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Motivational Assessment of Non-Treatment Buprenorphine Research Participation in Heroin Dependent Individuals

Gina Papke and Mark K. Greenwald

Substance Abuse Research Division, Dept. of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, MI

Abstract

Background—Heroin abuse remains an important public health problem, particularly in economically disadvantaged areas. Insight into this problem is gained from interviewing addicted individuals. However, we lack systematic data on factors that motivate heroin users to participate in non-treatment research that offers both financial incentives (compensation) and non-financial incentives (e.g., short-term medication).

Aim—To better understand the relative importance of several types of personal motivations to participate in non-treatment buprenorphine research, and to relate self-motivations to social, economic, demographic and drug use factors.

Methods—Heroin dependent volunteers ($N = 235$ total; 57 female and 178 male; 136 African American, 86 Caucasian, and 13 Other) applied for non-therapeutic buprenorphine research in an urban outpatient setting from 2004–2008. We conducted a semi-structured behavioral economic interview, after which participants ranked 11 possible motivations for research participation.

Results—Although the study was repeatedly described as non-treatment research involving buprenorphine, participants often ranked some treatment-related motivations as important (wanting to reduce/stop heroin use, needing a medication to get stabilized/detoxify). Some motivations correlated with income, heroin use, and years since marketing of buprenorphine. Two dimensions emerged from principal component analysis of motivation rankings: (1) treatment motivation vs. greater immediate needs, and (2) commitment to trying alternatives vs. a more accepting attitude toward traditional interventions. In summary, heroin addicts' self-motivations to engage in non-therapeutic research are complex – they value economic gain but not exclusively or primarily – and relate to variables such as socioeconomic factors and drug use.

Keywords

Research participation; motivation; heroin dependence; buprenorphine

1. Introduction

Participation in biomedical research studies of addiction is important because society at large and specific subgroups may benefit. Presently, however, information about substance

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Correspondence: Mark Greenwald, Department of Psychiatry and Behavioral Neurosciences, Substance Abuse Research Division, 2761 East Jefferson Ave., Detroit, MI 48207, USA, Tel: +1 313 993 3965, Fax: +1 313 993 1372, mgreen@med.wayne.edu.

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abusers' motives for research participation is quite limited. Improved knowledge of participants' motivations could help researchers understand ethical and scientific implications of their work, and address the representativeness of their findings. On the one hand, this problem needs to be approached in a population-specific manner, i.e., the motivations of healthy volunteers, patients in clinical trials, drug abusers generally, or specific types of drug abusers, may substantially differ. Thus, until we have systematic data, it would seem advisable to qualify conclusions based on participant sample characteristics. On the other hand, literature outside the addiction field can provide a basis for understanding certain types of research participant motives.

Published studies have examined motivation for research involvement across widely varying groups including racial and ethnic minorities (Castillo et al., 2011) and healthy individuals (Farre et al., 1995; Stunkel and Grady, 2011). A substantial literature derives from clinical trials research involving adult patients with an array of non-HIV medical conditions (Jenkins and Fallowfield, 2000; Criscione et al., 2003; Dixon-Woods and Tarrant, 2009; Wasan et al., 2009; McCann et al., 2010), pediatric patients and their parents (Harth and Thong, 1990; Tait et al., 2003; Chantler et al., 2007), psychiatric patients (Andresen et al., 2010), HIV patients with unknown drug use characteristics (Ross and Jeffords, 1994; Wendler et al., 2008), drug abusers (Timmermans and McKay, 2009), and non-treatment seeking drug abusers with HIV risk (Slomka et al., 2007).

One systematic review concluded that medical patients who are applying for clinical trial research are motivated by personal benefit (Edwards et al., 1998). Other data suggest a more nuanced perspective, such that patients engage in clinical trials with "conditional altruism," meaning that participation may benefit others, but the individual also perceives some personal gain or "diffuse reciprocity" (McCann et al., 2010; Locock and Smith, 2011). Given that treatment-seeking medical patients desire some personal benefit from research participation, we hypothesize that drug-dependent individuals who are not presently seeking treatment are also likely to be motivated (perhaps more so) by concerns about personal benefit. However, this idea has not been systematically evaluated in prior studies.

Generally speaking, studies with substance abusing individuals present investigators with a unique spectrum of challenges. Such individuals are often stigmatized for their drug use, yet some may genuinely wish to change their lifestyle; and they are often impoverished, with legitimate need for money/resources to live, yet the lay public may perceive their motives as purely selfish. This perception is complicated by the frequent use of incentive payments for research participation and attendant ethical issues, even if these incentives are consistent with the prevailing labor market and not judged to be coercive by institutional review boards (Ackerman, 1989; Wilkinson and Moore, 1997; Singer et al., 1998; Erlen et al., 1999; Bayoumi and Hwang, 2002; Emanuel, 2004). Few studies have specifically examined drug-dependent participants' research motivations and, in one report, only injection heroin users were interviewed (Fry and Dwyer, 2001).

Among illegal drug using participants in prior studies, monetary gain was the most common reported personal benefit, but those findings also suggest that monetary value alone was not enough to engage participants (Fry and Dwyer, 2001; Slomka et al., 2007). For instance, in addition to economic gain, injecting drug users in Australia endorsed being motivated by citizenship (e.g., provide information that could help solve societal problems), non-specific altruism (e.g., to help in general), personal satisfaction/benefit (e.g., curiosity and to improve insight), and benefits to drug users (e.g., dispel stigma and inform the public about drug issues; Fry and Dwyer, 2001). Further research is thus warranted to understand motivational factors, including separation of financial gain from other benefits, and to differentiate the

motives of drug abusers from those of other subgroups that have been studied in prior research.

