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Ethics in Psychiatric Research: A Review of 25 Years of NIH-funded Empirical Research Projects

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Abstract

Background—This paper reviews the past 25 years of empirical research funded by the National Institutes of Health (NIH) on matters of ethics in psychiatric research.

Methods—Using the NIH RePORTER and Medline databases, we identified 43 grants and 77 publications that involved the empirical study of a matter of ethics in research involving mental health service users.

Results—These articles provide original and useful information on important topics, most especially the capacity to consent and the voluntariness of consent. For example, participants who share a diagnosis vary widely in levels of cognitive impairment that correlate with decisional capacity, and capacity to consent can be enhanced easily using iterative consent processes. Few articles address matters of justice or benefits in research, particularly from the perspectives of participants. No articles address matters of privacy, confidentiality, or researcher professionalism.

Conclusions—Despite the usefulness of data from the studies conducted to date, current research on research ethics in psychiatry does not adequately address the concerns of service users as expressed in recent publications.

Keywords

research ethics; vulnerable subjects; psychiatric ethics; informed consent; decisional capacity; mental health consumers

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The age of great systems of psychiatry— for example, Freudian or Jungian psychoanalysis —has largely passed into the age of eclectic evidence-based practice. Medicine today values practices that are based upon empirical research rather than speculative theory. Research allows us to understand causal factors that contribute to a disorder, including genetic, environmental, and behavioral factors, and the interactions between them. Understanding causal factors may someday assist us in preventing major mental illnesses or providing more effective and sustainable treatment for all affected. In the meantime, it helps us to predict the natural course of disorders, to treat or manage their symptoms, and to offer a prognosis. The scientific enterprise is further reinforced in medicine by the fact that it can be highly profitable when translated into medical treatments (Moses 2005).

Over the past two decades an analogous shift in emphasis from theory to empirical data has occurred in the ethics of research (Borry et al. 2006; Sugarman and Sulmasy 2010). Whereas ethics was once largely the domain of philosophers and religious scholars, today many seek evidence-based ethics (Roberts 2000; Sieber 2006; Stanley et al. 1987). Several journals are dedicated to the publication of empirical studies on ethical issues, such as *Ethics & Behavior*, the *Journal of Empirical Research on Human Research Ethics (JERHRE)*, and *AJOB: Primary Research*. While some empirical ethics studies are purely descriptive (e.g., describing public attitudes toward ethical issues), others are experimental and seek to improve the way that we offer protections in research (Kon 2009).

What are the requirements for ethical research that might be investigated empirically in psychiatric research ethics? We propose the following eight primary requirements for ethical research, drawing from federal regulations for human subjects research (45CFR46) (National Commission 1979) and recent surveys of ethical issues in the field (DuBois 2008; Roberts and Roberts 1999).

1. **Consent is informed**. The consent of participants should follow a process of learning salient information about the prospective study (National Commission 1979). This process should be bi-directional and iterative. The objective is not merely the presentation of information, but the potential participants' understanding and appreciation of information, enabling a reasoned decision to accept or decline participation in the study (Grisso and Appelbaum 1998).

2. **Consent is voluntary**. The consent of participants should be neither coerced nor unduly influenced. Many factors may threaten voluntariness in research, particularly when participants are institutionalized, seriously ill, or in a social role that demands deference to the decisions of others (National Bioethics Advisory Commission 2001).

3. **Individuals and communities benefit**. Health research should benefit participants or communities by generating new knowledge that may contribute to the understanding, prevention, or treatment of illnesses and diseases (National Commission 1979). To provide benefits, research must be scientifically sound and address a question of value (Emanuel et al. 2000).

4. **Risks of harm are managed and proportionate**. Participants should not be exposed to unnecessary risks, the risks they are exposed to should be proportionate to the anticipated benefits, and risks that are greater than minimal should be monitored and evaluated regularly to determine whether changes are required in the study design or consent information (National Commission 1979).

5. **Distributive justice and social justice inform study design**. Ordinarily, the individuals or at least the populations that assume the burdens of participating in research should be targeted to receive the benefits of the research. Exceptions to this should be disclosed during the consent process and should occur only for appropriate reasons rather than for convenience (National Commission 1979). Research questions and the reporting of results should be sensitive to the possibility of stigmatizing groups by creating or reinforcing negative stereotypes (King 2005).

6. **Privacy and confidentiality are respected**. Access to individuals and their sensitive information is restricted or granted only with consent (Emanuel et al. 2000). This may require significant logistical measures, including de-identifying data sets, linking identifiers to data using separately stored codes, restricting access to data through firewalls and passwords, and obtaining certificates of confidentiality to protect against subpoena of data (Sieber 2001).

7. **Professionalism guides researcher behavior**. Professionalism requires researchers to manage and disclose financial conflicts of interest as well as conflicting roles (e.g., researcher and medical service provider) (DuBois 2008). It also requires researchers to abide by the general rules for the responsible conduct of research (e.g., avoiding falsification, fabrication, and plagiarism) (Bulger et al. 2002).

