SPECIFIC AIMS

Legitimate prescription opioid use during adolescence has been associated with later prescription opioid misuse and substance use disorder symptoms during adulthood.[1,2] Thus, primary prevention interventions for older adolescents and young adults at the time of prescribing are imperative. With several million opioid prescriptions dispensed to adolescents and young adults each year in the United States,[3] providers are uniquely positioned to address and mitigate opioid risks for these vulnerable groups. Indeed, despite a recent plateauing in prescribing rates, opioid-related poisonings, prescription misuse, opioid use disorder and unintentional overdose deaths continue to increase among our youth, suggesting an unrelenting effect of the opioid crisis and an urgent need for action.[4-7] Recognizing the urgency for action, state laws have been widely enacted that, among other requirements, mandate informed consent for patients as well as parents of minors who are prescribed opioids. While the intent of such laws is to lessen the impact of the opioid crisis by increasing risk awareness, it is not clear whether such laws are sufficient to enhance risk understanding and mitigate risky behaviors without adversely impacting effective pain management.

We previously demonstrated that opioid risk awareness alone (i.e., knowledge that adverse effects like addiction and excessive sedation can occur) was ***not*** related to safer opioid decision-making among parents, whereas higher risk perceptions and analgesic risk avoidance preferences were strongly related.[8] We have since similarly demonstrated that risk perceptions and analgesic preferences (but ***not*** simple risk awareness) were strongly associated with intentions to misuse prescription opioids among a large sample of adolescents and emerging adults.[9] Finally, desire for pain and other symptom relief remains the most common motive for prescription opioid misuse among adolescents and young adults.[10,11] Thus, modifiable targets to reduce risky prescription opioid decisions among adolescents/emerging adults include opioid risk perceptions, analgesic risk/benefit preferences and safe pain management knowledge.

Our current research (R01DA044245) examines the ability of our interactive Scenario Tailored Opioid Messaging Program (STOMP) to shift these modifiable factors in a way that will improve parental opioid decision making and handling while simultaneously ensuring good pain management of their children. This intervention, thus, provides an innovative, balanced approach to address both the primary prevention of opioid-related adverse outcomes and effective pain management. Relevant to this supplement, we will modify STOMP messages and test their impact on opioid risk perceptions and risky decision-making among older adolescents and emerging adults who make most if not all analgesic treatment decisions for themselves.

Supplemental funding via PA-18-591 will enable us to expand the target population of our current project to include older adolescents and emerging adults who are prescribed opioids for an acute pain condition and who are among those at highest risk for misuse. Specifically, funding will allow us to modify our STOMP messages to address the risks of opioid misuse and personal strategies to manage symptoms, and compare the effect of these STOMP messages to routine opioid analgesic consent information. These objectives fall within the scope of our currently funded project, but effectively expand our target enrollment to address the high priority need for primary prevention among youth. Thus, with supplemental funding, we aim to test the following hypothesis:

1) Examine whether modified STOMP messages will improve opioid risk understanding, enhance misuse risk perceptions, improve analgesic self-efficacy, and opioid decision-making among older adolescents and emerging adults (ages 15-24) who are prescribed opioids for post-procedure pain management. We hypothesize that older adolescents and young adults who are randomized to the intervention (versus routine opioid information/consent) will exhibit; **(H1)** Greater and sustained understanding of the potential risks of opioid misuse **(H2)** Decreased intentions to medically or non-medically misuse opioids for personal use, or share (divert) personal prescriptions with others.

2) Examine whether enhanced STOMP messaging will mitigate persistent/recurrent opioid use and later misuse among older adolescents and emerging adults. We hypothesize that opioid misuse risk perceptions mediate the relationship between prescription opioid use and later misuse, and that by enhancing risk perceptions, rates of opioid misuse intentions will decrease.

With adequate funding, we have the unique ability to expand and test translatable strategies that could effectively mitigate adverse outcomes related to opioid prescribing. Our multidisciplinary team's expertise related to opioid risks and pain management practices for youth and opioid misuse, combined with our ability to efficiently recruit and retain research subjects in clinical studies (current loss-to-follow-up is < 15%) supports the natural extension of our current project and will ensure completion within the timeframe of our current grant. This additional work will not only increase the impact of our research, but will lay the necessary foundation for a future longitudinal study of prescription opioid misuse among adolescents and emerging adults.

