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Review

The need for evidence-based research ethics: A review of the substance abuse literature

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Abstract

Participants in substance abuse research may be vulnerable for multiple reasons. International research ethics guidelines and policy statements require that researchers provide extra protections when conducting research with vulnerable subjects, but it is uncertain which measures best protect vulnerable individuals. Concerns about vulnerability have been translated into only the vaguest regulatory requirements, and very little empirical data exist to guide researchers and ethics review committee members who want to protect participants. This article reviews two bodies of substance abuse research ethics literature. First, "normative" articles, that is, articles that discuss ethical issues that may arise in substance abuse research, are discussed. The resulting taxonomy of ethical issues then guides a review of empirical studies on issues like the informed consent process and the use of financial incentives in substance abuse research. While the ethical issues in substance abuse research are numerous and well-documented, the evidentiary base for addressing these issues is inadequate. If any one major theme emerged from the existing studies, it is that many well-intentioned, protectionist concerns – about recruitment incentives, consent comprehension, and drug administration studies – are not supported by empirical data. While these findings are at best tentative, they suggest how research on research ethics might ultimately benefit participants.

Keywords: Research ethics; Substance abuse; IRB

Contents

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1. Introduction

The current regulatory system for research protections (45CFR46) identifies several populations as uniquely vulnerable and affords special protections to participants who enroll in studies that target these populations. Among the specially protected groups are pregnant women, fetuses, and neonates (subpart B), prisoners (subpart C), and children (subpart D). No explicit special protections exist for individuals with substance abuse disorders. However, the U.S. National Bioethics Advisory Commission (NBAC, 2001) encourages researchers to consider six kinds of vulnerability in the process of determining appropriate research protections: cognitive or communicative vulnerability; institutional vulnerability (i.e. being subject to the formal authority of another); deferential vulnerability (i.e. being informally subject to the authority of another); medical vulnerability; economic vulnerability; social vulnerability. Thus, individuals with substance abuse problems can be considered vulnerable insofar as their addictions contribute to or accompany economic hardship, comorbid psychiatric or cognitive disorders, social stigmatization, and incarceration or other involvement in the legal system (Gorelick et al., 1999; McGovern, 1998; NBAC, 1998).

Concerns about research participant vulnerability have been translated into only vague regulatory requirements (DuBois, 2005). For example, in the U.S., the so-called "Common Rule", which guides the institutional review board (IRB) review process, states:

> When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, [IRBs should ensure that] additional safeguards have been included in the study to protect the rights and welfare of these subjects. (46.111(b))

There are some advantages to vague regulations: they leave room for researchers and IRBs to adopt those protections that take into account the specific needs of a participant group and the specific resources that a research environment presents. Nevertheless, vague requirements for "additional safeguards" for vulnerable participants also place a heavy burden on researchers and IRB members who may want to protect participants (and minimize institutional liability) but may not know how best to accomplish these goals.

One way to determine IRB best practices is through empirical research (Sieber, 2004; Stanley et al., 1987). Just as evidence-based medicine may improve patient outcomes, evidence-based research ethics may enhance the ethical conduct of research (Newman et al., 2001; Roberts, 2000). Through a comprehensive literature review, this article seeks to determine the extent to which substance abuse research has a body of evidence upon which to base ethical best practices. Relevant empirical studies will be reviewed to determine what existing data can teach us and what evidentiary gaps exist.

2. Method

2.1. Literature review on ethical issues in substance abuse research

Broad subject heading terms were used in multiple combinations to search the Medline (1966 through September 2005), PsycINFO (1967 through September 2005), Sociological Abstracts (1965 through September 2005), and Kennedy Center ETHX (1976 through September 2005) databases to find (1) theoretical articles on ethical issues in substance abuse research and (2) empirical studies that explore variables related to ethical issues in research with participants with substance abuse problems. Due to differences in indexing terminology, different terms were used in different databases in an effort to maximize the number of articles retrieved. Only articles available in English were included; letters, commentaries in response to other articles, news articles, and journal issue introductions were also excluded. In the Medline database, in addition to general subject headings such as "Research Ethics" and "Human Experimentation [Ethics]", additional searches were conducted using the terms "privacy" and "confidentiality", "informed consent", and "decision-making capacity", three primary topics in research ethics that may not have been subsumed under general headings. Abstracts of retrieved articles were reviewed in order to determine which articles were truly relevant. Articles were included if ethical issues in research with participants with substance abuse problems are a primary focus. Many articles were excluded at this stage because they were not relevant to human subjects research, substance use/abuse research, and/or research ethics. Terms used for each database search, the total number of articles retrieved (excluding duplicates), and the final number of articles included in the literature review are listed below in Table 1.

In addition to the initial database searches, reference lists of retrieved articles were reviewed for any relevant articles that might have otherwise been missed ("snowballing technique"). An additional five articles were recommended to the authors by colleagues (including one reviewer). These methods and articles are also listed in Table 1. The fact that multiple searches using similar search terms in several databases retrieved so many different articles that had substance abuse research ethics as a primary focus suggests that indexing methods are inconsistent. This may present a problem for those attempting to determine best practices.

Theoretical articles were reviewed to develop a comprehensive list of key ethical issues pertaining to substance abuse research. From this list, related issues are organized according to the three Belmont principles, which traditionally govern research ethics: respect for persons, beneficence, and justice (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979).

Under each heading, ethical issues specific to conducting research with individuals who may abuse drugs or alcohol are discussed. Relevant empirical studies are reviewed and their potential applications to ethical research practices outlined. Gaps in knowledge and areas of dispute or uncertainty that may be clarified by empirical data are identified. Areas for future empirical research are suggested.

3. Results

3.1. Respect for persons: informed consent, decision-making capacity, and voluntariness

For informed consent to be valid, comprehension and voluntariness are required (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979; Penslar and Porter, 1993). Special ethical concerns related to comprehension and decision-making capacity arise in substance abuse research due to the nature of addiction as well as the potential for participants to be intoxicated or experiencing acute drug withdrawal during the informed consent process (College on Problems of Drug Dependence, 1995; Kleber, 1989; Sugarman,