In the present work, we examined reasons why out-of-treatment heroin abusers participate in laboratory-based non-therapeutic research that involved short-term inpatient buprenorphine maintenance followed by outpatient dose tapering. Participants were screened during the first few years after buprenorphine received U.S. Food and Drug Administration (FDA) approval and entered the U.S. market for treating opioid dependence. Although this research was clearly advertised and explained as non-therapeutic, the timing of this research enabled us to gauge participants' interest in buprenorphine, general treatment seeking (despite the non-therapeutic purpose), and alternative motives – thereby offering a balance to financial motivation. During screening for this research, participants ranked 11 *a priori* reasons for involvement. Socioeconomic, demographic, drug use and trait factors were also assessed. We compared motivational rankings and correlated them with other data obtained during the screening process.

2. Methods

2.1. Participants and setting

The Wayne State University Institutional Review Board approved all experimental procedures. Heroin-dependent males and females, ages 18 to 56 years old, were recruited by newspaper advertisements and word-of-mouth referral in the Detroit/metropolitan area.

We communicated at least three times to all participants that this was not treatment research. First, the IRB-approved study advertisement stated, “short-term maintenance on buprenorphine (an alternative to methadone) is included but this is not a treatment study” and that “only volunteers who are ... not seeking treatment will be accepted;” the advertisement also referred to the nature of the study, medical/psychiatric screening, a residential stay, overall length of participation, and potential earnings. Second, during the initial telephone interview the recruiter repeated all the above information, asked if they were still interested in continuing, and then collected further basic information from the candidate (e.g., sex, age, recent substance use, medical or psychiatric conditions that might need treatment). Third, during informed consent, the experimenter again explained to the participant that this was non-treatment research. All volunteers were also informed during the consent process that if, at any time they preferred treatment, they would be given a referral and discontinued from the research. However, no participant requested a treatment referral. Based on repeated self-report assessment prior to obtaining informed consent, participants were thus determined by these *a priori* criteria to be non-treatment seeking despite any quasi-treatment motivation they may have indicated subsequently by their motivation rankings (i.e., reduce/stop use).

Data were collected during the screening phase for three similar laboratory-based opioid pharmacology research studies, which were registered as NIH clinical trials NCT00218309 (Greenwald and Hursh, 2006), NCT00218361 (Greenwald and Steinmiller, 2009), and NCT00608504 (Greenwald, 2010). For each study, candidates were told during the initial telephone interview and again during in-person screening that the study involved a minimum 10-day outpatient induction onto buprenorphine, two further weeks of buprenorphine maintenance during a continuous inpatient stay, and a standardized three-week outpatient buprenorphine dose taper (Greenwald, 2008). Screening for these studies was conducted from 2004 to 2008 during the initial few years after sublingual buprenorphine tablets received FDA approval (October 2002) and entered the U.S. market (early 2003) for treating opioid dependence. Thus, for these heroin-dependent individuals buprenorphine was a relatively novel option – it had not yet been established as a standard

of care for opioid dependence – when these programmatically related research studies were conducted in this urban setting.

2.2. Measures

2.2.1. Motivations for research participation—Based on communications with participants in our opioid dependence non-treatment research studies that occurred prior to the present investigation, the senior investigator (MKG) and staff recruiter generated 11 motivations for research participation that former heroin-dependent individuals had reported. Presently, we assessed the relative importance of these 11 motivations, which were listed in the following standard order (verbatim) on the rating sheet: Amount of money that can be earned; Reduce or stop using heroin (“blow”); Need a medication to get stable/detoxed; Can’t afford treatment right now; Curious about buprenorphine; Don’t like methadone; Like the idea of a 2-week inpatient stay (get off the street, free room and board); The program is close to where I live; Someone I know participated here; Get a free health screening; Curious why I can’t stop using heroin.

Instructions were as follows: “Several factors may have influenced you to seek out this research study. First, read through the choices below. Then, decide how important the following factors were in deciding to participate in this study. Put them in order from 1 = most important, to 11 = least important.” Thus, the participant was asked to rank-order his/her motivations in the present time for the particular study.

At the end of a standardized behavioral economic semi-structured interview that characterized past 30-day heroin use patterns in these individuals (section 2.2.2), each participant ranked these 11 motivations from most important (1) to least important (11). As noted under Data Analysis (section 2.3), these rank scores were reversed to facilitate statistical analysis and interpretation. The interviewer was available to answer the participant’s questions and to assist in scoring when there was a rank tie (which was allowed). The interview and motivation ratings were collected on the first day of the screening process. Due to multiple procedures and time limitations, other assessments sometimes had to be deferred to the second visit (usually 2–3 days later). Some participants were also excluded prior to the return visit (e.g., certain medical conditions, participant was lost to contact). For these reasons, the sample sizes for secondary measures are smaller than primary measures (see tables herein).

2.2.2. Other screening assessments—The Shipley Institute of Living Scale was used to estimate IQ (Zachary, 1991), and participants had to score at least 80 to be included in these studies.

