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Design of the NIDA clinical trials network validation study of tobacco, alcohol, prescription medications, and substance use/misuse (TAPS) tool

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ABSTRACT

Background: Substance use and its associated use disorders are under-detected and under-treated in primary care. There is a need for a clinically useful brief screening and assessment instrument to identify primary care patients with substance use, sub-threshold substance use disorder (SUD), and SUD to facilitate brief intervention and treatment.

Methods: We describe the design of the recently completed National Drug Abuse Treatment Clinical Trials Network's tobacco, alcohol, prescription medications, and substance use/misuse screen and brief assessment tool validation study. Study aims included to: develop a 2-stage screening and brief assessment tool (TAPS Tool) to detect substance use, problem use, and SUD among adult primary care patients; examine the validity of both the screen component and the TAPS Tool by comparing them to reference standard screening and assessment measures of no use, problem use, and SUD; and determine the feasibility and acceptability of the self-administration and interviewer-administration of the tool. The design included a pilot testing phase (n = 30) and the main study of 2000 adult primary care participants who were randomly assigned in counter-balanced order to have the interviewer-administration or the self-administration of the TAPS Tool followed by the other administration format. Participants' views of feasibility, acceptability and preference for format of self-administration versus interviewer-administration of the TAPS Tool were assessed. Criterion measures of use and DSM-5 SUDs were administered.

Discussion: The TAPS Tool study builds on prior work to develop a 2-stage clinical tool for facilitating the adoption of screening, brief assessment and treatment for SUDs in primary care.

1. Introduction

Substance use disorders (SUDs) are under-treated in primary care. In 2014, 8.4% of the US population aged ≥18 years (an estimated 20.2 million Americans) were estimated to have a past-year alcohol or drug use disorder [1]. However, only 2.5 million adults received alcohol/drug use related treatment at a hospital, behavioral or mental health facility [1]. These numbers demonstrate a huge gap between the need for and receipt of SUD treatment. Primary care provides a natural location for providers to screen for problem substance use and identify SUD, provide interventions, and make referrals to appropriate specialty care [2]. SUDs may affect almost every major organ system, and result in significant morbidity, lost work productivity, and premature mortality [3–5]. The economic costs associated with tobacco, alcohol, and illicit/nonmedical drug use are estimated to be over $700 billion annually [6]. To facilitate screening for substance use and SUD detection during routine healthcare contacts, providers need screening and assessment instruments that provide accurate and clinically useful information, and can fit into busy clinical workflows.

Smith et al. [7] examined a single-question screener for identifying unhealthy alcohol use among adults in primary care ("How many times in the past year have you had X or more drinks in a day?" where X = 4 for women and 5 for men). The single-question screen was 81.8% sensitive and 79.3% specific for identifying unhealthy alcohol

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use. Smith et al. [8] also reported a single-question screener for identifying drug use ("How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" The single-question screener was 81.8% sensitive for detecting current drug use. Self-administered screening tools, such as computer self-administered versions of the single-item screening question [9] and a 4-item Substance Use Brief Screen (SUBS) for tobacco, alcohol, illicit, and prescription drug use [10] have performed well. These findings indicate feasibility of developing a quick screen for problem substance use. However, such screeners are not designed to distinguish between use of specific substances and risk levels. National Institute on Drug Abuse (NIDA)'s quick screen asks about use of several substances in one instrument, but it has not been validated [11].

The Alcohol, Smoking and Substance Involvement (ASSIST) 3.0 is a comprehensive assessment tool; however, its length deters routine use in primary care [12]. Based on secondary analysis of the multisite data, Ali et al. [12] derived a shorter "ASSIST-Lite" version that showed promising results in identifying problem substance users (sensitivity range: 0.8–1.0; specificity range: 0.7–0.8). The ASSIST-Lite has yet to be field tested to establish its clinical utility. We adapted the ASSIST-Lite and NIDA's quick screen to develop the TAPS Tool tailored to US population needs. This tool was designed for both patient self-administration and interviewer administration, and utilized an electronic platform (iPad), which has the potential to facilitate the integration of screening results into an electronic health record (EHR) system.

2. Materials and methods

2.1. Study aims

NIDA's National Drug Abuse Treatment Clinical Trials Network's (CTN) Tobacco, Alcohol, Prescription medications, and other Substance use (TAPS) Tool study sought to develop and validate a 2-stage screening and brief assessment tool (i.e., a 2-part instrument) to screen and assess adult primary care patients for tobacco, alcohol, non-medical prescription drug, and illicit drug use and problems related to their use. This combined screening and brief assessment tool was evaluated via self-administration and via interviewer-administration.

The aims of the study were to:

- Develop a 2-stage screening and brief assessment tool (TAPS Tool) to detect substance use, sub-threshold SUD, and SUD (tobacco, alcohol, prescription medications, and illicit substances) among adult primary care patients;
- Examine the concurrent validity of both the screen component and the TAPS Tool by comparing them to reference standard for screening and assessment measures for substance use, sub-threshold SUD, and SUD; and
- Determine the feasibility and acceptability of the self-administration and interviewer-administration of the TAPS Tool among these patients.