SIGNIFICANCE OF THIS SUPPLEMENT

Adolescents and emerging adults, themselves, are vulnerable to opioid-related adverse outcomes given high rates of pain and exposure to prescribed opioids. More than 90% of healthy youth report recent pain for which most have self-treated with analgesics.[13-15] Additionally, more than 3 million opioid prescriptions are dispensed annually to manage pain in this population.[3,16,17] These early pain and opioid exposures not only pose immediate threats to the well-being of our youth, but formulate analgesic perceptions that contribute to future use, misuse and abuse. For instance, 5% to 12.5% of opioid-naïve adolescents persistently or recurrently use a prescribed opioid following surgery or injury,[18,19] presenting a high risk for dependence and later misuse. Furthermore, we and others have found that legitimate use and misuse of opioids during adolescence are highly associated with misuse during early and mid-adulthood.[1,20,21] Adolescents who are prescribed opioids by 12th grade are 33% more likely to misuse opioids by 23 years of age – even if they have no history of illicit substance use.[1] Additionally, medical and non-medical use of prescription opioids during adolescence is associated with an increased risk (50% and 260%, respectively) of substance use disorder symptoms at age 35.[2] Lastly, even higher over-the-counter analgesic use during adolescence doubles the risk of later opioid misuse, underscoring the relationship between pain and the potential for opioid misuse.[20]

The need for pain relief is the most common motivation for self-reported prescription opioid misuse among adolescents and young adults.[11,22] Our Co-Is, Drs. Boyd and McCabe and colleagues found that prescription opioid misuse among adolescents and emerging adults is largely motivated by a need for pain relief and is influenced, in part by the perception that opioids are safe when prescribed by a doctor.[11] Even when under the care of a physician for pain, 1 in 4 adolescents are non-adherent to their opioid prescriptions, sometimes doubling their doses to relieve pain.[23] Additionally, easy access to personal, family or friends' prescriptions provide the most common source for adolescents who misuse opioids to self-treat pain or for other reasons.[24] One third of adolescents misuse their own past prescription and 56% that of a friend or family member who, in 80% of cases had the drug prescribed to them.[20,22,25-29] Thus, healthcare providers are the most common original source for prescribed opioids that are misused by adolescents and, therefore, provide a critical avenue for risk mitigation and primary prevention interventions.

Poor analgesic and opioid risk knowledge and perceptions contributes to risky misuse behaviors among adolescents and emerging adults. We recently surveyed 972 healthy community youth aged 15-24 years of age and found that nearly half had taken a prescribed opioid for pain and of these, 32% reported past misuse (i.e., taking more of the drug, taking it more frequently, or using it for an unrelated condition) and 26% indicated a willingness to misuse a prescribed opioid to manage pain.[9] Similar to findings from our studies of parents, we demonstrated that intentions to misuse a prescribed opioid were strongly associated with lower perception of opioid misuse risk and stronger preferences for analgesic benefit or pain relief (vs. analgesic risk avoidance). We also found that past opioid misuse experience helped explain opioid misuse intentions. Importantly, we found no association between simple awareness of serious opioid-related adverse outcomes (e.g., addiction, excessive sedation, respiratory depression) and willingness to misuse a prescription opioid.

Other studies of risky decision-making have demonstrated that adolescents and young adults respond more to the possibility of short-term benefit or reward (such as pain relief or other effects) than to the potential long-term and rare risks (such as addiction).[33] College students also assign less risk to prescription analgesics than to other substances, and perceived harm is highly associated with higher risk of nonmedical misuse.[34,35] These data may be, in part, explained by risk reappraisal that occurs after prescription analgesic use (or misuse), in that

experience with positive benefits and no adverse outcomes may lead to downward reappraisal of riskiness.[36] Together, such data indicate a critical need to enhance prescription opioid risk perceptions and pain management understanding at the time of initial exposure and prior to risk reappraisal.

Ongoing knowledge gap with regard to youth risk: Although brief interventions have been shown to reduce risky behaviors such as drinking and driving, and other substance use,[37] to date, no studies have examined the efficacy of interventions toward shifting prescription opioid risk perceptions and reducing misuse behaviors in adolescents and young adults. Expanding our parent study can begin to fill this gap. Based on our preliminary data among adults and decision theory, we believe that our tailored opioid risk messaging intervention will improve risk knowledge and perceptions, minimize risky decisions, AND at the same time will enhance analgesic self-efficacy and pain outcomes for older adolescents and emerging adults.