The behavioral economic interview of heroin purchasing and use behaviors and results have been described in detail elsewhere (Roddy and Greenwald, 2009; Roddy et al., 2011). Briefly, a semi-structured format lasting about 20–30 min was used to elicit comprehensive responses pertaining to past-month income (all sources including legitimate employment, public assistance, bartering arrangements, and illegal/sheltered income), heroin seeking/purchasing routines (e.g., number of dealers, drug price, estimated purity, distance and round-trip time to purchase heroin, dollar amount purchased per episode, number of weekly purchases), and consumption of heroin (e.g., \$10 bags per day, pattern of use across a typical 24-hr day), and non-heroin expenditures (e.g., legal and illegal substances, food, shelter/utilities, personal items).

The 38-item Stanford Time Perception Inventory (Zimbardo, 1992) was used to measure participants’ time orientation rooted in the Past (8 items; e.g., “I prefer the old and familiar to the new and challenging”), Present/Hedonistic (9 items; e.g., “I believe that getting

together with friends to party is one of life's most important pleasures"), Present/Fatalistic (8 items; e.g., "I think that it's useless to plan too far ahead because things hardly ever come out the way you planned"), and Future (16 items; e.g., "When I want to achieve something, I set goals and consider specific means for reaching those goals"). This instrument has previously been used with heroin abusers and found to differentiate their time orientation from healthy controls (Petry et al., 1998).

The 30-item version of the Impulsive Relapse Questionnaire (Krebaum et al., 2001; see Adinoff et al., 2007) was used to measure aspects of impulsive (relapse to) drug use. This questionnaire has empirically derived subscales related to Capacity for Delay (9 items; e.g., "It takes me a while, weighing the pros and cons, before I decide to use again"), Automaticity (6 items; e.g., "When I start using drugs again, it's not planned"), Speed (4 items; e.g., "When I decide to use drugs again, it takes less than a few minutes before I actually use"), Control Deficit (6 items; e.g., "I crave for less than one day before I start using again"), and Denial (5 items; e.g., "A few minutes before I start using again, I'm sure I won't"), and a Total score.

2.3. Data analyses

Participants were included in this data set if they reported daily heroin use for at least the past year and they completed the behavioral economic interview and motivation rankings. Demographic measures were available for all participants but, as indicated, other measures were available only on subsets of the overall sample. For each participant, time since buprenorphine was marketed was coded by calendar year of screening (2004 [$n = 60$], 2005 [$n = 45$], 2006 [$n = 46$], 2007 [$n = 46$], and 2008 [$n = 38$]).

Data analyses were conducted using SPSS version 19. First, we reversed the direction of rankings prior to analyses so that high scores reflect high research motivation (which is easier to understand). Second, we computed Spearman rank correlations between the 11 motivations for research participation. Third, we computed Spearman correlations between motivations and questionnaire measures that participants completed.

Next, we computed Spearman correlations between participant motives and heroin use variables including duration of heroin use, route of use (injection vs. non-injection), any lifetime heroin overdose and number of heroin quit attempts; and past 30-day purchasing/ use variables including percent of income spent on heroin, $\log_{10}$ purchase time (minutes), $\log_{10}$ unit purchase amount (U.S. dollars), $\log_{10}$ number of weekly purchases, and "weekly heroin investment" (product score of the latter three measures; Greenwald et al., manuscript under review). For the subset of 46 participants who qualified for the laboratory studies and were stabilized on buprenorphine 8 mg/day for two outpatient weeks prior to inpatient admission, we computed Spearman correlations between motivations and whether the subject initiated opioid abstinence (yes or no) as defined by at least one opioid-free urine specimen (out of six possible).

Finally, we conducted a principal component analysis, and computed Pearson correlations of the derived factor scores with other behavioral measures of interest. All results were considered significant using two-tailed tests at $p < .05$.

3. Results

3.1. Sample demographics

Research motivation ranking data were available for 235 participants (Sex: 57 female and 178 male; Race: 136 African American, 86 Caucasian, and 13 Other). Overall, mean [M] + 1 standard deviation [SD] participant age was 44.3 + 8.3 years, educational level was 12.3 +

1.5 years, Shipley IQ score was $103.2 + 11.5$, and duration of heroin use was $21.6 + 11.7$ years.

3.2. Ranking of research motivations

The highest mean motivation to participate was to reduce/stop heroin use, followed by the opportunity to earn money, needing a medication to get stabilized/detoxify, curiosity why s/he can't stop using heroin, curious about buprenorphine, can't afford treatment right now, like the idea of a two-week inpatient stay, dislike methadone, get a free health screen, proximity to research program, and know someone who participated. Mean + 1 SD ranks are presented in the left column of Table 1.

The most frequent top-ranked choices were reducing/stopping heroin use ($n = 90$ [38.2%]), earning money ($n = 59$ [25.1%]), curiosity why s/he can't stop using heroin ($n = 55$ [23.4%]), needing medication to get stable/detoxify ($n = 16$ [6.8%]), and all other reasons ($n = 15$ [6.4%]). The most frequent top two-ranked motivations (regardless of order within the pair) were reducing/stopping heroin use and needing medication to stabilize/detoxify ($n = 48$), reducing/stopping heroin use and curiosity why s/he can't stop using heroin ($n = 36$), reducing/stopping and earning money ($n = 34$), earning money and curious why s/he can't stop using heroin ($n = 22$), earning money and needing medication to stabilize/detoxify ($n = 13$), needing medication to stabilize/detoxify and curiosity why s/he can't stop using heroin ($n = 6$), and all other combinations ($n = 76$).

