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Research Strategy

SIGNIFICANCE

Definitions and Importance of Problem: Non-medical use of prescription drugs has been defined as "using a psychotherapeutic drug, even once, that was not prescribed for you, or that you took for only the experience or the feeling it caused"[10]. In addition, medical misuse of prescription drugs[4, 16] refers to taking a medication at a higher or more frequent dose then prescribed. This application focuses on both kinds of misuse (non-medical and medical) of prescription stimulant medications (PSM; e.g., Adderall, Ritalin) which are the fastest growing class of illicit drugs[20, 21]. PSM misuse is most prevalent among adolescents and young adults[11, 15-19] with college students at high risk for PSM misuse[20]. Given the academic and other pressures faced by college students, PSM are likely to be misused by students to stay awake and alert in order to complete their work and study for exams. PSM have a high potential for abuse due to their reinforcing properties, and improper use can have potentially serious health effects, especially for individuals with underlying cardiac conditions. McCabe and colleagues suggested that college campuses provide an "ideal environment" to foster PSM misuse, due to increased access to substances on campus, cultural acceptability for substance use, and peer pressure,[20] and also suggested college students may be at higher risk for PSM misuse, given the higher accessibility of different medications on campus, and the likelihood of students sharing their prescriptions with others[25]. For example, in a Canadian study, 78% of college students who engaged in PSM misuse reported obtaining the PSM from a friend or acquaintance holding a prescription for it[26]. College students who had PSM prescriptions are often approached or invited to divert these medications with up to 60% of those holding a prescription reportedly giving away or selling their PSM[4, 16, 179, 181].

Prevalence Rates and Consequences. Epidemiological trends indicate an increase in PSM misuse among young adults and college students, and rates are at their highest level in 15 years, which poses a growing public health concern[20, 21, 23, 181]. Estimated prevalence rates vary widely; in over 25 studies of college student PSM misuse conducted through 2009[180], estimates ranged from a low of 5.9% for past 30 days, to a high of 36% for lifetime prevalence in a general sample and 55% for lifetime rate in a fraternity sample[4, 24, 27, 28, 180]. Our own work has revealed that, by the fourth year of college, at least 31% of students have engaged in PSM misuse at least once in their lifetime, and annual prevalence peaks during the third year of college at approximately 20%[1]. In addition to rising prevalence rates, there are many consequence of PSM: headaches (33% of users), stomachaches (33%), irritability (62%), sad mood (25%), and sleeping difficulties (72%)[4, 29]. PSM misuse has also been associated with health issues including cardiovascular failure, jitteriness, hyperthermia, seizures, and anxiety[12, 186]. Compared to students who do not, those who misused PSM also had more social difficulties, had lower GPA, and reported concerns about their academic performance[29-31]. Our research has also found students who misuse PSM skip classes more frequently and spend less time studying than those who do not use or who use only as prescribed[27, 147].

PSM Misuse and Co-occurrence of AOD. We have consistently shown that PSM misuse is also a marker for heavy AOD involvement as it seldom occurs in isolation[1, 145-147]. Students who engage in PSM misuse are at risk for a host of issues related to alcohol and marijuana use compared to those who do not use PSM and those who use but do not misuse (i.e., take the PSM as prescribed), including being more likely to have used other drugs, to report frequent binge drinking, and more likely to drive after binge drinking than other college students[4, 29-30, 33, 36-37, 131]. Adolescents and young adults have particularly high rates of concurrent poly-drug use with up to 90% of past-year PSM misusers reporting using other drugs, particularly marijuana[31, 33-35]. Students who misuse PSM are more likely to meet diagnostic criteria for dependence on alcohol and marijuana, and are more likely than students abusing other drugs to report any drug related problems and to experience nine out of ten drug related consequences as assessed by the Drug Abuse Screening Test-10 (DAST-10)[32-33]. Thus, in addition to harm related to PSM misuse per se, considerable harm is related to the co-occurrence of PSM misuse with excessive alcohol, marijuana, and other drug use.

Dearth of Interventions and Missed Opportunities. Given the prevalence and consequences of PSM misuse on college campuses, the high co-occurrence with alcohol and marijuana, and the academic and public health implications, innovative prevention and treatment approaches are critically necessary[14, 20, 33, 39-41]. However, there are currently *no documented efficacious interventions* targeting college students who misuse PSM. The proposed study explicitly leverages expert knowledge (Arria) from existing NIDA-funded research on risk factors for PSM with expertise in screening and brief intervention (SBI) for college student alcohol and marijuana misuse by leaders in the field (Geisner, Kilmer, Larimer, Lee, Cimini) to develop and test such an intervention on three college campuses, in order to attack the problem of PSM misuse and bridge this important research and service gap. Consistent with other interventions in the college setting, we propose to

use brief interventions whose primary target will be PSM misuse; however there is evidence that these types of interventions will have secondary effects/reductions on other substance use[166]. Thus, our approach is significant as it has the potential to be both efficacious and highly efficient for reducing PSM misuse and related comorbid alcohol and marijuana use in a high-risk population (i.e., college students).

Evidence for Brief Interventions with College Students. The proposed intervention builds on the success of existing Brief Motivational Interviewing (MI)[168] strategies such as Brief Alcohol Screening and Intervention for College Students (BASICS)[5,6], but adapts the approach to focus on PSM misuse in addition to comorbid alcohol and marijuana misuse. The BASICS program incorporates personalized feedback regarding normative perceptions and actual norms, motives for using, and strategies to minimize negative consequences from alcohol use, and has been deemed by the NIAAA Task Force on College Drinking Prevention as a Tier 1 Intervention[63, 64]. Several theories underlie BASICS, including Social Comparison[65] and Social Learning Theory[66] which suggest people compare themselves to others as a way to evaluate appropriateness of their own behavior and learn by watching others. While BASICS targets alcohol use, other substances have been the focus of in-person feedback-based interventions patterned after BASICS. For example, an in-person, personalized feedback intervention (PFI) for marijuana designed and evaluated by members of our team showed reductions in number of joints used and a trend toward fewer consequences compared to controls[169]. Thus, adapting PFIs to address PSM misuse is timely and fills a critical need.

Prior research suggests that college students' beliefs about the health risks and academic benefits of PSM are malleable, and that intervening on academic beliefs may reduce likelihood of future PSM misuse[170].To date, however, we are aware of only *one intervention study* with PSM, and it sought to change college students' expectancies regarding benefits of PSM rather than misuse per se[171]. Looby and colleagues' intervention involved presenting the student with research-based information about the lack of evidence for a cognitive enhancement effect from PSM, and inviting the student to personalize that information based on feedback about how their own cognitive performance and subjective mood and arousal changed in response to a placebo substituted for methylphenidate. While the trial[171] did not show a reduction in PSM misuse, which may have been due to their decision to focus on PSM initiation among stimulant-naïve students, it did demonstrate the efficacy of a face-to-face intervention for changing college students' expectancies about PSM. The proposed work will build on our expertise in brief interventions by presenting personalized feedback about students' experiences with and beliefs surrounding PSM misuse alongside information about actual norms, outcomes, and effects to elicit personally relevant reasons for changing. Translating this strategy into a more clinically feasible approach, the proposed intervention will leverage MI strategies as an alternative way of encouraging students to personalize research-based information. By developing discrepancies between values and goals of importance to the student (e.g., "everyone is using these and I want to do well academically too") and ways in which the status quo could be in conflict with these (e.g., a minority of students report use, and those who use have lower grades), the feedback is designed to prompt contemplation of and a commitment to change.