2.2. The TAPS Tool

The TAPS Tool was designed as a two-step screening and brief assessment tool. The screening component (TAPS-1) was adapted from the NIDA Quick Screen V1.0 [11], which asked about frequency of use in the past 12 months of tobacco, alcohol above guideline-recommended daily limits (≥5 drinks/day for men, ≥4 drinks/day for women), illicit drugs, and non-medical use of prescription medications (sedatives, opioids, and stimulants). TAPS-1 was designed to quickly identify the presence of any unhealthily substance use. The brief assessment component (TAPS-2) was a modified version of the ASSIST-Lite [12], and it assessed use in the past three months of tobacco, alcohol, six different classes of illicit drugs, and other drugs. TAPS-2 provided information about specific substances and generated a score corresponding to the patient's risk level that could be used to guide clinical actions.

2.3. Pilot testing of the TAPS Tool

Before the conduct of the main study, pilot testing with 30 adult primary care patients across three study sites (Baltimore, MD; New York, NY; Kannapolis, NC) was conducted to provide feedback on their comprehension of the TAPS Tool items and feasibility, including technical issues of using the iPad, such as seeing and reading the text, using touchscreen, and audio. Research staff at each site recruited participants in the waiting room of each site until 10 patients completed the pilot study. Research staff approached patients in the waiting room, introduced themselves, and asked if they would be willing to hear about a study to provide advice to researchers about a new brief health survey. A purposeful sampling approach was used to recruit an approximately equal number of men and women, and an approximately equal number of participants from each of the 5 age groups (18–24, 25–34, 35–49, 50–64, 65 years or older) in order to obtain feedback from participants of various age and sex groups. Other demographic characteristics were not used to select participants for the pilot test. Patients who expressed interest in the study were brought to a private room to discuss the study and complete the informed consent process and the pilot data collection. A total of 30 adult participants completed the pilot study (10 from each of the 3 sites with a balanced age/sex distribution: Baltimore, MD; New York City, NY; Kannapolis, NC).

During the administration of the TAPS Tool questions, participants were asked to 'think aloud' as they completed the screening items [13], and the research staff observed the participant's use of the iPad, asked about any visible difficulty, probed for cognitive errors, and made text notes describing any problems that participants encountered. Upon completion of the tool, participants were asked to respond to a brief survey regarding the feasibility (e.g., time required to complete [in minutes]; user-friendliness [Likert scale 1 to 5]; need for assistance: [yes/no with comment box]), acceptability (e.g., comprehension of the items [yes/no with comments box], likelihood of responding accurately [Likert scale]), and preference for format (self-administration versus interviewer-administration [preference choice vs. no preference]) of the tool in primary care settings (Table 1). Each participant of the pilot study was paid $20 for their time and contribution to the study.

Based on the pilot study findings, the study team made some modifications to address technical issues related to use of the iPad: (a) using a screen cover to reduce screen glare, (b) adding a brief tutorial to give participants an option to practice on the iPad before completing the self-administration of the TAPS Tool, (c) using a guided access feature

Table 1
A brief survey of views on use of the TAPS Tool.

How much do you agree with the following statements on a scale of 1–5 where:
1 = strongly disagree
2 = disagree
3 = neither agree nor disagree
4 = agree
5 = strongly agree
Q1. These questions were easy to understand.
Q2. I was comfortable answering these questions.
Q3. I answered these questions as honestly as I could.
Q4. I would be willing to answer questions like these at my doctor's office.
Q5. I think my friends would answer these questions honestly at their doctor's office.
Q6. The iPad touch screen was easy to use.
Q7. I would prefer that a person asked me these questions in the doctor's office instead of answering them myself on an iPad.
Q8. I would prefer answering these questions on an iPad instead of having a person ask me.
Q9. The voice recording was helpful.
Q10. I would be comfortable sharing my answers about drug use with my doctor.

in system settings to lock the iPAD into the app that disabled the home button and prevented participants from wandering out of the app; (d) locking the screen in landscape with the volume button on top to prevent pressing on volume button while holding the iPAD against the desk; and (e) changing the color background of the screen every other page to alert participants to the change in screen. The TAPS Tool items were refined slightly to improve the wording of the screening items (see Section 2.4.6). No major issues were identified regarding the time required to complete the TAPS Tool and preference of the administration format.

2.4. Main study (Fig. 1)

Following the pilot phase, 2000 adult primary care participants were randomly assigned in counter-balanced order to have the interviewer-administered version of the TAPS Tool first or the self-administered version first (each participant had the tool administered both ways). After completing both versions of the TAPS Tool, participants were surveyed on their views of feasibility, acceptability and preference for format of self-administration versus interviewer-administration of the TAPS Tool. After the survey was completed, the research staff administered reference standard measures of substance use, sub-threshold SUD, and SUD (i.e., the validity assessment portion of the study).