Table 1
Substance abuse research ethics search history

Database	Search terms	Retrieved[a]/included	Articles
Medline	Substance-related disorders OR substance abuse, intravenous OR alcoholism OR heroin dependence OR heroin OR addictive behavior OR substance abuse OR addiction OR addict OR addicts OR injection drug users[a] AND research ethics OR human experimentation [ethics]	36/5	Charland (2002), Hall et al. (2004, 2003), Hofman (2004) and Marshall et al. (2003)
Medline	[a]Same as above AND confidentiality OR privacy AND human experimentation	26/2	Cohen (2002) and McGovern (1998)
Medline	[a]Same as above AND comprehension OR decision making capacity OR mental competency OR decision making AND human experimentation	8/4	Appelbaum (1995), Brandon and Lisman (2000), Goldman (2000) and Sugarman (1994)
Medline	[a]Same as above AND informed consent AND human experimentation	12/6	College on Problems of Drug Dependence (1995), Cowan (1977), Fureman et al. (1997)[b], Mendelson (1991), Modell et al. (1993)[b] and Tucker and Vuchinich (2000)
PsychInfo	Drug abuse OR drug usage OR substance-related disorders OR alcohol abuse AND experimental subjects OR human subjects research AND experimental ethics OR ethics	9/7	Festinger et al. (2005)[b], Fischman and Johanson (1998), Forman et al. (2002)[b], McCrady and Bux (1999)[b], Ritter et al. (2003), Seddon (2005) and Sinha et al. (1999)[b]
Sociological Abstracts	Addict OR alcohol OR substance abuse AND research ethics	13/4	Allen (2002), Drobes and Anton (2000)[b], Dolinsky and Babor (1997) and Duval and Salmon (2004)
ETHX (Kennedy Center)	Alcoholism OR addiction AND scientific research ethics OR truth-telling OR informed consent in human experimentation OR privacy in health care OR confidentiality in health care	183/6	Brody and Waldron (2000), Buchanan et al. (2002), Fitzgerald and Hamilton (1997), Fry and Dwyer (2001)[b], Gorelick et al. (1999) and Harrison et al. (1995)[b]
Snowballing		15	Faillace et al. (1972)[b], Fitzgerald and Hamilton (1996), Kaufman et al. (2000)[b], Kleber (1989), Koocher (1991), Kranzler et al. (1990)[b], Loberg et al. (1988)[b], MacQueen et al. (1999)[b], National Advisory Council on Alcohol Abuse and Alcoholism (2005), National Advisory Council on Drug Abuse (2000), Ostini et al. (1993), Power (1989), Siegal et al. (1993), Wood and Sher (2000) and Wright et al. (1998)
Recommended by colleagues		5	Elman et al. (2001)[b], Reynolds et al. (2000)[b], Scott and White (2005)[b], Carroll et al. (1999)[b] and Gorelick et al. (1998)[b]
Total		54	

[a] Duplicates have been excluded.
[b] Designates an article presenting original empirical research.

1994). The ability of individuals with substance abuse problems to give adequate informed consent to participate in studies that involve the administration of drugs has been questioned, given that addicts are compulsively driven to use drugs and have difficulty abstaining from use (Charland, 2002; Cohen, 2002; College on Problems of Drug Dependence, 1995; Hall et al., 2003, 2004). Substance abuse is also linked with cognitive deficits and well as comorbid psychiatric disorders (e.g. schizophrenia, bipolar disorder) that may limit decision-making capacity (Gorelick et al., 1999).

The true voluntariness of consent to research participation can be questioned in instances where individuals are enrolled involuntarily in treatment programs, are incarcerated, or are faced with the threat of incarceration (Appelbaum, 1995; Duval and Salmon, 2004). Voluntariness is also questionable if research participation is the only available option for treatment (Ostini et al., 1993). The urgent importance of entering any kind of treatment program, as well as the fact that research-based treatment programs are often free or low-cost, may limit full consideration of the special considerations of research-based treatment.

Specific concerns regarding informed consent are raised when substance abuse research is conducted with minors. The capacity of children and adolescents to provide adequate informed consent for different kinds of research is contested (Baylis et al., 1999; Miller et al., 2004); having a substance abuse disorder adds to an already complex problem. Children who are prone to substance abuse also often have other risk factors that increase their vulnerability to research risks, such as cognitive disorders or disturbed parent–child interactions (Allen, 2002; Brody and Waldron, 2000). A minor's participation in any type

of research generally requires parental permission—with the minor's assent when feasible. However, when parental permission is not a reasonable requirement, federal regulations in the U.S. (45CFR46.408) allow IRBs to waive parental permission, thus enabling minors to give consent for themselves, as long as this consent is consistent with federal, state, or local laws (Wagener et al., 2004). Certain state guidelines allow minors to consent independently to substance abuse treatment in order to ensure access to care for adolescents who might otherwise be deterred. Where minors have a right to independently consent to treatment, they also usually have a right to consent to treatment-related research (Brody and Waldron, 2000). Realistically, adolescents rarely seek treatment on their own (Brody and Waldron, 2000). Entrance into treatment programs usually occurs in response to pressure from parents or school or law enforcement officials, which obviously influences an adolescent's decision-making (Brody and Waldron, 2000; Duval and Salmon, 2004). Treatment is often required as a condition of staying out of jail or remaining in school; sometimes judges or schools make direct referrals to research-based treatment programs.

Three studies were identified that examined comprehension of the informed consent process by injection drug users (IDUs) being recruited into HIV vaccine trials. Two of these studies found that IDUs adequately understood the informed consent process and scored as well on tests of comprehension as other non-substance-using participants (Harrison et al., 1995; MacQueen et al., 1999). Another study found that supplementary information such as videotapes or pamphlets improved understanding and knowledge retention (Fureman et al., 1997). More information on these studies is presented in Table 2.

These studies of comprehension have several limitations. First, they only assessed comprehension of informed consent materials at one or two time points directly after intervention. They also did not explore the more complex issue of decision-making capacity and the factors that influence it. Formal measures of decision-making capacity exist, and empirical studies of decision-making capacity have been conducted on individuals with schizophrenia, Alzheimer's disease, and other mental illnesses (Appelbaum, 1997; Carpenter et al., 2000; Hougham et al., 2003). Substance abuse research could benefit from similar studies. Furthermore, the studies of comprehension identified were limited to IDUs enrolling in HIV vaccine trials; none involved drug administration trials, treatment research, or research with minors.

The use of financial incentives to recruit individuals who abuse drugs or alcohol to participate in research raises ethical concerns (Buchanan et al., 2002; Seddon, 2005). These concerns regarding payment of substance abusers are part of a larger debate surrounding the potential undue influence of money in the recruitment of research participants in general (Grady, 2001). Due to the economic vulnerability of many individuals with alcohol and drug problems, it has been argued that some cannot say "no" to money offered by researchers (Charland, 2002; Koocher, 1991). If research involves the administration of addictive substances, care must be taken that trial participation does not provide incentives for people to participate in unhealthy behaviors (or disincentives for reducing or stopping drug use) (Cowan, 1977; Ostini et al., 1993). Some authors have expressed concern that individuals with substance abuse problems may use the money received for research participation to buy illegal drugs and question whether researchers have an ethical responsibility to prevent or minimize the misuse of these payments (College on Problems of Drug Dependence, 1995; Gorelick et al., 1999; Ritter et al., 2003). Payment incentives, as well as the potential for participants to be intoxicated or in a state of withdrawal, also raise concerns about the truthfulness and accuracy of self-reported information (Wright et al., 1998).