8. **Ethical processes are followed**. Human subjects research requires prospective review, and in some cases ongoing monitoring, by Institutional Review Boards (IRBs) or Research Ethics Committees (Emanuel et al. 2000). Clinical trials require monitoring and sometimes interventions by Data and Safety Monitoring Boards (DSMB) (Emanuel et al. 2000). Many research projects benefit from processes of community engagement (DuBois 2008; Ross 2010).

With funding from the National Institute of Mental Health (5R13MH079690) to examine the "best practices in mental health research ethics," this paper reviews the empirical research funded by the National Institutes of Health (NIH) on these eight ethical requirements in psychiatric research. It aims to provide an overview and evaluation of what has been funded, published, and learned over the past 25 years.

Methods

We searched for NIH-funded grants in the area of psychiatric research ethics using the NIH RePORTER (Research Portfolio Online Reporting Tools Expenditures and Results). RePORTER is a searchable online electronic database hosted at RePORT.nih.gov that provides access to a variety of data on NIH extramural research activities, including principal investigators, project summaries, publications, and patent information.[1] Currently, the RePORTER's repository has data on NIH projects dating from 1987 forward.

The NIH RePORTER query form contains 25 fields with varying levels of manipulation per item. We used the following search criteria:

- **Keywords**: ethics, ethic, ethical, "informed consent", privacy and confidentiality. Quotations are used to match exact terms. Terms must be searched independently; the query form does not allow the use of Boolean logic to search records. (While the terms "ethics," "ethic," and "ethical" were expected to capture all or most relevant studies, additional terms were used when results were not wholly unwieldy and unfocused, concepts we operationalized by capping returned results at 5,000 hits.)
- **Fiscal years**: All (1987-current (March 2011)).
- **Agencies**: National Institute of Child Health and Development (NICHD),National Human Genome Research Institute (NHGRI), National Institute of Mental Health (NIMH), National Institute of Neurological Disorders and Stroke (NINDS), National Institute on Aging (NIA), National Institute on Alcohol Abuse and Alcoholism (NIAA), National Institute on Drug Abuse (NIDA) and the Substance Abuse and Mental Health Services Administration (SAMHSA). These were considered the most likely to fund research related to a diagnosis found in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM).

[1]RePORTER replaces CRISP (Computer Retrieval of Information on Scientific Projects), which was initiated in 1998 and contained records dating from 1972. The CRISP database was taken offline December 30, 2009.

- **Funding mechanisms**: Research projects, research centers, other research-related, training/individual, interagency agreements and intramural research.
- **Activity codes**: All research project grants and research career awards.

All results were reviewed by at least one author to determine if the project synopsis met our inclusion criteria. To be included in our review, grants needed: (a) an empirical research component; (b) a focus on ethical issues in research; and (c) research participants with a cognitive, mental health, or substance abuse disorder listed in the Diagnostic and Statistical Manual of Mental Disorders-IV-TR (American Psychiatric Association, 2000)—excluding Mental Disorders Due to a General Medical Condition and secondary disorders such as Dementia Due to Head Trauma.

Using the relevant search results, we conducted a second search in RePORTER using the principal investigators (PI) to crosscheck and expand our results.

A search was then conducted to identify all relevant publications resulting from the grants that were funded in mental health research ethics. For each relevant grant, we examined the "Results" tab in RePORTER to identify publications associated with the grant. Because the NIH RePORTER cautions users that publications may not be posted and updated in a timely manner, a second search was conducted in the Medline (1987 through March 2011) to identify publications matching the grant funding number.

To be included in our review, a publication needed to meet the same criteria as the grants.

The three authors held three face-to-face meetings, during which they sorted grants and articles by topic. Sorting was done by consensus. During these meetings, grants and publications were further scrutinized to ensure that they met inclusion criteria, leading to the refinement of the dataset.

Results

In reporting results for grants and publications, we count a grant only once even when awards are made across multiple years and count a publication only once even when it lists funding from multiple grants.

What Has Been Funded?

Our initial RePORTER search yielded 4,481 search results (February 24, 2011). Many of these were redundant (e.g., multiple years of an R01), and most did not meet our inclusion criteria. The relevant PI search yielded no awards not already contained in the original search results.

A total of 43 grants (38 research and 5 career awards) met our inclusion criteria. Table 1 summarizes these grants by topic and funding agency.

Of the 9 NIH Institutes and Centers we investigated, 3 did not fund any grants matching our inclusion criteria: NHGRI, SAMHSA, and NIAAA; the remaining institutes funded between 1 and 24 grants.

Table 2 presents a list of the 43 grants by topic, principal investigator, title, and grant number.

What Has Been Published?

