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Assessing Informed Consent in an Opioid Relapse Prevention Study with Adults under Current or Recent Criminal Justice Supervision

Ashleigh A. Allen¹, Donna T. Chen², Richard J. Bonnie³, Tomohiro M. Ko¹, Colleen E. Suratt⁴, Joshua D. Lee^{5,6}, Peter D. Friedmann⁷, Michael Gordon⁸, Ryan McDonald⁵, Sean M. Murphy⁹, Tamara Y. Boney¹⁰, Edward V. Nunes¹¹, and Charles P. O'Brien¹⁰

¹University of Virginia Institute of Law, Psychiatry, and Public Policy, Charlottesville, VA, USA

²Center for Biomedical Ethics and Humanities, University of Virginia School of Medicine, Charlottesville, VA, USA

³University of Virginia School of Law, Charlottesville, VA, USA

⁴Department of Public Health Sciences, University of Virginia, Charlottesville, VA, USA

⁵Department of Population Health, New York University, New York, NY, USA

⁶Department of Medicine, Division of General Internal Medicine, New York University, New York, NY, USA

⁷Office of Research, University of Massachusetts Medical School-Baystate, Baystate Health, Springfield, MA USA

⁸Friends Research Institute, Baltimore, MD, USA

⁹Department of Healthcare Policy and Research, Cornell University, New York, NY, USA

¹⁰Treatment Research Center, University of Pennsylvania, Philadelphia, PA, USA

¹¹New York State Psychiatric Institute, Columbia University, College of Physicians and Surgeons, New York, NY, USA

Abstract

Concerns persist that individuals with substance use disorders who are under community criminal justice supervision experience circumstances that might compromise their provision of valid, informed consent for research participation. These concerns include the possibilities that desire to obtain access to treatment might lead individuals to ignore important information about research participation, including information about risks, or that cognitive impairment associated with substance use might interfere with attending to important information. We report results from a consent quiz (CQ) administered in a multisite randomized clinical trial of long-acting naltrexone to prevent relapse to opioid use disorder among adults under community criminal justice supervision—a treatment option difficult to access by this population of individuals. Participants

were required to answer all 11 items correctly before randomization. On average, participants answered 9.8 items correctly (89%) at baseline first attempt ($n=306$). At week 21 ($n=212$), participants scored 87% (9.5 items correct) without review. Performance was equivalent to, or better than, published results from other populations on a basic consent quiz instrument across multiple content domains. The consent quiz is an efficient method to screen for adequate knowledge of consent information as part of the informed consent process. Clinical researchers who are concerned about these issues should consider using a consent quiz with corrected feedback to enhance the informed consent process. Overall, while primarily useful as an educational tool, employing a CQ as part of the gateway to participation in research may be particularly important as the field continues to advance and tests novel experimental treatments with significant risks and uncertain potential for benefit.

Keywords

Informed consent; research ethics; substance use disorder; criminal justice supervision

1. Introduction

Informed consent is foundational to ethical clinical research as one important means for respecting persons and their autonomy (Emanuel, Wendler, & Grady, 2000). For informed consent to be valid, potential participants must be capable, voluntary, and adequately informed (Faden, Beauchamp, & King, 1986). To achieve this, researchers must disclose relevant information, including information about risks, potential benefits, alternatives, and the nature of research, and ideally participants should understand the disclosed information. However, studies show that these ideals are imperfectly achieved across a variety of conditions (Nishimura et al., 2013; Tam et al., 2015).

Additionally, concerns persist that individuals with substance use disorders who are under criminal justice supervision, including community criminal justice supervision (e.g., probation, parole), experience circumstances that might compromise their provision of valid, informed consent for research participation (Adler, 1995; DeMatteo, Filone, & LaDuke, 2011; Dugosh, Festinger, Croft, & Marlowe, 2010; DuVal & Salmon, 2004; Edens, Epstein, Stiles & Poythress, 2011; Festinger, et al., 2007; Rounsaville, Hunkele, Easton, Nich, & Carroll, 2008). These concerns include the possibilities that desire to obtain access to treatments might lead individuals to ignore important information about research participation (Anderson & DuBois, 2007; McCrady & Bux, 1999; Vaughn, Sarrazin, Saleh, Huber, & Hall, 2002) or that cognitive impairment associated with substance use might interfere with attending to important information (McCrady & Bux, 1999). Further, provisions to safeguard sensitive information disclosed by participants and information about confidentiality protections may be especially important to individuals with substance use disorders and criminal justice system involvement who are considering research participation (DuVal & Salmon, 2004). In light of these needs, an addictions research group at the University of Pennsylvania has been using consent quizzes since the 1970s as a tool for increasing the likelihood that consent is informed (Grabowski, O'Brien, & Mintz, 1979).