Web-Delivered Intervention. Derivatives of BASICS such as Web-based PFIs have been efficacious in reducing college student drinking [58-62]. Personalized normative feedback (PNF) interventions for college student alcohol use[67-68], which focus primarily on correcting misperceived descriptive norms by providing accurate normative feedback, have evolved from BASICS and resulted in significant effects on drinking [93-96]. There is reason to believe normative feedback may have a similar impact on PSM misuse given recent data suggesting widespread normative misperceptions for PSM[156]. Thus, **Study 1** aims to document accurate norms on each of the three participating campuses, in order to adapt normative feedback components of a PFI for PSM misuse. Consistent with preliminary research, we hypothesize that students' perceived norms of PSM will be greater than actual norms and these normative perceptions will relate to student's own PSM.

Costs associated with personalizing information via the Web are quite low, suggesting wide potential reach and resultant public health benefit of even modest improvements[42, 43, 45]. Internet-delivered tailored prevention or intervention materials have targeted a range of health behaviors with a variety of populations[42], including tobacco use[43-44, 47-52], depression and anxiety[53-57], and drinking[58-62]. Web approaches are attractive in a stepped care model due to cost-effectiveness, personalization, and widespread accessibility of the internet[42-44]. This approach may be ideal for students, as younger individuals not only wish to access health information through technology, but are critical of more traditional methods[46]. Thus, **Study 2** aims to reach college students who engage in PSM misuse through web screening and intervention[42]. We hypothesize that participants who receive the PFI will reduce PSM misuse assessed at follow-ups. We further expect reductions in perceived benefits of PSM and perceived descriptive norms for PSM, and increases in use of alternative behaviors to support academic success, and expect these changes will mediate impacts on PSM use at follow-ups. We

further expect secondary effects of the intervention on alcohol and marijuana use, and expect these reductions will partially mediate PSM outcomes (see Mediators below). Finally, we will explore PSM motives and demographics as potential moderators of intervention efficacy (see Moderators below).

In Person Feedback in Student Health and Counseling Centers. With well documented barriers related to implementing approaches developed in a lab setting or in the context of a research trial to "real world" clinical settings, Study 3 will test the efficacy of the PFI in a Student Counseling and Health Center at a large, diverse public university in the Northeastern U.S. Students presenting with medical and/or mental health concerns will be screened for PSM misuse as well as AOD use as part of their routine care and will be offered either an in-person session, the web-based PFI, or assessment only control based on random assignment. For practical purposes related to staff time in a busy clinical setting, web-based PFI, if effective with this population, would be preferable; however, if in-person PFI outperforms the web-based (or only under certain conditions for certain students), this will help identify how to best serve students who may be struggling. An important aspect of our in-person approach will be to use the student's past experiences with PSM as a starting point. An MI-trained interventionist will help the student to develop discrepancies, elicit change talk, provide students with opportunities to more thoroughly explore and question their beliefs, and offer alternatives by reviewing their personalized responses. MI has been an effective approach for other interventions, and it is an appropriate modality for this target population. Thus**, Study 3** aims to determine whether and for whom in-person implementation of the PFI is more efficacious than web-based PFI in reducing PSM misuse and co-occurring alcohol and marijuana use. We hypothesize both web- and in-person PFI will be more efficacious than control. We also hypothesize in-person intervention will be more efficacious than web, particularly at long-term follow-up (18-months), given some literature suggesting advantages of in-person PFI emerge over longer periods[200]. As with Study 2, we expect reductions in perceived benefits and norms of PSM and increases in alternative behaviors will mediate efficacy of both interventions, as will reductions in alcohol and marijuana use. We will explore demographics and PSM motives as moderators of overall and differential efficacy.

Moderators: Motives for PSM misuse and Demographics. Evidence suggests students misuse prescription stimulants for a variety of reasons[91-92, 159, 177]. Understanding motives for PSM misuse is important to identify necessary intervention components and to determine for whom interventions are most useful. Motivational models of substance use suggest behavior is motivated by different reasons, leading to theoretically and psychologically distinct behaviors[195, 196]. Different motivations are associated with unique patterns of use and consequences, influencing when or where one will use a substance, how frequently or how much one will use, and what consequences may occur[195, 196]. Studies of PSM use through alternative assessment methods (e.g., Twitter and Wastewater analysis)[182-184] have confirmed that PSM use among students peaks around mid-terms and finals, supporting that perceptions of academic benefit and academic motives lead to PSM misuse among students. Indeed, self-reported motives for use among students include improving concentration, to help with studying, enhance academic performance, and, with less frequency, to counteract effects of other drugs, lose weight, experiment, and/or get high[1, 3, 29, 91-92, 159, 177]. Overall, reasons for PSM misuse have been characterized into three main categories: academic motives, partying motives, and both academic and partying motives. The proposed intervention addresses each of these motives for PSM misuse. Students who engage in PSM misuse for academic reasons may benefit differently from those who use it more for recreational reasons. Each kind of user may benefit from alternative strategies to achieve desired academic and/or social outcomes rather than relying on PSM. Thus, the current study will explore whether student's motives for PSM misuse will moderate intervention efficacy. We will also explore whether characteristics including gender, race/ethnicity, and fraternity/sorority status moderate intervention effects.

