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Regulatory Issues Encountered when Conducting Longitudinal Substance Abuse Research

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Abstract

Objective—To summarize challenges unique to obtaining Institutional Review Board (IRB) approval for longitudinal substance abuse research, focusing on solutions and lessons learned.

Methods—Thirteen senior Principal Investigators with experience conducting research on substance abuse treatment and health services outcomes recalled instances from the prior 5 years when obtaining UCLA and non-UCLA IRB approval was hampered by differences in the interpretation of regulatory guidelines and how those differences were resolved.

Principal Findings—Comprehensive yet flexible research protocols regarding (1) informed and voluntary consent, (2) participant payment, and (3) re-contact efforts are essential for securing IRB approval of longitudinal substance abuse studies. Specific examples of lessons learned are provided.

Conclusions—Experiences can help researchers to provide appropriate and explicit justification for longitudinal substance abuse research protocols, thereby minimizing the burden and cost associated with meeting regulatory requirements as well as enhancing the efficiency, quantity, and quality of data collected.

Keywords

Institutional Review Boards; longitudinal substance abuse research; best practices

1. Introduction

Substance abuse continues to be a widespread and persistent public health problem in the United States, often occurring over the life course (Hser et al., 1997; Claus et al., 1999; Scott et al., 2005). The consequences of substance abuse account for a significant number of costly events such as emergency room visits, arrests, and incarcerations (ONDCP, 2004; SAMHSA, 2006; U.S. Department of Justice, Office of Justice Programs, 2005). To accurately capture the chronic nature of drug abuse and the course of recovery, researchers increasingly affirm the need to focus on the long-term interplay of multiple events over time such as drug use, health services utilization, psychosocial mediation factors, major life events, and intervention

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outcomes. A longitudinal perspective is particularly relevant to the chronic disease management concepts proposed in current health services policy and practice (McLellan, 2002; McLellan et al., 2000; Moos and Moos, 2005; Weisner et al., 2001).

Conducting longitudinal drug abuse research is challenging for numerous reasons, but particularly daunting for Principal Investigators (PI) is the application of research practices that are scientifically rigorous and, at the same time, adequately address concerns raised by Institutional Review Boards (IRB). IRBs are charged with protecting the rights and welfare of all human research participants and are guided by principles codified in federal and state statutes. These principles inform necessary oversight, but, sometimes problematically, they are also subject to interpretive changes over time. It is not uncommon for PIs and IRB members, who have different priorities, missions, and agendas, to occasionally differ on what constitutes appropriate research conduct. This difference of opinion encourages healthy debate and can result in improved research procedures, but, from a researcher perspective, it also generates lengthy correspondence, delays the initiation of data collection, and results in the expense of scarce resources. As IRBs become stricter (Oakes, 2002), fulfilling additional IRB-initiated human subjects protection requirements poses a significant research burden, one that can be compounded by other complications like the involvement of multiple regulatory agencies, IRB member turnover, changes in the interpretation of governing regulations, and conflicting state and agency statutes. While these issues are not unique to longitudinal substance abuse research, in this arena other noteworthy regulatory issues commonly arise.

During a longitudinal study the physical and emotional states of participants may change over the course of time. From enrollment to follow-up, substance abusers may transition in and out of various health and other service settings (e.g., drug or mental health treatment, jail or prison, homeless shelters), activities (e.g., using, in withdrawal or abstaining, criminally active, employed), economic circumstances, and physical or emotional health (e.g., mentally ill, medically or cognitively impaired) (Scott and White, 2005). This ongoing change in states precipitates the emergence of unanticipated issues during the life of a study, necessitating research protocols comprehensive and flexible enough to address diverse scenarios.