Pharmacotherapy is underutilized for drug-dependent criminal justice populations (Friedmann et al., 2012) despite substantial evidence of its effectiveness in reducing opioid use (Amato et al., 2005). Some authorities in the criminal justice system view pharmacotherapy as substituting one drug for another, particularly in regards to agonist therapy (methadone and buprenorphine) for opioid use disorders. For this reason, among others, many authorities in the criminal justice system discourage persons under criminal justice supervision from pursuing pharmacotherapy, and in particular agonist therapies (Bonnie, 2005; Friedmann et al., 2012). For these individuals, and for individuals disinterested in agonist therapies, acceptable pharmacotherapeutic options are often difficult to access. When a clinical trial provides an opportunity to obtain access to an opioid antagonist medication that is otherwise expensive and potentially difficult to access, such as extended-release naltrexone, concern exists that participants desiring to gain access to it through the clinical trial might ignore risks and other important information related to research participation.

Extended-release naltrexone has a number of risks that participants must be made aware of during the informed consent process. Participants receiving naltrexone injections may experience pain or infection at the site of injection, and there is risk of overdose death if participants try to overcome the effects of long-acting naltrexone by using large amounts of heroin or other opioids. After the effects of naltrexone wear off, participants are more sensitive to the effects of opioids, and the risks of overdose and death are increased if they use the same amount as they had previously used on a regular basis. Participants in the treatment-as-usual arm incur risks as well, including the risk of overdose death after a period of abstinence. Participants in both arms also may perceive more general risks of study participation, including that authorities in the criminal justice system would disapprove of their participation. Informing potential participants about safeguards put in place to protect their confidentiality, such as not sharing information about individuals' participation with criminal justice system authorities, contributes to informed decision-making.

With these concerns in mind, each site in a five-site randomized controlled trial testing extended-release naltrexone to prevent relapse to opioid dependence among adults with a history of opioid dependence (current or prior dependence) and current/recent criminal justice system (CJS) involvement required all participants to pass a consent quiz in order to demonstrate knowledge about the study as part of the informed consent process (Lee et al., 2015; Lee et al., 2016). This requirement provided the opportunity to analyze results from an informed consent quiz implemented in a large scale, real-world study of a pharmacological intervention which was commercially available but not yet FDA-approved for opioid relapse prevention and which was very difficult to access as a treatment option for this population.

2. Methods

2.1 The XR-NTX Relapse Prevention Effectiveness Study

The primary study was a five-site randomized controlled trial (RCT) evaluating the effectiveness of monthly injections of extended-release naltrexone (XR-NTX), a sustained-release full mu-opioid receptor antagonist, in preventing relapse to opioid dependence in individuals under current or recent CJS who preferred opiate-free treatment over methadone

or buprenorphine agonist maintenance treatment (Lee et al., 2015; Lee et al., 2016). A common protocol was approved by the local Institutional Review Boards (IRBs) and implemented at five independently NIDA-funded sites: University of Pennsylvania in Philadelphia, New York School of Medicine/Bellevue Hospital Center and Columbia University Medical Center in New York City, Rhode Island Hospital and Brown University in Providence, and Friends Research Institute in Baltimore (Lee et al., 2015). The Data and Safety Monitoring Board (DSMB) was hosted at the University of Pennsylvania. Participants were enrolled from February 2009 through November 2013. Oral naltrexone was initially approved by the FDA in 1984; extended-release naltrexone (Vivitrol) was FDA-approved in 2006 for treatment of alcohol dependence and received FDA approval for treatment and prevention of opioid dependence in 2010.

