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Introduction: Case Studies in the Ethics of Mental Health Research

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Abstract

This collection presents six case studies on the ethics of mental health research, written by scientific researchers and ethicists from around the world. We publish them here as a resource for teachers of research ethics and as a contribution to several ongoing ethical debates. Each consists of a description of a research study that was proposed or carried out and an in-depth analysis of the ethics of the study.

Keywords

Research ethics; international; case studies; mental health

Building Global Capacity in Mental Health Research

According to the World Health Organization (WHO), there are more than 450 million people with mental, neurological, or behavioral problems worldwide (WHO, 2005a). Mental health problems are estimated to account for 13% of the global burden of disease, principally from unipolar and bipolar depression, alcohol and substance-use disorders, schizophrenia, and dementia. Nevertheless, in many countries, mental health is accorded a low priority; for example, a 2005 WHO analysis found that nearly a third of low-income countries who reported a mental health budget spent less than 1% of their total health budget on mental health (WHO, 2005b).

Despite the high burden of disease and some partially effective treatments that can be implemented in countries with weaker healthcare delivery systems (Hyman et al., 2006), there exist substantial gaps in our knowledge of how to treat most mental health conditions. A 2007 *Lancet* Series entitled Global Mental Health claimed that the “rudimentary level of mental health-service research programmes in many nations also contributes to poor delivery of mental health care” (Jacob et al., 2007). Its recommendations for mental health research priorities included research into the effects of interactions between mental health

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and other health conditions (Prince et al., 2007), interventions for childhood developmental disabilities (Patel et al., 2007), cost-effectiveness analysis, the scaling up of effective interventions, and the development of interventions that can be delivered by nonspecialist health workers (Lancet Global Mental Health Group, 2007). All of these priorities require research in environments where the prevailing health problems and healthcare services match those of the populations the research will benefit, which suggests that research must take place all around the world. Similarly, many of the priorities identified by the Grand Challenges in Mental Health Initiative require focus on local environments, cultural factors, and the health systems of low- and middle-income countries. All the challenges "emphasize the need for global cooperation in the conduct of research" (Collins et al., 2011).

Notwithstanding the need for research that is sensitive to different social and economic contexts, the trend of outsourcing to medical research to developing countries shows no sign of abating (Thiers et al., 2008). Consequently, a substantial amount of mental health research will, in any case, take place in low- and middle-income countries, as well as rich countries, during the next few years.

The need for local research and the continuing increase in the international outsourcing of research imply that there is a pressing need to build the capacity to conduct good quality mental health research around the world. However, the expansion of worldwide capacity to conduct mental health research requires more than simply addressing low levels of funding for researchers and the imbalance between the resources available in rich and poor countries. People with mental health disorders are often thought to be particularly vulnerable subjects. This may be a product of problems related to their condition, such as where the condition reduces the capacity to make autonomous decisions. It may also result from social conditions because people with mental disorders are disproportionately likely to be poor, are frequently stigmatized as a result of their condition, and may be victims of human rights abuses (Weiss et al., 2001; WHO, 2005a). As a result, it is vitally important that the institutional resources and expertise are in place for ensuring that this research is carried out ethically.

Discussion at a special session at the 7th Global Forum on Bioethics in Research revealed the perception that many mental health researchers are not very interested in ethics and showed up a lack of ethics resources directly related to their work. This collection of case studies in the ethics of mental health research responds to that gap.

This collection comprises six case studies written by contributors from around the world (Table 1). Each describes a mental health research study that raised difficult ethical issues, provides background and analysis of those issues, and draws conclusions about the ethics of the study, including whether it was ethical as it stood and how it ought to be amended otherwise. Three of the case studies are written by scientists who took part in the research they analyzed. For these cases, we have asked scholars independent of the research to write short commentaries on them. It is valuable to hear how the researchers themselves grapple with the ethical issues they encounter, as well as to hear the views of people with more distance from the research enterprise. Some of the ethical issues raised here have not been discussed before in the bioethics literature; others are more common concerns that have not

received much attention in the context of international research. The case studies are intended to both expand academic discussion of some of the key questions related to research into mental health and for use in teaching ethics.

Case studies are an established teaching tool. Ethical analyses of such cases demonstrate the relevance of ethics to the actual practice of medical research and provide paradigmatic illustrations of the application of ethical principles to particular research situations. Concrete cases help generate and guide discussion and assist students who have trouble dealing with ethical concepts in abstraction. Through structured discussion, ethical development and decision-making skills can be enhanced. Moreover, outside of the teaching context, case study analyses provide a means to generate and focus debate on the relevant ethical issues, which can both highlight their importance and help academic discussion to advance.