Much has been written on the difficulty of conducting follow-up studies with “deviant” populations (Hansten et al., 2000; LaPorte et al., 1981; Mackenzie et al., 1987; Moos and Bliss, 1978; Walton et al., 1998; Wright et al., 1995). Also well-documented are techniques for successfully tracking, locating, and retaining substance-abusers in research (Cohen et al., 1993; Cottler et al., 1996; Desmond et al., 1995; Goldstein, 1977; Passetti et al., 2000; Ribisl et al., 1996; Sullivan et al., 1996). However, more recently, follow-up research practices are increasingly informed by a heightened sensitivity for privacy concerns (i.e., the Health Information Portability and Accountability Act [HIPAA]) as well as the utilization of technology-driven resources. Passed in 1996 and revised in 2004, HIPAA has contributed to an atmosphere of confusion and concern regarding the confidentiality of patient records, particularly in the substance abuse treatment realm, and whether methods for safeguarding personally identified health information adequately meet patient privacy regulations. The widespread use of computer-based search engines, databases, and communication methods means that accidental disclosure of sensitive information is more common, greater numbers of people are impacted, and the potential consequences are more significant (e.g., identity theft, computer crime). Together, these two forces have dramatically altered the environment in which the requirements of research and regulatory are mediated. Consequently, now more than ever before, the responsibilities assigned to regulatory agencies are expanding and standards for privacy and confidentiality change continually, usually in a direction that is more restrictive and cautionary.

It is in this new environment that PIs must successfully navigate the regulatory review process before initiating a study, an experience that can prove increasingly formidable as voiced in numerous recent publications featuring researcher-IRB interactions (Dougherty and Kramer, 2005; Fitch, 2005; Green et al., 2006; Koerner, 2005; Lincoln, 2005; Malone et al., 2006; Sansone et al., 2004). Only a handful of studies have documented variations in how IRBs handle health services research (Dziak et al., 2005; Gold and Dewa, 2005) or the research ethics review process itself (Fitzgerald et al., 2006) and none have provided guidance specific to longitudinal substance abuse research. Our purpose in this paper is to summarize challenges unique to attaining IRB approval to conduct longitudinal research on substance abuse, focusing on solutions and lessons learned.

2. Methods

Sponsored by UCLA's Center for Advancing Longitudinal Drug Abuse Research (CALDAR), this paper stems from one of CALDAR's primary themes of enhancing the efficiency, quantity, and quality of data collected for longitudinal research. Experiences with IRBs were provided by thirteen senior UCLA PIs who completed a one-on-one semi-structured interview with a postdoctoral fellow. Collectively, contributors had conducted over 100 Federal- and State-funded studies in substance use and health services outcomes for an average of 15 years. The participants were asked to recall and provide documentation of instances from the prior 5 years when obtaining UCLA and non-UCLA IRB approval for longitudinal substance abuse research was hampered by differences in interpretation of regulatory guidelines and how those differences were resolved. Copies of IRB correspondence were reviewed as needed. For context, findings were compared to relevant journal articles.

PIs identified three broad topics that we will briefly review: (1) creating an environment for informed and voluntary consent, (2) designing appropriate participant payment, and (3) balancing privacy rights and re-contact efforts. This paper is not an exhaustive account of regulatory difficulties likely to be encountered when conducting longitudinal drug abuse research, but is instead intended to capture current successful practices and serve as a preparatory resource for researchers planning to initiate studies of a similar longitudinal nature.

3. Findings

3.1. Creating an environment for informed and voluntary consent

Obtaining informed and voluntary consent from individuals who participate in longitudinal substance abuse research poses several distinct issues. Informed consent is not merely the act of agreeing to contribute to a research study, but is a continuous process in which competent and autonomous potential participants are invited to learn about the research procedures and asked to participate. In order to obtain informed consent, the prospective participant should be presented with sufficient and comprehensible information about the research protocol so that he or she can arrive at an intelligent, informed consent (Grunder, 1978). Informed consent must cover particular elements that include, but may not be limited to, these topics: study purpose and procedures, potential risks and discomforts, anticipated benefits to subjects and to society, alternatives to participation, payment for participation, possible commercial products resulting from the research, financial obligations, emergency care and compensation for injury, provisions for safeguarding confidentiality, procedures for withdrawal, identification of the investigators, and rights of the research subjects.

3.1.1. Extra protections for vulnerable populations—When substance abusers are presented with information about a longitudinal study they may be in a “vulnerable” state (i.e., intoxicated, suffering from withdrawal symptoms or co-occurring mental illness, or experiencing cumulative cognitive deficits associated with long-term use), which may impair

their ability to weigh the risks and benefits of the study and impede independent decision-making. Diminished autonomy is most commonly thought to exist among children because of their incomplete intellectual development and also among prisoners because of their altered societal status (Amdur, 2003). Vulnerable individuals such as these are considered to be deserving of extra protections designed to ensure respect for individual autonomy.