Participants in the primary study were individuals with a lifetime (current or prior) history of opioid dependence, as measured using structured assessment instruments based on DSM-IV criteria (i.e., MINI International Neuropsychiatric Interview and SCID Module E for Substance Use Disorders), and current or recent CJS-involvement defined as “currently serving an adjudicated sentence that includes community supervision (e.g., parole, probation, outpatient drug court programs, or other court-mandated treatment) or in the past 12 months arrested or incarcerated” (Lee et al., 2015; Lee et al., 2016). Study inclusion/exclusion criteria were chosen to maximize the potential for generalizability within acceptable safety parameters.

The control arm was treatment-as-usual (TAU) offering brief counseling and referrals to community treatment programs. For both arms, study visits were scheduled every two weeks for 6 months to gather research information, including urine tests. Follow-up visits were completed at 12 and 18 months post-baseline. In the primary outcome analysis, XR-NTX was an effective relapse prevention intervention, reducing relapse events overall and prolonging time-to-relapse. There were seven overdoses in the study, all of which occurred in the TAU arm. Study methods and outcomes have been published elsewhere (Lee et al., 2015; Lee et al., 2016).

2.2 Informed consent process

The informed consent process was approved by the local IRB at each of the five sites. Prescreening consisted of a telephone or in-person brief evaluation, during which an in-person screening visit was scheduled. At the in-person screening, individuals were informed that they needed to score 100% on a consent quiz in order to move forward in the study. They then participated in a standard informed consent process in which a summary of the study was provided and the research assistant/study coordinator reviewed the consent information with the prospective participant. Following this discussion, participants took a consent quiz (CQ) consisting of 11 True/False questions. Participants scoring less than 100% were provided feedback, given the opportunity to ask questions, and could re-take the CQ until they answered all questions correctly (up to five attempts). Once the participant scored 100%, he or she signed the consent form in person per standard International Congress on Harmonization (ICH) Good Clinical Practice guidelines.

2.3 Consent quiz instrument and data collection

The CQ instrument consisted of 11 True/False questions covering risks and potential benefits of study participation, the voluntary nature of and alternatives to participation, and study procedures (see Table 1 for quiz items). Trial investigators and University of Virginia ethics researchers adapted it from a consent quiz that has been used by the University of Pennsylvania researchers since the 1970s as a tool for increasing the likelihood that consent is informed (Grabowski, O'Brien, & Mintz, 1979). At week 21, participants who remained in the study completed the CQ instrument again for research purposes; for participants in the XR-NTX arm, this was the visit they received their last injection. No targeted preparation or re-consenting occurred, results were not immediately reviewed, and incorrect answers did not affect participants' eligibility to remain in the trial.

2.4 Data analysis

Available data from first administration of the CQ at baseline ($n=306$) and from week 21 ($n=212$) were used. Although 308 participants completed the CQ at baseline, results from 2 first administrations were unavailable. At week 21, 96 participants did not complete the CQ, either due to loss to follow-up or because they missed that specific visit. Descriptive statistics on CQ scores as measured by mean and median group score at baseline and 21 weeks and percentage of participants answering each question correctly at both time points were calculated.

Fisher's exact tests were used to evaluate differences in proportion of participants answering each question correctly by study arm at baseline and 21 weeks. Because the distributions of the CQ scores at baseline and Week 21 were skewed, nonparametric Mann-Whitney U tests were used to evaluate the difference in median CQ score at baseline and at week 21, by study arm. An independent t-test was used to test for a difference in mean change in CQ score between baseline and 21 weeks, by study arm. A paired t-test was used to evaluate mean change in individual participants' CQ scores between baseline and 21 weeks. A p -value level of 0.05 was used for all tests.