2.4.1. Study sample and sites

This study included adults recruited during their healthcare visits. The selection of study sites was based on the applicability of the expected findings to adults in the community, study cost, and feasibility. For consideration of the generalizability of study results to community-based primary care patients, the study was conducted in primary care clinics at multiple sites. Sites were selected from among clinics with the following characteristics:

- Primary care clinic.
- Clinic served a sufficient number of male and female patients that would be potentially eligible to participate in the study.
- Clinic had adequate space to accommodate study staff and activities.

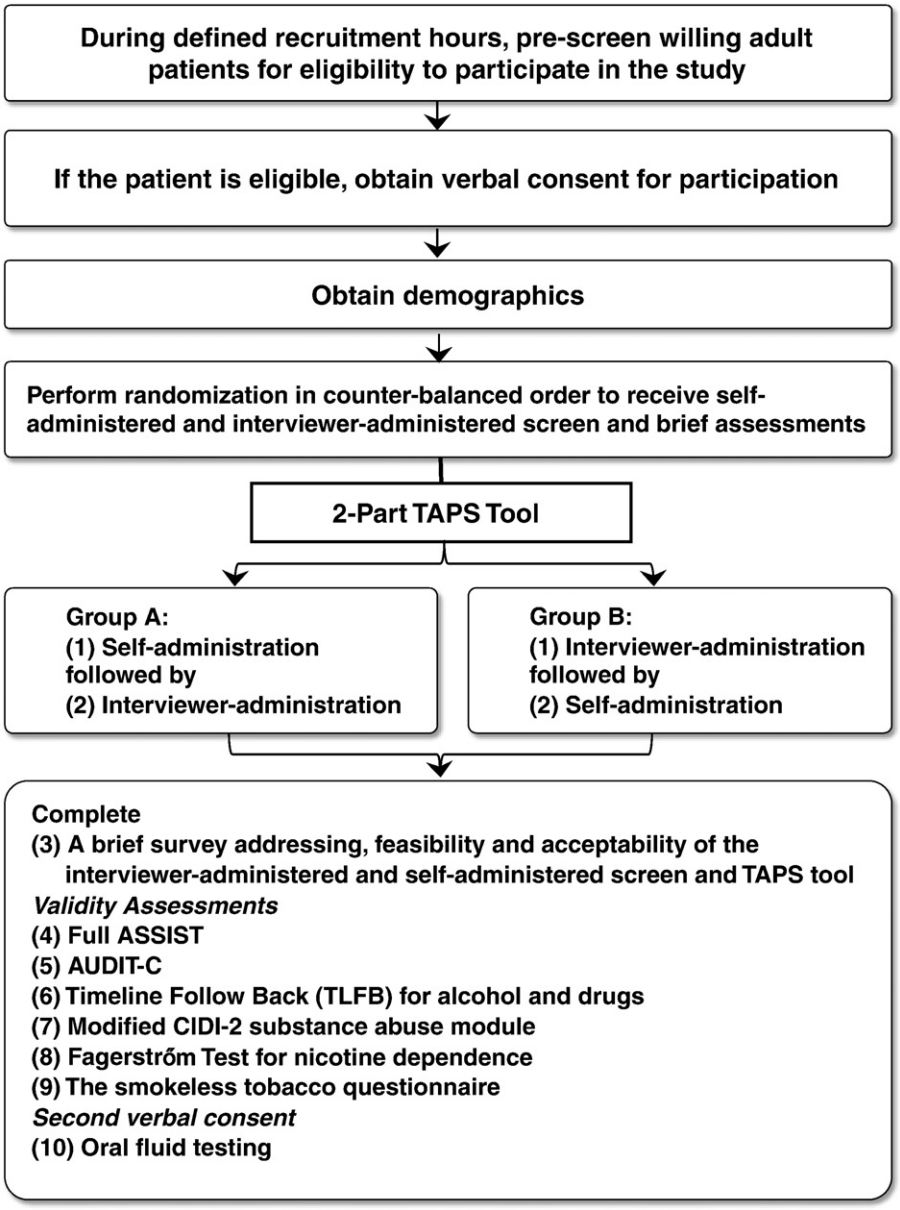

Fig. 1. Study flowchart of the main study: The 2-Part TAPS Tool.

Based on the consideration of the diversity in location and demographic characteristics of practices, 5 primary care practices from 4 states that were expected to serve an adequate number of women and nonwhite patients were included for this study (Baltimore, MD; New York City, NY; Richmond, VA; and two sites in Kannapolis, NC).

2.4.2. Inclusion and exclusion criteria

To increase the generalizability of study findings, the inclusion and exclusion criteria for study participants were broadly defined. Inclusion criteria were: primary care patients aged ≥18 years and ability to provide informed consent. Exclusion criteria were: inability to comprehend spoken English, inability to self-administer the iPad tool due to physical limitations, and previously enrolled in this study.