Extra protections are typically translated into practice as lengthy and complex consent forms. PIs strive to design forms that follow regulatory guidelines and are also informative and written in simple language. The last criteria is especially relevant to materials designed to convey information to chronic substance abusers, given their changing physical and emotional states, but also since many have low rates of educational attainment (Fothergill and Ensminger, 2006; Gfroerer et al., 1997; Kogan et al., 2005) or may be cognitively impaired (Hanson and Luciana, 2004; Prosser et al., 2006). But all too often during interactions between IRBs and PIs, consent forms become long and confusing, inadvertently contravening evidence on enhanced comprehension and memory of short and simple forms (Murphy et al., 1999), or omit information that later becomes crucial for conducting long-term follow-up.

3.1.2. Informed consent forms for longitudinal research—Consent forms for longitudinal research are particularly susceptible to verbosity and misapprehension. PIs must include specific language required by regulatory agencies and also find it useful to summarize prior interactions to help participants remember that they have enrolled in a longitudinal study. The combination of these two aims in one consent form can result in a document that decreases participant comprehension rather than improving it. Too much regulatory language, often perceived by participants as legalese, and historical or extraneous detail can trigger participant paranoia and undermine researcher credibility, deterring some from participating in the study.

As an example, one PI related an experience in which participants completing their 1-year follow-up interview were invited to provide saliva samples for substance abuse genotyping. These samples were collected as part of an innovative study supplement that had been funded after the parent study, which focused on health services utilization and outcomes following initial treatment, had been initiated. The PI developed a separate saliva consent form and during IRB review was directed to include verbatim language on participant rights to be informed of parental heritage via DNA testing. The PI's appeal to omit the language, because there was no intent to perform parentage tests and DNA samples had not been collected from parents, thus making such tests impossible, was denied. During the consent process research staff explained to participants reasons why the language was required but not applicable. Nevertheless participants were suspicious and voiced concerns that all of the current and prior study procedures were not being stated. Inclusion of extraneous information in the saliva consent form had effectively tainted participant perceptions of the entire study. In the end, research staff relied upon their rapport with participants, built over the life of the study, to calm fears and restore confidence in the research.

Conversely, sometimes consent forms do not provide enough information. Long-term follow-up studies may be conducted with participants last contacted many years ago before computer-based resources for locating people were available. However, new locating resources increase research efficiency and practicability, resulting in benefits that outweigh potential risks. This argument was successfully made by one PI who was granted IRB approval to utilize electronic search engines available in the public domain to locate participants who were last contacted 25 years previously. The PI reported that some participants were initially apprehensive at re-contact, primarily because participants could not understand how they had been located after so many years. Some worried that the study's association with Federal funding meant that investigators had access to information that violated their rights to privacy or that the research center was masquerading for other government entities. To address these concerns, research

staff explained how new technology had been used to locate participants. Additionally, the PI included in the latest consent form explicit agreement for possible future follow-up as well as the use of electronic records to re-locate participants later, making it an important document for explanation of privacy rights.

3.1.3. Refusals and their impact on longitudinal research—Regardless of the number of assessments that constitute a longitudinal study, to honor participant autonomy informed consent must be provided at each time-point. Re-consent is important because over time many participants may have difficulty remembering the research study or distinguishing it from clinical assessments done during their drug use history (Dennis et al., 2004). However, longitudinal researchers are particularly aware that each consent interaction explicitly affords the opportunity for refusal. Participants who previously agreed to be interviewed, even many times previously, may refuse participation. This may not be due to an aversion to study aims or protocols but more frequently due to impulsive decision-making related to their current mood or situation. Distinguishing between capricious and genuine refusals can be tricky. In some cases re-approaching participants at a later time yields a change of heart, while in others it is appropriate to discontinue interactions altogether. Longitudinal researchers are reluctant to accept a refusal without first confirming its sincerity. During some types of longitudinal analyses, one missing data point can trigger case-wide deletion, i.e., jeopardizing data about that participant not just at one time-point (where refusal occurred) but rather all data that has been painstakingly collected about that participant over years of work.

One example where the right to refuse was at risk of being impracticably broadened occurred when the IRB asked that the consent form include the right to withdraw any data that had been provided during the course of the study. This stipulation could have resulted in years of lost work if participants had dropped out of the study along with all of their data from multiple assessments. The PI responded with a reminder that the formerly approved procedures represented a high and appropriate degree of protection, participants had provided consent prior to data collection, and there was no precedent for such a limitless opportunity to delete or discard data. In this case the PI's appeal was granted and the study was approved.