2.5 Comparisons with other consent quiz studies

In order to place our findings in context, we compare our results for specific components of informed consent at baseline and week 21 with results for similar components from a large, systematic meta-analysis of 103 studies assessing participants' understanding of informed consent in clinical trials across a variety of disease categories (Tam et al., 2015). Because this meta-analysis excluded studies that involved participants with substance use disorders, we also compared our results to seven studies assessing knowledge of consent information by participants with a substance-use history (Table 2). From these studies, we gathered information about sample size, study population/trial purpose, and time of quiz administration. For intervention studies aiming to improve information retention, we included scores from baseline and follow-up in the control arm. We also gathered information about question format (True/False, multiple-choice, open-ended) because closed-response formats do not provide as much discrimination between levels of understanding as open-response questions and individuals tend to score higher on closed-

response instruments (Festinger et al., 2014; MacQueen, Chen, Ramirez, Nnko, & Earp, 2014).

3. Results

3.1 Participant characteristics

All participants had a lifetime history of opioid dependence, with 88% reporting heroin use, 49% reporting other opioid misuse, and 41% reporting injection drug use. Within 30 days prior to screening, 34% of participants reported any opioid misuse, with 24% using heroin and 19% misusing other opioids, 19% reported cocaine use, 12% reported heavy alcohol use, and 19% reported marijuana use; 57% of participants reported none of these within 30 days of the baseline visit. Only 9% of participants required opioid detoxification to enter the study. Eighty percent of participants were under current CJS supervision at baseline; 38% were on probation, 36% were on parole, and 6% were under some other type of CJS supervision. The remaining 20% of participants were not under CJS supervision at baseline, but had recent criminal involvement (i.e., arrest, incarceration, conviction, plea bargain 0-12 months prior to baseline). Mean age was 43.8 years ($SD = 9.3$). The vast majority of participants were male (85%). Half of participants identified themselves as African-American, 20% as Caucasian, 27% as Hispanic, and 3% as some other race or ethnic group. Participants reported an average of 11.5 years of education ($SD = 2.01$). Only 18% of participants were employed at baseline. Seventy-one percent of participants were insured, with 44% having Medicaid. Participant demographics by study arm are available elsewhere (Lee et al., 2016).

3.2 Overall results from consent quiz

Overall, 141 individuals (46.1%) answered all questions correctly on their first try, 58 (19.0%) missed one question, 56 (18.3%) missed two, and 51 (16.7%) missed three or more. Of the 165 individuals (53.9%) who missed at least one question, 156 of them (94.5%) scored 100% on their second try, 7 on the third try, one on the fourth try, and one participant took five tries. On first attempt at baseline, the mean score was 9.79 out of 11 (89.0%) ($SD = 1.49$) and the median score was 10. For the 212 participants who completed the CQ at week 21, the mean score was 9.53 (86.6%) ($SD = 1.71$) and the median score was 10. Mann-Whitney U tests found no significant difference in the median CQ scores at baseline or week 21 between individuals receiving XR-NTX versus TAU.

A paired t -test revealed a statistically significant decrease in mean CQ scores from baseline ($M = 9.86$, $SD = 1.45$) to week 21 ($M = 9.53$, $SD = 1.71$) for participants who were present at both time points; $t(210) = 2.49$, $p < 0.05$. Cohen's d for the comparison between baseline and week 21 scores was $d = 0.21$ confirming a small effect size. There was no significant difference in the mean change in CQ scores between baseline and week 21 for participants in the TAU arm ($M = -0.18$, $SD = 1.72$) and the XR-NTX arm ($M = -0.47$, $SD = 2.12$); $t(209) = 1.08$, $p = 0.281$.

3.3 Results from specific domains of informed consent

The proportions of participants who answered each item correctly are presented in Table 1. Nearly all participants correctly answered questions regarding the voluntary nature of participation (99.7% at baseline; 91.1% at week 21), the benefit conferred by XR-NTX, i.e. that it blocks the ability to get high on opiates (98.0% at baseline, 96.2% at week 21), and at least one important risk associated with study participation, i.e. that overdose is possible if after getting clean a participant uses the same amount of heroin they did before getting clean (96.7% at baseline, 93.9% at week 21). Nearly all participants recognized that different treatments were being administered and compared (96.7% at baseline, 96.7% at week 21) and the availability of alternative treatment if they were to withdraw from the study (93.1% at baseline, 90.6% at week 21).