Consistent with our inclusion criteria, we excluded publications that were primarily theoretical or lacked a focus on research ethics. In several cases, the theoretical papers appear to have grown out of the authors' empirical study of the field; for instance, their interviews or studies may have led them to develop a paper describing a general problem (Candilis et al. 2005; J. A. Fisher 2006a; Kim and Holloway 2010), offer recommendations (Depp and Lebowitz 2007; Stanley 1988), or develop a framework or taxonomy for the field (J. A. Fisher 2006b; Rabins and Black 2010; Sieber and Stanley 1988).

In the end, 77 articles met our inclusion criteria. Table 3 provides references to the 77 articles divided by topic.

What Have We Learned?

As noted earlier, this paper aims to provide an overview and evaluation of the past 25 years of NIH-funded empirical studies and publications related to psychiatric research ethics. Accordingly, we do not present methodological details from most publications discussed here and we have generally excluded discussion of reviews and surveys that focus on multiple topics. (Some review articles were included if they were systematic, focused on a specific topic and empirical data, and contributed something new to the literature.) To facilitate a coherent presentation of the relevant publications, we present results as responses to 9 overarching research questions that we found to be most prominently addressed by the included studies.

1. How should we assess capacity to consent to research?—As noted above, the focus of this review is restricted to ethics in research. Accordingly we have excluded from review the extensive literature on capacity to consent to treatment. This is also appropriate as the context of research introduces distinct elements—concepts such as randomization, and dual roles (e.g., physician and researcher) that can be confusing to patients who become participants.

Dunn et al. (2006b) reviewed 10 instruments that were developed to assess capacity to consent to research or some dimension thereof (e.g., understanding of consent information). Of these, the best validated is the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) (Appelbaum and Grisso 2001). While the instrument was developed with foundation funding, NIH-funded studies of capacity to consent to research have used the MacCAT-CR more than any other instrument. For the purposes of studying consent to research, the MacCAT-CR has several advantages. First, it assesses all four of the components generally considered essential to capacity to consent—understanding, appreciation, reasoning, and ability to express a clear and stable choice (Grisso and Appelbaum 1998; Roth et al. 1977). Second, its items refer to standard hypothetical protocols allowing results to be compared across studies and populations. Third, it has demonstrated excellent validity and reliability across studies. While it lacks a fixed cut off point for decisional capacity, Kim et al. (2007) found that a MacCAT-CR score of 20 had a sensitivity of .84 and specificity of .80 when scores were compared to those of 3 trained psychiatrist-raters. (Participants were labeled as lacking capacity when at least 2 of 3 psychiatrists made the determination; thus, a MAcCAT-CR score ≤ 20 indicated a lack of decisional capacity within their study population). Most other instruments fall short in at least some of these regards.

However, other instruments may be preferable in screening participants for inclusion in a study because they are simpler and more directly relevant to the task at hand. For example, the University of California San Diego Brief Assessment of Capacity to Consent (UBACC)

consists of 10 items scored from 0 – 2; takes less than 5 minutes to administer; has a validated cut off score (14.5) and excellent inter-rater reliability; and its items refer to the particular research protocol being used in a study (Jeste et al. 2007). In contrast, the MacCAT-CR takes approximately 30 minutes to administer; lacks a cut-off score; and its items do not refer to the actual research protocol in question.

2. What are risk factors for incapacity to consent?—Many of the publications funded by grants on decisional capacity report on basic research on the neurocognitive deficits associated with schizophrenia and bipolar without directly assessing the relationship of these deficits to capacity to consent (Depp et al. 2008; Depp et al. 2007; Moore et al. 2006; Palmer et al. 2009; Palmer et al. 2010; Savla et al. 2011; Wilk et al. 2004). In what follows, we focus on the relationship of diagnoses to capacity to consent.

A series of studies indicate that a number of diagnoses correlate with MacCAT-CR scores that are significantly lower than those of healthy controls. These include schizophrenia (Candilis et al. 2008; Jeste et al. 2006; Palmer et al. 2005; Stiles et al. 2001); the mania associated with bipolar disorder even during periods of minimal symptoms (Depp et al. 2007; Palmer et al. 2007); intellectual disabilities (mental retardation) (C. B. Fisher et al. 2006); and Alzheimer's disease/mild cognitive impairments (Karlawish 2008; Rubright et al. 2010). In contrast, the depression typical of major depressive disorder appears not to present a significant risk of reduced capacity (Stiles et al. 2001), though Palmer found some decrease of scores on understanding correlated with depression among patients with bipolar (Palmer et al. 2007).

3. Do the diagnostic risk factors for incapacity to consent generally indicate that psychiatric patients cannot consent to research?—While the previous section identified some psychiatric diagnoses that present risk factors for incapacity to consent, data also support four important qualifications of this finding. To simplify presentation and focus on the largest data sets, we restrict our focus to the diagnosis of schizophrenia.

First, while the MacCAT-CR scores of people with schizophrenia are often lower than those of healthy controls, several studies found that their mean scores were, in the judgment of experts, nevertheless adequate to consent to a research study (Dunn 2006; Jeste et al. 2006; Saks et al. 2006).