SCIENTIFIC PREMISE

Heightening opioid risk perceptions, strengthening opioid risk aversion values and enhancing positive, non-opioid pain relieving practices at the time of opioid prescribing are theory-based strategies to mitigate future prescription opioid misuse among older adolescents and young adults. Similar to adults, older adolescents and young adults have been found to exhibit cognitive appraisal of risks and benefits during risky decision-making.[38-41] It has also been suggested that behaviors may be best modified in this age group by enhancing risk perceptions and risk avoidance values.[33] Enhancing gist risk perceptions (i.e., global perceptions about health risks) has been found to decrease risky intentions such as drinking and driving or unprotected sex.[41] Conversely, giving verbatim or quantitative information about low rates of negative outcomes (e.g., overdose, addiction) is believed to provide a "rational calculus of risk promotion" that endorses risk-taking and intentions, particularly among youth who focus on higher rates of short-term benefit.[41] Novel prevention strategies aimed at enhancing risk perceptions and shifting reward preferences (i.e., strengthening the perceived benefits of health-promoting behaviors via gain-framing or positive outcome messages[42]) are, therefore, likely to be more successful in reducing risk-taking among adolescents than giving detailed risk rate information. Lastly, interventions that include visual aids have been found to be highly effective and memorable means to change and sustain risk perceptions and risky behavioral intentions among young adults.[42]

Our interactive Scenario Tailored Opioid Message Program (STOMP) intervention was developed based on Fuzzy Trace Theory (FTT) with an aim to change the mental model of risk perceptions and shift preferences in a direction that will reduce risky opioid decisions and enhance best analgesic practices. FTT describes how information (both taught and experienced) is processed to create mental representations ranging from precise data to fuzzy or simple gist representations. Based on this theory and consistent with other neurodevelopmental theories, risky decision-making is a function of the mental representations (verbatim and gist) of the options at hand (e.g., to misuse a prescribed drug or not). In addition to mental representations, reward sensitivity (i.e., the degree to which someone is benefit preferent), time preferences (i.e., desire for immediate reward over later ones), and opportunity (i.e., availability) also factor into risky decision-making. Thus, opioid misuse among adolescents and young adults reflects, to varying degrees, the degree to which the risk-taker desires the positive effect of the drug (reward), the ready availability of the drug, and the risk-taker's cognitive appraisal of the option to misuse (riskiness). While opioid misuse behavior may initially be goal-directed (i.e., to obtain pain relief or benefit), the slippery slope to addiction is sharper

with opioids than, perhaps, other controlled substances. Thus, primary prevention of misuse behavior must begin with initial exposure to the drug. FTT suggests that the most appropriate and, perhaps, most malleable targets to prevent initial opioid misuse are the mental representations of options, that is, of opioid risk perception and analgesic preferences.[41]

INNOVATION

- This extension of our parent project is a natural extension of our innovative, interactive STOMP intervention to a group of older adolescents and young adults who are vulnerable to opioid misuse.
- Our intervention aligns with the National Drug Control Strategy with an overall goal to increase risk recognition, prevent opioid-related adverse events and minimize the capacity for future misuse.
- Our intervention uniquely combines scenario-tailored risk decision exercises with tailored risk messages and evidence based advice. Thus, the information has the ability to enhance target perceptions and improve competency or self-efficacy.

Our multidisciplinary team brings expertise in acute post-procedure pain management, adolescent substance use behaviors (with a particular emphasis on prescription opioid misuse among adolescents and emerging adults),[10,11,22,26,28,43] tailored decision-aid technology and evaluation of educational and behavioral interventions in the clinical setting.[44-47] Increasing Dr. Malviya's effort from a consulting role to an active co-investigator will bring a more prominent role regarding effective pain management strategies and interpretation of data.

APPROACH

With this supplement, we aim to expand the target population identified in our parent study to include older adolescents and emerging adults (ages 15-24 years) who are beginning to or are solely making analgesic decisions for themselves following a painful procedure.

We will adapt STOMP messages to specifically address the risks of personal misuse of opioid analgesics and the potential risk of sharing prescribed opioids with others. We will modify the analgesic messages that address safe and effective pain management strategies and early opioid weaning.

Using modified surveys but similar procedures as the parent project, we will test the effect of STOMP on the outcomes: opioid risk perceptions, misuse intentions and behaviors, persistent use and left-over disposal intention.

Expanded sample inclusion and justification: We will recruit up to 600 English speaking patients, aged 15-24 of all races who are expected to receive an opioid prescription for acute, short-term postoperative pain following elective ambulatory or short stay (<48 hrs) orthopedic, sports medicine, or other surgical procedures.

Sample exclusions: We will exclude patients who are undergoing emergency procedures, cannot self-report their pain, have a hematologic-oncologic, kidney or liver condition (precluding the usual analgesic prescription patterns), or who have been recently treated for chronic pain. We will exclude subjects with significant mental health history that includes diagnoses with treatment for severe depression, bipolar disorder, psychoses, suicidal ideation.