2.4.3. Sample size

To determine an appropriate sample size, we performed simulations to calculate the precision of the estimates (specificity and sensitivity) as a function of prevalence and sample size. Precision was defined as 95th percentile of half-width of the 95% confidence interval. For specificity, most of the half-width values were below 0.06. That is, we would get a fairly precise estimate of specificity irrespective of the sample size, even with a sample size as small as 400. In contrast, estimates of sensitivity are more impacted by substance use prevalence and sample size, as for a condition with a low prevalence and a small sample size, there will be few observations with which to calculate sensitivity. We expected to have good precision of sensitivity on substances that were of moderate levels of prevalence (such as cannabis and cocaine which are between 5% and 15%) with a sample size of 2000 where the precision is <0.125 (with estimates of precision of specificity of <0.03). Based on prior data from primary care adult patients [14], we did not expect to have a prevalence of less than perhaps 4–5% for any substances of interest except methamphetamines, inhalants, or hallucinogens. Thus, with a sample size of 2000, and given the expected prevalence of use in the study population, we anticipated having sufficient precision to validate the TAPS Tool for detection of any unhealthy or hazardous use for major substance classes and for detection of SUD.

2.4.4. Recruitment and informed consent procedures

At each site, research staff consecutively approached each patient following a pre-determined pattern in the waiting area, and interested patients were screened for eligibility. To avoid interrupting patient care, the logistics of conducting screening in a medical setting required that the screening process be relatively brief. During defined recruitment hours, research staff screened primary care patients who were possibly eligible for the study. Depending on the patient flow, patients would be approached either prior to or after the evaluation by a clinician. For each day of screening, the number of patient refusals and other reasons for patient inability to participate were recorded on a recruitment form. The research staff screened patients according to the study operations manual procedures.

Informed consent was obtained in a two-step process. In the first step, eligible patients who agreed to participate in the study were provided with an IRB-approved informed consent information sheet. The IRB waived written informed consent because it was a minimal risk study, and the consent form would be the only place in which the name of the participant would be recorded. The information sheet included a description of all significant elements of the study; the assessment interview and questionnaires; risks and benefits of study procedures; alternatives to participation in the study; confidentiality; $20 payment for participation; a statement that participation is voluntary and that the patient may withdraw at any time; and information about whom to contact with questions. Patients read the informed consent information sheet, expressed verbally their understanding of the key elements of the study, and gave oral consent to participate in the study.

After completing the study assessments, participants were asked to provide informed consent to participate in the second step of the study in which they would provide an oral fluid sample for testing drug use (amphetamines, methamphetamine, MDMA, cocaine/metabolite, opiates, oxycodone, phencyclidine, THC, barbiturates, benzodiazepines, and methadone). They were told that drug testing data collected would not link to their name or other identifiers and that they were free to refuse to provide the oral fluid sample. They were informed they would receive an additional $10 for providing the sample. Participants were not asked to provide consent for the oral fluid test until after they completed all other study assessments, in order to avoid biasing the self-reported data. Data collection and all study interviews were conducted in a private room.

2.4.5. Randomization and blinding

We sought to determine the validity of the interviewer-administered and self-administered versions of the TAPS Tool, which was incorporated into randomization. After providing the initial informed consent, participants were randomly assigned to one of two groups according to a block randomization procedure within site. Group A completed the self-administered TAPS Tool and then a face-to-face interviewer-administered TAPS Tool. Group B completed the interviewer-administered TAPS Tool followed by the self-administered version. The randomization procedure was conducted through a centralized and web-based process set up by the Clinical Trials Network Data and Statistics Center (DSC) statistician. Participants were not blinded to study group. The research staff (interviewer) was blinded to the sequence of self-administration vs. interviewer-administration until after the patient provided informed consent.

2.4.6. Study assessments

2.4.6.1. The 4-item screen component (TAPS-1) of the TAPS Tool (modified NIDAMED Quick screen). The TAPS Tool consists of a 4-item screen for tobacco use, alcohol use, prescription medication misuse, and illicit substance use in the past 12 months (TAPS-1) (Table 2) and a brief assessment (i.e., a modified version of the ASSIST-Lite (TAPS-2) (Table 3) [12]. The 4 screening items were based on previous reports [7,8,11,15] and modified for the present study by asking "how often"

Table 2
The 4-item screen of the TAPS Tool.

Stage I - Substance use screening questions: The 4-item screen
The screen will consist of one stem question with 4 substance categories. (Instructions: The following questions are about the past 12 months) Question - In the past 12 months, how often have you: 1. Used any tobacco (for example, cigarettes, e-cigarettes, cigars, pipes, or smokeless tobacco)? 2. [Males] Had 5 or more drinks containing alcohol in one day?[Females] Had 4 or more drinks containing alcohol in one day? [Only the version specific to participant's gender will be administered]. ▪ 1 standard drink is about 1 small glass of wine (5 oz), 1 beer (12 oz), or 1 single shot of liquor 3. Used any drugs including marijuana, cocaine or crack, heroin, methamphetamine (crystal meth), hallucinogens, ecstasy/MDMA? 4. Used any prescription medications just for the feeling, more than prescribed, or that were not prescribed for you? Prescription medications that may be used in this way include: ▪ Opiate pain relievers (for example, OxyContin, Vicodin, Percocet, methadone). ▪ Medications for anxiety or sleeping (for example, Xanax, Ativan, Klonopin). ▪ Medications for ADHD (for example Adderall or Ritalin). **Response options:** Daily or almost daily, Weekly, Monthly, Less than monthly, Never

Table 3
Brief assessment questions of the TAPS Tool.