Only three empirical studies were identified that explored the use of payment incentives for research with substance abusers. Two studies found that payment is effective in recruiting hard-to-reach substance users to participate in research and an important motivating factor in attendance at follow up visits (Festinger et al., 2005; Reynolds et al., 2000); however, there was no evidence that payment is coercive, undermines voluntariness, or increases drug use in the short-term (Festinger et al., 2005). Another study found that payment does not differentially affect participation according to income level or employment status (Reynolds et al., 2000). One study suggests that drug users participate in research (at least in low-risk survey research) not simply for monetary gain but also with the hope of benefiting others (Fry and Dwyer, 2001). More information on these studies is presented in Table 2.

Existing research suggests that participants do not view payments as coercive and that payments are not correlated with increased substance use in the short term; however, this research is limited. It would be useful to examine the views of participants on issues related to payment, such as impact on voluntariness and truth-telling and alternative compensation methods (i.e. as opposed to cash payments). More empirical research could lend support to specific institutional practices and policies—for example, whether to prohibit, mandate, or otherwise regulate payment to research participants. No studies were identified that looked at the effect of drug or alcohol addiction, withdrawal symptoms, or intoxication on participants' voluntariness or truth-telling. Studies exploring issues of voluntariness in research with participants in forced treatment programs or situations in which treatment was only available (or affordable) through research participation are also needed.

3.2. *Beneficence: preventing harm and providing benefits*

3.2.1. Experimental administration of drugs and alcohol. Some types of substance abuse research carry greater than minimal risk without direct benefit to participants. It is difficult to study in a controlled manner the physiological mechanisms and immediate effects of drugs by observing their use in a "natural" environment. Therefore, drugs of abuse (including alcohol) and medications that could potentially be used in the treatment of drug dependence are sometimes administered in a controlled research setting in order to understand basic mechanisms of brain function or to learn more about the physiological causes and consequences of addiction (Charland, 2002; Cowan, 1977; Dolinsky and Babor, 1997; Fischman and Johanson, 1998; Wood

Table 2
Empirical research on issues related to informed consent

Author/year	Population	Study design	Findings
Comprehension of informed consent			
Fureman et al. (1997)	IDUs recruited for enrollment in an HIV vaccine study ($n = 186$)	Evaluation of the impact of a pamphlet and a videotape on knowledge of information from informed consent immediately and after 1 month	Both the pamphlet and the videotape increased knowledge immediately following the informed consent process The videotape increased knowledge retained after 1 month
Harrison et al. (1995)	Individuals screened for enrollment in an HIV vaccine study including IDUs ($n = 119$)	Comparison study of rate of recruitment, proportion eligible, and degree of comprehension of informed consent procedures between IDUs and non-IDUs	High levels of comprehension of the informed consent process were observed in volunteers who were also IDUs
MacQueen et al. (1999)	IDUs recruited for enrollment in an HIV vaccine study ($n = 193$)	Survey to assess comprehension and willingness to participate before and after a group educational session as well as barriers to and motives for participation in an HIV vaccine study	Overall, comprehension levels were high at baseline and improved at follow-up; IDUs comprehended the information needed to make a fully informed decision
Use of payment incentives			
Festinger et al. (2005)	Drug addicts enrolling in treatment research ($n = 350$)	2×3 parametric design; participants randomly assigned to receive different magnitudes of payment incentives in either cash or gift certificates for participating in a 6-month follow-up research study which included urinalysis and assessment of perceptions of having been coerced to participate	Perceptions of coercion were uniformly low across all study conditions There was no significant main effect for the magnitude of payment or the mode of payment on the level of perceived coercion, nor was there an interaction effect Higher payments and cash (as opposed to gift certificate) payments were significantly correlated with increased follow up attendance
Reynolds et al. (2000)	Crack cocaine and IDUs ($n = 1427$)	Correlation study using targeted sampling plan to evaluate the role of incentives in recruitment of research participants	Use of monetary incentives enhanced recruitment of hard to reach populations such as drug users Variables such as level of income, source of income, and current work situation were not associated with recruitment; cash incentives had value for all participants, not just those with low monthly incomes
Fry and Dwyer (2001)	IDUs recruited to participate in a survey on illegal drug use ($n = 154$)	Survey on reasons for participating in research	Reasons reported for research participation include not only economic gain but also altruism, citizenship, and drug user activism

IDU, injection drug user.

and Sher, 2000). Some new drugs are also screened for abuse or addictive potential (sometimes referred to as clinical abuse liability testing) (College on Problems of Drug Dependence, 1995; Mendelson, 1991).

Guidelines for safe and ethical experimental administration have been published by both the National Institute on Drug Abuse's (NIDA) National Advisory Council on Drug Abuse (NACDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) (National Advisory Council on Alcohol Abuse and Alcoholism, 2005; National Advisory Council on Drug Abuse, 2000). However, debate continues over identification of the appropriate participants to recruit for this type of research (Brandon and Lisman, 2000; Fischman and Johanson, 1998; Kleber, 1989), the ability of participants to refuse participation or truly "volunteer" (Charland, 2002; Goldman, 2000; Tucker and Vuchinich, 2000), and the potential addictive and other physiological risks. Using individuals who have a history of substance abuse for clinical abuse liability testing regardless of the substance raises ethical concerns, especially because of the common problem of polydrug abuse.

Uncertainties regarding the physical and addictive risks of participation in administration studies could be elucidated with empirical data. There are no systematic data on immediate negative outcomes or physical risks of the administration of drugs or alcohol reported in the literature (Wood and Sher, 2000). However, several studies followed participants after completion of cocaine and alcohol administration studies to determine the effects of participation on substance use patterns. In two studies involving the administration of cocaine in an experimental setting, no adverse health events were reported (Elman et al., 2001; Kaufman et al., 2000). In one study, reported frequency of cocaine use did not increase as compared to baseline (Kaufman et al., 2000). In another study, neither frequency of cocaine use nor addiction severity increased after participation in the study as compared to a group that did not participate in the administration study (Elman et al., 2001). Unfortunately, sample sizes in both studies were very small. More information on these studies is presented in Table 3.