3.1.4. Prisoners—From one follow-up interview to another, it is not uncommon for substance abusers participating in a longitudinal study to become incarcerated or be released from jail or prison, making it difficult for PIs to know at study initiation whether to include special precautions to protect prisoner rights. Similarly, without anticipating that some participants may be incarcerated at follow-up, PIs are also likely to neglect to ensure prisoner-specific review requirements have been fulfilled.

The decision to participate in research must be made without any pressure from outside sources (Grunder, 1978), making the inclusion of inmates problematic. More than other prospective participants, prisoners may feel coerced to participate in studies, acting out of a misapprehension that such “good behavior” will please legal authorities and enhance their chances of release. To protect inmates, federal law requires that several extra conditions be satisfied prior to IRB approval (Prentice et al. 2002). For example, precautionary protocols must be designed to prevent research participation from affecting parole board decisions and to avoid coercive compensation. Furthermore, a prison representative must be present at IRB review of any study involving incarcerated populations.

This last condition negatively impacted one long-term follow-up of substance-abusing individuals subject to review by two separate IRBs, one of which agreed to defer to the decisions of the other. Unfortunately, although the PI had indicated that prisoners would account for a portion of the study population, the prisoner representative happened to be absent from the meeting when the project was re-approved during annual continuing review by the prevailing

IRB. This omission was revealed when, to meet federal requirements, the subordinate IRB requested documentation that a prison representative had participated in the approval meeting. The oversight was corrected several months later when the prevailing IRB reviewed the project again with the prison representative in attendance. However, so much time had lapsed that the subordinate IRB's approval had expired and the PI was invited to resubmit the protocol as a new study. The PI decided that re-submitting the project was not worthwhile because the subordinate IRB's approval was primarily needed for the use of administrative data records, which were determined to be of limited use and could be supplanted by equivalent self-reported data. While the PI understood that it was appropriate for the study to receive prisoner advocate review and approval and that the subordinate IRB was justifiably fulfilling its role by taking an active interest in the conduct of the research, the PI was equally frustrated with the bind the study faced and the apparently limited amount of flexibility and celerity the two IRBs were able to employ in trying to resolve the situation. In the end, the PI chose to rely only on the approval of the prevailing IRB. While this issue was resolved with an uncommon tactic, from this experience it was learned that IRBs can make mistakes, which may impact the study in ways that are beyond the control of PI. Also, it was learned that it is prudent for PIs to assume that a proportion of participants will be incarcerated at follow-up. Consequently, to minimize IRB-related delays as illustrated by this example, PIs must pro-actively communicate with IRBs to ensure that prisoner-specific protocols and review requirements are met before data collection begins.

3.1.5. Lessons learned—Longitudinal research on substance abuse raises some unique but not insurmountable regulatory issues related to voluntary and informed consent. Although the process may be influenced by participants' changing emotional and physical states, there is no empirical evidence indicating that substance users, even those with co-occurring mental disorders or cognitive deficits, are incapable of providing informed consent (McCrady and Bux, 1999; Walker et al., 2005). Drug craving and drug use should not automatically exclude individuals from research, especially since such sample selection restrictions may bias findings and result in failure to recognize issues relevant to this population (College on Problems of Drug Dependence, 1995).

Longitudinal substance abuse researchers can do several things to create an environment conducive to obtaining true informed consent. First, when designing study protocols, PIs must include procedures to: ensure that consent occurs when participants are not acutely intoxicated or in withdrawal; evaluate refusals for sincerity (i.e., allow for re-contact of insincere refusals); and address the likelihood that the proportion of the sample deemed deserving of special precautions (e.g., incarcerated or cognitively deficient) will change over time. Second, PIs must design consent forms that: observe regulatory guidelines and reference prior study activities but do not compromise clarity and conciseness; include explicit language to permit contact at some future time point following study completion; and, as applicable, ask for permission to use electronic records to locate participants later. Finally, PIs should be prepared to: appeal unwarranted precedents, especially those that limit the scientific rigor of the study such as deletion of prior data upon refusal to participate in ongoing research; treat consent as a process and develop strong rapport with participants to secure continued participation despite new consent requirements that may upset participants; and start the IRB process early, especially when multiple IRBs are involved or when the study includes participants who were last contacted many years ago, as time will be needed to mediate unexpected or unusual events. Withdrawing a study from IRB review is typically not an option available to researchers and, in any case, should be considered only in extreme and rare instances. Instead, researchers are better served by working collaboratively and pro-actively with their IRBs. Utilizing the appeals process and working closely to understand the viewpoints and responsibilities of IRB members will improve communications and facilitate future researcher-IRB interactions.