Second, groups of individuals sharing a diagnosis are far from homogeneous. Standard deviations on the MacCAT-CR are often fairly large, and while many participants do not manifest capacity to consent, most do (Candilis et al. 2008; Dunn et al. 2007; Jefferson et al. 2008; Jeste et al. 2006).

Third, the risk factors for decisional incapacity associated with the psychiatric diagnoses listed above may be no greater than those associated with several medical conditions (Basso et al. 2010; Luebbert et al. 2008).

Fourth, Palmer et al. (2005), Palmer and Savla (2007), and Dunn (2006) report that negative symptoms (such as short term memory deficits) are more predictive of incapacity to consent than positive symptoms (such as delusional beliefs or hallucinations). Thus, someone could have persistent delusional beliefs associated with a psychotic disorder and retain decisional capacity because these beliefs are not relevant to understanding and evaluating the research protocol in question.

4. How can we enhance capacity to consent?—Several studies have attempted to improve the outcomes of consent processes, focusing above all on participants'

understanding of consent information. The only intervention that has been repeatedly and consistently found to enhance participant understanding and appreciation of consent information is an iterative approach to the consent process. This involves presenting information, assessing an individual's understanding and appreciation, and then discussing material that appears to be poorly understood or appreciated (Dunn 2006; Mittal et al. 2007; Moser et al. 2006; Palmer et al. 2007; Stiles et al. 2001). Rubright et al (2010) confirmed that a one-page summary of information can usefully supplement such an iterative approach with participants with mild cognitive impairments.

Several studies have also evaluated the presentation of information using alternative media (e.g., videos or slide presentations) rather than standard consent forms. The results of such studies have been mixed (Jeste et al. 2008; Mittal et al. 2007). In contrast to an earlier review by Flory and Emanuel (2004), a review by Jeste (2008) found many positive outcomes. However, these outcomes were frequently participant satisfaction rather than participant understanding and appreciation of information (Henry et al. 2009; Jimison et al. 1998). Moreover, they typically compared the media intervention only to standard consent processes rather than the iterative approaches that have been demonstrated to be effective at improving understanding and appreciation of consent information as well as effective in terms of cost. Nevertheless, in a randomized trial, use of a DVD yielded better outcomes measured by the UBACC and MacCAT-CR than standard consent forms (Jeste et al. 2009).

5. What should we do when patients lose the capacity to consent?—When patients lose the capacity to consent to clinical research, few options exist. Patients may be routinely excluded from research participation. Some states allow proxies to make decisions regarding research participation, and some allow the use of research advanced directives.

Stocking et al. (2006), Kim et al. (2005), Kim et al. (2009) and Karlawish et al. (2009) found that most patients with dementia (83%–96%) are willing to cede participation decisions to a proxy. However, some data indicate that proxies frequently make different decisions regarding research participation than patients would (Stocking et al. 2006).

Stocking et al. (2007) found that research advanced directives do not achieve all of their intended goals. They found that the directives failed to affect enrollment rates or facilitate the decisions of proxies.

Structured interviews with nationally-known experts on dementia and research ethics, dementia researchers, and dementia caregivers and advocates found unanimously that the dissent (refusal to participate) of dementia patients should be binding if it is unequivocal or sustained after an effort to relieve concerns; and near unanimity that assent should be required whenever an individual has the ability to assent (some were unsure regarding observation-only studies—that is, they might not require assent for such minimal risk studies) (Black et al. 2010). Kim et al. (2010) found that a deliberative democracy process with family members and surrogate decision- makers for patients with Alzheimer's disease produced more favorable attitudes toward family decision making regarding research participation.

Of five protections offered in research—confidentiality protection, IRB review, Data and Safety Monitoring Board (DSMB) review, informed consent, and surrogate decision makers —surrogates were rated lowest by participants with schizophrenia in terms of protectiveness and influence on their willingness to participate (Roberts et al. 2004a).

6. Why do participants enroll in research and is consent adequately voluntary?—Roberts et al. (2006e) and Roberts et al. (2006c) found generally positive

views toward research and high levels of willingness to volunteer, with participants endorsing strongly the exercise of autonomy and altruism as motives. Candilis et al. (2006) found that nearly two-thirds of participants expressed willingness to participate in a hypothetical drug trial. Among those willing, altruism was the most commonly endorsed motive (80%). However, many of these participants (50%) also evidenced the so-called therapeutic misconception, seeking health benefits from participation.

Depp and Lebowitz (2007) reviewed three mental health clinical trials that used an effectiveness/public health study design rather than the traditional efficacy design. Effectiveness designs involve less homogenous study populations, non-academic settings, and allow participants and clinicians to influence dosing and even assignment to study arms. The purpose is to increase the generalizability of research by better resembling real, post-trial treatment conditions. Adherence to the intervention is typically treated as an outcome rather than a variable to control. The authors argue that the benefits of effectiveness designs are significant and outcomes of the three studies reviewed justify further use of these models, in part because they better meet the needs of participants and thereby enhance retention and adherence to protocols.