Six studies collected follow-up data from alcoholics who had participated in alcohol administration research. Two of these

Table 3
Empirical research on administration of substances

Author/year	Population	Study design	Findings
Kaufman et al. (2000)	Occasional, IV-naïve cocaine users who were administered cocaine IV ($n = 25$)	Follow up study to determine whether cocaine use patterns changed following investigational IV cocaine administration	Investigational cocaine exposure did not lead to adverse health events in any subject No subjects reported IV cocaine use or altered frequency of cocaine use after participation
Elman et al. (2001)	Non-treatment seeking cocaine dependent individuals following cocaine infusion in a brain imaging study ($n = 21$); compared with cocaine dependent subjects who did not receive the infusion ($n = 19$)	Follow up study to determine if cocaine use or rating on an addiction severity scale increased after infusion of cocaine in an experimental setting	The infused and non-infused groups did not differ in terms of frequency of cocaine use or addiction severity at 5 and 10 months. Both groups showed significant reductions in frequency of cocaine use
Drobes and Anton (2000)	Non-treatment seeking alcoholics ($n = 25$)	Follow up survey to determine the impact of participation in an alcohol administration study	Subjects reported significant reductions in drinking quantity and frequency; no subjects reported increased drinking following study participation
Sinha et al. (1999)	Non-treatment seeking alcoholics who participated in an alcohol self-administration study ($n = 21$)	Three-month follow up study to determine effects of alcohol administration on subsequent drinking	Participants had significantly reduced total number of drinking days as well as drinks consumed per occasion compared with baseline levels
Modell et al. (1993)	Recently abstinent chronic, severe alcoholics ($n = 16$)	Short-term monitoring of effects of administering small amounts of alcohol	No evidence that experimental administration of alcohol to abstinent alcoholics causes desire for more alcohol, precipitates immediate relapse, or creates any behavioral problems
Kranzler et al. (1990)	Alcoholics in inpatient treatment administered ethanol in a lab-based study ($n = 15$); comparison group not administered ethanol ($n = 21$)	Six-month follow up study to determine the effects of lab-based ethanol administration on disulfiram compliance	There were no immediate adverse effects of ethanol administration Days of disulfiram use (measure of compliance) did not differ at follow up; treatment outcome did not appear to suffer as a consequence of ethanol exposure
Loberg et al. (1988)	Alcoholics hospitalized for treatment who participated in experimental drinking study ($n = 20$); comparison group ($n = 20$)	One-year follow up study to measuring alcohol consumption and social and psychological adjustment	Participating in drinking experiments while hospitalized for treatment did not negatively affect subsequent alcohol consumption or social/psychological adjustment as compared with those who did not participate in the experimental study
Faillace et al. (1972)	Alcoholic patients who received beverage alcohol in progressively reduced amounts for 32 days ($n = 14$); similar group of alcoholics who did not participate in same treatment study ($n = 14$)	Six-month follow up study to compare outcomes on occupational, residential and interpersonal adjustment, abstinence, and global adjustment measures	Alcoholics who are given alcohol in a controlled manner tend not to be adversely affected

IV, intravenous.

studies involved non-treatment-seeking alcoholics (Drobes and Anton, 2000; Sinha et al., 1999), three involved alcoholics in treatment at the time of the administration study (Faillace et al., 1972; Kranzler et al., 1990; Loberg et al., 1988), and one involved recently abstinent alcoholics (Modell et al., 1993). None of the six studies reported any immediate adverse events or increases in the frequency or amount of alcohol consumption in the short-term. No other negative outcomes were reported, including problems with social/psychological adjustment (Loberg et al., 1988) or poor disulfiram adherence (Kranzler et al., 1990). More detailed information regarding these studies is presented in Table 3.

As in the cocaine administration follow-up studies, sample sizes in these alcohol administration follow-up studies were very small, and not all studies used comparison groups. Study data are difficult to compare as each study used different outcome measures and collected data at different time points. Most studies relied on self-reported data; only two used biological markers to corroborate self-reports. All studies used either treatment-seeking or non-treatment-seeking participants exclu-

sively. It would be useful to compare differences in outcomes for treatment-seeking participants and non-treatment-seeking research participants since ethical discussions often suggest that the potential risks differ between these two groups of substance abusers.

3.2.2. Privacy and confidentiality. Another potential harm of research participation is loss of privacy and confidentiality.[1] Maintaining confidentiality of participants' personal information is essential in substance abuse research. In some studies, merely agreeing to participate or appearing at research sites identifies one as an illegal drug user (Scott and White, 2005). Personal information about private, socially undesirable, or illegal behaviors or HIV status is often collected (Ostini et al., 1993) or in some cases even observed (Power, 1989). Breach of confidentiality could result in damage to reputation, personal relationships, loss of employment, or criminal prosecution (Buchanan et al., 2002; Fitzgerald and Hamilton, 1996, 1997). For participants who are prisoners, their parole or personal safety could be jeopardized by breach of confidentiality (Siegal et al., 1993).

The development of trust is essential to gathering accurate information from participants. In the U.S., Certificates of Confidentiality (http://www.grants1.nih.gov/grants/policy/coc/) protect personally identifiable research information by allowing researchers to refuse to disclose information collected for research purposes in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. However, the full extent of their effectiveness and cover in terms of protecting participants is yet to be determined (Duval and Salmon, 2004; Hofman, 2004). There are times when federal state regulations and laws mandate breach of confidentiality, for example, in instances of child or elder abuse or neglect, or danger to self or others (Fitzgerald and Hamilton, 1997; Gorelick et al., 1999; Wright et al., 1998). Confidentiality related to substance use in adolescent populations (Brody and Waldron, 2000) and during pregnancy (Marshall et al., 2003) is an especially sensitive matter; some states have used information from health care providers about perinatal substance abuse to charge women with child abuse. Federal regulations regarding the release of information on minors are somewhat different than research regulations, which were developed with adults in mind. In navigating the tension between protecting the confidentiality of information disclosed in trust and legal and ethical duties to report, researchers may strike a balance by disclosing conditions under which they would breach confidentiality (Kleber, 1989).

Only one identified empirical study addressed confidentiality issues. In a survey of federally-funded substance abuse researchers, McCrady and Bux (1999) reported that most had policies to break confidentiality in cases where child abuse or homicidality/suicidality was reported. However, not all researchers reported informing participants of these policies (McCrady and Bux, 1999). This suggests that more research on privacy and confidentiality in substance abuse research is warranted. For example, little is known regarding what research participants understand regarding the privacy protections that are offered to them, what information participants wish to be kept confidential and why, and when confidentiality concerns lead participants to lie or conceal information. Such research could provide evidence-based guidance to researchers on how to appropriately manage confidentiality issues.