3.2. Designing appropriate participant payment

Unlike participants involved in short-term studies (e.g., cross-sectional surveys, time-limited clinical trials), substance abusers enrolled in longitudinal research typically contribute to the study at multiple time-points over several years or even decades. In return for their continued contribution, participants commonly expect to be monetarily compensated with an amount that reflects the current fair market value of their time. Moreover, they may expect that payments increase over time. The perceived value of payments has been found to be a key factor in increasing participation rates (Reilly et al., 2000; Festinger et al., 2005; Rosado et al., 2005), and this is particularly salient to longitudinal studies that are necessarily dependent on data that has been accumulated over time. Inappropriate or undesirable payment protocols (e.g., a gift certificate instead of cash) can result in feelings of discrimination (Seddon, 2005) or demoralization and participation refusal. However, providing appropriate monetary payments to substance abusers over the life of a longitudinal study can generate IRB concerns that are rooted in principles intended to prevent coercion of vulnerable populations, and fears that monetary payments will be used by this population to obtain illegal substances to continue the same behavior that is under investigation in the research study.

3.2.1. The ethics of coercion vs. compensation—Voluntary consent to participate in a study implies that there is an absence of coercion to participate. Specifically, individuals should not feel forced to participate due to the direct influence of other individuals (e.g., researchers, prison guard, treatment staff) or the allure of a payment that is too valuable to resist. Especially concerning are situations where payments may induce people to participate in studies without considering its risks and benefits other than the benefit of the payment itself (Gordon et al., 2003). To protect participants from coercive payments, IRBs must determine whether a proposed payment is a reimbursement or an inducement. A payment is considered a reimbursement when it is meant to compensate for direct expenses resulting from study participation (e.g., transportation, parking, child care, time lost from work, and food). Reimbursements are not considered coercive. In contrast, an inducement is intended to encourage participation in return for financial gain (Gordon et al., 2003). An inducement is considered coercive because it violates the fundamental ethical standard that research participation be completely voluntary without the influence of outside sources such as financial gain.

3.2.2. Need for flexible payment options—Prior to IRB approval, PIs are required to explain all protocols and procedures including payment practices. However, designing appropriate payments for longitudinal studies is complicated by changes in participant states during the course of the study. PIs may not know at study initiation whether special precautions are needed to protect prospective participants because the current status of individual participants is unknown until after re-contact has been made. Consequently, payment options may not be flexible enough to allow for all contingencies. For example, non-cash payments may be more suitable for current substance abusers or treatment clients because they may be overly vulnerable to the influence of payments (Seddon, 2005). Active users may be primarily motivated by interests in earning cash to purchase drugs (Sieber and Sorensen, 1992) without proper consideration of research participation risks. Similarly, payment to mentally or medically ill participants might be more appropriate when accompanied by specialized informed consent procedures (i.e., an evaluation of mental status) to preclude coercion or exploitation. Parenting mothers may respond better to payments for child-related or household items (e.g., grocery vouchers or gift cards to a household retailer). Payment of incarcerated individuals must also be carefully considered as this practice is sometimes viewed as: (1) an effectual reward for criminal behavior; (2) the endorsement of inequitable compensation for prisoners (who are often paid less for the same interview as non-incarcerated participants on the basis that the value of money is greater in a controlled setting); and, (3) in some cases,

unjust to jail and prison staff whose hourly wage is less than the payment for research participation (Seddon, 2005).

PIs should also keep in mind that offering payments to friends and family who help contact participants for follow-up poses other regulatory concerns. One study received IRB approval to offer family members and friends a \$10 referral reward if participants scheduled a follow-up interview, while in another study this same procedure was rejected by a different IRB as an invasion of participant privacy. In yet another study, the PI expressed the need for caution when alerting significant others about the availability of payments, especially money, since participants may be coerced by their family or friends who are motivated by the chance of receiving money themselves. PIs reported that spouses, more than any other associate, serving as gatekeepers may be inappropriately influenced by payments, either denying access to the respondent or coercing their participation.