Modified recruitment strategy and informed consent: All participants ages 15-17 will be recruited with parental consent-assent document, either by phone or in person prior to surgery. We will recruit young adults by phone or in person prior to surgery. When potential participants are recruited by phone, we will then email an e-consent (e-parental permission/assent) for electronic signature as well as the baseline survey link, to be completed prior to surgery. All participants will be assigned a study ID and asked to complete the online survey prior to the day of surgery. This method allows the participant to complete the baseline survey in private, at home, without the added time pressure of the day of surgery. On the day of surgery, we will review all ongoing aspects of the study (i.e., additional surveys, timing, and collection of perioperative data).
For subjects approached in person before surgery, we will obtain written informed consent and have the participant complete the baseline survey immediately thereafter and prior to surgery.

Inclusion of women and minorities: Our sample will include male and female young adults with an expected regional distribution of race and ethnicity (see Inclusion of Minorities in parent project for breakdown). Our studies will have the unique ability to elucidate the contribution of sex and race on opioid perceptions, decisions, and risk behaviors, as we will control for these variables in the analyses.

Feasibility: During 2017, more than 600 patients aged 15-24 underwent outpatient or short stay procedures and received an opioid prescription at discharge. We will allow 24 months to recruit subjects and collect data which should be sufficient given our target population, our collective clinical and research experience and that of our project manager. We expect that recruitment will be similar to if not better than past studies given the low risk nature of the study. As with our parent study, a modest monetary incentive will be provided in order to maximize participation and reduce the loss to follow-up.

Potential benefits of the proposed research to the subjects and others: Participation offers the potential benefit for young adults to gain knowledge and awareness of opioid risks and to develop effective pain management and risk reduction competencies. The knowledge gained from our studies is directly translatable into practice with the potential to reduce the risks of opioids to young adults.

Protection against risk (see Parent Protection of Human Subjects for more detail): Our opioid messages are developed with the guidance of pediatric pain and risk communications experts. The intervention poses no more than minimal risk to adolescents or young adults but may instead, offer potential benefit in terms of risk reduction, self-efficacy and pain management competency.

We will minimize the risk for breach of confidentiality of all participants by training of study team members, use of electronic and physical security measures for data capture and storage, and by employing a Certificate of Confidentiality (automatic for NIH funded studies). Unique study identifiers (ID) for each subject will permit linkage between surveys and follow-up data while maintaining the privacy of every participant. ID links between subjects and their data will be kept separately in an encrypted file. Data will only be stored on fire-walled databases which will limit access only to those assigned appropriate permissions.

Routine management will not be altered and we will exclude those who cannot, by nature of their underlying condition be safely prescribed the usual combination of opioids and non-opioids for postoperative pain. We will record all adverse events and will review non-serious AEs

quarterly and serious AEs as they are learned to determine the relationship to study participation and actions needed, if any (see DSMP).

Data and safety monitoring plan (DSMP): Our study specific DSMP provides details of how we will collect, review, evaluate and manage adverse events that may happen as part of routine care or study participation.

Group assignment (same as parent study): Patients will be randomly assigned a priori by computer generated randomization to either the Control Group (i.e., Routine provider written/verbal analgesic instruction) or one of two Intervention Groups: STOMP written (prose) feedback (i.e., Routine provider information plus the STOMP written feedback or our enhanced STOMP Video feedback (i.e., Routine provider information plus STOMP Video feedback).

Outcomes

Aim 1) Opioid risk perceptions, misuse risk perceptions, intentions to medically misuse, non-medically misuse or divert left-over opioids

Aim 2) Persistent opioid use after surgery, left-over opioid retention

Measurements (only modifications from parent grant are described)

- **Opioid risk knowledge:** Participant's awareness of common and critical opioid risks will be assessed using the ADE knowledge instrument, where participants use nominal responses to record which are possible when taking opioids or when opioids are in the home.[7,8,124] These items were developed with established content and face validity and, together with risk perceptions, were found to have predictive validity.[7,8]

- **Opioid risk perceptions:** Perceived seriousness of opioid risks (e.g., excessive sedation, misuse, addiction) will be assessed using a 6 point Likert scale where 0=Not serious to 5=Extremely serious.[7,8,46] We have previously demonstrated predictive validity of these items toward situational and analgesic decisions.[7,8,46] Perceived risk severity has been shown to predict intention and health behavior.[82]