Stage II - Brief assessment questions (modified ASSIST-Lite)		
(Instructions: The following questions are about the PAST 3 MONTHS ONLY)		
1) Did you smoke a cigarette containing tobacco?	Yes [1] No [0]	→ *No: Skip to Q2*
1a Did you usually smoke more than 10 cigarettes each day?	Yes [1] No [0]	
1b Did you usually smoke within 30 min after waking?	Yes [1] No [0]	*Tobacco score: __ [0–3]*
2) Did you have a drink containing alcohol?	Yes [1] No [0]	→ *No: Skip to Q3*
2a On any occasion, did you have 5 or more drinks containing alcohol in a day (for men)/4 or more drinks containing alcohol in a day (for women)? *	Yes [1] No [0]	
2b Have you tried and failed to control, cut down or stop drinking?	Yes [1] No [0]	*Alcohol score:* __ [0–4]
2c Has anyone expressed concern about your drinking?	Yes [1] No [0]	
* 1 Standard drink is about 1 small glass of wine (5 oz), or 1 beer (12 oz), or 1 single shot of liquor		
3) Did you use marijuana (hash, weed)?	Yes [1] No [0]	→ *No: Skip to Q4*
3a Have you had a strong desire or urge to use marijuana at least once a week or more often?	Yes [1] No [0]	
3b Has anyone expressed concern about your use of marijuana?	Yes [1] No [0]	Marijuana score: __ [0–3]
4) Did you use cocaine, crack, or methamphetamine (crystal meth)?	Yes [1] No [0]	→ *No: Skip to Q5*
4a Did you use cocaine, crack, or methamphetamine (crystal meth) at least once a week or more often?	Yes [1] No [0]	
4b Has anyone expressed concern about your use of cocaine, crack, or methamphetamine (crystal meth)?	Yes [1] No [0]	Stimulant score: __ [0–3]
5) Did you use heroin?	Yes [1] No [0]	→ *No: Skip to Q6*
5a Have you tried and failed to control, cut down or stop using heroin?	Yes [1] No [0]	
5b Has anyone expressed concern about your use of heroin?	Yes [1] No [0]	Heroin score: __ [0–3]
These next questions are about taking prescription medications just for the feeling, more than prescribed, or that were not prescribed for you. Please do NOT report use of 'over the counter' medications.		
6) Did you use a prescription opiate pain reliever (for example, Percocet, Vicodin) not as prescribed or that was not prescribed for you?	Yes [1] No [0]	→ No: Skip to Q7
6a Have you tried and failed to control, cut down or stop using an opiate pain reliever?	Yes [1] No [0]	
6b Has anyone expressed concern about your use of an opiate pain reliever?	Yes [1] No [0]	Opioid score: __ [0–3]
7) Did you use a medication for anxiety or sleep (for example, Xanax, Ativan, or Klonopin) not as prescribed or that was not prescribed for you?	Yes [1] No [0]	→ *No: Skip to Q8*
7a Have you had a strong desire or urge to use medications for anxiety or sleep at least once a week or more often?	Yes [1] No [0]	
7b Has anyone expressed concern about your use of medication for anxiety or sleep?	Yes [1] No [0]	*Sedative score:* __ [0–3]
8) Did you use a medication for ADHD (for example, Adderall, Ritalin) not as prescribed or that was not prescribed for you?	Yes [1] No [0]	→ *No: Skip to Q9*
8a Did you use a medication for ADHD (for example, Adderall or Ritalin) at least once a week or more often?	Yes [1] No [0]	
8b Has anyone expressed concern about your use of a medication for ADHD (for example, Adderall or Ritalin)?	Yes [1] No [0]	Prescription Stimulant score: __ [0–3]
9) Did you use any other illegal or recreational drug (for example, ecstasy/molly, GHB, poppers, LSD, mushrooms, special K, bath salts, synthetic marijuana ('spice'), whip-its, etc.)? What did you take?		Not scored –

rather than on "how many days" did the participant use substances. The five response options for the screening questions were based on the response categories used in the ASSIST that allow creating risk-level scores [16]. Based on the pilot study findings, they were modified for easier comprehension by replacing the option "once or twice" with "less than monthly". Pilot study findings indicated some confusion about the term tobacco 'product', soda versus alcohol, definition of a drink, and the meaning of methamphetamine; hence, we dropped 'product' from the tobacco question, revised the alcohol use question to indicate 'drinks containing alcohol,' provided the information for what constitutes a standard drink, and revised the methamphetamine wording as methamphetamine (crystal meth). The pilot study findings also indicated that participants often were unclear about the meaning of prescription medications. To increase clarity, examples for opioid pain relievers (e.g., OxyContin, Vicodin, Percocet, Methadone), medications for anxiety or sleeping (e.g., Xanax, Ativan, Klonopin), and medications for attention deficit hyperactivity disorder (ADHD; e.g., Adderall, Ritalin) were added to the question (Table 2). We also replaced "in the past year" with "in the past 12 months" to increase the clarity of the reference period [17].