Mediators: Alcohol and Marijuana Comorbidity with PSM Misuse. Given the high correlation between PSM misuse and AOD, it is possible to conceptualize motives for PSM misuse as related to consequences of AOD. For students who report partying motives for PSM, the relationship between AOD use and PSM misuse is intuitively obvious in light of a shared propensity hypothesis. In some cases, students are seeking feelings of euphoria or a buzz from PSM[1, 145] just as they do with other substances. In other cases, the appeal of PSM is in its ability to deliver wakefulness, which allows the user to extend a drinking session and thereby consume more alcohol[1, 147]. Yet even when the motives for PSM misuse appear to be purely academic, PSM misuse may still be closely linked to AOD use as a compensatory strategy, whereby students turn to PSM in hopes of making up for the classes and study time they missed as a result of their AOD use, or possibly to manage side-effects of their alcohol and/or marijuana use. In the context of the college setting, heavy alcohol use has been associated with lower GPA, less engagement with faculty, and increased sleepiness[160-162]; conceivably, PSM could be used to combat and counter problems with fatigue and tiredness. Marijuana use is associated with deficits in attention, concentration, and memory, and this impact is more pronounced the more frequently
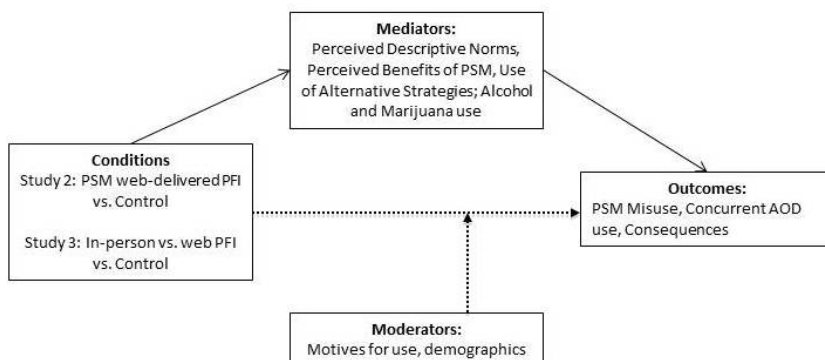
someone uses, though shows improvement with sustained abstinence[163-165]. In fact, longitudinal analyses our team has conducted support the conclusion that PSM occurs in the context of AOD-related declines in academic performance[147]. Specifically, increases in alcohol and marijuana use over time appear to contribute to declines in class attendance, which in turn contribute to declines in GPA, and this cascade of events is strongly predictive of students engaging in PSM misuse for studying. In an intervention focused solely on reducing PSM misuse, most PSM misusers would have little room for decreasing their misuse due to the episodic use patterns (primarily around mid-terms and finals). Thus, in addition to directly targeting PSM misuse through a PFI, another reason for this application's significance stems from its focus on reducing PSM misuse directly as well as targeting intervention components for co-occurring alcohol and marijuana misuse (mediators in Studies 2 and 3). We hypothesize that PFI will lead to reductions in comorbid alcohol and marijuana use, and that reductions in alcohol and marijuana use will serve to mediate reductions in PSM misuse. By focusing holistically on the student's underlying substance use problems, an intervention targeting PSM misusers could have a substantial impact on a subset of college students who are at particularly high risk for co-occurring AOD use and associated consequences. Delivery of intervention components will be targeted to high risk times in the academic calendar to maximize benefits.

Mediators: Beliefs, Perceptions, and Alternatives. Guided by the Health Belief Model, our approach targets students' beliefs about benefits of PSM, based on evidence that higher perceived benefits and positive beliefs about PSM predict greater likelihood of use[25, 27, 31, 170, 171, 176, 177, 178]. Such beliefs can be impacted by academic and health-related information[170]. According to the prototype-willingness model, motivation that drives behavior can be used to reduce thoughts associated with the behavior itself[170]. That is, given that PSM is primarily academically motivated, the proposed intervention will leverage the student's underlying academic motives to create ambivalence about PSM misuse and cultivate motivations toward increasing alternative behaviors (i.e., regular class attendance, studying, sleep) and bolstering academic self-efficacy. At the same time, the intervention will also provide information about risk-factors accompanying PSM misuse as supported by the literature (i.e., increased AOD, lower GPA), which will help students develop less favorable perceptions about PSM and thereby reduce their own likelihood of future use. We hypothesize reductions in expected benefits of PSM will mediate efficacy of both web-based (Study 2 and 3) and in-person (Study 3) PFIs.

Next, we will target students' descriptive norms about how many of their peers engage in PSM misuse. Similar to research with alcohol, it has been suggested that college students over-estimate the prevalence of PSM use/misuse on their campuses, which may contribute to an erroneously held view of the normality of this behavior[80, 167]. For example, in one study[176] 71.4% of students reported PSM misuse among their peers, however only 9.2% actually used them. In another study[8], 60% of college students knew someone who used. Our own recent study[156] demonstrated that almost all college students (89%) inaccurately perceived the typical student as having used PSM (medically or non-medically) at least once in their life. Such misperceptions were associated with their own higher PSM misuse as well as higher hazardous drinking, prompting the suggestion that interventions aiming at correcting norms may be useful[80, 156]. We hypothesize reductions in perceived descriptive norms for PSM use will mediate both web- (Study 2 and 3) and in-person (Study 3) PFI efficacy. Finally, the perceived benefits of healthier alternatives such as reducing AOD use, getting adequate sleep, studying regularly, and attending class will be targeted. Protective Behavioral Strategies (PBS)[81-87] have been related to reductions in problem drinking and account for treatment effects in college and community samples[64, 88, 82-84, 89-

Theoretical Framework for Study: Figure 1 shows our heuristic model.

Mediators: Perceived Descriptive Norms, Perceived Benefits of PSM, Use of Alternative Strategies; Alcohol and Marijuana use

Conditions
Study 2: PSM web-delivered PFI vs. Control
Study 3: In-person vs. web PFI vs. Control

Outcomes: PSM Misuse, Concurrent AOD use, Consequences

Moderators: Motives for use, demographics

90], thus it is important to develop and test healthier alterantives for PSM misuse. We hypothesize that increased use of alternative strategies to achieve desired academic and social benefits will mediate efficacy of both web-based (Study 2 and 3) and in-person (Study 3) PFI.

(b) Innovation:
The proposed research is innovative for several reasons:
1. ***Novel interventions to be adapted from existing methodology and tested with PSM:*** There have been no interventions of any kind developed for students who misuse PSM, and only one published intervention has targeted delay of onset of PSM through changing expectancies in this population. Lessons learned from prior

research on brief interventions[88, 98-100] will be applied to intervening with PSM misuse and comorbid AOD use in college students, representing an innovative response to this multi-faceted issue. The proposed feedback includes components uniquely relevant to PSM and the behaviors surrounding their misuse (e.g., diversion of medication). With the potential for attention problems interfering with full, sustained review of lengthy personalized feedback by the student, the current study breaks feedback down into concrete sections strategically delivered over the course of the quarter/semester. Students can go back and view the salient components of the intervention as often as they wish, also meeting the needs of a sample with potential attention challenges. Understanding factors influencing outcomes (e.g., motives, concurrent use with other substances) will help to further identify how to target interventions to maximize gains. Once the adapted materials are tested, larger trials can provide more evidence and aid in dissemination. Programming used for the intervention is easy to modify and relatively inexpensive to adapt for other campuses. Thus, this low cost[104-105], brief, personalized intervention fills an important gap in the services available at present for college students who misuse PSM.

2. **Collaboration between a team of experts.** The research project will be conducted by a team with expertise in the epidemiology and treatment of PSM and co-occurring AOD use. We have been instrumental in understanding the risk factors and correlates of PSM in college students and in developing and testing efficacious in-person and web-delivered SBI/PFIs with college populations. Perceived descriptive norms and the overestimation of peers' risk behaviors are pivotal in the development and maintenance of college student drinking and marijuana use, and correcting these misperceptions is effective at reducing both use and related harms.[69, 70-79] Our team has been at the forefront of developing and testing such interventions[5, 71, 74, 88, 93, 108-110, 134, 137, 138, 143, 144]. Given that no interventions have been developed or tested with college students who misuse PSM, we are uniquely qualified to adapt and test evidence based treatments in reducing the misuse of PSM.