- **Analgesic self-efficacy:** Analgesic self-efficacy will be measured using a six item scale where participants will score their confidence to safely and effectively give and stop analgesics when managing their pain and other symptoms.[126-128] Self-efficacy is the perceived confidence to perform specific behaviors to attain effective health outcomes.[129] Measures of medication self-efficacy mediate symptom management and health behavior and predict medication behavior and therapeutic change.[130]

- **Opioid decision-making:** Situational decisional exercises will be modified to assess opioid use and potential misuse decision-making. We recently used similar decision-making scenarios to assess misuse intentions among 15-23 year olds, and demonstrated significant associations between risk understanding, past misuse behavior and misuse intentions.[9] Four scenarios will assess participants' 1) willingness to misuse opioids either by taking higher doses (or more frequent dosing) of the personal prescription, 2) intention to misuse a previously prescribed opioid prescription for ongoing pain 3) intention to use a friend's

prescribed opioid for ongoing pain 4) pain and symptom relief when opioid-related adverse events are present.

- **Analgesic adherence:** Participants will record postoperative analgesics administered, self-reported pain scores (i.e. 0-10 Numeric Rating Scale), and adverse effects the follow-up surveys. Opioids will be converted to oral morphine equivalents, and opioid and non-opioid consumption will be reported as total mg/kg given. Adherence will be reported as the percentage used of the total opioid and non-opioid doses prescribed. The number of left-over doses of opioids will be calculated at discontinuation (amount dispensed minus amount used). We will assess intention to keep left-overs and reasoning at follow-up.

- **Pain interference:** The PROMIS Adult Pain Interference Short Form will also be used to measure how much pain is interfering with participants' activities at 1 and 2 weeks.[48,49]

- **Adverse side effects:** Participants will document all analgesic-related side effects using the follow-up surveys.[7] We will also review the clinic notes (6 months) for surgical and analgesic-related calls, return visits to the clinic or hospital, and analgesic refill orders, and persistent pain documentation.

Measurements of Contributing Factors

- **Key biologic and other characteristics of the participant:** Participants will record their demographics including sex and race and ethnicity.

- **Substance Use**: We will use the ASSIST measure for adults as a gross measure of risk factors for substance use disorder.[50]
- **Pain history and opioid familiarity:** History of participant pain, opioid and non-opioid use will be assessed with simple categorical items.[8,46]

- **Pain relief preference (PR-Pref):** This instrument assesses the participant's desire to provide pain relief relative to their desire to minimize ADE risks. The instrument includes 7 risk–benefit items[7,8,46] similar to those used to assess the importance patients place on chronic medication benefits versus their concern for adverse effects.[145-147] Agreement with each statement is ranked on a 5 point Likert scale from strongly disagree (-2) to strongly agree (+2), to yield a total score ranging from -12 to +12, where lower numbers indicate a preference for risk avoidance, higher numbers pain relief, and the middle range, indifference or ambivalence.[145,147] We previously have demonstrated the instrument's internal consistency, construct and predictive validity (higher scores predict parental opioid administration).[46]

- **Surgical factors:** The procedure, prior injury, duration of surgery, all perioperative analgesics given and details of participant's prescription and analgesic instructions will be recorded from the medical record.

Study Procedures (SEE TABLE 1 BELOW)

Group assignment: Participants will be randomly assigned a priori by computer generated randomization to one of the three groups: the Control Group (i.e., Routine provider

ten/verbal analgesic instruction), the STOMP written feedback (intervention) Group: (i.e., Routine provider information plus the STOMP written feedback) or the enhanced STOMP Video Feedback (intervention) Group (i.e., Routine provider information plus the STOMP Video feedback).

All baseline and follow-up surveys are completed by the subjects using a Qualtrics survey link via their own smartphone or computer (or our iPAD if completed in person) to ensure completeness and privacy. Subjects will enter only an assigned, unique ID number with no other identifying information. STOMP (either written or video groups) will be provided together with each decision exercise (built into the survey itself). The electronic survey includes appropriate logic and prompts to minimize the potential for missing items.

Subjects will be texted/emailed survey links on day 0 (day before or on surgery), day 7, day 14, 1 & 3 months after discharge. Table 1 depicts the study assessments completed at each timepoint. These will be automatically scheduled via our umich gmail system. On each of the survey days, we will also send a text SMS reminder to participants (automated using the same process as our parent study). Subjects can opt to complete surveys via email link (Qualtrics) or via paper/pen (returned via mail). No more than 1 additional text reminder for each will be sent to subjects who have not completed their follow-up surveys.