3.3. Inter-relationships between motivations

Table 1 lists all significant Spearman rank correlations among the motivations for participation. The two highest correlations were that motivation to earn money was inversely related to interest in reducing/stopping heroin use, and that motivation to stabilize/detoxify was inversely related to the individual's curiosity about his/her inability to stop using heroin. Higher motivation to earn money was related to: less interest in needing medication to stabilize/detoxify, less curiosity about why subjects could not stop heroin use, less concern about being unable to afford treatment and less dislike of methadone. Also, there were positive correlations between several measures of potential treatment intent including reducing/stopping heroin use, needing a medication to stabilize/detoxify, and inability to afford treatment. Higher curiosity about buprenorphine as a motivation was related to less motivation based on inability to afford treatment, less need for medication to stabilize/detoxify, less motivation to reduce/stop heroin use, less motivation for a free health screen, and less motivation for an inpatient stay.

3.4. Inter-relationships between motivations, demographic factors, buprenorphine marketing duration, and questionnaire trait measures

Sex, age, educational level, and duration of heroin use were not significantly associated with any of the motivations. Race was significantly related to one motivation: Whites reported the highest curiosity about buprenorphine, followed by African Americans and other racial groups, $M + 1$ SD rank [percentage ranking their curiosity about buprenorphine among their top two motives] = $6.9 + 2.5$ [18.6%], $6.1 + 2.6$ [11.0%], and $5.9 + 2.9$ [6.1%], respectively, $F(2,234) = 3.14$, $p < .05$.

A pattern of significant correlations was observed for three participant motives (see Table 2 columns). First, greater need for medication to stabilize/detoxify was related to longer time since buprenorphine marketing, lower present time orientation (Hedonism and Fatalism) and higher future orientation scores on the Stanford Time Perception Inventory. Second, increased curiosity about buprenorphine was associated with higher impulsiveness scores on the Impulsive Relapse Questionnaire (total score and the Automaticity and Speed subscales).

Third, increased desire for free health screening was associated with lower present time orientation scores (Stanford Time Perception Inventory Hedonism and Fatalism).

Longer time since buprenorphine marketing (as well as a longer period of conducting buprenorphine research at our site) was associated with increased participant motivation for medication to stabilize/detoxify and knowing someone who had participated at our research site. In contrast, curiosity about buprenorphine as a reason for participating did not significantly correlate with time since buprenorphine marketing.

3.5. Inter-relationships between *motivations* and heroin use

As shown in Table 3, participants' increased curiosity about buprenorphine was related to a greater time/money "investment" in their current pattern of purchasing heroin: longer purchase times (i.e., traveling farther to dealer) and increased purchase amount, offset by fewer weekly purchases (efficiency). Increased motivation to earn money was associated with shorter heroin purchase time (proximity to dealer). Some other motivations (e.g., desire for money, preference for an inpatient stay, and proximity to the program) were also related to heroin acquisitive behavior.

Fifty-six participants completed participation motivation ratings and qualified for the laboratory studies, but only 46 participants completed outpatient buprenorphine induction. Of the 46, higher motivation to reduce/stop heroin use was unexpectedly associated with less likelihood of achieving any opioid abstinence during buprenorphine induction. Qualifying for vs. exclusion from the laboratory research was not significantly related to any motivation, but rates of qualifying were significantly higher for whites than African Americans, 51.7% vs. 33.7%, $\chi^2 = 5.95$, $p < .02$. Those who qualified reported a shorter duration of lifetime heroin use (18.3 vs. 22.5 years, $F[1,232] = 5.47$, $p < .03$), and spending a higher proportion of income on shelter (8.5% vs. 3.3%, $F[1,233] = 16.96$, $p < .001$).

3.6. Inter-relationships between *motivations* and income and expenditures

Higher past 30-day $\log_{10}$ total income was associated with higher motivation based on reducing/stopping heroin use ($r = 0.137$) and less concern about proximity to the research program ($r = -0.147$). Spending a higher proportion of past-month income on shelter was associated with greater preference for an inpatient stay ($r = 0.184$), and with less motivation based on program proximity ($r = -0.132$). Motivation due to money earning potential was not related to past-month income or expenditures.

3.7. Motivational patterns

Participants' primary motivation and top-two motivations (see frequency distributions above) were not significantly related to demographics, heroin use, or trait measures. Based on inter-correlations (Table 1), we reduced the dimensionality of these varied motivations using principal component analysis (PCA). We excluded the two lowest-ranked motivations in the sample (proximity to the program and knowing someone else who had participated) because these motivations did not explain significant variance. We conducted PCA with the remaining 9 motivations and limited the empirical solution to two components using Varimax rotation. The resulting factor scores for each participant were saved for further analyses, reported next.

The following motivations significantly loaded on Factor 1: more motivated by reducing/stopping heroin use (0.720), more motivated by needing a medication to stabilize/detoxify (0.645), more motivated by an inability to afford treatment (0.584), less motivated by earning money (-0.460), less motivated by an inpatient stay (-0.417), less motivated by free

health screening (−0.351), and less curious why s/he could not stop using heroin (−0.292). We interpret higher scores on this factor as reflecting greater treatment motivation.

The following motivations significantly loaded on Factor 2: Less dislike of methadone (−0.626), more motivated by prospect of an inpatient stay (0.505), less curious why s/he could not quit heroin use (−0.484), more motivated by earning money (0.476), less curious about buprenorphine (−0.452), and more motivated by needing a medication to stabilize/detoxify (0.313). We interpret higher scores on this factor as reflecting greater acceptance of *status quo* (low resistance to methadone, inpatient and detoxification, with relatively low curiosity about exploring quitting or buprenorphine)).