3. **Shift current clinical practice paradigms in real world healthcare settings:** The proposed project reaches beyond laboratory research by testing the study interventions in a campus-based primary health and mental health care setting, offering the opportunity to address issues of capacity-building, intervention fidelity, and cost-effectiveness as interventions are prepared to be taken to scale through dissemination. Study 3 is a natural extension of nearly a decade of work in building service delivery capacity by the Principal Investigator (Dr. Cimini), and practitioners at the Health Center and Counseling Center of the University at Albany, SUNY. With funding support from the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment (SAMHSA-CSAT), Albany has built both research and service-focused infrastructures to deliver and evaluate SBI for alcohol use with fidelity in both the Health Center and Counseling Center. Based on the strength of our project results, we have received the attention of the White House Office of National Drug Control Policy, and our published work related to this project has informed the President's 2009 and 2012 National Drug Control Strategy. Because there are currently more than 21.6 million individuals enrolled in colleges and universities across the nation (U.S. Department of Education, 2012), many of whom seek medical and mental health services from agencies within their institutions of higher education for presenting problems unrelated to their drug use, early intervention for PSM and AOD use within a college or university setting as part of routine medical and mental health care is a promising, innovative, cost-effective, and evidence-based strategy to investigate through research. The proposed study will assist both researchers and practitioners in identifying key implementation considerations when applying what has been learned in the laboratory to busy health and mental health care settings facing competing service demands, limited resources, and associated challenges to intervention fidelity. It will identify what is most important so we can take such interventions to scale across the nearly 4500 colleges/universities in the U.S.

4. **Excellent potential for national dissemination based on the linkages that exist among the project team members and their broader networks of both scientists and practitioners**. This application seeks to create an approach to early intervention for college students who engage in misuse of PSM by adapting web-based brief interventions. With PSM misuse gaining attention in the scientific literature and popular media, interest in responding effectively on college campuses is at an all-time high. With existing partnerships with national organizations already committed to addressing this issue (e.g., Drs. Geisner, Kilmer, & Larimer working with NASPA; Drs. Cimini & Kilmer working with Dartmouth's National College Health Improvement Program), statewide initiatives that emphasize efforts to bring science to practice (e.g., Dr. Arria's leadership role in the Maryland Collaborative to Reduce College Drinking and Related Problems, Dr. Kilmer's position as chair of Washington's College Coalition for Substance Abuse Prevention), and successful efforts to translate research findings for everyone from parents to policy makers, this team is uniquely positioned to focus on dissemination with an emphasis on "real world" applications on and relevance to college campuses.

(c) Approach

Preliminary/Pilot Studies: Dr. Arria is synonymous with the study of PSM and has conducted the largest longitudinal study to date (the NIDA-supported College Life Study) addressing the linkages between college students' AOD use—including PSM—and outcomes such as academic performance and persistence, post-college employment as well as on motives for PSM misuse[27, 41, 145-149]. Drs. Geisner, Larimer, Kilmer, and Lee have conducted or collaborated on numerous studies of college student substance use (alcohol, marijuana, and PSM) and related problems directly relevant to the proposed research[88, 106-108, 143-144, 156, 169]. We have conducted several RCTs of in-person feedback interventions for alcohol and marijuana, in addition to RCTs of computer- and web-delivered feedback for alcohol as a stand-alone intervention, with between-subjects effect sizes ranging from medium to large on normative perceptions (d = .61-.96) and drinking behavior (d = .35-.97) relative to assessment only[93, 96]. Dr. Cimini and her team have been translating research findings on prevention and intervention using a public health approach to a large public university-based primary health and mental health care delivery setting[150-155]. Our research team has demonstrated 1) a thorough knowledge of conducting research with college students who use and misuse PSM; 2) success in developing and evaluating efficacious interventions, including computer/web feedback and in-person feedback, in reducing alcohol use, 3) success in adapting feedback-based interventions for a variety of other presenting problems, including marijuana, gambling, and mood disorders, and for adapting them to in-person, real world settings; 4) success in establishing the role of normative misperceptions and AOD use as critical aspects of intervening with PSM misuse. Our work also demonstrates feasibility of our recruitment, retention, and intervention procedures.

1) ***Misuse of Prescription Stimulant Medication***. For the past decade, Dr. Arria has led the NIDA-funded College Life Study (CLS), which included over 1250 young adults originally enrolled as college students. She has focused on understanding the antecedents and consequences of all forms of substance use during college, and in particular on PSM. Her team has numerous publications[1, 27, 41, 145-149, 159, 174, 178] on the risk factors for PSM misuse and longitudinal interrelationships between PSM misuse and other forms of drug use, and academic variables. Two recent studies at UW have also included items regarding PSM misuse. In the first (R01AA012547; Larimer PI, Kilmer, Lee Co-Is, Geisner collaborator), a random sample of 1477 students completed a web survey of stimulant use, of whom 3.8% reported misuse of their own PSM and 9.8% reported misuse of another's PSM in the past year. In the second study, Kilmer and colleagues completed a survey of lifetime use among students 18-25 and found that 19% reported PSM misuse. Results also support a need to correct misperceptions; despite 81% having never used PSM, 89% believed the typical student had used for non-medical reasons at least once[156]. Drs. Geisner, Kilmer, and Larimer have also recently begun (July 2014) a collaborative project with the National Association of Student Personnel Administrators (NASPA) to better understand trends, perceptions, motives, and effects related to PSM misuse. The UW team will lead a 9 campus initiative to develop and conduct surveys and in-person focus groups with students and administrators to explore implications for prevention campaigns and make suggestions for intervention development – information from this project will undoubtedly set the stage for even greater success with the proposed research.

2) ***Alcohol Use Interventions.*** We have been involved in development, implementation, and evaluation of individual-focused alcohol prevention approaches targeting at-risk students for 10-30 years. Drs. Larimer & Kilmer were part of the original development team for BASICS and related brief motivational PFI, which are currently recognized as among the best approaches for addressing college student problem drinking[6, 98-100]. The general approach[6] has been found to result in significant reductions in alcohol consumption among heavy drinking students for up to four years[5, 134,135]. Dr. Larimer has been PI of 4 studies of BASICS and related brief web-based PFIs for alcohol (R01AA010772; R01AA012547; U01AA014742; R01 AA018276); Drs. Kilmer, Lee, and Geisner served as Co-Is or collaborators on these studies. Data from the first of these four studies supported in-person PFI among fraternity members as well as provided support for perceived norms as predictors of alcohol use and consequences[134, 137-140]. The second project supported use of mailed PFI as a universal prevention strategy[88] with significant effects on drinking 12-months post-intervention, and expanded our understanding of the relation between high-risk drinking and comorbid problems including depression[141]. Both projects demonstrate our ability to successfully conduct large scale intervention studies with college students. We recently demonstrated web-based PFI was efficacious for reducing the escalation of alcohol use across the transition out of high school for youth in the U.S. & Sweden[142].