3.2.3. Treatment referrals. Ethical concerns arise regarding the inclusion of treatment-seeking versus non-treatment-seeking addicts in different types of research (Cowan, 1977; Kleber, 1989). Some argue that researchers conducting non-therapeutic substance abuse research have a duty to provide participants with information, counseling, and/or referrals to treatment (Koocher, 1991). One study reported observing participants who mistook researchers for addiction counselors or other treatment specialists (Wright et al., 1998) and may therefore have been seeking treatment assistance by enrolling in research. This would illustrate the so-called "therapeutic misconception", which has attracted significant attention in the broader sphere of clinical research (Appelbaum, 2002; Hochhauser, 2002; Horng and Grady, 2003). There is also a concern that if the participant is interested in treatment, research participation may delay entry into treatment; however, none of the studies reviewed found that participation in substance abuse studies adversely affects future participation in therapy. It has been suggested that (non-therapeutic) research and treatment be coupled so that treatment directly follows research (Cohen, 2002). Therefore, subjects volunteering for research are also committing to treatment. Another alternative would be to assess individuals' preferences prior to recruitment for a specific study (or type of study) and refer them appropriately (Gorelick et al., 1999).

There has been no empirical research relating to any of these concerns. Data from participants in non-therapeutic substance abuse research regarding their reasons for participation, treatment preferences, and prior treatment-seeking behaviors are needed in order to help substance researchers adequately and efficiently serve the treatment needs of all research participants.

3.2.4. Placebo-controlled trials. The ethicality of randomized studies that involve the use of placebo or "no treatment" groups has also been questioned as potentially placing participants at increased risk because individuals desiring treatment for their addiction are randomized to receive no treatment (Brody and Waldron, 2000; Ostini et al., 1993). The most common "empirical" approach to the ethical evaluation of placebo controls in other areas of research is a meta-analysis of the actual harms and benefits experienced by participants across groups in specific placebo-controlled trials. For example, a meta-analysis of the use of FDA data dispelled common ethical myths about

[1] Interestingly, the Belmont Report does not discuss either privacy or confidentiality. Because privacy refers to "having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others" (Penslar, Institutional Review Board Guidebook, Chap. 3, Section D), it is sometimes treated under the heading of "respect for persons", which encompasses concerns about autonomy and consent. We have treated it under the Belmont heading of "beneficence" because it is one of the most common sources of harm in behavioral research.

the use of placebo controls in depression studies. The study found that placebo compared favorably with experimental therapies and active comparators and that rates of suicide and attempted suicide were actually lower in placebo groups than in the active intervention groups (Khan et al., 2000). Our literature review did not find any similar studies in the field of substance abuse research. However, the reason for this may largely pertain to the nature of the placebo-controlled trials typically performed in substance abuse research. Placebo-controlled trials are generally considered ethically controversial only when a known effective treatment exists and is being withheld (World Medical Association, 2004). Where no known effect treatment exists, the use of placebo is uncontroversial. Moreover, if a study provides psychosocial treatment for control group participants as well as for groups receiving study medication, then at least one potentially effective treatment is being provided, thus meeting the criteria of "clinical equipoise" frequently used in justifying the risk–benefit ratio in clinical trials (Freedman, 1987).

3.3. Justice in recruitment and subject selection

As noted in the introduction, individuals who abuse substances may be vulnerable within a research context. Yet, while the concern that vulnerable participants may be exploited in research is valid, denying or hindering access to participation in the name of justice and protection may ironically create an injustice and harm individuals because research may be beneficial to participants and their communities (Kahn et al., 1998). Research participants should be representative of the entire population of individuals affected by a certain condition or likely targets of a tested intervention; women and minorities must be adequately represented (NIH Revitalization Act of 1993, P.L. 103-43). Attention must be paid to the fairness of sampling and recruitment practices (Sieber and Sorensen, 1991). For example, targeting potential participants only at previously-used or obviously accessible sites runs the risk of over- or under-representing individuals from these sites. This may not only skew data but may overburden some individuals with research participation while denying others access to studies (Gorelick et al., 1999). While there may be valid safety or scientific reasons for excluding members of specific groups from participation (e.g. the group cannot provide valid data on an important dependent variable), categorical exclusion of any group (such as individuals who are HIV-positive, have co-morbid psychiatric disorders, or are pregnant) from participation strictly for convenience is unethical as it will limit the extension of potential research benefits to those excluded groups (Kahn et al., 1998; Ostini et al., 1993).

Two studies addressed the representativeness of participants in drug treatment research. One study compared participants in two clinical trials for the treatment of cocaine dependence to a random sample of individuals being treated in outpatient clinical settings (Carroll et al., 1999). Research participants were more likely to be younger, White, and on public assistance and more likely to report employment problems and more consistent and intense cocaine use. Gorelick et al. (1998) reviewed published studies of pharmacological cocaine treatment and compared characteristics of participants to individuals from a national population-based survey who reported seeking treatment for a cocaine-related problem. The authors determined that research participants were fairly comparable in basic sociodemographic characteristics to the larger population of treatment-seeking individuals, with the important exception of race/ethnicity. Over 25% of studies included only White participants; 31% of studies reviewed had no African-American participants, and two-thirds of studies included no Hispanics/Latinos. In the future, studies could examine not only the representation of special populations within studies, but also whether data on special populations are analyzed in a culturally, racially, or ethnically sensitive manner—e.g. by not treating majority population data as "normal" or by avoiding comparisons that do little other than contribute to stigmatization (Philleo and Brisbane, 1997; Corbie-Smith et al., 2004); whether benefits and burdens are fairly distributed; and what is the effect of recruitment incentives on the representation of individuals from various socioeconomic groups.

3.4. Other empirical studies: researcher knowledge and practices

Additional published studies were identified that suggest variation exists in ethical knowledge and practices among substance abuse researchers. One study of research personnel found that not all individuals conducting research – even experienced addiction treatment staff members – are familiar with human subjects protections related to informed consent (Forman et al., 2002). In this study, an educational intervention significantly improved the correctness of staff beliefs regarding human subjects protections. Interestingly, a substantial percent of staff remained unsure about the risks associated with participant payments even though the educational session addressed this concern. Another study of federally-funded alcohol and drug abuse researchers reported that many study protocols employed procedures to minimize coercion of substance-abusing participants; two-thirds of researchers surveyed used an objective means to determine competence to give informed consent and to measure comprehension of consent forms (McCrady and Bux, 1999). More research is needed on the current beliefs and practices of substance abuse researchers to identify areas of needed education and training as well as best practices and creative, effective solutions to common problems.

4. Conclusion

Researchers are often highly frustrated with research regulations and IRBs, but it is unlikely that researchers are frustrated because they are unconcerned with the well-being of participants. We have no reason to believe, for example, that researchers disagree with the fundamental ethical principles that undergird our research regulations: respect for persons, beneficence, and justice (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979). Moreover, enlightened researchers believe that, at least in the long

run, treating participants well will improve their chances of obtaining quality data (Sieber, 1992). Research that demonstrates respect and ethical concern for participants is more likely to succeed in enrolling participants and obtaining honest participation (Centers for Disease Control and Prevention et al., 1998; Fisher and Wallace, 2000). Rather, it appears that researchers are primarily frustrated when they believe that IRB decisions hinder research without actually promoting the interests of research participants (American Psychological Association, 2001; De Vries et al., 2004; DuBois, 2004).