Participants' Factor 1 scores did not significantly correlate with any measure except Shipley IQ score ($r = -0.150$, $p < .03$). In contrast (see Table 4), higher Factor 2 scores – “*status quo* acceptance” – correlated with higher Present Fatalism scores (Stanford Time Perception Inventory) and a pattern of more habitual investment in one's heroin purchasing (i.e., more frequent weekly purchases, shorter purchase times, and lower unit purchase amounts).

4. Discussion

This study aimed to determine heroin-dependent individuals' motivational priorities to participate in non-therapeutic buprenorphine research. Some prior work has explored altruistic versus personal motivations for research participation among drug users (Fry and Dwyer, 2001; Slomka et al., 2007). However, a more detailed examination of personal motivations has not yet been conducted and no clinical pharmacology study has focused on buprenorphine-related motivation. Extant studies have focused mostly on motivations of medical patients volunteering for clinical trials, rather than drug abusers. Furthermore, the data from these studies offer a mixed picture regarding participant motivation, particularly in terms of separating financial gain from other personal or altruistic benefits. Thus, the present study fills a gap in our knowledge about the inclinations of out-of-treatment drug abusers to be attracted to research not simply because it offers compensation, but also the prospect of experiencing potential beneficial effects of a novel medication (at the time this study was conducted).

The first significant finding of our study is that economic gain is an important but not necessarily primary benefit that motivates heroin users. Despite clear and repeated information in the study advertisements, telephone screen, and consent form/discussion that volunteers were applying for a non-therapeutic study, these heroin dependent individuals most frequently described their primary motivation as stopping/reducing heroin use. Participants were also repeatedly instructed that they could be referred to a clinic if at any time they desired treatment, but no participants did. Thus, despite affording them opportunities to disengage from research and pursue treatment, participants' overt behavior was partly discrepant from their verbal behavior. This dissociation could reflect a few possibilities: Participants may exhibit demand characteristics (i.e., self-reporting quasi-therapeutic intent to please the experimenter); they could be ambivalent about their current motivation; or – despite instructions to rate their current motivation – their intent could have reflected a desire to stop/reduce heroin use in the future rather than immediately. This latter interpretation (reminiscent of delay discounting) is consistent with our finding that higher Present Orientation (Hedonistic/ Fatalistic scale scores on the Stanford Time Perception Inventory) were negatively related, whereas higher Future Orientation was positively related, to wanting to take a medication to stabilize/detoxify from heroin. Thus, because we created a context in which participants could readily obtain treatment referral yet did not, it appears that participants' reported motivation to stop/reduce heroin use without acting on that expression is likely to be endogenous, and is unlikely to reflect coercive influence of the

research process or threaten the participant's autonomy. In fact, being able to identify participants with a future orientation who are interested in receiving a medication provides an opportunity for researchers to track participant's postexperimental outcomes. Furthermore, if research involvement were to result in the participant altering their motivation in favor of seeking treatment, this would be an additional personal benefit to them.

Earning money was participants' second most frequent primary motivation, followed by curiosity about why they could not stop using heroin. Therefore, our results echo prior studies mentioned above that identified the non-exclusive importance of money among other potential factors that were assessed (Fry and Dwyer, 2001; Stunkel and Grady, 2011). Previous research has indicated that participants from lower socioeconomic strata view study payment as a source of income (Slomka et al., 2007). The present results indicate that participants with lower income ranked financial gain as a more important research motive than those with higher income. In contrast, participants with higher income were more motivated by the prospect of reducing/stopping heroin use. Also, we noted an economic tradeoff effect: Those who spent a greater percentage of their income on shelter reported higher motivation due to the free inpatient stay required for the study. Thus, heroin users may view research participation as part of an "informal economy" (Slomka et al., 2007), in which study compensation and living arrangements can help to maintain their lifestyle. We believe these findings do not pose an ethical problem for conducting this type of research with substance abusers. Institutional Review Boards dictate the need to standardize research compensation, and participants' income levels are outside the experimenter's control. Economic principles dictate that individuals will consume commodities (in this case, participate in scientific research) based on cost/benefit considerations. In this regard, the participant is acting as a rational consumer, who is entitled to engage in transactions that afford access to economic substitutes that meet his/her needs.

Surprisingly, we found that higher curiosity about buprenorphine was related to *less* emphasis on treatment-oriented reasons for participation (less ability to afford treatment, less need for medication to stabilize/detoxify, less motivation to reduce/stop heroin use, less motivation for a free health screen, and less motivation for inpatient stay). Buprenorphine-curious individuals also reported more highly "invested" heroin purchasing habits (longer purchase times, offset by larger episodic purchase amounts), suggesting more severe addiction. These relationships could mean that curiosity about buprenorphine reflects novelty seeking – either without adequate knowledge of, or without commitment to, benefits that buprenorphine might provide. This interpretation is consistent with the positive correlations we found between higher buprenorphine curiosity and higher impulsivity on subscales of the Impulsive Relapse Questionnaire. A related finding from a treatment study in our clinic is that heroin-dependent, cocaine-abusing individuals scoring high on Novelty Seeking (Tridimensional Personality Questionnaire; Cloninger et al., 1991) were retained at significantly higher rates than low novelty seekers early during treatment with buprenorphine and contingency management, however, they were significantly more likely to drop out later (Helmus et al., 2001). Thus, in future research of this type, it would be useful to distinguish the motivational patterns of higher vs. lower novelty-seeking participants.