The vast majority of participants answered correctly regarding their ability to withdraw from the study at any time (86.9% at baseline, 81.1% at week 21) and the possibility of a painful lump at the site of XR-NTX injections (85.0% at baseline, 79.7% at week 21). Participants least frequently demonstrated knowledge of specific study procedures related to the frequency of visits required of people receiving the XR-NTX injection (74.5% at baseline, 80.6% at week 21.)

While proportions were similar at baseline for participants who correctly answered “false” to the question “researchers will tell my probation or parole officer (PO) that I am in the study” and ultimately randomized to TAU and XR-NTX arms (90.2% vs 91.5%), at week 21, more participants in the TAU arm answered “false” than in the XR-NTX group, (99% vs 88.9%, $p = 0.003$).

3.4 Comparison with other consent quiz studies

The percentage of participants in our study answering questions correctly was higher than the pooled percentage of participants reported by the meta-analysis (Tam et al., 2015) for each comparable component of informed consent (Table 1).

Our study participants’ mean CQ score of 89.0% is consistent with the consent quiz scores from the two most directly comparable studies, both of which used a True/False quiz with a substance-dependent, though not necessarily CJS-involved population; their average scores were 90% ($SD=10.6$) and 87.1% ($SD=9.2$) respectively (Harrison et al., 1995; Kiluk et al., 2010). Not surprisingly, scores from our study are higher than those measured using open-ended consent quizzes (Table 2).

4. Discussion

Participants in this clinical trial performed as well as clinical trial participants across multiple disease categories on a basic consent quiz. There are a number of potential explanations for participants’ high quiz scores relative to other studies, including: the consent quiz developed for this study being easier to understand than other quizzes, other quizzes covering more detailed information, or, as mentioned earlier, the closed-ended item type contributing to elevated scores. Although it is possible that other quizzes covered more detailed information, our consent quiz was designed to cover the most vital concepts,

including important risks and potential benefits, burdens of participation, the voluntary nature of participation, alternatives to joining the research study, and confidentiality provisions. As such, tested information included complex concepts such as how extended-release naltrexone affects one's ability to get high on opiates as well as the risks for overdose and death under several circumstances.

Like many others, our investigators chose a True/False format to reduce burden on the study participants who were already completing many instruments at screening. Given this format, if participants were merely guessing we would expect an average score of 50% (5-6 items correct of 11); yet on average participants answered 9.79 items (89%) correctly on their first quiz suggesting they were not guessing. An average score of 9.53 (86.6%) correct after 21 weeks without formal repeat presentation of the information suggests that information was stored in some way in the participants' long-term memories, reinforced through experience, and was sufficiently retrievable to their working memory to discern whether a particular statement about the study was true or false. We did not test their knowledge before engaging in the informed consent process, so it is possible that some of the information on the test is common knowledge amongst this community of individuals, some of whom have participated in other clinical trials.

Consent quizzes can identify topics that are confusing to participants and provide an opportunity to clarify misunderstandings about risks and benefits or study procedures. Having information about which consent quiz items are frequently answered incorrectly can also help researchers determine which aspects of their informed consent process should be revised or given more attention. Although not ideal for ascertaining depth of understanding (MacQueen et al., 2014; Tam et al., 2015), True/False or multiple choice instruments are commonly used to test knowledge given their efficiency and ease of use particularly when assessing on a large-scale (Grady et al, 2017; Kiluk et al., 2010; MacQueen et al., 2014; Rounsaville et al., 2008; Tam et al., 2015) and we argue they are likely to be used if consent quizzes are widely adopted as a screening tool or prerequisite to study entry. For situations in which investigators want further assurance that information can be brought to mind by participants without the external prompt provided by closed-ended question formats, open-ended methods such as teach-back are useful, although more time is required. These methods have been employed to assess comprehension among a variety of populations considered vulnerable to inadequate informed consent (Festinger et al., 2010; Krieger et al., 2015; Kripalani, Bengtzen, Henderson & Jacobson, 2008).