Roberts et al. (2004b) interviewed participants with schizophrenia who were already enrolled in research study. Eighteen percent felt pressured by doctors or nurses to enroll in the study, with a mean rating of 2.21 out of 5 on the degree of pressure felt. Women reported feeling more pressure than men. Dugosh et al. (2010) developed a measure of perceived coercion to enroll in a study for criminally involved substance abusers. They found that many participants felt they could not say “no” to entering the study (14%) and many more felt it would help their court case (51%).

Roberts et al. (2002) found participants reported that payments would increase their likelihood of joining a study. The influence was rated very high for a blood draw study and low for a placebo-controlled medication trial. (A recommendation of the trial by their physician ranked as high or higher than payments across all study types.) Participants with schizophrenia have also reported that they would require more significant payments for studies involving greater risk (Dunn et al. 2009).

In a series of studies, Festinger and colleagues learned that cash payments to drug users are not associated with new drug use or perceived coercion but rather with better study retention with less effort (Croft et al. 2007; Festinger et al. 2005; Festinger et al. 2008).

Festinger et al. (2009) discovered that cash payments for correct answers on a test assessing knowledge of consent information significantly increased recall of consent information. Whereas most studies have assumed that the manner of presentation of information or the cognitive capacity of participants were the determining factors in tests of understanding, this study demonstrates that motivation (e.g., financial incentives) may play a significant role.

7. What are the primary risks in research participation and how are they viewed by participants and researchers?—Avila et al. (2001) reviewed 655 challenge studies, that is, studies that intentionally seek to provoke psychiatric symptoms in order to understand their etiology and sequelae. They found that challenge studies are common in medical and psychiatric research, and the purpose and procedures are similar in both domains. Given the similarities, the authors question why challenge studies in psychiatry attract increased ethical review and oversight.

Kim (2003) reviewed data on the benefits and burdens of exposing psychiatric research participants to placebos. Use of placebo in antidepressant and antipsychotic trials is not

related to increased mortality by suicide. However, direct data on long-term effects are lacking, and only minimal data exist on participants' perspectives and experiences with placebos

Moser (2005) observed that during medication-free schizophrenia clinical trials participants' ability to reason decreases significantly. Thus, while medication-free research may not lead to increased mortality by suicide, it may have some harmful side effects.

Kim and Holloway (2003) modeled the impact of enrolling in an 8-week placebo-controlled clinical trial versus individualized psychiatric treatment for a patient with moderate depression, low risk of suicide, no comorbid conditions and no health insurance. They estimated that the participant in a clinical trial would have a chance of treatment response 25% lower than in individualized treatment. In 2003, an uninsured participant could expect to save $164 for every 10% of response sacrificed by entering a clinical trial.

Roberts et al. (2006d) surveyed patients with schizophrenia and psychiatrists to determine how they rated the risk level of 12 different research procedures. Both groups rated 4 procedures as posing risk greater than those encountered in daily living: psychotic symptom induction, medication discontinuation for 2 weeks, giving a new experimental medication, and a spinal tap. Ratings of patients and psychiatrists were congruous (i.e., not statistically different).

Roberts et al. (2003b) found that both psychiatrists and patients with schizophrenia characterized as "moderately harmful" a psychopharmacological trial that involved a "wash out" period leading to re-emergence of serious symptoms. Participants indicated a relatively low likelihood of willingness to participate in such a trial; but indicated that the likelihood would be increased by both payments and the recommendation of their treating physician. Similarly, Roberts et al. (2006b) found that willingness to participate in a study was inversely related to the perceived level of risk posed by the study. Both of these findings—that risks decrease and payments increase willingness to participate—were confirmed by Dunn et al. (2009).

Kim et al. (2006) found that psychiatrists require that participants demonstrate a higher level of capacity to consent to enroll in a higher risk than a lower risk study.

Prentice et al. (2005) defined optimistic bias as the belief that one is less likely than others to experience adverse events in a research study, a bias that could adversely affect the quality of decisions to enroll in a study. They found that participants with schizophrenia exhibited lower levels of optimistic bias than healthy comparison participants.

8. What justice concerns do participants have?—In a series of interviews with 100 ethnically diverse and economically disadvantaged drug users, Fisher (2010) and Oransky et al. (2009) learned that participants had a variety of concerns about matters of social justice with nonintervention studies on HIV risk. These included fears of stigma and legal troubles and concerns that they would receive fair payment for their participation—balanced by a concern that these payments could be coercive. They also found high levels of skepticism among participants about the truthfulness of researchers. Fisher (2010) found that an educational session on HIV vaccine trials with participants yielded significantly increased levels of trust in researchers to disclose the risks of research; however, most participants remained doubtful that drug company funded research would be reported honestly (77%), and most believed that researchers find it more acceptable to use drug addicts as guinea pigs for HIV vaccine trials than people who are better off (73%).