While the ethical issues that arise in research conducted with potentially vulnerable participants who abuse substances are numerous and well documented, the evidentiary base for addressing these issues is clearly inadequate. The empirical studies that do exist are often suggestive, but their sample sizes are typically too small to generalize to the larger population of participants. If any one major theme emerged from the existing studies it is that many well-intentioned, protectionist concerns – about recruitment incentives, consent comprehension, and drug administration studies – may be overstated. Policies based on such protectionist concerns may indeed hinder research without actually promoting the interests of participants. For example, the studies reviewed generally found that comprehension of informed consent information was adequate; therefore, excluding participants with substance abuse disorders may unjustly stigmatize them and disregard their autonomy. Some studies found that payments to participants did not contribute to perceived coercion or higher rates of substance use; therefore, insisting upon no or very low payment may be unfair and may unnecessarily reduce researchers ability to recruit participants. Finally, studies that indicated that experimental administration of addictive substances does not carry a significant addictive risk may suggest that prohibiting such research will unnecessarily constrain our ability to gain information that is potentially beneficial to the participant population. However, too little data exist to definitively settle any of the current debates regarding protectionist policies.

We realize that there are many challenges to conducting empirical studies on ethical issues in human subjects research (Sachs et al., 2003). First, researchers may be reluctant to study ethical issues in their own projects out of fear that findings may reflect badly on them or harm future recruitment efforts. Yet, recruiting participants from the studies of other investigators may be even more challenging given privacy protections.

Secondly, ethical concepts in research such as competency and autonomy are imprecise and difficult to operationalize. Empirical studies on ethics are often vague in their stated objectives and in the concepts that are the targets of their study (Miller, 2002; Tancredi, 1995). Clear conceptual understanding about the topic or problem being examined is required, and individuals with training and experience in empirical research methods may not be as expert in these conceptual areas (Sugarman, 2004). Greater collaboration and training specific to empirical research on ethics is needed in the field of substance abuse. Ultimately, ethics in research and IRB review will only become evidence-based when researchers and funding bodies decide that it merits greater attention than it has received to date.

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References

Allen, D., 2002. Research involving vulnerable young people: a discussion of ethical and methodological concerns. Drugs: Educ. Prev. Policy 9, 275–283.

American Psychological Association, 2001. Research Ethics: Comments Submitted by APA on the Draft of the NBAC Report on Ethical and Policy Issues in Research Involving Human Participants. American Psychological Association, http://www.apa.org/science/comment_nbac-01.html (retrieved December 29 2004).

Appelbaum, P.S., 1995. Consent and coercion: research with involuntarily treated persons with mental illness or substance abuse. Account. Res. 4, 69–79.

Appelbaum, P.S., 1997. Patients' competence to consent to neurobiological research. In: Shamoo, A.E. (Ed.), Ethics in Neurobiological Research with Human Subjects: The Baltimore Conference on Ethics. Gordon and Breach Publishers, Amsterdam, pp. 253–264.

Appelbaum, P.S., 2002. Clarifying the ethics of clinical research: a path toward avoiding the therapeutic misconception. Am. J. Bioeth. 2, 22–23.

Baylis, F., Downie, J., Kenny, N., 1999. Children and decision-making in health research. IRB 21, 5–10.

Brandon, T., Lisman, S., 2000. Introduction to the special section on empirical underpinnings of the ethics of alcohol administration in research settings. Psychol. Addict. Behav. 14, 315–318.

Brody, J., Waldron, H., 2000. Ethical issues in research on the treatment of adolescent substance abuse disorders. Addict. Behav. 25, 217–228.

Buchanan, D., Khoshnood, K., Stopka, T., Shaw, S., Santelices, C., Singer, M., 2002. Ethical dilemmas created by the criminalization of status behaviors: case examples from ethnographic field research with injection drug users. Health Educ. Behav. 29, 30–42.

Carpenter Jr., W.T., Gold, J.M., Lahti, A.C., Queern, C.A., Conley, R.R., Bartko, J.J., Kovnick, J., Appelbaum, P.S., 2000. Decisional capacity for informed consent in schizophrenia research. Arch. Gen. Psychiat. 57, 533–538.

Carroll, K.M., Nich, C., McLellan, A.T., McKay, J.R., Rounsaville, B.J., 1999. 'Research' versus 'real-world' patients: representativeness of participants in clinical trials of treatments for cocaine dependence. Drug Alcohol Depend. 54, 171–177.

Centers for Disease Control and Prevention, Department of Health and Human Services, National Institutes of Health, Food and Drug Administration, Health Resources and Services Administration, Substance Abuse and Mental Health Services Administration, Indian Health Service, 1998. Building Community Partnerships in Research: Recommendations and Strategies. http://www.minority.unc.edu/reports/cdc1998/CttyPartInResCDC1998.pdf (accessed May 18, 2006).

Charland, L.C., 2002. Cynthia's dilemma: consenting to heroin prescription. Am. J. Bioeth. 2, 37–47.

Cohen, P.J., 2002. Untreated addiction imposes an ethical bar to recruiting addicts for non-therapeutic studies of addictive drugs. J. Law Med. Ethics 30, 73–81.

College on Problems of Drug Dependence, 1995. Human subject issues in drug abuse research. Drug Alcohol Depend. 37, 167–175.

Corbie-Smith, G., Miller, W.C., Ransohoff, D.F., 2004. Interpretations of "appropriate" minority inclusion in clinical research. Am. J. Med. 116, 249–252.

Cowan, D., 1977. Ethical considerations of metabolic research in alcoholic patients. Alcohol Clin. Exp. Res. 1, 193–198.

De Vries, R., DeBruin, D.A., Goodgame, A., 2004. Ethics review of social behavioral, and economic research: where should we go from here? Ethics Behav. 14, 351–368.

Dolinsky, Z., Babor, T., 1997. Ethical, scientific, and clinical issues in ethanol administration research involving alcoholics as human subjects. Addiction 92, 1087–1097.

Drobes, D.J., Anton, R.F., 2000. Drinking in alcoholics following an alcohol challenge research protocol. J. Stud. Alcohol. 61, 220–224.

DuBois, J.M., 2004. Is compliance a professional virtue of researchers? Reflections on promoting the responsible conduct of research. Ethics Behav. 14, 383–395.

DuBois, J.M., 2005. Vulnerability in research. In: Bankert, E., Amdur, R. (Eds.), Institutional Review Board: Management and Function. Jones and Bartlett, Boston, pp. 337–340.