3) ***Adapting PFI for Illicit Substance Use and Other Disorders.*** We have adapted web-based PFI for in-person and online interventions for marijuana use[144] (R21 DA025833), and comorbidity of substance use disorders and disordered gambling[71] (R01DA025051). Drs. Lee (PI), Kilmer (Co-I), and Larimer (Co-I) developed a PFI for marijuana that, in an RCT, resulted in intervention effects for amount used and consequences[169]. Dr. Geisner adapted PFI to address the comorbidity of depressed mood and alcohol

misuse[109], and this combined intervention is efficacious in reducing misperceived drinking norms, which were related to changes in alcohol use for those with comorbid heavy drinking and depressed mood[110]. She has adapted this intervention for the web (R21: AA019993) and recently finished data collection with similar recruitment and up to 90% retention rates. Response rates and retention across all studies are comparable to those proposed in the current application. Dr. Cimini and her team have implemented and evaluated the effectiveness of evidence-based interventions and prevention practices addressing college drinking and drug use across a variety of contexts (including patients in university-based primary health and mental health care settings, student-athletes, mandated students, and first-year students) and intervention delivery formats (including individual, group, peer-delivered, computerized, mass media, and Web-delivered feedback formats). This prior research-to-service experience within the University at Albany's clinical service delivery settings has resulted in the ability to implement these interventions in a standardized manner with a high degree of intervention integrity and fidelity, and to provide a thorough evaluation of these programs using a comprehensive set of assessment measures. Based on rigorous peer review, the brief alcohol intervention developed by Dr. Cimini and her team has been listed in SAMHSA's National Registry of Evidence-based Programs and Practices, recognized for both quality of research and readiness for dissemination. Thus, the current study builds on a strong base of preliminary data in support of the proposed intervention and feasibility of the methodology*.

4) ***Perceived norms and AOD as theoretical mediators***: We have completed 5 RCTs evaluating efficacy of computer/internet delivered PNF for alcohol use among college students[93-95,142]. Consistent with our proposed research hypotheses, drinking reductions in all studies were mediated by changes in perceived norms for the typical student, providing additional support for the correction of normative misperceptions as an active theoretical mechanism for intervention efficacy. Kilmer and colleagues[143] also investigated the impact of norm misperception on illicit drug use. 5990 participants provided information on use, perceptions, and consequences of marijuana use. Two-thirds of participants reported no marijuana use, but 98% of respondents incorrectly predicted the "typical student" used marijuana at least once per year. Estimates of peer use and use by the typical student each added significantly to separate equations predicting variance in drug use and in related consequences. Dr. Cimini has collected preliminary data at UAlbany supporting misperceptions of the norm for PSM misuse. Specifically, students were asked "Within the last school year, do you think the typical student at your school used any of the following prescription drugs (for stimulants) that were not prescribed to him/ her?" Results indicated 74% of students perceived that the typical student used stimulants within the last year, though the actual rate of use on that campus was reported at 25%. Drs. Kilmer and Geisner recently published a paper on normative misperceptions of PSM[156]. Their research similarly found that students overestimated PSM misuse by other students and those normative estimates were associated with student's own higher PSM use. Living in a fraternity or sorority was related to higher PSM use and perceived norms. Finally, higher normative perceptions were associated with higher hazardous drinking. Thus, our preliminary studies and bio-sketches demonstrate our ability to successfully conduct this research.

Study Methodology *Overview*: The proposed RCT aims to examine the efficacy of a PFI for reducing PSM misuse. Study 1 will document normative perceptions on each of the 3 participating campuses. Study 2 will examine the efficacy of a web-delivered PFI adapted and expanded from models like BASICS which will contain tailored information on normative misperceptions of PSM misuse, contrasting commonly held misconceptions about the benefits of PSM with research-based information about the actual effects of PSM, and learning and study strategies as alternatives to PSM misuse compared to a control condition, as well as components targeting comorbid alcohol and marijuana misuse. For Study 3, an in-person individually-delivered PFI (adapted from web format to face-to-face) addressing PSM and AOD misuse will be compared to the web-delivered PFI tested in Study 2 and to an assessment only control. The two studies will evaluate outcomes with respect to both short-term (6 months) and longer-term (12 and 18 months) reductions in four substance-related outcomes: (a) the perceived norms and benefits of PSM misuse, (b) PSM misuse frequency, (c) marijuana use frequency, and (d) alcohol use frequency and quantity.

Setting: Participants will be recruited from three universities: The University of Washington (UW), the University of Maryland College Park (UMCP), and University at Albany, State University of New York (UAlbany). UW is located in Seattle, WA and UMCP is located nine miles from Washington DC, with each school's total undergraduate enrollment of more than 30,000. UAlbany, which is one of four SUNY University Centers, is classified as a Research II and NCAA Division I institution with more than 12,000 undergraduate students. All three universities are coeducational and very diverse with regard to race, ethnicity, religion, gender, age, disability, and sexual orientation.

Studies 1 & 2 Recruitment Procedures: A total of 8,172 undergraduates for Study 1 and 15,732 for Study 2 aged 18 to 24 (age restricted in order to maintain comparability with prior SBI/PFI interventions with college students) will be randomly selected from the University Registrars' databases across the 3 sites. Students will be emailed an invitation to log on to a secure web browser, read a consent statement and indicate their willingness to participate in the study. Approximately 50% of invited students will respond to the invitation (Study 1 N=4,086 and Study 2 N=7,866).

Studies 1 & 2 Screening for Eligibility: For *Study 1*, all students randomly selected from the registrars' databases will be eligible to complete a 30-minute survey via a secure server, regarding PSM use, PSM misuse, normative perceptions, AOD use, and other relevant constructs. Participants will be paid $20 for completing the survey. Following completion of Study 1, we will select and invite focus group participants at UW to get subjective impressions of and suggestions surrounding feedback components and modules drafted for the purposes of this application (see Appendix B). We will conduct 5 focus groups of 8-10 individuals at the UW involving Study 1 participants who indicate willingness to participate and who have used PSM in the past. We will use focus groups in an iterative fashion and provide intervention refinement following feedback elicited about the treatment materials. We will then conduct an additional 2-3 focus groups for final reactions and input to the PFI intervention. Investigators will then meet to decide what changes (if any) should be made to the intervention prior to implementing the PFI for Study 2, based on transcripts and detailed notes taken during the focus groups and the consistency of participant feedback regarding various components. Groups will be conducted in person, led by two interviewers, and recorded. The primary interviewer will guide discussion through open-ended questions, while the secondary interviewer takes notes and observes responses. For *Study 2*, eligibility will be determined based on a brief web-based, self-administered screening questionnaire. Screening items will assess PSM use, PSM misuse, consequences, alcohol, marijuana, and other drug use. There are two main eligibility criteria for Study 2. First, to allow for studying academic outcomes, participants must be undergraduate students in their second semester or later at the university, have an anticipated graduation date at least 18 months in the future, and be planning to remain at their home university for at least 18 months. Second, to study possible reductions in PSM misuse but to include all students who maybe engaging in risky behaviors, participants must have engaged in PSM misuse once or more in the past month and/or 6 or more times in the past year. Based on prior studies[4, 24, 27, 28, 112, 156], we expect 14%-20% will meet criteria for PSM misuse and agree to participate. Students will be paid $10 for completing screening for Study 2. Up to six reminders to participate will be emailed[111]. The IRB at each institution will approve all procedures.