2.4.6.2. Brief assessment component (TAPS-2) of the TAPS Tool (modified ASSIST-Lite). We modified the ASSIST-Lite items to reflect the current context of drug use in the United States and to improve comprehension, in response to the pilot study's findings. *First*, we replaced "did you use cannabis?" with "Did you use marijuana (hash, weed)?" to increase the clarity for primary care patients. We replaced "cannabis" with "marijuana" to be consistent with the wording in the major US drug use surveys [18]. *Second*, the ASSIST-Lite combines use of illicit stimulants, cocaine and prescription stimulants into a single category. To better understand prescription drug misuse, we distinguished between prescription stimulants, and illicit stimulants (e.g., cocaine and methamphetamine) by using two separate questions to assess nonmedical prescription stimulant use and illicit stimulant use. *Third*, the ASSIST-Lite combines use of heroin and prescription opioids into a single group. We used separate questions to assess heroin use and nonmedical prescription opioid use. *Fourth*, the ASSIST-Lite includes an open-ended question "Did you use any other psychoactive altering substance?" to assess drug use that may not captured. To increase clarity, we replaced the question with "Did you use any other illegal or recreational drug (for example, ecstasy/molly, GHB, poppers, LSD, mushrooms, special K, bath salts, synthetic marijuana ('spice'), whip-its, etc.)"; these examples were chosen to reflect recent drug use trends in the United States [18].

2.4.6.3. A brief survey of views on use of the TAPS Tool. Participants completed a brief survey on their view of the TAPS Tool's feasibility, acceptability, and their preference for format of administration (Table 1).

2.4.6.4. Validity assessment measures. The selection of assessments was based on consideration of their reported validity, the need for comprehensive data for each substance assessed, as well as costs of data collection in terms of participant time, staff time and training, and feasibility of completion. Therefore, assessment questions were limited to those that have demonstrated clinical value and could contribute directly to the objectives of this study.

Validation assessment measures for the TAPS Tool were interviewer administered and included: (a) full ASSIST to determine substance-specific use information and scores for each substance [16,19], (b) 30-day Timeline Follow Back (TLFB) to determine alcohol, nonmedical prescription drug use, and illicit substance use [20], (c) modified Composite International Diagnostic Interview-2 (modified CIDI-2) in which extant CIDI items were mapped onto the DSM-5 SUD classifications, to assess 12-month SUD [21–23], (d) Fagerström Test for Nicotine Dependence (FTND) to assess current nicotine dependence [24,25], (e) AUDIT-C to assess problem alcohol use, as it is the most widely used measure for alcohol use in primary care [26,27], (f) the smokeless tobacco questionnaire [28,29], and (g) oral fluid drug testing for amphetamines, methamphetamine, MDMA, cocaine/metabolite, opiates, oxycodone, phencyclidine, THC, barbiturates, benzodiazepines, and methadone) [30,31]. All participants were administered all validation assessment measures by research staff.

2.4.7. Data collection

As participants completed the self-administered and interviewer-administered TAPS Tool, research staff recorded the time spent administering the interview and any interruptions, while the computer program recorded the time spent completing the iPad version [in minutes]. Research staff also recorded the number of times the participant requested assistance, and the type of assistance requested (reading, comprehension, use of the iPad, or other recorded in comments box).

Following completion of the two formats for the TAPS Tool, participants were asked to complete a brief survey asking about the feasibility (e.g., user-friendliness; need for assistance), acceptability (e.g., comprehension, likelihood of responding accurately, user friendliness), and preference for format (self-administration and interviewer-administration) of the tool in primary care settings. After the survey was completed, research staff administered validation assessment measures of substance use, sub-threshold SUD, and SUD.

Subsequently, participants were asked to provide an additional verbal informed consent (see above) to undergo oral fluid testing for the presence of common drugs of abuse. Once collected, oral fluid was sent to an outside laboratory for analysis (Intercept® immunoassay; OraSure Technologies, Bethlehem, Pennsylvania). To aid in the interpretation of drug test results, individuals were asked, as part of the testing procedures, if they were currently taking any drugs as prescribed by their health care provider(s) from a list of prescription opioids, benzodiazepines, and stimulants. Research Staff had medication picture cards from the National Survey on Drug Use and Health as a reference in case a participant was unable to recall the name of a medication.