Higher motivation to reduce/stop heroin use was unexpectedly associated with less likelihood of achieving any opioid abstinence (i.e., one opioid-free urine sample) during the outpatient buprenorphine induction period. By definition, the participants who qualified for the laboratory research and received buprenorphine were generally healthier (having passed the medical and psychiatric screening), and could therefore differ in other ways from the remaining participants. However, there were no significant differences in research

motivations between study qualifiers and non-qualifiers. One possible explanation for this unexpected finding, which was not assessed here, is that study qualifiers may have had high expectations regarding buprenorphine's efficacy (e.g., based on peer or internet discussion) that exceeded their ability to initiate opioid abstinence during medication induction. Participants who qualified reported shorter lifetime duration of heroin use (also related to being younger); thus, study qualifiers may have been less committed to behavior change than non-qualifiers.

Although being motivated by knowing someone who had participated at our research site was among the least important motivations overall, we found that the longer buprenorphine had been marketed (and had been researched in our laboratory) from years 2004 – 2008, the more participants were motivated by an affiliated participant in our laboratory research, or wanting a medication to stabilize/detoxify in these studies. To the extent that local heroin abusers often know one another and some participated in these studies, and then communicated by word-of-mouth (which is a major referral source for our research program), it is likely that this time-related increase in participant motivation due to knowing someone has to do with peer education and diffusion (Davey, 2007). Similarly, increased appeal of buprenorphine during this period may reflect its diffusion via community-based opioid treatment providers (Ducharme et al., 2007; Rieckmann et al., 2011). Few previous research studies with substance abusers have examined such trends; although this outcome is not surprising, it is useful to have empirical confirmation of this trend. Such knowledge may help researchers plan for recruiting and maximizing rates of participation in future substance abuse studies of novel medications.

Finally, principal component analysis of motivation rankings revealed two higher-order dimensions of participant research motivation. High scores on the first factor seem to reflect higher treatment motivation (i.e., more motivated by reducing/stopping heroin use, needing a medication to stabilize/detoxify, and inability to afford treatment, while less motivated by earning money). High scores on this second factor seem to reflect participants' acceptance of the *status quo* (i.e., lack of curiosity about novel, alternative treatments relative to traditional methods for opioid dependence treatment). These two dimensions may parsimoniously characterize the motivational set of heroin addicts applying for non-therapeutic research, and further research should be conducted to investigate these aspects. This outcome has theoretical utility, in that past studies have explored multiple reasons for research participation, but the independence of these different motivations is not well understood. These data may help generate items for developing novel questionnaires to assess research motives in future studies.

It is important to note that this investigation is limited to heroin-dependent individuals who applied for buprenorphine research during the initial few years after it was introduced in the U.S. market. The results are also limited based on the motivations that were presented to participants, i.e., other motivations may exist that we overlooked such as altruistic motives. Therefore, it is not clear whether our results generalize to the entire population of heroin abusers, or apply only to the subset interested in buprenorphine. Nonetheless, lessons from this experience could be germane to clinical research with other new medications for the treatment of substance use disorders as they are introduced in Phase I and II trials. The necessity of an inpatient stay may have further limited the pool of participants (e.g., fewer females due to child or family care responsibilities) and the generality of our findings. Notably, we did not observe significant sex differences in our analyses.

We conclude from our results that heroin abusers' motivation to participate in non-therapeutic buprenorphine research is multifactorial and is correlated with income, drug use and personality traits. No single motive uniformly inspired research participation; instead,

patterns of motivations emerged across individuals. This research addresses important ethical issues, particularly with regard to participant autonomy, that have generally not received systematic empirical attention in prior studies (either with medical patients or substance users). The present findings suggest that out-of-treatment heroin abusers are attracted to this non-therapeutic research (which was made clear at multiple points in the screening process) by a mixture of perceived personal benefits that include both economic and quasi-therapeutic motives. Yet, participants did not avail themselves of the opportunity to obtain treatment referral, and it seems unlikely that the research environment was coercive. Rather, it appears that individuals bring to the research setting various traits (e.g., different levels of impulsivity, orientation toward the future such as improving their health), economic characteristics (e.g., income and expenditures), and drug use patterns, and these different phenotypes may relate to their pattern of motivation. These issues do not appear to compromise either the participant's autonomy or the ethics of the research. Nonetheless, given the paucity of programmatic work in this field (particularly with substance abusers) these are preliminary conclusions. Further research is warranted to improve our knowledge of these motivations, which could be used to facilitate recruitment of substance-using individuals in urban communities for such research, educate institutional review boards and, under appropriate circumstances, to provide a bridge for interested individuals between non-therapeutic and therapeutic environments.