Study 2 Baseline and Randomization: The web-based screening survey will automatically generate an eligibility determination. Students who are ineligible will be shown a message thanking them for their interest in the study and directing them to campus resources that are available to them if they wish to discuss AOD issues. Those meeting the eligibility criteria above will automatically be directed to complete the baseline assessment measures. Once baseline is completed, students will be randomly assigned to either an intervention group (PFI) or assessment only control (AOC) group. Those in the intervention will immediately receive online personalized feedback (see below) on their PSM misuse, academics, and links to alternatives. Over the course of the quarter/semester, students in the intervention group will receive a link to view 4 additional modules surrounding PSM misuse, AOD use, Consequences, and Beliefs/Motives about PSM use. The AOC group will receive a "thank you" screen providing referrals/emergency numbers. Students will be assessed at 6, 12 and 18 months post-baseline using similar email invitations and reminders (expected retention 90% based on past research). Participants will be paid $20, $25, and $30 for each follow-up survey. Students who indicate significant alcohol or drug dependence will be contacted and referred (See Human Subjects). We will make any indicated adjustments/refinements to feedback based on findings prior to Study 3.

Study 3 Recruitment, Randomization & Assessment Procedures: All students who present for services at the University at Albany Health Center and University Counseling Center will be invited to complete a brief, web-based assessment of their PSM and AOD (identical to Study 2) in order to assess eligibility for Study 3 before meeting with their service provider. Routine screening is already part of ordinary clinical practice at UAlbany Health and Counseling Centers, and annually more than 1300 unique individuals visit these centers and complete routine screening. Our own pilot data suggests more than 2/3 of heavy illicit substance users make at least one visit to a campus health clinic annually, indicating these settings are ideal for identifying non-treatment-seeking at-risk PSM users. During the student's medical or counseling appointment, the provider will review the Screening Questionnaire and will refer eligible students to the study using a referral script similar to ones from prior studies successfully conducted in this setting. The same eligibility criteria will be used: students must have misused PSM once or more in the past month and/or 6 or more times in past year.

Students agreeing to participate in the study will be emailed an invitation to log onto a secure web browser,

read a consent statement and indicate their willingness to participate in the study. Those indicating their consent will immediately be routed to the baseline survey which will be used to generate the web-delivered or in-person PFI content and for which they will receive $20. Following baseline, participants will be randomly assigned to one of three conditions (n = 100 per condition). For Study 3, students will be randomly assigned to either a web-delivered PFI (as in Study 2), a one-session face-to-face brief intervention delivered in an MI style using the PFI as generated in the web condition, or an assessment only control group.

Participants will complete a battery of web-based follow-up assessments at 6, 12, and 18 months post-baseline for which they will receive $20, $25, and $30, respectively. Participants will additionally complete a brief post-intervention assessment of satisfaction with services and convenience of the intervention, and at each assessment they will be asked whether they have sought other drug treatment since the intervention to control for possible confounding treatment effects. These data will help determine the ideal interventions for the service delivery settings in regard to ease of access and utilization by participants.

Study 3 Training and Ongoing Supervision of Interventionist: One potential method for maintaining or enhancing the efficacy of individual brief interventions for college students seeking campus health and mental health care beyond the life of a research project is to train and supervise existing service providers to deliver the feedback interviews. The current approach will provide training to enhance existing knowledge of the UAlbany Counseling and Health Center staff regarding PSM misuse, and will utilize an existing provider imbedded in the Counseling Center staff at UAlbany to provide the in-person interventions. The provider will complete specific additional training related to both the MI process and PSM, alcohol, and marijuana content of the proposed intervention, and will participate in weekly supervision meetings with Drs. Cimini and Rivero. In addition, all intervention sessions will be audio-recorded and reviewed for adherence to the protocol and MI competence using existing protocols developed for use in prior funded projects at UAlbany and UW. The interventionist will also complete an adherence checklist after each individual session, to indicate which components were covered in each intervention session. Scores on adherence/competence measures and checklists will be reviewed and included as a covariate in secondary analyses of intervention efficacy.

Measurement and Assessment Procedures: Measures will be completed via a secure web survey, using DatStat Illume and will last 30-45 minutes. Measures selected are in Appendix A.

PSM Measures		
PSM Use	DV	▪ PSM Timeline Followback (TLFB) - Quantity and past-30-day frequency of PSM misuse[188] ▪ Medical Use, Medical Misuse, and Non-Medical Use Questionnaire[23, 80]
PSM Consequences	DV	▪ Drug Abuse Screening Test (DAST)[32] ▪ The CAGE Questionnaire – Stimulant Use[189] ▪ Prescription Stimulant Use Consequences[4]
PSM Motivations	Moderator	▪ Prescription Stimulant Use Motives Questionnaire[91] ▪ Motives for Not Using[9]
PSM Norms and Attitudes	Mediator	▪ Prescription Stimulant Norms Rating Form[74] ▪ Attitudes about PSM and Diversion[4] ▪ Prescription Stimulants Expectancy Questionnaire (PSEQ-II)[187]
AOD Measures		
AOD Use	DV/Mediator	▪ Quantity/Frequency/Peak Alcohol Use Index[6] ▪ Daily Drinking Questionnaire[113] ▪ Alcohol and Marijuana Timeline Followback (TLFB)[9,10] - Quantity and past-30-day frequency of marijuana and alcohol use, (use days, heavy episodic drinking, and typical and peak BAC ▪ ASSIST[132] - Other drug use
AOD Consequences	DV	▪ Rutgers Alcohol Problem Index (RAPI)[191] ▪ Rutger's Marijuana Problem Index (RMPI)[169,192,193]
Reasons for Not Using	Moderator	▪ Attributions for Limiting or Abstaining from Illicit Drugs (ALAID)[9]
Other Measures		
Demographic Characteristics	Covariate/ Moderators	▪ Standard questions will be used to assess age, sex, sexual orientation, race/ethnicity, parental education level, number of hours per week working for pay, religiosity, and current living arrangement
Academic Characteristics, Skills and Outcomes	Feedback	▪ Learning and Study Strategies Inventory, 2nd edition (LASSI)[175] ▪ Relapse Prevention/Protective Behaviors Scale[190] ▪ Satisfaction with Academic Progress and Skills ▪ Factors affecting Academic Performance ▪ Activities/Options that Could Improve Grades or Academic Progress