After completing the interview, participants were compensated ($20 if they completed the interview only and $30 if they completed both the interview and the oral fluid testing) and thanked for their participation. Individuals who met criteria for an alcohol or drug use disorder were offered local substance use treatment referral resources, while those with current tobacco use were given the number for their state's quitline.

2.4.8. Duration of study and visit schedule

Within 10 months (August, 2014–April, 2015), the study recruited a total of 2000 adults aged ≥18 years who completed study assessments. Each participant was seen only once (no follow-up visits). Initial screening and all assessments occurred during the participant index visit. The total duration of individual participation in the study ranged from about 30 min to 1 h (depending largely on how many substances the participant reported having used).

2.4.9. Training procedures

All research staff received the Good Clinical Practices (GCP) and Human Subjects Research Protection (HSRP) training, protocol specific training, database training, and protocol specific assessment training applicable to their specific roles and responsibilities, before the study initiation.

2.4.10. Safety assessment

This study was considered a minimal risk study (survey and oral fluid collection only), as it did not include a behavioral or pharmacological intervention. Any adverse event would be reported on an adverse event form. The only expected risk to participants would be a loss of confidentiality which was minimized by not obtaining signed informed consent and through anonymous data collection. Any breach of confidentiality would be reported on a protocol deviation form.

2.4.11. Subject discontinuation

All participants were allowed to withdraw consent at any stage of the study. In addition, research staff or Lead Investigator would remove the participant from the study when there was evidence that continuing in the study might be harmful to the participant.

2.4.12. Data management

This study used a centralized Data and Statistics Center (DSC). The DSC was responsible for the development of electronic case report forms and the clinical study database, ensuring data integrity, and training site and participating study site staff on applicable data management procedures. A web-based distributed data entry model was developed and implemented to ensure that guidelines and regulations surrounding the use of computerized systems were upheld.

2.4.13. Data analysis

Unlike an intervention trial that sought to examine a specific outcome in relation to an intervention, the focus of this study was to identify a set of questions useful for detecting adults with use, sub-threshold SUD, and SUD. Separate analyses were specified to examine the validity of the screener alone (the 4-item TAPS-1) alone and the full TAPS Tool (2-stage screening and brief assessment tool). Sensitivity, specificity, and area under a receiver operating characteristic curve (AUC) were the statistical measures selected to assess each item of the 4-item screen and the TAPS Tool score against the study's reference criterion measures. The Full ASSIST, AUDIT-C, TLFB, modified CIDI-2, Fagerström, and Oral Fluid Testing were criterion measures assessed in separate analyses for each corresponding substance (tobacco, alcohol, cannabis, etc.) as appropriate. For example, agreement statistics were planned between the marijuana score on the TAPS Tool and on the ASSIST; similar analyses were planned between the marijuana score on the TAPS Tool and the DSM-5 subthreshold problem use or SUD classification based on responses to the CIDI-2. For guiding clinical actions, the analyses of the DSM-V criteria (CIDI-2) would be the primary focus. For instance, to evaluate concordance between TAPS Tool and CIDI, the following binary categorical variables for a given substance use would be created from the CIDI: subthreshold problem use or higher (≥1 SUD criterion endorsed vs. 0), SUD or higher (≥2 SUD criteria vs. 0–1 criteria), and moderate or higher SUD (≥4 SUD criteria endorsed vs. 0–3 criteria). For each of these criterion categories, ROC analysis for each possible cut-point on the TAPS Tool would be conducted; and AUC, sensitivity, specificity, positive predictive value, and negative predictive value would be obtained. For identification of subthreshold problem use, cutoffs would be selected that maximized sensitivity. For identification of SUD, cutoffs would be selected that were both higher than the cutoff for problem use and had higher sensitivity. Exploratory analyses also would be specified to explore whether sensitivity, specificity, and AUC differ as a function of factors such as gender, race/ethnicity, and education level.

Regarding the order in administration of the TAPS Tool (self-administered vs. interviewer-administered) and substance use prevalence, we would use generalized estimating equation (GEE) analysis to determine whether there were differences in prevalence for each substance use in relation to the order of administration and instrument (self-

administered vs. interviewer-administered). A two-way crossed model would be fitted to determine the presence of the interaction between order and instrument. A significant interaction effect would suggest a difference in the participants' responses to self-administered vs. interviewer-administered TAPS Tool due to order of administration. Finally, participant-reported feasibility measures of the TAPS Tool (Table 1) would be summarized at the end of the study to assess its feasibility. In these analyses, missing data and dropouts were expected to be relatively minimal, as the study did not include follow-up assessments. In cases where data from one instrument was missing, the missing data were not included in the analyses. No imputation for missing data was conducted.