People working in mental health research can benefit most from case studies that are specific to mental health. Even though, as outlined below, many of the same ethical problems arise in mental health research as elsewhere, the details of how they arise are important. For example, the nature of depression and the variation in effectiveness of antidepressive medication make a difference to how we should assess the ethics of placebo-controlled trials for new antidepressants. Moreover, seeing how familiar ethical principles are applied to one's own research specialty makes it easier to think about the ethics of one's own research. The cases in this collection highlight the commonalities and the variation in the ethical issues facing researchers in mental health around the world.

The current literature contains some other collections of ethics case studies that may be useful to mental health researchers. I note four important collections here, to which interested scholars may want to refer. Lavery et al.'s (2007) *Ethical Issues in International Bio-medical Research* provides in-depth analyses of ethically problematic research, mostly in low- and middle-income countries, although none of these cases involve mental health. Cash et al.'s (2009) *Casebook on Ethical Issues in International Health Research* also focuses on research in low- and middle-income countries, and several of the 64 short case descriptions focus on populations with mental health problems. Two further collections focus on mental health research, in particular. Dubois (2007) and colleagues developed short and longer US-based case studies for teaching as part of their “Ethics in Mental Health Research” training course. Finally, Hoagwood et al.'s (1996) book *Ethical Issues in Mental Health Research with Children and Adolescents* contains a casebook of 61 short case descriptions, including a few from outside the United States and Western Europe. For teachers and academics in search of more case studies, these existing collections should be very useful. Here, we expand on the available resources with six case studies from around the world with extended ethical analyses.

The remainder of this introduction provides an overview of some of the most important ethical issues that arise in mental health research and describes some of the more significant ethics guidance documents that apply.

Ethical Issues in Mental Health Research

The same principles can be applied in assessing the ethics of mental health research as to other research using human participants (Emanuel et al., 2000). Concerns about the social value of research, risks, informed consent, and the fair treatment of participants all still apply. This means that we can learn from the work done in other areas of human subjects research. However, specific research contexts make a difference to how the more general ethical principles should be applied to them. Different medical conditions may require distinctive research designs, different patient populations may need special protections, and different locations may require researchers to respond to study populations who are very poor and lack access to health care or to significant variations in regulatory systems. The ethical analysis of international mental health research therefore needs to be tailored to its particularities.

Each case study in this collection focuses on the particular ethical issues that are relevant to the research it analyzes. Nevertheless, some issues arise in multiple cases. For example, questions about informed consent arise in the context of research with stroke patients, with students, and with other vulnerable groups. To help the reader compare the treatment of an ethical issue across the different case studies, the ethical analyses use the same nine headings to delineate the issues they consider. These are social value, study design, study population, informed consent, risks and benefits, confidentiality, post-trial obligations, legal versus ethical obligations, and oversight.

Here, I focus on five of these ethical issues as they arise in the context of international mental health research: (1) study design, (2) study population, (3) risks and benefits, (4) informed consent, and (5) post-trial obligations. I close by mentioning some of the most important guidelines that pertain to mental health research.

Study Design

The scientific design of a research study determines what sort of data it can generate. For example, the decision about what to give participants in each arm of a controlled trial determines what interventions the trial compares and what questions about relative safety and efficacy it can answer. What data a study generates makes a difference to the ethics of the study because research that puts human beings at risk is ethically justified in terms of the social value of the knowledge it produces. It is widely believed that human subject research without any social value is unethical and that the greater the research risks to participants, the greater the social value of the research must be to compensate (Council for International Organizations of Medical Sciences [CIOMS], 2002; World Medical Association, 2008). However, changing the scientific design of a study frequently changes what happens to research participants, too. For example, giving a control group in a treatment trial an existing effective treatment rather than placebo makes it more likely that their condition will improve but may expose them to adverse effects they would not otherwise experience. Therefore, questions of scientific design can be ethically very complex because different possible designs are compared both in terms of the useful knowledge they may generate and their potential impact on participants.

One of the more controversial questions of scientific design concerns the standard of care that is offered to participants in controlled trials. Some commentators argue that research that tests therapeutic interventions is only permissible if there is equipoise concerning the relative merits of the treatments being compared, that is, there are not good reasons to think that participants in any arm of the trial are receiving inferior treatment (Joffe and Truog, 2008). If there is not equipoise, the argument goes, then physician-researchers will be breaching their duty to give their patients the best possible care (Freedman, 1987).

The Bucharest Early Intervention Project (BEIP) described in the case study by Charles Zeanah was a randomized controlled trial comparing foster care with institutional care in Bucharest, Romania. When designing the BEIP, the researchers wrestled with the issue of whether there was genuine equipoise regarding the relative merits of institutional and foster care. One interpretation of equipoise is that it exists when the professional community has not reached consensus about the better treatment (Freedman, 1987). Childcare professionals in the United States were confident that foster care was superior, but there was no such confidence in Romania, where institutional care was the norm. Which, then, was the relevant professional community?