References

- Ackerman TF. An ethical framework for the practice of paying research subjects. *IRB*. 1989; 11:1–4. [PubMed: 11650243]
- Adinoff B, Rilling LM, Williams MJ, Schreffler E, Schepis TS, Rosvall T, Rao U. Impulsivity, neural deficits, and the addictions: the "oops" factor in relapse. *J. Addict. Dis.* 2007; 26(Suppl. 1):25–39. [PubMed: 19283972]
- Andresen EL, Wilson KA, Castillo A, Koopman C. Patient motivation for participating in clinical trials for depression: validation of the motivation for clinical trials inventory-depression. *Int. Clin. Psychopharmacol.* 2010; 25:7–16. [PubMed: 19901843]
- Bayoumi AM, Hwang SW. Methodological, practical, and ethical challenges to inner-city health research. *J. Urban Health.* 2002; 79:S35–S42. [PubMed: 12473697]
- Castillo AG, Jandorf L, Thelemague LD, King S, Duhamel K. Reported benefits of participation in a research study. *J. Community Health.* 2011 Epub before print.
- Chantler TEA, Lees A, Moxon ER, Mant D, Pollard AJ, Fitzpatrick R. The role familiarity with science and medicine plays in parent's decision making about enrolling a child in vaccine research. *Qual. Health Res.* 2007; 17:311–322. [PubMed: 17301340]
- Cloninger CR, Przybeck TR, Svrakic DM. The Tridimensional Personality Questionnaire: US normative data. *Psychol. Rep.* 1991; 69:1047–1057. [PubMed: 1784653]
- Davey M, Latkin C, Hua W, Tobin K, Strathdee S. Individual and social network factors that predict entry to drug treatment. *Am. J. Addict.* 2007; 16:38–45. [PubMed: 17364420]
- Dixon-Woods M, Tarrant C. Why do people cooperate with medical research? Findings from three studies. *Soc. Sci. Med.* 2009; 68:2215–2222. [PubMed: 19394741]
- Ducharme LJ, Knudsen HK, Roman PM, Johnson JA. Innovative adoption in substance abuse treatment: exposure, trialability, and the Clinical Trials Network. *J. Subst. Abuse Treat.* 2007; 32:321–329. [PubMed: 17481455]
- Emanuel EJ. Ending concerns about undue inducement. *J. Law Med. Ethics.* 2004; 32:100–105. [PubMed: 15152431]
- Erlen JA, Sauder RJ, Mellors MP. Incentives in research: ethical issues. *Orthop. Nurs.* 1999; 18:84–87. [PubMed: 10410052]
- Farre M, Lamas X, Cami J. Sensation seeking amongst healthy volunteers participating in phase I clinical trials. *Br. J. Clin. Pharmacol.* 1995; 39:405–409. [PubMed: 7640147]

- Fry C, Dwyer R. For love or money? An exploratory study of why injecting drug users participate in research. *Addiction*. 2001; 96:1319–1325. [PubMed: 11672496]
- Greenwald MK. Opioid abstinence reinforcement delays heroin lapse during buprenorphine dose tapering. *J. Appl. Behav. Anal.* 2008; 41:603–607. [PubMed: 19192863]
- Greenwald MK. Effects of experimental unemployment, employment and punishment analogs on opioid seeking and consumption in heroin-dependent volunteers. *Drug Alcohol Depend.* 2010; 111:64–73. [PubMed: 20537815]
- Greenwald MK, Hursh SR. Behavioral economic analysis of opioid consumption in heroin-dependent individuals: effects of unit price and pre-session drug supply. *Drug Alcohol Depend.* 2006; 85:35–48. [PubMed: 16616994]
- Greenwald MK, Steinmiller CL. Behavioral economic analysis of opioid consumption in heroin-dependent individuals: effects of alternative reinforcer magnitude and post-session drug supply. *Drug Alcohol Depend.* 2009; 104:84–93. [PubMed: 19464125]
- Greenwald MK, Steinmiller CL, Iliwarska E, Lundahl LH, Burmeister M. manuscript under review. BDNF Val⁶⁶Met genotype is associated with drug-seeking phenotypes in heroin-dependent individuals.
- Harth SC, Thong YH. Sociodemographic and motivational characteristics of parents who volunteers their children for clinical research: a controlled study. *BMJ*. 1990; 300:1372–1375. [PubMed: 2372582]
- Helmus TC, Downey KK, Arfken CL, Henderson MJ, Schuster CR. Novelty seeking as a predictor of treatment retention for heroin dependent cocaine users. *Drug Alcohol Depend.* 2001; 61:287–295. [PubMed: 11164693]
- Jenkins V, Fallowfield L. Reasons for accepting or declining to participate in randomized clinical trials for cancer therapy. *Br. J. Cancer*. 2000; 82:1783–1788. [PubMed: 10839291]
- Locock L, Smith L. Personal benefit or benefiting others? Deciding whether to take part in clinical trials. *Clin. Trials*. 2011; 8:85–93. [PubMed: 21163854]
- Krebaum, SR.; Jackley, PK.; Adinoff, B. The Impulsive Relapse Questionnaire: Development and Validation (version date: 03/11/02); Scientific Meeting of the Research Society on Alcoholism and the 11th Congress of the International Society for Biomedical Research on Alcoholism; 2002.
- McCann SK, Campbell MK, Entwistle V. Reasons for participating in randomized controlled trials: conditional altruism and considerations for self. *Trials*. 2010; 11:31. [PubMed: 20307273]
- Petry NM, Bickel WK, Arnett M. Shortened time horizons and insensitivity to future consequences in heroin addicts. *Addiction*. 1998; 93:729–738. [PubMed: 9692271]
- Rieckmann TR, Kovas AE, McFarland BH, Abraham AJ. A multi-level analysis of counselor attitudes toward the use of buprenorphine in substance abuse treatment. *J. Subst. Abuse Treat.* 2011 Epub ahead of print.
- Roddy JK, Greenwald MK. An economic analysis of income and expenditures in heroin-using research volunteers. *Subst. Use Misuse*. 2009; 44:1503–1518. [PubMed: 19938929]
- Roddy JK, Steinmiller CL, Greenwald MK. Heroin purchasing is income- and price-sensitive. *Psychol. Addict. Behav.* 2011; 25:358–364. [PubMed: 21443296]
- Ross MW, Jeffords K. Reasons for entry into and understanding of HIV/AIDS clinical trials: a preliminary study. *AIDS Care*. 1994; 6:77–82. [PubMed: 8186281]
- Singer E, Van-Hoewyk J, Maher MP. Does payment of incentives create expectation effects? *Public Opin. Q.* 1998; 62:152–164.
- Slomka J, McCurdy S, Ratliff EA, Timpson S, Williams ML. Perceptions of financial payment for research participation among African-American drug users in HIV studies. *J. Gen. Int. Med.* 2007; 22:1403–1409.
- Stunkel L, Grady C. More than the money: a review of the literature examining healthy volunteer motivations. *Contemp. Clin. Trials*. 2011; 32:342–352. [PubMed: 21146635]
- Tait A, Voepel-Lewis T, Malviya S. Participation of children in clinical research: factors that influence a parent's decision to consent. *Anesthesiology*. 2003; 99:819–825. [PubMed: 14508312]
- Timmermans S, McKay T. Clinical trials as treatment option: bioethics and health care disparities in substance dependency. *Soc. Sci. Med.* 2009; 69:1784–1790. [PubMed: 19819059]