Sample Size Determination

Our sample size is based on our recent findings that 26% of adolescents/young adults indicated a willingness to misuse a prescribed opioid for pain management. We need 426 participants (142/group) to detect a clinically important effect of the STOMP intervention on misuse intention (i.e., decrease to 13%; 95% confidence and 80% power). This sample will be more than sufficient to detect an expected mean difference in opioid misuse risk perception between either intervention group and the control (MD 0.56, SD 1.21; sample needed = 122) and to test for a modest effect of the interventions in a factorial design (estimated eta squared 0.14; sample needed = 147). To allow for 30% loss to follow-up and to account for missing data, we will recruit up to 600 participants.

Table 1. Sequence of study assessments

Measures	Time 0 Baseline (preop)	Time 0.1 (Immediately Post-Session)	Time 1 (7 days)	Time 2 (14 days)	Time 3 (1 month)	Time 4 (3 months)
Demographics	x					
Pain, Analgesic and Misuse History	x					
Pain relief Preference	x			x		
Opioid knowledge/ risk perceptions	x	x		x	x	x
Opioid misuse risk perceptions	x	x		x	x	x
Scenario (situational) decision-making	x			x	x	x
Analgesic self-efficacy	x	x				
Pain interference			x	x	x	x
Opioid left-over disposal				x	x	x

Analgesic use and ADEs			x	x	x	x
Perioperative data	x					
Analgesic refill data				x		

TA ANALYSES

Generalized estimating equations (GEE) will be used to model both continuous (i.e., negative binomial and Gaussian) and binary outcomes (i.e., binomial) for each aim.[151,152] All models will include both time-varying measures (e.g., opioid risk perceptions) and time-invariant covariates (e.g., sex, race, etc.) and will use either an independent or exchangeable correlation structure to correct for within subject correlations. Analyses will use Stata's (STATA/SE v.13; STATA Corp., College Station, TX) 'xtgee' option as appropriate. All hypotheses per our conceptual model (Figure 3) will be tested at the 0.05 alpha level. Standardized coefficients and adjusted odds ratios will be computed to determine the relative effect size for each of the key independent variables.

Missing data: The use of electronic surveys with built-in prompts for incomplete items will reduce the potential for missing responses. Patients will be contacted by phone, text or email (per their preference) to promote ongoing recording of postoperative data and to reduce the potential for missing data and LTF. We have used similar procedures to successfully ensure complete data and minimize loss to follow-up.[8,25,94,153]

Any remaining missing data on surveys (e.g., assist or PR-Pref) will be examined for randomness and we will impute only partial non-response (e.g., missing 1 to 2 items of PR-Pref or assist) using a horizontal (i.e., per individual) approach. Largely incomplete or total survey non-response will be examined for non-randomness and potential bias (e.g., missing DAST-10). These missing data will not be imputed, however, outcomes will be compared for persons with missing vs. complete data to determine selection bias. We have adjusted our sample size to account for the potential for missing data. We will use pairwise deletion to use the available, complete cases to test our hypotheses.

Aim 1: Using GEE, we will examine the association between the STOMP intervention and the outcomes (risk seriousness perception, and situational opioid decisions). It is hypothesized that, compared to controls, patients who receive the STOMP intervention will have 1) enhanced risk perceptions (continuous measure) and 2) improved opioid decisions (scenario-based). Hypotheses 1 and 2 will be tested using both main and interaction effect models. In the main effects models, STOMP group assignment is our binary independent variable of interest. Time by intervention interaction effect models will be used to examine whether the STOMP group has improved opioid risk perceptions and decisions at the follow-up assessments compared to the control group. It is expected that there will be no difference between the intervention group and control group at baseline. However, significant interaction effect terms should emerge for the intervention group at the follow-up assessments.

Anticipated Problems and Solutions:

The main potential limitation to achieving our aims is the efficient recruitment of eligible subjects and the potential LTF. Modest monetary incentives will be given for baseline and follow-up surveys which we've found to enhance recruitment rates and minimize LTF in high enrollment studies ($25 after completion of 1 month follow-up; $25 after receipt of 3 month follow-up survey).[95,153] Participants will receive reminders by text, phone or email (per preference) which we have used to successfully reduce LTF and boost return of diaries in our previous longitudinal pain studies.[8,46,153] We will evaluate our recruitment and retention rates quarterly to determine whether we are on target or whether we need to enhance our recruitment plan.

HUMAN SUBJECTS PROTECTIONS (Same as Parent Project with the following modifications)

For this supplement, we expand our subject involvement to include up to 6005 English speaking adolescents and young adults (ages 15-24) who are prescribed opioids for acute, short-term postoperative pain following elective ambulatory/ short-stay surgical procedures. Males and females of all races will be recruited.