Duval, G., Salmon, C., 2004. Research note: ethics of drug treatment research with court-supervised subjects. J. Drug Issues 34, 991–1005.

Elman, I., Krause, S., Karlsgodt, K., Schoenfeld, D.A., Gollub, R.L., Breiter, H.C., Gastfriend, D.R., 2001. Clinical outcomes following cocaine infusion in non-treatment-seeking individuals with cocaine dependence. Biol. Psychiat. 49, 553–555.

Faillace, L.A., Flamer, R.N., Imber, S.D., Ward, R.F., 1972. Giving alcohol to alcoholics: an evaluation. Quart. J. Stud. Alcohol. 33, 85–90.

Festinger, D., Marlowe, D., Croft, J., Dugosh, K., Mastro, N., Lee, P., DeMatteo, D., Patapis, N., 2005. Do research payments precipitate drug use or coerce participation? Drug Alcohol Depend. 78, 275–281.

Fischman, M.W., Johanson, C., 1998. Ethical and practical issues involved in behavioral pharmacology research that administers drugs of abuse to human volunteers. Behav. Pharmacol. 9, 479–498.

Fisher, C., Wallace, S., 2000. Through the community looking glass: reevaluating the ethical and policy implications of research on adolescent risk and psychopathology. Ethics Behav. 10, 99–118.

Fitzgerald, J.L., Hamilton, M., 1996. The consequences of knowing: ethical and legal liabilities in illicit drug research. Soc. Sci. Med. 43, 1591–1600.

Fitzgerald, J.L., Hamilton, M., 1997. Confidentiality, disseminated regulation and ethico-legal liabilities in research with hidden populations of illicit drug users. Addiction 92, 1099–1107.

Forman, R.F., Bovasso, G., Woody, G., McNicholas, L., Clark, C., Royer-Malvestuto, C., Weinstein, S., 2002. Staff beliefs about drug abuse clinical trials. J. Subst. Abuse Treat. 23, 55–60.

Freedman, B., 1987. Equipoise and the ethics of clinical research. New Engl. J. Med. 317, 141–145.

Fry, C., Dwyer, R., 2001. For love or money? An exploratory study of why injecting drug users participate in research. Addiction 96, 1319–1325.

Fureman, I., Meyers, K., McLellan, A.T., Metzger, D., Woody, G., 1997. Evaluation of a video-supplement to informed consent: injection drug users and preventive HIV vaccine efficacy trials. AIDS Educ. Prev. 9, 330–341.

Goldman, M., 2000. The culture of science and the ethics of alcohol administration in research. Psychol. Addict. Behav. 14, 335–341.

Gorelick, D., Pickens, R., Bonkovsky, F., 1999. Clinical research in substance abuse: human subject issues. In: Pincus, H., Lieberman, J., Ferris, S. (Eds.), Ethics in Psychiatric Research: A Resource Manual for Human Subjects Protection. American Psychiatric Association, Washington, DC, pp. 177–194.

Gorelick, D.A., Montoya, I.D., Johnson, E.O., 1998. Sociodemographic representation in published studies of cocaine abuse pharmacotherapy. Drug Alcohol Depend. 49, 89–93.

Grady, C., 2001. Money for research participation? Does it jeopardize informed consent? Am. J. Bioeth. 1, 40–44.

Hall, W., Carter, L., Morley, K.I., 2003. Addiction, neuroscience, and ethics. Addiction 98, 867–870.

Hall, W., Carter, L., Morley, K.I., 2004. Neuroscience research on the addictions: a prospectus for future ethical and policy analysis. Addict. Behav. 29, 1481–1495.

Harrison, K., Vlahov, D., Jones, K., Charron, K., Clements, M., 1995. Medical eligibility, comprehension of the consent process, and retention of injection drug users recruited for an HIV vaccine trial. J. Acq. Immune Defic. Syndr. Hum. Retrovirol. 10, 386–390.

Hochhauser, M., 2002. Therapeutic misconception and recruiting doublespeak in the informed consent process. IRB 24, 11–12.

Hofman, N.G., 2004. Toward critical research ethics: transforming ethical conduct in qualitative health care research. Health Care Women Int. 25, 647–662.

Horng, S., Grady, C., 2003. Misunderstanding in clinical research: distinguishing therapeutic misconception, therapeutic misestimation, and therapeutic optimism. IRB 25, 11–16.

Hougham, G., Sachs, G., Danner, D., Mintz, J., Patterson, M., Roberts, L.W., Siminoff, L., Sugarman, J., Whitehouse, P.J., Wirshing, D.A., 2003. Empirical research on informed consent with the cognitively impaired. IRB 25, S26–S32.

Kahn, J.P., Mastroianni, A.C., Sugarman, J., 1998. Beyond Consent: Seeking Justice in Research. Oxford University Press, Oxford, New York.

Kaufman, M., Levin, J., Kukes, T., Villafuerte, R., Hennen, J., Lukas, S., Mendelson, J., Renshaw, P., 2000. Illicit cocaine use patterns in intravenous-naive cocaine users following investigational intravenous cocaine administration. Drug Alcohol Depend. 58, 35–42.

Khan, A., Warner, H., Brown, W., 2000. Symptom reduction and suicide risk in patients treated with placebo in antidepressant clinical trials: an analysis of the food and drug administration database. Arch. Gen. Psychiat. 57, 311–317.

Kleber, H., 1989. Drug abuse liability testing: human subjects issues. In: Fischman, M.W., Mello, N. (Eds.), Testing for Abuse Liability of Drugs in Humans. National Institute on Drug Abuse Monograph Series, Washington, DC, pp. 341–356.

Koocher, G., 1991. Questionable methods in alcohol research. J. Consult. Clin. Psychol. 59, 246–248.

Kranzler, H.R., Dolinsky, Z., Kaplan, R.F., 1990. Giving ethanol to alcoholics in a research setting: its effect on compliance with disulfiram treatment. Br. J. Addict. 85, 119–123.

Loberg, T., Laberg, J., Andresen, S., Larsen, G., 1988. Do drinking experiments have a negative effect on alcoholics' recovery? Br. J. Addict. 83, 1429–1437.

MacQueen, K.M., Vanichseni, S., Kitayaporn, D., Lin, L., Buavirat, A., Naiwatanakul, T., Raktham, S., Mock, P., Heyward, W., Des Jarlais, D., Choopanya, K., Mastro, T., 1999. Willingness of injection drug users to participate in an HIV vaccine efficacy trial in Bangkok, Thailand. J. Acq. Immune Defic. Syndr. 21, 243–251.

Marshall, M.F., Menikoff, J., Paltrow, L.M., 2003. Perinatal substance abuse and human subjects research: are privacy protections adequate? Men. Retard. Dev. Disabil. Res. Rev. 9, 54–59.