In this study, participants scored well in all domains of informed consent included in the quiz. In particular, a high percentage of participants correctly answered questions regarding the voluntariness of their participation in the study and the alternative choices they could make, cornerstones of informed consent. Participants also accurately recognized risks of trial participation – an important finding because this study, which tested a pharmacological intervention, entailed more risks than studies that include only psychosocial interventions. Week 21 scores are especially encouraging since CQ performance at that visit did not preclude participants from remaining in the study which could have decreased motivation to answer accurately. Yet, results suggest that participants were not answering in a random fashion.

Of the questions in the risk/benefit domains, 21.9% of participants at baseline incorrectly answered the question “It is possible, although very difficult, to overdose with heroin while taking naltrexone.” It is unclear whether participants answered this question incorrectly because the concept was difficult to understand or because the question was phrased in a confusing way. Participants might have answered “False” to this question for semantic reasons while in fact understanding the risk of overdose. For example, a participant may answer “False” to this question if he or she believes that it is *easy* to overdose with heroin while taking XR-NTX. Rewriting this question would allow better ascertainment of participants’ knowledge. From an educational perspective, this question, even though worded in a complex way, provided researchers with the opportunity to reiterate this important potential risk.

Performance between the XR-NTX and TAU study arms differed on only one CQ item: “The researchers will tell my probation or parole officer (PO) that I am in the study.” The study was designed to discourage direct referrals from POs and avoid direct communications between researchers and POs to minimize the possibility of real or perceived coercion. At baseline, correct responses to this question were approximately equal between participants ultimately randomized to the XR-NTX and TAU arms (90.2% and 91.5%). However, at week 21, 99% of the TAU group correctly answered “false” while only 88.9% of the XR-NTX group answered “false.” We suspect that some of the participants receiving XR-NTX may have asked the researchers to share this information with a PO when the conditions of their probation or parole require that they receive treatment of some kind. Site investigators reported that they did receive requests along these lines.

Our study has limitations. The CQ instrument we used was not psychometrically validated. Nevertheless, it was developed mainly to efficiently test knowledge of basic consent information as part of the informed consent process and to serve as a basis for further consent discussion. When the XR-NTX study was designed, there were some psychometrically validated instruments assessing quality of informed consent (see for example, Joffe et al., 2001), but no instruments had yet been psychometrically validated for CJS-involved individuals with substance use disorders (Festinger et al., 2014).

The current trial did not collect information about whether any participants were excluded from the trial because they were unable to score 100% on the quiz after multiple attempts, although investigators did not indicate this as a major impediment to recruitment. Indeed, such occurrences are likely to be rare with appropriate educational support, as clinical populations of all types can demonstrate knowledge of informed consent information when given such support (Nishimura et al., 2013) including clinical trial participants with cognitive impairments due to conditions such as schizophrenia-related psychosis (Wirshing, Wirshing, Marder, Liberman, & Mintz, 1998). Nevertheless, more research speaking to this point would help inform future investigators in planning for using consent quizzes in this manner. Further, although the current study included some participants who required detoxification in order to participate, no enrolled participants were actively using opioids at the time of enrollment. Future studies could examine the consent quiz performance of clinical trial participants who are actively using substances for studies seeking to enroll these individuals. If these studies encounter participants who have extreme difficulty

demonstrating comprehension or retention of information communicated during the consent process, researchers should consider how their comprehension can be enhanced.

It is unclear why participants continue to score well at week 21, but we speculate that knowing ahead about the need to score 100% correct on a consent quiz and opportunity for corrective feedback may have attuned participants to the information disclosed. Experiential knowledge garnered from study participation likely also contributed. It is possible that participants remembered the precise questions after 5 months, although we consider it unlikely. Perhaps reviewing important information in a simple quiz format used as part of the consent process contributed to improved understanding and retention of the information over time. This hypothesis could be investigated in more detail in future research studies. In their 1979 publication, Grabowski et al. report that independent investigators at the Veterans Administration found that participants who had to pass a CQ were all aware of the general nature of the study they were in, whereas 27% of individuals participating in studies without a consent quiz were both unaware of the general nature of the study in which they participated, as well as unaware that they were participating in research.