Sampling Plan and Recruitment: Given that adult patients, themselves, are the target population, we will contact potential participants at the time of surgery scheduling, in the preoperative clinic, or by phone or mail prior to the day of surgery to allow ample time to make an informed decision about taking part in the study and to allow time for completion of baseline surveys (prior to surgery). Participants will be provided a verbal synopsis of the study as well as a comprehensive written consent form. Study procedures will not proceed until consent documents are signed.

Potential Risks:

- This study poses no more than minimal risk to participants who are aged 15-24. The primary risk to participants is potential for breach of confidentiality. Given our data collection and handling procedures as outlined in the parent study and re-emphasized below, the potential for breach is extremely unlikely.
- Some adverse effects following surgery and during analgesic use are expected. We will be closely recording all opioid and surgery-related adverse events and will report these per our parent study DSMP and board review.

Protection against risks:

Confidentiality: We will minimize the risk of confidentiality breach by assuring privacy during our recruiting/consenting procedures, through the use of surveys and paperwork containing no identifiers (only assigned study ID links), and the maintenance of linkage lists, databases, etc. on institutional computers (protected by the use of secure login procedures). Consent forms will be stored separately from datasheets, to avoid the additional possibility of linking materials. A Certificate of Confidentiality has been granted by NIH to further protect study participants from breach of confidentiality.

Adverse Events: To ensure that our intervention poses no risk to safe or effective pain management, we will monitor all adverse events related to routine care (e.g., opioid-related drug effects, surgical events, and unplanned hospitalization) per our DSMP to determine whether either group (intervention or control) has been placed at greater risk for these events. Serious and non-serious events will be reviewed and reported as outlined in the DSMP.

Potential Benefits of the Research to Human Subjects: Since the nature of this study is to enhance and motivate safe use and management of opioid analgesics, those who take part and who are randomized to the intervention(s) might benefit from this knowledge and skill building program. Of note, our pilot data also showed that being in the Control group enhanced awareness of opioid-related ADEs (though did not have a significant effect on hypothetical decisions). Additionally, this study has the potential to yield information and interventions that may benefit participants in the future. This potential benefit of our ability to improve participant knowledge and decision-making around opioid risks far outweighs the minimal risks posed by study participation.

Importance of Knowledge to be Gained: High rates of prescription opioid misuse among adolescents and young adults and strong motivation for pain relief suggest a considerable lack of understanding of effective and safe use of prescription opioids and other analgesics. To date, educational interventions have not adequately addressed both the benefits and risks of opioid analgesics. Adolescents, therefore, continue to place themselves at risk for serious opioid-related adverse events including death and misuse. Our study will yield important information about new and innovative ways to provide older adolescents and young adults with the skills and information necessary to make safe and sound analgesic decisions – particularly with respect to high risk periods such as the postoperative period. The knowledge gained from this research is imperative to optimize the safety of opioid analgesics in the hands of adolescents and young adults.

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CAUTION: IF YOU HAVE PRINTED THIS CONSENT FOR USE WITH PARTICIPANTS, IT IS NOT THE IRBMED APPROVED VERSION. Access the approved/watermarked consent from the Documents Tab in the main study workspace. The approved/watermarked document *will not* contain this cover page and *will* have the approval watermark present in the header.

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INSTRUCTIONS FOR EDITING THIS DOCUMENT

1. Turn on Track Changes.
2. Make necessary changes in consent, and update the footer intended for study team version control.
3. Upload the revised consent into Section 10-1, maintaining the IRBMED standard naming convention as follows:
   - **Consent - Tracked**
   - **Consent -** *Concise Subtitle* **– Tracked** (provide a subtitle when there are multiple consents associated with the study)
   - **Assent - Tracked**
   - **Parental Permission/Assent - Tracked**
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NOTES:

Words identified above in bold must not be changed; words identified in italics may be modified by the study team. Informed consent subtitles should be a one or two word descriptor, such as**: Consent – *Genetic* – Tracked** or **Consent – *Blood Draw* - Tracked**.

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DO NOT delete any documents or stacks of documents from eResearch; these are retained for historical and regulatory reference purposes.

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---------- IRB OFFICE USE ONLY ----------

Study ID: HUM00147378 / Continuing Review ID: CR00078558

Approval Date: 8/21/2019

Document Finalized: 8/21/2019 12:00 PM

University of Michigan
Electronic Consent To Be Part Of A Research Study

Name of Study and Researchers

Title of Project: Evaluating an Interactive Opioid Risk Education Program (**STOMP** – **S**cenario-**T**ailored **O**pioid **M**essaging **P**rogram) for Young Adults

Principal Investigator: Terri Voepel-Lewis, PhD, RN

Funding Source: National Institute of Health

GENERAL STUDY Information

This study does not replace or interfere with your routine care in any way.