McCrady, B., Bux, D.J., 1999. Ethical issues in informed consent with substance abusers. J. Consult. Clin. Psychol. 67, 186–193.

McGovern, T.F., 1998. Vulnerability: reflection on its ethical implications for the protection of participants in SAMHSA programs. Ethics Behav. 8, 293–304.

Mendelson, J., 1991. Protection of participants and experimental design in clinical abuse liability testing. Br. J. Addict. 86, 1543–1548.

Miller, F.G., 2002. Ethical significance of ethics-related empirical research. J. Natl. Cancer Inst. 94, 1821–1822.

Miller, V.A., Drotar, D., Kodish, E., 2004. Children's competence for assent and consent: a review of empirical findings. Ethics Behav. 14, 255–295.

Modell, J., Glaser, F., Mountz, J., 1993. The ethics and safety of alcohol administration in the experimental setting to individuals who have chronic, severe alcohol problems. Alcohol Alcohol. 28, 189–197.

National Advisory Council on Alcohol Abuse and Alcoholism, U.S. Department of Health and Human Services, 2005. Recommended Council Guidelines on Ethyl Alcohol Administration in Human Experimentation. National Advisory Council on Alcohol Abuse and Alcoholism, http://www.niaaa.nih.gov/Resources/ResearchResources/job22.htm (accessed May 18, 2006).

National Advisory Council on Drug Abuse, 2000. Recommended Guidelines for the Administration of Drugs to Humans. National Advisory Council on Drug Abuse, http://www.nida.nih.gov/Funding/HSGuide.html (accessed May 18, 2006).

National Bioethics Advisory Commission, 1998. Research Involving Persons with Mental Disorders that may Affect Decision-making Capacity. Volume I: Report and Recommendations. National Bioethics Advisory Commission, http://www.georgetown.edu/research/nrcbl/nbac/capacity/TOC.htm (accessed May 18, 2006).

National Bioethics Advisory Commission, 2001. Ethical and Policy Issues in Research Involving Human Participants. Volume I: Report and Recommendations. National Bioethics Advisory Commission, http://www.bioethics.gov/reports/past_commissions/nbac_human_part.pdf (accessed May 18, 2006).

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. National Commission for the Protection of Human Subjects of Biomedical and Behavioral

Research, http://www.nihtraining.com/ohsrsite/guidelines/belmont.html (accessed May 18, 2006).
Newman, E., Willard, T., Sinclair, R., Kaloupek, D., 2001. Empirically supported ethical research practice: the costs and benefits of research from the participants' view. Account. Res. 8, 309–329.
Ostini, R., Bammer, G., Dance, P., Goodwin, R., 1993. The ethics of experimental heroin maintenance. J. Med. Ethics 19, 175–182.
Penslar, R.L., Porter, J.P., 1993. Institutional Review Board (IRB) Guidebook. Office for Human Research Protections, http://www.hhs.gov/ohrp/irb/irb_guidebook.htm (accessed May 18, 2006).
Philleo, J., Brisbane, F., 1997. Cultural Competence in Substance Abuse Prevention. National Association of Social Workers Press, Washington, DC.
Power, R., 1989. Participant observation and its place in the study of illicit drug abuse. Br. J. Addict. 84, 43–52.
Reynolds, G., Fisher, D., Cagle, H., Johnson, M., 2000. The role of employment cycles and incentives in the recruitment of drug users. Adv. Med. Sociol. 7, 289–300.
Ritter, A., Fry, C., Swan, A., 2003. The ethics of reimbursing injection drug users for public health research interviews: what price are we prepared to pay? Int. J. Drug Policy 14, 1–3.
Roberts, L.W., 2000. Evidence-based ethics and informed consent in mental illness research. Arch. Gen. Psychiat. 57, 540–542.
Sachs, G., Hougham, G., Sugarman, J., Agre, P., Broome, M., Geller, G., Kass, N., Kodish, E., Mintz, J., Roberts, L., Sankar, P., Siminoff, L., Sorenson, J., Weiss, A., 2003. Conducting empirical research on informed consent: challenges and questions. IRB 25, S4–S10.
Scott, C., White, W., 2005. Ethical issues in the conduct of longitudinal studies of addiction treatment. J. Subst. Abuse Treat. 28, S91–S101.
Seddon, T., 2005. Paying drug users to take part in research: justice, human rights, and business perspectives on the use of incentive payments. Addict. Res. Theory 13, 101–109.
Sieber, J., 2004. Empirical research on research ethics. Ethics Behav. 4, 397–412.
Sieber, J., Sorensen, J., 1991. Conducting social and behavior AIDS research in drug treatment clinics. IRB 14, 1–5.
Sieber, J.E., 1992. Planning Ethically Responsible Research: A Guide for Students and Internal Review Boards. Sage Publications, Newbury Park, CA.
Siegal, H., Carlson, R., Falck, R., Reece, R.D., Perlin, T., 1993. Conducting HIV outreach and research among incarcerated drug abusers: a case study of ethical concerns and dilemmas. J. Subst. Abuse Treat. 10, 71–75.
Sinha, R., Krishnan-Sarin, S., Farren, C., O'Malley, S., 1999. Naturalistic follow-up of drinking behavior following participation in an alcohol administration study. J. Subst. Abuse Treat. 17, 159–162.
Stanley, B., Sieber, J., Melton, G., 1987. Empirical studies of ethical issues in research: a research agenda. Am. Psychol. 42, 735–741.
Sugarman, J., 1994. Toward achieving meaningful informed consent in AIDS vaccine trials with injection-drug users. AIDS Publ. Policy J. 9, 167–172.
Sugarman, J., 2004. The future of empirical research in bioethics. J. Law Med. Ethics 32, 226–231.
Tancredi, L.R., 1995. The limits of empirical studies on research ethics. Ethics Behav. 5, 217–236.
Tucker, J., Vuchinich, R., 2000. Creating a research context for reducing risk and obtaining informed consent in human alcohol studies. Psychol. Addict. Behav. 14, 319–327.
Wagener, D.K., Sporer, A.K., Simmerling, M., Flome, J.L., An, C., Curry, S.J., 2004. Human subjects challenges in youth-focused research: perspectives and practices of IRB administrators. Ethics Behav. 14, 335–349.
Wood, M., Sher, K., 2000. Risk of alcohol consumption in laboratory studies involving human research participants. Psychol. Addict. Behav. 14, 328–334.
World Medical Association, 2004. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. World Medical Association, http://www.wma.net/e/policy/b3.htm (accessed May 18, 2006).
Wright, S., Klee, H., Reid, P., 1998. Interviewing illicit drug users: observations from the field. Addict. Res. 6, 517–535.