		• Primary Academic Outcomes: GPA
		• Academic Behaviors
		• College Engagement[194]
Satisfaction	Covariate	• Participants' satisfaction with interventions (assessed post intervention)

Personalized Feedback Intervention (PFI) Materials: Intervention materials for the web-PFI will be programmed using the Datstat Illume Software Development Kit. Custom programming will link feedback to the baseline survey to populate feedback fields with personalized information related to participants' PSM misuse, AOD use, consequences, norms, and academic behaviors. We have previously utilized this system (R01AA012547; R01AA012529; R01AA016099; R21AA019993; R21DA019257) to program feedback with multiple conditions, and protocols can be adapted for the current study. We will track feedback completion via Illume, including number and length of times spent reviewing feedback and will control for these in analyses[115]. Due to the possibility of attention difficulties in this population, feedback will not be a lengthy, single administration, but include 5 customized modules for participants to review over the quarter/semester.

Prescription Stimulant Medication Misuse PFI. The intervention is comprised of personalized feedback presented in text and graphic format, and each component is followed by a link to tips for making changes if and when the participant is contemplating or ready to commit to change. These tips will include general relapse prevention strategies, as well as information about the importance of regular class attendance, study habits, and sleep habits for academic success. General educational tips/strategies for time management, as well as initiating behavior change will also be included. The first component of the feedback targets ***PSM and academics***, including student's own prescription stimulant use frequency, satisfaction with academic progress and grades, factors identified by the student as interfering with academic performance, sense of their time management and study skills, impact of alcohol and marijuana use on academic/cognitive factors, student-identified actions that could improve academic success, and resources for getting assistance with academic support. The second component targets ***PSM and perceived norms***, including perceived and actual past year use, perceived and actual past-quarter/semester frequency, requests to divert PSM (both requests to others and to themselves), perceptions surrounding diversion, attitudes about helping others, and what the science shows about academic impact. By building a discrepancy between student's own PSM misuse and that of others, as well as correcting their perceptions of other's use (norms reduction) and beliefs about PSM, the intervention will reduce PSM misuse. This component ends with campus-specific resources for assessment and support. Component three addresses ***PSM and unwanted effects***, with a review of consequences related to PSM use, the science behind PSM misuse, and a link to alternative strategies. In the fourth component, ***Reasons/Motives for using PSM*** are addressed, including when during the academic year the student tends to use, motives for PSM use, and reasons to limit/avoid use. The final component reviews ***Alcohol, Marijuana, and Drug Interactions***. For marijuana use, participants will receive personalized feedback about frequency of use, consequences, and perceived norms; for alcohol use, they will receive information on frequency, quantity, norms, BAC and related effects, and consequences. The section ends with information on drug interactions. Appendix B includes a draft of proposed feedback, to be refined and programmed during the start-up phase.

Face-to-Face Personalized Feedback Intervention. The face-to-face intervention is an enhanced version of the web-based PFI described above.The intervention will be adapted by Dr. Cimini's team in consultantion with the UW research team to be appropriate for in-person delivery. The face-to-face intervention will consist of a 1.5-hour intervention intended to discuss the student's PSM misuse, AOD use, and review personalized graphic feedback. The interventionist will use motivational interviewing principles[168] throughout, including expressing empathy, developing discrepancies, rolling with resistance, and supporting self-efficacy. Review of personalized feedback will be used to facilitate the building of discrepancies by illustrating areas in which the student's AOD use may be in conflict with important goals or could be incongruent with the student's impression of the impact of their use. In the review of feedback, the provider listens for and reflects "change talk" (statements made by the student that indicate concern or need for change), and can elicit "change talk" with evocative questions and other strategies suggested by Miller and Rollnick[168]. While the layout of the feedback is consistent across participants, individual content within domains on the feedback will be directly tailored to the individual based on his/her baseline survey responses. Further, the motivational discussion with each participant is tailored to their responses to the feedback, level of readiness to change, and interest in particular feedback topics. Specifically, because MI involves a variety of active listening strategies (simple and complex reflections, open questions, affirmation, and strategic responses to resistance) the conversation is inherently tailored to each participant's unique reaction to the feedback and his or her concerns, questions, and goals. The personalized graphic feedback illustrates the impact of PSM misuse and AOD use in multiple domains to facilitate a conversation about patterns of use and consequences.

Data Analysis: Prior to performing inferential tests of hypotheses, univariate and bivariate descriptive statistics

will be conducted to examine the distributions of and correlations among key study variables.

Evaluation of Specific Aims:

Aim 1: To examine whether perceived norms of PSM differs from the "actual" prevalence as estimated by the screening sample, the actual prevalence will be subtracted from the perceived prevalence. A one-sample t-test will be used to assess whether the difference score is statistically significantly greater than 0. If the difference score is a non-normal distribution, we will instead use a non-parametric Wilcoxon sign rank test.

Aim 2: Evaluate efficacy of interventions. We will first examine effects of the intervention on perceived norms, benefits of PSM, and use of alternative strategies as separate outcomes using linear mixed models (a.k.a. hierarchical linear or multilevel models[120]). This project will have 5 repeated measures, yielding up to 6,000 Level 1 observations (repeated-measures) across 1,200 Level 2 (people). The following equation represents a basic analytic model for Aims 2 and 3:

<u>Level 1:</u> $Y_{ti} = \pi_{0i} + \pi_{1i}(Post)_i + \pi_{2i}(Month6)_i + \pi_{3i}(Month12)_i + \pi_{4i}(Month18)_i$

<u>Level 2:</u> $\pi_{0i} = \beta_{00} + \beta_{01}(Tx)_i + \beta_{02}(Site)_i + r_{00i}$

$\pi_{1i} = \beta_{10} + \beta_{11}(Tx)_i + \beta_{12}(Site)_i$

$\pi_{2i} = \beta_{20} + \beta_{21}(Tx)_i + \beta_{22}(Site)_i$

$\pi_{3i} = \beta_{30} + \beta_{31}(Tx)_i + \beta_{32}(Site)_i$

$\pi_{4i} = \beta_{40} + \beta_{41}(Tx)_i + \beta_{42}(Site)_i$

where *Post, Month6, Month12*, and *Month18* are dummy codes for follow-up visit such that the reference time point is baseline; *Tx* represents randomly assigned treatment condition; *Site* represents the study site; i indexes participants; r_{00i} represents a random effect for the intercept; and Y_{ti} represents the outcome for each individual, i, at each time, t. β_{11} - β_{41}, are primary coefficients as they compare treatment conditions for the difference in the outcomes from baseline to each of the follow-up visits. The model assumes conditional independence, given random-effects and (multivariate) normality of Level 2 random-effects. As additional analyses, we will also specify time as a continuous variable in order to assess differences between intervention and control groups in slopes over time.