In spite of its limitations, our study has several strengths. First, to the best of our knowledge, this study has the largest sample size of any to assess knowledge of informed consent information with clinical trial participants who had a substance use disorder, with $n=306$ at baseline, compared with $n=130$ in the next largest study (Rounsaville et al., 2008). Additionally, this study is one of few to reassess knowledge of consent information at a follow-up time-point. By examining participants' scores on a consent quiz administered as part of a standard informed consent process in a clinical trial in which the experimental treatment is desirable, difficult to obtain, and potentially risky, this study speaks to concerns that research participants might ignore information presented during the informed consent process to access a difficult-to-obtain relapse prevention medication and makes an important contribution to the body of literature regarding research consent.

Further reports of experiences related to implementation and routine use of consent quizzes could help investigators interested in using consent quizzes learn what is feasible and how to implement such a program. Studies designed to compare different testing modalities and implementation practices to determine how best to ascertain knowledge of important informed consent information and to enhance informed consent for a particular study while limiting the burden put on clinical trial participants who already complete large batteries of forms are critically important to help guide researchers in this regard.

5. Conclusions

Persons with a history of opioid dependence and current/recent CJS involvement enrolled in this clinical trial testing naltrexone for relapse prevention can attend to information communicated to them as part of the informed consent process sufficiently to score 100% correct on a true/false consent quiz and also can demonstrate knowledge of important concepts for at least as long as 21 weeks. These individuals perform as well as, or better than, other clinical trial groups on a basic consent quiz instrument across multiple content domains. The consent quiz is an efficient method to screen for adequate knowledge of

consent information as part of the informed consent process. Clinical researchers who are concerned about these issues should consider using a consent quiz with corrected feedback as one way to enhance the informed consent process.

We suggest that the primary purpose of the consent quiz is firstly an educational, and secondly a quality improvement tool. However, there may be instances where a participant does not demonstrate adequate knowledge of the informed consent information, even after repeated instances of corrected feedback. In these cases, the participant should not be enrolled in the trial in question, and the consent quiz would function as a gatekeeping device. In the future, trials that use consent quizzes should track whether and under what circumstances participants are excluded due to failing to pass a consent quiz in order to better inform and improve this process. Overall, while primarily useful as an educational tool, employing a CQ as part of the gateway to participation in research may be particularly important as the field continues to advance and tests novel experimental treatments with significant risks and uncertain potential for benefit.

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Declaration of interest:

Dr. Lee has received investigator initiated study funding and study drug in-kind from Alkermes and Reckitt Benckiser for additional studies. Dr. Friedmann was paid an honorarium and received reimbursement for travel for attendance at an Indivior Advisory Board Meeting and served as a roundtable leader for Orexo. Dr. Gordon received investigator initiated study funding and study drug in-kind from Alkermes for an additional study. Dr. Nunes received: study drug in-kind from Alkermes/Cephalon, Inc., Reckitt-Benckiser, and Duramed Pharmaceuticals for additional studies; web-based behavioral intervention for a research study from HealthSim, LLC; devices under investigation and reimbursement for travel for investigators' meeting from Brainsway. Dr. Nunes was paid an honorarium and received reimbursement for travel for attendance at a Lilly Advisory Board Meeting in January 2012 and received educational materials from Otsuka America Pharmaceutical, Inc. in 2013. He serves on an Advisory Board for Alkermes. Dr. O'Brien has served as a consultant to Alkermes.

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Table 1

Performance on consent quiz questions, by question type.