The equipoise requirement is justified by reference to the role morality of physicians: for a physician to give her patient treatment that she knows to be inferior would violate principles of therapeutic beneficence and nonmaleficence. As a result, the equipoise requirement has been criticized for conflating the ethics of the physician-patient relationship with the ethics of the researcher-participant relationship (Miller and Brody, 2003). According to Miller and Brody (2003), provided that other ethical requirements are met, including an honest null hypothesis, it is not unethical to assign participants to receive treatment regimens known to be inferior to the existing standard of care.

A subset of trial designs that violate equipoise are placebo-controlled trials of experimental treatments for conditions for which proven effective treatments already exist. Here, there is not equipoise because some participants will be assigned to placebo treatment, and ex hypothesi there already exists treatment that is superior to placebo. Even if we accept Miller and Brody's (2003) argument and reject the equipoise requirement, there remain concerns about these placebo-controlled trials. Providing participants with less effective treatment than they could get outside of the trial constitutes a research risk because trial participation makes them worse off. Moreover, on the face of it, a placebo-controlled trial of a novel treatment of a condition will not answer the most important scientific question about the treatment that clinicians are interested in: is this new treatment better than the old one? Consequently, in situations where there already exists a standard treatment of a condition, it has generally been considered unethical to use a placebo control when testing a new treatment, rather than using the standard treatment as an active-control (World Medical Association, 2008).

Some psychiatric research provides scientific reasons to question a blanket prohibition on placebo-controlled trials when an effective intervention exists. For example, it is not unusual for antidepressive drugs to fail to show superiority to placebo in any given trial. This means that active-control trials may seem to show that an experimental drug is equivalent in

effectiveness to the current standard treatment, when the explanation for their equivalence may, in fact, be that neither was better than placebo. Increasing the power of an active-control trial sufficiently to rule out this possibility may require an impractically large number of subjects and will, in any case, put a greater number of subjects at risk (Carpenter et al., 2003; Miller, 2000). A 2005 trial of risperidone for acute mania conducted in India (Khanna et al., 2005) was criticized for unnecessarily exposing subjects to risk (Basil et al., 2006; Murtagh and Murphy, 2006; Srinivasan et al., 2006). The investigators' response to criticisms adopted exactly the line of argument just described:

> A placebo group was included because patients with mania generally show a high and variable placebo response, making it difficult to identify their responses to an active medication. Placebo-controlled trials are valuable in that they expose the fewest patients to potentially ineffective treatments. In addition, inclusion of a placebo arm allows a valid evaluation of adverse events attributable to treatment v. those independent of treatment. (Khanna et al., 2006)

Concerns about the standard of care given to research participants are exacerbated in trials in developing countries, like India, where research participants may not have access to treatment independent of the study. In such cases, potential participants may have no real choice but to join a placebo-controlled trial, for example, because that is the only way they have a chance to receive treatment. In the Indian risperidone trial, the issue of exploitation is particularly stark because it seemed to some that participants were getting less than the international best standard of care, in order that a pharmaceutical company could gather data that was unlikely to benefit many Indian patients.

This is just one way in which trial design may present ethically troubling risks to participants. Other potentially difficult designs include washout studies, in which participants discontinue use of their medication, and challenge studies, in which psychiatric symptoms are experimentally induced (Miller and Rosenstein, 1997). In both cases, the welfare of participants may seem to be endangered (Zipursky, 1999). A variant on the standard placebo-controlled trial design is the withdrawal design, in which everyone starts the trial on medication, the people who respond to the medication are then selected for randomization, and then half of those people are randomized to placebo. This design was used by a Japanese research team to assess the effectiveness of sertraline for depression, as described by Shimon Tashiro and colleagues in this collection. The researchers regarded this design as more likely to benefit the participants because for legal reasons, sertraline was being tested in Japan despite its proven effectiveness in non-Japanese populations. Tashiro and colleagues analyze how the risks and benefits of a withdrawal design compare with those of standard placebo-controlled trials and consider whether the special regulatory context of Japan makes a difference.