3.3.3. Successful payment strategies—IRBs have considered a range of payment strategies to be appropriate for longitudinal research. These include: non-cash payments such as gift certificates and grocery scrip for current substance users, i.e., those in treatment; payment that reflects the economic standards of the day (approximately \$10 to \$15 per hour interviewed in 2006) but is low enough so that it would be more efficient and less restrictive to earn money for drugs outside of the research; payments that increase with each interview completed over time; dividing large payments into separate smaller amounts that must be collected incrementally per research activity (i.e., \$5 for a urine sample, \$20 for an interview, \$20 for a medical exam, \$5 for referring a friend); cash to reimburse travel expenses; modest bonus payments (beyond the main payment) for participants who respond promptly or who pre-complete some study forms prior to the actual study interview; payment to friends and family who help with re-contact; and for incarcerated participants, either placing on their trustee account an amount less than what is paid for the same interview done with a non-incarcerated individual or offering to provide full payment to a non-incarcerated friend or family member.

3.3.4. Lessons learned—When considering the amount and type of payment for participation in a longitudinal substance abuse research study, incorporating a range of payment options is essential. There is some concern that voluntary consent is violated by excessive payments. Substance using participants, especially those who are incarcerated, are considered a vulnerable population that is easily induced by financial gain. However, participants may perceive a relatively low or undesirable payment as patronizing, jeopardizing their decision to remain enrolled in the study. It is worth remembering that even among the substance-abusing population, variation exists in reasons for study participation, understanding and expectations of procedures, and feelings of freedom to participate or refuse (Grady, 2001). In fact, evidence indicates that among substance abusing research participants, payments are generally not spent on drugs (Festinger et al., 2005). Instead reasons for participation include citizenship, altruism, and “drug user activism” (Fry and Dwyer, 2001). Enjoyment of behavioral research participation and receipt of associated non-monetary benefits has been documented among other vulnerable populations (Carey et al., 2001). Similarly, many substance abusers may participate in research not just for the money but also for other reasons such as the opportunity to contribute to research that may benefit fellow substance abusers in the future. Diverse strategies can be utilized to ensure that payments are desirable enough to facilitate and maintain participation rates while simultaneously appropriate so as not to be coercive.

3.4. Balancing privacy rights and re-contact efforts

Many substance users have a transient and chaotic lifestyle that hinders efforts to track them for longitudinal studies, necessitating frequent and creative contact strategies. There is often no evidence that participants actually receive mail or phone messages about the study, and

some participants may be more responsive to letters, or phone calls, or a combination of both types of contact strategies. Systematic procedures employing various types of communication at different time-points are most effective (Hall et al., 2003; Scott, 2004).

3.4.1. Multiple and frequent contact attempts—While multiple and frequent contact attempts may enhance follow-up rates, many IRBs consider them to be an invasion of privacy. One PI stated that as few as two mailing attempts were allowed with their study of a prison sample. In another example, telephone calls were prohibited altogether and research staff had to rely entirely on letters. Interviews had last been conducted with participants more than 10 years earlier and so predictably many had moved and could not be reached through their last known address. After one year of attempted contact by mail and a response rate of only about 20%, the PI requested IRB re-review. The PI explained that such a restrictive contact method was compromising the response rate, thereby jeopardizing findings as well as future funding, and the appeal to allow for telephone calls was granted. In yet a third longitudinal study, many subjects ignored the initial mailed invitation to participate in the 25-year follow-up interview, viewing the unopened envelope as just more “junk mail” or forgetting about it in the midst of ongoing daily activity. Upon receipt of subsequent requests (by mail and telephone), many participants were prompted to respond, often after a period as long as 6 months after the initial invitation.