3. Discussion

The triple-aim of healthcare reform (i.e., better health, better care, lower costs) supports the implementation of integrated behavioral healthcare in primary care to improve the overall population health and lower the cost of healthcare per capita [32]. Comorbid medical and SUD conditions are a substantial disease burden and a cost driver, which may be related to poor treatment adherence, greater morbidity, and hospitalizations [3,33,34]. Failure to identify and treat SUD could further increase a variety of health risks associated with comorbid SUD and medical illnesses that are highly costly [3]. Having a clinically useful 2-stage screening and assessment tool for use in daily practice is an initial step to improve case identification for appropriate intervention. Screening for substance use, Brief Intervention, and Referral to Treatment (SBIRT) strategies have been promoted as a primary care model to help integrate SUD care [35]. These programs could benefit from a valid screening and assessment instrument such as the TAPS Tool that can both screen for substance use quickly and assess problem levels of tobacco, alcohol, prescription drugs, and illicit drug use to guide clinical interventions.

The TAPS Tool study is poised to make a unique contribution to the field in multiple ways. First, it is the largest study of its kind conducted in the US primary care setting. The single-item screener from Smith et al. [7,8] suggest the feasibility of developing a screen for identifying substance use. Participants of Smith et al. [7,8] were recruited from a single site, an urban safety-net hospital located in a community where the prevalence of substance use problems was high, and participants were asked the questions through face-to-face interview. To enhance the generalizability of study findings, the TAPS Tool study was designed to be a multi-site study that recruited a diverse sample of primary care patients from 5 practices in four different US states (i.e., not limiting to a local region) to compare both the self-administration (e.g., an iPad) that would permit electronic adoption by EHR systems and interviewer-administration of the iPad-delivered tool.

In addition, the existing single-item screeners, while potentially useful for triage, focus on the use of one substance class (alcohol, or drug). Use of more than one substance is common among adult substance users. A screener of multiple substances in primary care is potentially desirable because it can quickly provide more granular information than a single-item screener. Accordingly, we examined a 4-item screen component (TAPS-1) of the TAPS tool for multiple substances (tobacco, alcohol, prescription medications, and illicit drugs) to enhance the efficiency of rapid substance use screening. The 4-item screen (TAPS-1) also has the potential to be easily integrated into regular clinical workflows as a stand-alone instrument.

Further, single-item screeners alone are unable to provide an assessment of level of problem use. In a busy or resource-limited clinical setting, a 2-stage screen and brief assessment tool that would permit rapid screening for substance use, plus targeted assessments for a subset of patients who screen positive for further evaluation, is needed for efficiency in busy practice settings. As learned from screening for depression in primary care, a 2-stage approach has advantages of lowering the patient burden and provider time costs [36]. We designed the study to examine the validity of the screen component alone (TAPS-1) and the validity of the 2-stage screening and assessment tool (TAPS Tool) to allow flexible adoption by practices based on their patient population, workflow, and caseload. Moreover, we tested the 4-item screen for the 12-month status of substance use using language for timeframe (i.e., in the past 12 months) adopted by the NIH PhenX Toolkit (www.phenx.org) for the DSM-5 based SUDs to facilitate cross-study comparisons and to increase the likelihood of adoption of the screening tool by the research community.

Taken together, the TAPS Tool study addressed a timely need to develop a quick screen for early identification of recent or current tobacco, alcohol, nonmedical prescription drug, and illicit drug use; and a combined screening and brief assessment tool for detection of risk levels of substance use to inform optimal clinical management among adults in primary care settings.

3.1. Limitations and strengths

The TAPS Tool study had some limitations. Like studies of Smith et al. [7,8], it used a cross-sectional design and it was not possible to examine test re-test reliability over a longer time frame. In a future study, prospectively collected outcome data would help to determine the TAPS Tool's predictive validity. In addition, the same research staff administered all reference measures to the same patient, and this may produce a potential source of bias because the research staff was aware of the TAPS Tool responses when s/he administered the other assessments. The oral fluid sample provided limited information for assessing sensitivity and specificity of the TAPS Tool because of some missing data (participant refusal to provide the sample), a short time window of drug detection (<1 week), and a lack of collecting oral fluid testing for tobacco and alcohol use. Finally, research is needed to evaluate the TAPS Tool's validity in clinical settings where the patients' substance use information is shared with providers.

Notwithstanding these limitations, the design of the present study's instruments builds on prior work and contain clinically important features – including brevity, comprehensiveness (covering tobacco, alcohol, nonmedical prescription drugs, and illicit drugs), use of an electronic platform to facilitate links to EHR systems, comparison between patient self-administration or interviewer administration to allow the flexibility to fit into a variety of clinical workflows, creation of actionable risk-score categories, and availability in the public domain for dissemination and adaption to facilitate adoption of screening and brief assessment in primary care [8,33,37–39]. Identification of problem substance use is an important step to increase intervention in medical settings, and the TAPS Tool validation study represents an important step forward in this regard.

Institutional review board approval

This NIDA CTN study (CTN-0059) was approved by the Duke University Health System Institutional Review Board; Friends Research Institute, Inc. Institutional Review Board; New York University School of Medicine Institutional Review Board; and Virginia Commonwealth University Institutional Review Board (ClinicalTrials.gov Identifier: NCT02110693).

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Disclosures

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