9. How do IRBs handle mental health research protocols?—Luebbert et al. (2008) observed that IRB members are significantly more likely to view psychiatric research participants as being more vulnerable to coercion and having less decisional capacity than research participants with medical diagnoses even when the severity of the latter's illnesses was likely to engender cognitive comorbidities. The authors were critical of the tendency to overinflate the vulnerabilities of psychiatric patients while underestimating the vulnerabilities of medical patients. In this regard, IRB members' attitudes resembled those of the general public as found by Muroff et al. (2006). In a survey of 3140 adults in the US, respondents were less supportive of psychiatric research than general medical research primarily due to concerns about decisional capacity.

It is important that IRBs have the scientific and community expertise necessary to review protocols. Catania et al. (2008) learned that 95% of IRBs that regularly review mental health research protocols have one or more mental health experts on their committees. But further research is needed to determine the specific expertise they possess (e.g., clinical vs. research expertise) and whether community representatives adequately include mental health service users or those familiar with the concerns of service users.

Discussion

This article reviewed the content of publications emerging from the 43 grants that the NIH funded from 1987–2011 in the area of psychiatric research ethics. At least five conclusions can be drawn from the review.

First, many important things have been learned about the ethics of psychiatric research. For example, participants frequently retain capacity to consent even in the face of positive symptoms associated with serious mental disorders; understanding of consent information can be enhanced through iterative consent processes; and cash payments to drug users are not associated with new drug use or perceived coercion but rather with better study retention with less effort. These data will be useful to researchers, IRBs, and participants, and much of it can be used to fight stereotyping and prejudice against individuals with psychiatrics illnesses.

Second, surprisingly few studies used qualitative methods, and very few of the PIs are sociologists or ethnographers. This is somewhat surprising given that so many aspects of ethics are subjective (e.g., what we consider beneficial, private, or stigmatizing) and socially complex (e.g., influenced by religion, culture, education, and context). Mental health service users have criticized this focus on "objective," quantitative data to the neglect of more qualitative data on themes that are difficult to quantify but are important to those with psychiatric illnesses (Campbell 2009; Del Vecchio and Blyler 2009).

Third, there has been a greater focus upon participants with schizophrenia than with other diagnoses. Forty-seven percent of publications in our review focused on individuals with schizophrenia. This may be due to convenience (the individuals to whom psychiatric researchers have access) or to the fact that most studies focus upon matters of consent and schizophrenia poses a potential threat to decisional capacity. In either case, it would be beneficial to focus upon new populations—including people with depression, Post-traumatic Stress Disorder (PTSD), bipolar disorder, and anxiety disorders, which combined affect millions throughout the world—to expand understanding of psychiatric illnesses and avoid stigmatizing people with schizophrenia.

Fourth, some agencies have not sponsored any research on matters of ethics in research involving participants with psychiatric diagnoses—even when their research focus would

make this reasonable. Given that psychiatric disorders may manifest in childhood and that they may have a strong genetic component, we expected that NICHD and NHGRI would have funded some projects in these areas. This may be due to the funding priorities of the agencies or to a lack of competitive investigators seeking funding for such projects.

Fifth, many important topics have not been addressed adequately (or at all) and some of these may be the topics of most interest to mental health service users. Very few studies addressed matters of benefits or justice in research; no studies examined matters of privacy or professionalism (e.g., conflicts of interest) in psychiatric research. Rather, *77 percent of publications addressed informed consent in research—most of these (61%) focused on decisional capacity*. As noted in the first point above, this research has been valuable—for researchers, IRBs, and participants alike. Moreover, Roberts et al. (2000) found that psychiatric patients and psychiatric researchers agreed that voluntariness and capacity should be viewed as significant factors in determining whether and how individuals are allowed to participate in research. However, the disproportionate number of research projects on capacity to consent may reinforce outdated assumptions about the relationship between mental disorders and decisional capacity, and they divert resources from the study of topics that may be of greater importance to service users.

In the introduction we noted the shift from theoretical speculation to evidence-based practices in psychiatry and even in the ethics of psychiatric research. It is important to recall that research is just one of several ways of generating a sense of understanding of mental disorders. Various cultures, religions, and literary works of art have engaged the subject of mental illness and produced very different pictures of phenomena such as schizophrenia. Above all, each individual living with a diagnosis will have a different perception of its origins, meaning, and implications. Some reject the notion of a diagnosis altogether, viewing it as the byproduct of contemporary medical culture more than a trait of the individual (Pilgrim 2007).

