participation in this study. If a patient prefers not to be paid in cash, they can be reimbursed with a $30 gift card instead.

   Healthcare provider participants will be reimbursed $350 for baseline assessments, attendance at our high-quality Motivational Interviewing training, and attendance at our baseline focus group. Additionally they will be reimbursed $50 for completing post-trial assessments and attending a post-trial focus group. Hospital Clinical Staff will be paid $20 for their participation in focus groups or interviews in this study. These focus groups or interviews may occur up to 3 times throughout the study and therefore they will be paid up to $60.

3. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.

   There are no costs to any study subjects incurred as part of participation in the research.

4. **In Case of Injury:** This section is required for any research involving more than minimal risk. N/A
   a. Will medical treatment be available if research-related injury occurs?
   b. Where and from whom may treatment be obtained?
   c. Are there any limits to the treatment being provided?
   d. Who will pay for this treatment?
   e. How will the medical treatment be accessed by subjects?

   This study does not entail physical procedures that may cause injury. No compensation is available for emotional injury. All patients enrolled in study are currently receiving health care at the study-sponsoring hospital.