- Wasan AD, Taubenberger SP, Robinson WM. Reasons for participation in pain research: can they indicate a lack of informed consent? *Pain Med.* 2009; 10:111–119. [PubMed: 18657219]
- Wendler D, Krohmal B, Emanuel EJ, Grady C. ESPIRIT Group. Why patients continue to participate in clinical research. *Arch. Int. Med.* 2008; 168:1294–1299. [PubMed: 18574086]
- Wilkinson M, Moore A. Inducement in research. *Bioethics.* 1997; 11:373–389. [PubMed: 11655117]
- Zachary, RA. Shipley Institute of Living Scale: Revised Manual. Los Angeles, CA: Western Psychological Services; 1991.
- Zimbardo, PG. Stanford Time Perception Inventory Manual. Stanford, CA: Stanford University; 1992.

Table 1
Significant Spearman Correlations Among Research Motivation Rankings ($N = 235$)

Research Motivation (Mean Rank + 1 SD)	Reduce/stop heroin use	Earn money	Medication to stabilize/ detoxify	Curious can't stop heroin	Bupre- norphine	Can't afford treatment	Like inpatient stay	Dislike methadone	Free health screen	Proximity to program
Reduce heroin use (9.16 + 2.29)										
Earn money (8.02 + 2.79)	-0.391									
Need medication (7.92 + 2.28)	0.227	-0.211								
Curious can't stop (7.76 + 2.83)	-0.228	-0.222	-0.360							
Buprenorphine (6.37 + 2.61)	-0.134		-0.189							
Can't afford treatment (5.61 + 2.40)	0.231	-0.196	0.156	-0.197	-0.204					
Like inpatient stay (5.20 + 2.68)	-0.135				-0.136	-0.194				
Dislike methadone (5.18 + 2.57)		-0.129	-0.136			-0.138	-0.256			
Free health screen (4.76 + 2.24)	-0.164		-0.137		-0.149					
Proximity to program (3.42 + 2.11)	-0.170					-0.151			-0.209	
Know someone (2.60 + 2.08)				-0.169			-0.130		-0.160	

Bold indicates $p < .001$; non-bold indicates $p < .05$.

Table 2
Significant Spearman Correlations Between Research Motivation Rankings, Demographics and Questionnaire Measures

	Reduce/stop heroin use	Earn money	Medication to stabilize/ detoxify	Bupre- norphine	Can't afford treatment	Dislike methadone	Free health screen	Know Someone
# Years since buprenorphine marketed (235)			0.145					0.134
Shipley IQ (222)	-0.160	0.204						
STPI Present Hedonism (102)			-0.237				-0.313	
STPI Present Fatalism (102)			-0.242				-0.264	
STPI Future (102)			0.236					
IRQ Total (101)				0.232				
IRQ Automaticity (101)				0.218	-0.304			
IRQ Speed (101)				0.314				
IRQ Control Deficit (101)						-0.218	-0.214	

Bold indicates $p < .001$; non-bold indicates $p < .05$. Parenthesized numbers (left column) indicate sample size available for this correlation. STPI = Stanford Time Perception Inventory and IRQ = Impulsive Relapse Questionnaire; see text for description.

Table 3
Significant Spearman Correlations Between Research Motivation Rankings and Heroin Use Measures

	Reduce/stop heroin use	Earn money	Buprenorphine	Like inpatient stay	Proximity to program
Log ₁₀ Heroin purchase time (234)		-0.183	0.186		-0.179
Log ₁₀ Heroin purchase amount (234)			0.227	-0.130	
Log ₁₀ Heroin weekly purchases (234)			-0.185		
Log ₁₀ "Heroin investment" (232)			0.178	-0.143	-0.221
Any opioid abstinence during buprenorphine induction (46)	-0.321				

Bold indicates $p < .001$; non-bold indicates $p < .05$. Parenthesized numbers (left column) indicate sample size available for this correlation.

Table 4

Significant Pearson Correlations of Research Motivation Factor 2 Scores with Other Measures

Measure	N	r
STPI Present Fatalism	102	−0.239
Log ₁₀ Heroin Purchase Time	234	−0.177
Log ₁₀ Heroin Purchase Amount	234	−0.184
Log ₁₀ Heroin Weekly Purchases	234	0.136
Log ₁₀ Heroin “Investment”	234	−0.170

See text for description of Factor 2 loadings and interpretation. STPI = Stanford Time Perception Inventory (see text).