Describing the attitudes of many mental health service users, Campbell (2009) writes:

> They view the focus on evidence-based practices as paternalistic, following a ‘top-down’ medical model that is not congruent with the recovery vision articulated by users. Most evidence-based research supports the status quo because it looks at recovery through the lens of symptoms, recidivism, and treatment outcomes and not the promotion of wellness outcomes such as empowerment, self-efficacy, meaning in life, and hope (Marzilli 2002). (Campbell 2009, 114)

We know that service users frequently have different priorities for psychiatric research than do many psychiatric researchers. For example, the top 3 priorities articulated by NIMH in 2007 included:

- Integrative science of brain and behavior science
- Diagnostic tests and biomarkers
- Genetic and environmental risk architecture (National Institute of Mental Health 2007)

In contrast, service users frequently prioritize research on:

- Alternative treatment approaches (such as nutrition or self-help)
- Undesirable side-effects of treatment and iatrogenic harms
- Qualitative research on consumer needs, involuntary treatment, cultural issues, etc (Campbell et al. 1993; Del Vecchio and Blyler 2009)

We have reason to believe that a similar discrepancy may exist regarding priorities for research on matters of psychiatric research ethics. In focus groups with mental health service users, DuBois and Campbell observed that consumers frequently articulated concerns with:

- The privacy and confidentiality of medical records and research data
- Effects of washout studies (abrupt withdrawal from medications either to provoke symptoms or establish a medication-free baseline for research purposes)
- Stigma and disrespectful treatment
- Inadequate payments for time (DuBois 2008; DuBois and Campbell 2006)

This discrepancy in priorities is somewhat speculative given a relative paucity of research on the priorities of service users; however, this very paucity is simultaneously an indication of the problem hypothesized.

This review has limitations. It was not comprehensive, but rather focused upon NIH-funded research. Foundations, particularly the National Alliance for Research on Schizophrenia and Depression (NARSAD) and the MacArthur Foundation, have funded many important projects; some leading researchers have been funded primarily through such foundations.[2] Moreover, this review did not aim to address the quality of the published research, as would a Cochrane's review.

Nevertheless, this review clearly indicates that we need to expand the range of research questions investigated to include matters of benefits, justice, and privacy in research, as well as the methods used to ensure that rich qualitative data are gathered on the subjective experiences of participants. Doing so will yield rich data of interest not only to IRBs, researchers, and ethicists, but above all to service users who are most deeply affected by psychiatric research.

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Table 1

Number of Grants Funded within Topic Areas by Institute and Overall*

	NIMH	NIDA	NINDS	NCRR	NIA	NICHD	NHGRI	SAMHSA	NIAAA	Total
Informed Consent: Comprehension and Decisional Capacity	19	2	1	0	7	1	0	0	0	30
Informed Consent: Voluntariness and Willingness to Participate	1	2	0	1	0	0	0	0	0	4
Benefits	0	0	0	0	0	0	0	0	0	0
Risks and Harms	1	1	0	0	0	0	0	0	0	2
Social and Distributive Justice	0	0	0	1	0	0	0	0	0	1
Privacy and Confidentiality	1	1	0	0	0	0	0	0	0	2
Conflicts of Interest / Other Professionalism	0	0	0	0	0	0	0	0	0	0
Ethical Processes and IRB Review	2	2	0	0	0	0	0	0	0	4
GRAND TOTAL	**24**	**8**	**1**	**2**	**7**	**1**	**0**	**0**	**0**	**43**

*Grants were assigned to a topic using their Project Summaries found in RePORTER rather than the topics represented in the publications citing the grant number. These frequently differed.

Table 2

Grants Meeting Inclusion Criteria (N=43)

PI	Grant Title	Grant #
Black, B	Assent and Dissent in Dementia Research	R21AG030036
Black, B	Ethical Aspects of Dementia Research	K01AG021091
Bogart, C	Confidentiality Intervention: Effects on Collaboration	R03MH061031
Candilis, P	Competence of Human Subjects to Consent to Research	K01MH001851
Carpenter, W	Research Ethics in Schizophrenia	R01MH058898
Catania, J	IRBs and Ethical Issues in Psychiatric Research	R01MH064696
Coors, M	Ethical Issues in Broad Data Sharing for Addiction Research: Best Research Practices	R01DA029258
Dunn, L	Proxy Decision Making for Alzheimer Disease Research	R01AG027986
Dunn, L	Enhancing Informed Consent in Late-Life Psychosis	K23MH066062
Festinger, D	Improving the Ethics of Consent in Drug Abuse Research	R01DA016730
Festinger, D	Ethics of Participant Payment in Drug Abuse Research	R01DA013408
Festinger, D	Contingency Management for Cocaine Dependence: Cash vs. Vouchers	R01DA021621
Fisher, CB	Participant Perspectives on Drug Use/HIV Research Ethics	R01DA015649
Fisher, CB	Consent Capacity of Adults with Mental Retardation	R01HD039332
Fisher, CB	Ethical Challenges for Research Extenders Responsible for the Integrity of Community Research	R21RR026302
Fisher, J	Informed Consent in Private Sector Mental Health Research	F31MH070222
Jeste, D	DVD Consent for Research in Older Schizophrenia Patients	R01MH067902
Jimison, H	Multimedia Tool for Enhancing Informed Consent Process	R41MH057175
Johnson, M	Evidence-Based Ethics and Mental Health Research with Prisoners	R01MH082872
Johnson, M	HIV, Drugs, and Prisoners: Barriers to Epidemiologic and Intervention Research	R01DA020357
Karlawish, J	Consent Methods and Participation in Geriatric Clinical Research	R01MH071643
Karlawish, J	Improving Informed Consent in Alzheimer Disease Research	R01AG020627
Kim, S	Ethics of Surrogate Consent for Dementia Research	R01AG029550
Kim, S	Capacity to Appoint a Proxy for Research Consent	R01MH0750230
Kim, S	Therapeutic Misconception and the Ethics of Sham Surgery Controls in PD Research	R01NS062770
Kim, S	Competence to Consent in Schizophrenia Research	K23MH064172
Koenig, B	Translating Addiction Genomics Research into Practice: Examining Ethics and Policy	R01DA014577
Lidz, C	Informed Consent and the Therapeutic Misconception	R01MH058097
McKay, M	Informed Consent in AIDS and Mental Health Research	R01MH058566
Mintz, J	Consenting to Psychiatric and Medical Treatment Research	R01MH058100
Moser, D	Informed Consent and Medication Status in Schizophrenia	R03MH064535
Palmer, B	Enhancing Consent for Alzheimer Research	R01AG028827
Palmer, B	Capacity to Consent to Research on Bipolar Disorder	R01MH064722
Roberts, L	Vulnerability and Informed Consent in Clinical Research	M01RR000997
Roberts, L	Ethics and Safeguards in Psychiatric Research	R01MH074080
Roberts, L	Psychiatric Research Ethics: Science and Safeguards	K02MH001918
Sachs, G	Dementia Research: Informed, Proxy, and advance consent	R01AG015317