Question [correct answer]	% Participants answering correctly at baseline, prior to randomization <i>n</i> =306				% Participants answering correctly at 21 weeks <i>n</i> =212				Component of informed consent	% Participants understanding same component in meta-analysis (95% CI)
	All	XR-NTX	TAU	All	XR-NTX	TAU	All	XR-NTX		
Q1. I am free to decide whether or not to be in this study. [True]	99.7	100.0	99.3	98.1	97.2	99.0			Voluntary nature of participation	74.7 (67.9–80.5)
Q2. When taking naltrexone, I can still get high on opiates (drugs like heroin, Percodan, Oxycontin, methadone, buprenorphine). [False]	98.0	98.7	97.4	96.2	94.4	98.1			Potential benefits of the study	74.0 (65.0–81.3)
Q3. If I get clean for a period of time and use the same amount of heroin I did before getting clean, I could overdose. [True]	96.7	97.4	96.1	93.9	94.4	93.3			Potential risks and side-effects	67.0 (57.4–75.4)
Q4. I can choose whether or not I get the naltrexone injection in this study. [False] ^a	79.8	83.0	76.6	79.7	75.9	83.7			Randomization/No therapeutic misconception	52.1/62.4 (41.3–62.7)/(50.1–73.2)
Q5. Once I start in this study, I have to continue until the end. [False]	86.9	85.0	88.9	81.1	81.5	80.8			Freedom to withdraw at any time	75.8 (70.6–80.3)
Q6. It is possible, although very difficult, to overdose with heroin while taking naltrexone. [True]	78.1	80.4	75.8	65.6	63.0	68.3			Potential risks and side-effects	67.0 (57.4–75.4)
Q7. People can get a painful lump in the buttock from the naltrexone injection that is bad enough to require surgery. [True]	85.0	87.6	82.4	79.7	81.5	77.9			Potential risks and side-effects	67.0 (57.4–75.4)
Q8. The researchers will tell my probation or parole officer (PO) that I am in the study. [False]	90.8	91.5	90.2	93.9	88.9	99.0			Confidentiality	66.2 (55.3–75.7)
Q9. If I decide not to be in the study, I can try to get into any regular drug treatment program I want, including methadone or buprenorphine. [True]	93.1	93.5	92.8	90.6	89.8	91.3			Availability of alternative treatment if withdrawn	64.1 (53.7–73.4)
Q10. Some people will not get the naltrexone injection, but will come back twice a month to complete interviews and give urine samples as part of the study. [True]	96.7	96.1	97.4	96.7	94.4	99.0			Knowing that treatments were being compared	62.9 (45.5–77.5)
Q11. People getting the naltrexone injection will only need to come to the study once a month. [False]	74.5	72.5	76.5	77.8	80.6	75.0			Study procedures	N/A

Note. The studies included in the Tam et al. (2015) meta-analysis assessed understanding at varied time-points. Participants from studies with later assessments were less likely to understand confidentiality or to be able to name at least one risk.

This question could potentially be interpreted as asking whether the participant may refuse an injection—for which the correct answer is “True.”_g

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Table 2

Baseline consent quiz scores of clinical trial participants with a history of substance use disorders.

Study	Mean baseline CQ score (<i>SD</i> ^a)	Quiz type (# of questions)	Time of administration	Population/primary trial type	<i>n</i>
Harrison, Vlahov, Jones, Charron, & Clements, 1995	90.6% (10.6)	True/False (17)	Baseline	Injection drug user participants in a placebo-controlled HIV vaccine trial	39
Current XR-Naltrexone study	89.0% (13.5)	True/False (11)	Baseline	Participants with a history of opioid dependence and current/recent CJ involvement, in a relapse-prevention RCT (XR-NTX vs. TAU)	306
Kiluk, Nich, & Carroll, 2010	87.1% (9.2)	True/False (14)	Baseline	Substance-dependent (not further specified) participants in a community-based RCT of cognitive-behavioral therapy or standard drug counseling for treatment of substance dependence disorder	76
Rounsaville et al., 2008	84.8%	Multiple choice (4)	Baseline	Marijuana-dependent, CJ-involved participants, referred by a PO in a RCT trial of four outpatient treatments for marijuana dependence	130
Festinger et al., 2014	69%	Open-ended (15)	Baseline	Substance-dependent, drug court clients in a drug court hosted trial examining different schedules of judicial hearings and treatment	52 ^b
Festinger et al., 2009	42%	Open-ended (15)	1–2 weeks after informed consent	Substance-dependent, drug court clients in a drug court hosted trial	17 ^b
Festinger et al., 2010	37% (13.8)	Open-ended (16)	2 weeks after informed consent	Substance-dependent, drug court clients in a drug court hosted trial	45 ^b
Festinger et al., 2007	35%	Open-ended (17)	2 weeks after informed consent	Substance-dependent, drug court clients in a drug court hosted trial	85

^a *SD* reported when available.

^b Participants from the consent as usual arm.