3.4.2. Personal identifiers—To conduct longitudinal studies, PIs must necessarily record and archive participant identifiers so that later follow-up is possible. Social Security Number and date of birth, in addition to full name and other personal identifiers, are especially useful since these items tend to remain unique despite name changes resulting from marriage or divorce. Personal data can be kept confidential by restricting access and taking precautions to prevent any potentially damaging information from being disclosed to unintended sources (Amdur, 2003). These procedures are usually articulated in protocols explained to participants in the informed consent process. In keeping with principles of privacy and confidentiality, plans to re-contact participants are also usually included in the consent form. But, as experienced by one PI, complications occur when an unexpected opportunity arises to extend the length of a study and prior consent forms do not include a statement regarding plans to re-contact participants beyond original timeframes. In this example, the original consent form stated that follow-up interviews would be conducted 6 and 12 months later. After the initial study had ended, the PI was awarded funding to conduct a 5-year follow-up on the same population. The IRB refused to grant approval for the new follow-up since participants had not been asked about re-contact previously. The PI maintained that unexpected re-contact would not pose a substantial risk because, first, it did not raise significantly different human subject protection concerns than contacting a new cohort of individuals (participation is voluntary and informed consent must be provided in both cases) and, second, the majority of participants would be interested in further follow-up since they had not discontinued participation during prior interactions. The appeal was granted.

3.4.3. Family members and friends—Family members and friends often provide emotional and economic support to substance abusers (Kumpfer et al., 2003; Clark, 2001), making them ideal individuals to contact when attempting to locate participants for long-term follow-up. One PI stated:

Investigators have the task of obtaining consent within relatively few attempts to contact participants. The restrictions do not allow the investigators to develop a rapport with participants through multiple mailings and reminder calls. Given this, investigators must be creative and resourceful on how to successfully retain participants. It is crucial to convince the participant as well as those in their network (e.g., family members, friends, neighbors) that completing the follow-up interview is

beneficial to both the participant (e.g., payments), to society at large, and to others like themselves (e.g., those that may benefit from the research) at the initial interview. Keeping the interest of participants to remain in the study is an art as well as a science, and relationship-building is vital.

Despite the benefits of building relationships with family and friends of participants enrolled in a longitudinal study, there can be a number of problematic issues associated with implementation of such contacts. The researcher must be careful to avoid revealing personal participant information, particularly when a participant's life course has dramatically changed since the last contact and current friends and family have no idea about their past substance-abusing lifestyle. Conversely, participants who have relapsed may feel embarrassed that they have "let down" the interviewer with whom they formed a personal bond. In both situations participants may avoid follow-up, introducing inadvertent attrition bias. All PIs agreed that as the "face" of the study it is the research staff that most influences participant decisions to respond to re-contact attempts and it is the PI's responsibility to ensure that staff are trained to ameliorate embarrassment among participants with an empathetic and caring attitude. PIs noted their IRB's request for assurances that interviewing staff are well-trained, the nature of the study is described with non-stigmatizing words in letters and phone messages, for example by referencing "a public health study" instead of "drug abuse research," and that protocols are in place to maintain participant privacy during day-to-day research activities.

3.4.4. Using administrative records to supplement self-reported follow-up data

—When designing a longitudinal substance abuse study, PIs may decide to acquire administrative records on participants as a supplement to (or in lieu of) data obtained from face-to-face follow-up interviews. Official records provide a historical perspective on events, and they exist on most activities relevant to research on longitudinal substance abuse and services utilization outcomes, such as treatment for drug use, medical or mental illness, arrests, incarcerations, motor vehicle accidents, receipt of government aid, and morbidity and mortality. Death records are especially useful to obtain prior to initiating follow-up interviews since with this information PIs can avoid contacting grieving relatives and reserve locating efforts for individuals who are still alive and able to participate. Records extraction can be accomplished only if the researcher has obtained permission from the agency that maintains the data and has also recorded the variables needed to link data, most commonly full name, Social Security Number, and date of birth. Plans to acquire administrative data on individuals must also be stated in the consent form, although, even with participant consent, this procedure typically raises a number of IRB concerns. One PI met IRB opposition after having received supplemental funding to acquire administrative data from a source that was not specifically named in the protocol or consent form. IRB board members felt that the original consent language was too broad and asked that it be modified to explicitly name the agency and the variables to be provided. The PI explained that participants had already signed a consent form that listed the parent organization of the agency that would provide the data, and also summarized the nature of the data without naming the actual variables. Additionally, the PI argued that it would be impracticable to re-locate and re-consent the more than 20,000 people who had already agreed to participate in the study and plans to minimize potential risks associated with sharing data were extraordinarily cautious. The IRB approved the request to acquire data. In three other longitudinal studies, acquisition of administrative data prompted IRB interest in distinctions between public and private data, adequate data security procedures, and protocols regarding data destruction and archival. In two of these studies, approval was facilitated by the fact that both had resulted from legislative mandates. The other study was so large and utilized data on a population that had last been contacted more than 10 years ago that re-consent was impracticable and a waiver of written consent was granted.