Study Purpose: This study will help us evaluate our new pain management education program, STOMP, that is meant to teach patients about some safe and effective ways to manage pain after surgery.

Voluntary: Taking part in this study is voluntary. Your choice of whether or not to take part will not affect the care you receive at the University of Michigan. Some of the questions may make you feel uncomfortable. If a question makes you uncomfortable, you can just skip it and go to the next question.

Who: We will recruit up to 600 young adults (ages 15-24) who are having surgery that is typically associated with pain during recovery.

Study procedures:

Surveys:

- Those who take part will complete 5 brief surveys over 3 months. These surveys ask about your pain and pain reliever knowledge/perceptions, your past pain reliever use and other drugs you have used in the past.
- The survey also asks about your preferences for pain relief, beliefs about pain reliever risks and what you might do to take care of your pain under specific conditions.

Here is the survey schedule:

Before Surgery	1 week after surgery	2 weeks after surgery	1 month after surgery	3 months after surgery
Baseline survey (20 mins)	<5 min survey	10 min survey	10 min survey $25	10 min Final survey $25
Past pain/symptom experience; Perceptions	Pain/ pain reliever use	Pain/ pain reliever use Perceptions	Pain/ pain reliever use; Perceptions	Pain/ pain reliever use; Perceptions

Education: With the first survey, two thirds of those who take part will get new information about how to manage pain. Who gets this information is decided randomly, like flipping a coin..

Health Information: Lastly, we will separately collect information about your surgery and recovery (through 3 months after surgery only) from your medical record.

Risk to Privacy: All surveys will be completed on your smartphone, an iPad or computer.

To keep your personal information private, we will give you a study ID number that you yourself will enter on all surveys. This ID will help us to link your surveys together and with the surgery information we record separately without disclosing your identity in our databases or in any analysis.

No one outside our study team will be able to figure out whose surveys belong to you or others in the study. All identifiers will be destroyed once the study is complete.

Benefits: Some people who take part may learn something from being in this study that will help them better manage pain at home after surgery. Additionally, your part in the study will help us learn how we might improve the care we give to surgical patients in the future.

Clinical Trial: A description of this clinical trial will be available on http://www.clinicaltrials.gov/, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

With appropriate permissions, your de-identified information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

Protecting your privacy: To further protect your privacy, this research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information or documents, that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information or documents, protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIH, which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, such as child abuse and neglect, or harm to self or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

Payment

Those who take part will be paid up to $50 based on survey completion as noted in the table above.

The University of Michigan accounting department will need your name, address, payment amount, and related information for tax reporting purposes.

AUTHORIZATION TO RELEASE PROTECTED HEALTH INFORMATION

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by contacting the researchers listed below (under Contact Information).

Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Demographic information
- Personal identifiers

It's possible that the researchers or others will need access to information about you during or after this study. For example:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- The University of Michigan or a government agency may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to, make sure the study is done safely and properly, learn more about side effects, or analyze the results of the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- Federal or State law may require the study team to give information to the Food and Drug Administration (FDA) or other government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

As a rule, the researchers will continue to use information about you until the study is over and will keep it secure until it is destroyed. Limited information about you may continue to be used after the study is over, for other research, education, or other activities. But use of this information would not reveal your identity.

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information see http://www.med.umich.edu/hipaa/npp.htm. Note that once your information has been shared with others, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Contact Information

To find out more about the study, to ask a question or express a concern about the study, or to talk about any problems you may have as a study subject, you may contact one of the following:

Principal Investigator: Terri Voepel-Lewis PhD, RN Mailing Address: 1540 E. Medical Center Dr., Mott Children's Hospital, Ann Arbor, MI 48109-4245 Telephone: 734 936-0734 Email: terriv@umich.edu	Study Coordinator: Monica Weber, RN, BSN, CCRP Mailing Address: 1540 E. Medical Center Dr., Mott Children's Hospital, Ann Arbor, MI 48109-4245 Telephone: 734 936-0734 Email: monij@umich.edu

You may also express a concern about a study by contacting the Institutional Review Board:

University of Michigan Medical School Institutional Review Board (IRBMED)

2800 Plymouth Road

Building 520, Room 3214

Ann Arbor, MI 48109-2800
734-763-4768

E-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study, you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

SIGNATURES

Research Subject:

I understand the information printed on this form. My questions so far have been answered.

Signature of Subject: _____ Date: _____

Name (Print legal name): _____