PI	Grant Title	Grant #
Stanley, B	Informed Consent in Aged Psychiatric Patients	R01MH041734
Stanley, B	Psychotropic Drugs, Competency, and Commitment in Mentally Ill	R01MH041735
Stiles, P	Understanding Research Consent Disclosures	R03MH056346
Stone, H	Law and Ethics of Drug Addiction Genetics Research	R01DA020119
Tait, R	IRB Member Assessment of Decisional Capacity in Psychiatric and Medical Research	R01MH075958
Weinfurt, K	PREMIS: Preventive Misconception in HIV Prevention Trials	R21MH092253

Table 3

Publications by Topic from Grants Meeting Inclusion Criteria

Topic	#	Author/Date
Informed Consent: Comprehension and Decisional Capacity	47 (61%)	Black et al. 2008; Black et al. 2010; Candilis et al. 2008; Depp et al. 2008; Depp et al. 2007; Dunn, 2006; Dunn et al. 2006a; Dunn and Jeste 2003; Dunn et al. 2006b; Dunn et al. 2007; C. B. Fisher 2010; C. B. Fisher et al. 2006; C. B. Fisher et al. 2008; Henry et al. 2009; Jefferson et al. 2008; Jeste et al. 2006; Jeste et al. 2008; Jeste et al. 2007; Jeste et al. 2009; Jimison et al. 1998; Karlawish et al. 2009; Kim et al. 2007; Kim and Caine, 2002; Kim et al. 2002; Kim et al. 2009; Kim et al. 2005; Kim et al. 2010; Lidz and Appelbaum 2002; Lidz et al. 2004; Mittal et al. 2007; Moore et al. 2006; Moser et al. 2006; Moser et al. 2005; Palmer, 2006; Palmer et al. 2009; Palmer et al. 2005; Palmer et al. 2007; Palmer and Savla, 2007; Palmer et al. 2010; Rubright et al. 2010; Saks et al. 2006; Savla et al. 2011; Stiles et al. 2001; Stocking et al. 2006, 2007, 2008; Wilk et al. 2004
Informed Consent: Voluntariness and Willingness to Participate	12 (16%)	Candilis et al. 2006; Croft et al. 2007; Dugosh et al. 2010; Dunn et al. 2009; Festinger et al. 2009; Festinger et al. 2005; Festinger et al. 2008; Karlawish 2008; Roberts et al. 2004a; Roberts et al. 2006b; Roberts et al. 2002; Roberts et al. 2003b
Benefits	2 (3%)	Depp and Lebowitz 2007; Roberts et al. 2006c
Risks and Harms	11 (14%)	(Avila et al. 2001; Dunn et al. 2006c; Kim 2003; Kim et al. 2006; Kim and Holloway 2003; Muroff et al. 2006; Prentice et al. 2005; Roberts et al. 2006a; Roberts et al. 2006d; Roberts et al. 2006e; Roberts 2003b)
Social and Distributive Justice	1 (1%)	(Oransky et al. 2009)
Privacy and Confidentiality	0	
Conflicts of Interest / Other Professionalism	0	
Ethical Processes and IRB Review	2 (3%)	(Catania et al. 2008; Luebbert et al. 2008)
Review Articles / Surveys on Multiple Topics	2 (3%)	(Dunn et al. 2006a; Roberts et al. 2003a)
Total Publications	77	