3.4.5. Lessons learned—Privacy and confidentiality regulations are intended to prevent potentially sensitive information from being disclosed and also guide research procedures for re-contact. Based on our experiences, limitations regarding when, how, and number of times participants can be contacted, or whether participants can be indirectly contacted through family members and friends, should be flexible. However, to gain IRB approval to re-contact participants for long-term follow-up, it is essential for PIs to demonstrate that: there is value in multiple, frequent, and varied contact attempts; follow-up cannot occur without the collection of participant identifiers; there are adequate protocols for securing participants' personal information; and research interviewers have been trained in research ethics and are tactful and skilled at projecting an empathetic and caring attitude. Acquiring administrative records on participants requires appropriate consent, and PIs should be prepared to explain measures taken to minimize potential risks. Further, researchers must anticipate and address IRB concerns that contacting subjects indirectly through friends and family may increase the risk that sensitive information will be disclosed. Finally, methodological research on these re-contact issues is needed to assist both PIs and IRBs in their decision-making processes.

4. Conclusion

Variability exists across IRBs and time and the information presented in this paper was collected from a limited set of researchers at one university who discussed experiences related to their psychosocial studies. There are likely critical regulatory issues relevant to the medical field and related disciplines that are not covered in this paper. However, the researchers who contributed to this paper are affiliated with a large substance abuse research center that probably has the largest portfolio of longitudinal studies in the world and, collectively, over the past 30 years these investigators have conducted numerous long-term follow-up studies on a wide and diverse range of drug-abusing populations. From these experiences, it is clear that ethical review of research is necessary and, in the current environment of heightened privacy concerns and widespread availability technological resources, PIs conducting longitudinal drug abuse research in particular are obligated to articulate not only their intent but also specific procedures for respecting participant rights.

Researchers and IRB members do not always agree, but they can often work together to resolve their differences. There are times when IRB members have not previously dealt with certain issues, and in other situations, researchers have not adequately addressed the risks associated with particular study features. When research needs and regulatory concerns collide, PIs and IRB members are often best served by raising awareness of one another's issues by engaging in on-going dialogue. Greater understanding among IRB members of the oddities and idiosyncrasies common to longitudinal substance abuse research and more appreciation among PIs of the roles and responsibilities fulfilled by regulatory entities, will benefit both arenas and, more often than not, facilitate solutions that are satisfactory to both parties.

The value of anticipating necessary protocol changes and building in time to accommodate modifications to study activities cannot be emphasized enough. Longitudinal studies are likely to precipitate events that require particular attention and planning, for example, the desire to conduct further follow-up with research subjects, increases in incentive amounts, addition or modification of forms, and contacting incarcerated research subjects. Researchers benefit by anticipating how their study might evolve and how IRBs might react to the original protocol, as well as to the changes it may undergo. IRBs are as active and as invested as ever in reviewing research protocols, and interacting with IRB members can be a time-consuming and expensive process. However these are also good reasons for researchers to incorporate a sufficient amount of resources into their study plans to accommodate the time and funding needed to secure approval for longitudinal studies that involve human subjects. Also, individual investigators, particularly junior investigators, within research centers might find it useful to create a

centralized mechanism for learning from one another's IRB experiences, principally by utilizing a core set of staff who routinely prepare IRB applications and respond to related correspondence and thus have acquired the expertise, communication skills, and rapport needed to navigate the IRB process successfully. Researchers can learn from experiences like ours to provide appropriate and explicit justification for protocols, thereby minimizing the burden and cost associated with meeting regulatory requirements.

Balancing the interests of research participants with the needs of scientifically rigorous procedures requires compromises and plays out in at least three areas: (1) informed and voluntary consent, (2) participant payment, and (3) re-contact efforts. Comprehensive yet flexible research protocols are essential for securing IRB approval of longitudinal substance abuse studies, on the one hand, and enhancing the efficiency, quantity, and quality of research data collected, on the other.

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