We will then examine effects on PSM, marijuana, and alcohol use and consequences. These outcomes are integers, bounded at zero, and often times positively skewed. Because of potential violations of regression assumptions that can arise due to the non-normal distribution, we will use a generalized form of the linear mixed model (GLMM) with a Poisson distribution in order to more appropriately model these outcomes as counts[117]. Count regression coefficients are connected to the outcome via a natural log link and are commonly exponentiated (e^{β}) to yield rate ratios (RRs) describing the proportional increase in the outcome for a 1-unit increase in the predictor (e.g., Treatment (1) compared to Control (0)).

To assess mediation hypotheses, we will utilize an approach that has been used by co-investigators with similar data to the proposed study[197]. Kenny et al.[198] described mediation using multilevel models for longitudinal treatment data similar to the present data. Specifically, Kenny et al. focused on change in the direct treatment pathways from a model without the mediator to a model with the mediator (i.e., the common c and c' pathways in the mediation literature). In the present context, that is the treatment cross-level interactions with time (β_{11} - β_{41}) for the model presented above compared to one in which mediators are included as Level 1 time-varying covariates. We will use this approach and consider the percent reduction in effects after the mediator is included in the model. In Neighbors et al[199], this approach was extended using a nonparametric bootstrap[199] to allow estimation of the indirect path without making normality assumptions on the sampling distribution of the indirect effect. Perceived benefits and norms of PSM, use of alternative strategies, and alcohol and marijuana use will be included as the Level 1 time-varying mediators of interest and PSM use and consequences will be modeled as the outcomes. To assess moderators of efficacy, we will include level 2 covariates for baseline levels of motivations of PSM and demographic characteristics as well as their interactions with treatment in the GLMM.

Aim 3: Efficacy of in-person and web-based interventions. GLMM Poisson regression will be also used to test the efficacy of the web-based PFI and in-person MI on reducing PSM use and consequences. Using the basic model equation, dummy variables rather than a single treatment indicator will be included as Level 2 covariates for web-based PFI and in-person MI such that the reference will be the control group. In addition to comparisons of the two intervention groups to the control, we will also conduct post-estimation general linear contrasts to compare effects of the web-based PFI and in-person MI on the PSM outcomes.

Missing data and attrition. Our prior research has been successful at retaining participants with 85-93% retention over 6 months or longer. GLMMs provide unbiased estimates in the presence of missing data as long as it can be considered ignorable. Missing data are ignorable if they are either missing completely at random or missing at random after accounting for measured variables in analysis, including outcome at earlier time

points[120]. As seen in previous studies, little efficiency is lost in GLMMs with 10%-20% missing data.

Power. Because count outcomes will typically require a larger sample size to detect effects than continuous outcomes, we assess power for the GLMMs for PSM use. Thus, power estimates for the GLMM will be conservative for the linear mixed models. For Aim 2, we are not aware of power analysis software to estimate power for GLMMs; thus, we used a simulation-based approach. Simulations based on models that contain "true" effects can provide an estimate of power. Two-hundred datasets were generated based on the model in equation 1 where estimates for fixed and random-effects were guided by previously collected data of similar interventions for reducing problem alcohol use and the existing literature. The GLMM model was fit to each dataset and specific output were saved (e.g., regression coefficients, p-values). The percentage of datasets with statistically significant effects (i.e., $p<.05$) for a given hypothesis provides a simulation-based estimate of power for this hypothesis. A number of simulation runs were conducted varying the size of the fixed-effects. These simulations revealed a sample size of 600 per treatment condition will yield power > 0.80 given the magnitude of the treatment x time-dummy interaction coefficient was -.13 or smaller. Assuming no baseline differences in the outcome, this would correspond to a rate ratio of .87 at a given follow-up time point (i.e., a 13% decrease in PSM use for PNF intervention compared to control). Given our power to detect fairly small effects of the Aim 2 intervention, we would expect reasonable power to detect mediated and moderated effects as well. For Study 3 planned analyses of the web-based and in-person interventions, we also ran similar sets of simulations to assess power for varying effect sizes. We used similar estimates of random effects, but allowed the fixed effect of the intercept to be higher given the high risk sample and we specified a sample size of 100 per arm (300 total). Based on the simulations, we would expect power of .80 or higher to detect coefficients -.3 or smaller which corresponds to a RR of .74.

Timeline:

	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
STUDY PREPARATION / DISSEMINATION																																																												
HIRE & TRAIN STAFF	●	●	●	●																																																								
OBTAIN HUMAN SUBJECTS APPROVAL	●	●	●	●	●																																																							
PROGRAM AND TEST ASSESSMENTS		●	●	●	●							●	●	●																																													
DATA ANALYSIS AND DISSEMINATION							●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
STUDY 1 (ALL SITES)																																																												
NORMS DOCUMENTATION SURVEY						●	●	●	●	●																																																	
FOCUS GROUPS (UW ONLY)									●	●																																																	
PFI DEVELOPMENT/PROGRAMMING/TESTING												●	●	●	●																																												
STUDY 2 (ALL SITES)																																																												
SCREENING																●	●	●																																									
BASELINE & INTERVENTION																●	●	●																																									
6, 12, & 18 MONTH FOLLOWUPS																		●	●				●	●			●	●																															
STUDY 3 (UALBANY ONLY)																																																												
SCREENING															●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●																													
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6 MONTH FOLLOWUP																					●	●	●	●	●	●	●	●	●	●	●	●	●	●																									
12 MONTH FOLLOWUP																												●	●	●	●	●	●	●	●	●	●	●	●	●																			
18 MONTH FOLLOWUP																																	●	●	●	●	●	●	●	●	●	●	●	●	●	●												

Limitations of the Proposed Research: We have considered and taken steps to address study limitations. One limitation is the use of self-report measures; we considered collateral respondents and clinical interviews for diagnostic purposes, but rejected these on the basis of substantial research supporting validity of self-report in substance use research[125-129] and cost-effectiveness[126]. An additional limitation is related to the assessment of PSM misuse – while several measures for alcohol have strong reliability and validity, measures to document and describe PSM misuse and practices are relatively less established. However, by approaching assessment of practices related to the use of PSM in multiple ways, our study will appropriately capture use that is occurring and can contribute to assessment strategies/approaches. Although a potential limitation would be related to a small sample size (due to not meeting recruitment or retention targets), we are confident we can recruit at least 50% of initial contacts. Steps to improve recruitment and retention of representative samples, already proven effective in other studies across members of the research team, include compensation and maintenance of updated addresses. Although use of the internet for data collection may pose limitations, we have found no difference between web- and paper measures in prior research[130]. Despite limitations, the proposed research is a novel intervention to fill a gap in a high risk population. Results can be applied on campuses wishing to use effective, brief and inexpensive interventions to prevent and reduce PSM misuse.