Study Population

The choice of study population implicates considerations of justice. The Belmont Report, which lays out the ethical foundations for the United States system for ethical review of human subject research, says:

> Individual justice in the selection of subjects would require that researchers … should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978)

Two distinct considerations are highlighted here. The first ("individual justice") requires that the researchers treat people equally. Morally irrelevant differences between people should not be the basis for deciding whom to enroll in research. For example, it would normally be unjust to exclude women from a phase 3 trial of a novel treatment of early-stage Alzheimer disease, given that they are an affected group. Some differences are not morally irrelevant, however. In particular, there may be scientific reasons for choosing one possible research population over another, and there may be risk-related reasons for excluding certain groups. For example, a functional magnetic resonance imaging study in healthy volunteers to examine the acute effects of an antianxiety medication might reasonably exclude left-handed people because their brain structure is different from that of right-handed people, and a study of mood that required participants to forego medication could justifiably exclude people with severe depression or suicidal ideation.

The second consideration requires that we consider how the research is likely to impact "social justice." Social justice refers to the way in which social institutions distribute goods, like property, education, and health care. This may apply to justice within a state (Rawls, 1971) or to global justice (Beitz, 1973). In general, research will negatively affect social justice when it increases inequality, for example, by making people who are already badly off even worse off. The quotation from the Belmont Report above suggests one way in which research might violate a requirement of social justice: people who are already badly off might be asked to participate in research and so be made worse off. For example, a study examining changes in the brain caused by alcohol abuse that primarily enrolled homeless alcoholics from a shelter near the study clinic might only put at further risk this group who are already very badly off. An alternative way in which research can promote justice or injustice is through its results. Research that leads to the development of expensive new attention deficit hyperactivity disorder medication is likely to do little, if anything, to make the world more just. Research on how to improve the cognitive development of orphaned children in poor environments (like the BEIP) is much more likely to improve social justice.

This last point suggests a further concern about fairness—exploitation—that frequently arises in the context of international collaborative research in developing countries. Exploitation occurs, roughly, when one party takes "unfair advantage" of the vulnerability of another. This means that the first party benefits from the interaction and does so to an unfair extent (Wertheimer, 1996). These conditions may be met in international collaborative research when the burdens of research fall disproportionately on people and institutions in developing countries, but the benefits of research, such as access to new treatments, accrue to people in richer countries. A number of case studies in this collection

raise this concern in one way or another. For example, Virginia Rodriguez analyzes a proposed study of the genetic basis of antisocial personality disorder run by US researchers but carried out at sites in several Latin American countries. One of the central objections raised by one of the local national research ethics committees with regard to this study was that there appeared to be few, if any, benefits for patients and researchers in the host country.

Risks and Benefits

Almost all research poses some risk of harm to participants. Participants in mental health research may be particularly susceptible to risk in several ways. First, and most obviously, they may be physically or psychologically harmed as a result of trial participation. For example, an intervention study of an experimental antipsychotic may result in some serious adverse effects for participants who take the drug. Less obvious but still very important are the potential effects of stopping medication. As mentioned above, some trials of psychoactive medications require that patients stop taking the medications that they were on before the trial (*e.g.*, the Japanese withdrawal trial). Stopping their medication can lead to relapse, to dangerous behavior (like attempted suicide), and could mean that their previous treatment regimen is less successful when they attempt to return to it. Participants who were successfully treated during a trial may have similar effects if they do not have access to treatment outside of the trial. This is much more likely to happen in research conducted with poor populations, such as the Indian mania patients.

The harms resulting directly from research-related interventions are not the only risk to participants in mental health research. Participation can also increase the risks of psychosocial harms, such as being identified by one's family or community as having a particular condition. Such breaches of confidentiality need not involve gross negligence on the part of researchers. The mere fact that someone regularly attends a clinic or sees a psychiatrist could be sufficient to suggest that they have a mental illness. In other research, the design makes confidentiality hard to maintain. For example, the genetic research described by Rodriguez involved soliciting the enrollment of the family members of people with antisocial personality disorder.

The harm from a breach of confidentiality is exacerbated when the condition studied or the study population is stigmatized. Both of these were true in the case Sana Loue describes in this collection. She studied the co-occurrence of severe mental illnesses and human immunodeficiency virus risk in African-American men who have sex with men. Not only was there shame attached to the conditions under study, such that they were euphemistically described in the advertisements for the research, but also many of the participants were men who had heterosexual public identities.

Informed Consent

Many people with mental disorders retain the capacity (ability) and competence (legal status) to give informed consent. Conversely, potential participants without mental problems may lack or lose capacity (and competence). Nevertheless, problems with the ability to consent remain particularly pressing with regard to mental health research. This is partly a

consequence of psychological conditions that reduce or remove the ability to give informed consent. To study these conditions, it may be necessary to use participants who have them, which means that alternative participants who can consent are, in principle, not available. This occurred in the study of South African stroke patients described by Anne Pope in this collection. The researcher she describes wanted to compare the effectiveness of exercises designed to help patients whose ability to communicate was compromised by their stroke. Given their communication difficulties and the underlying condition, there would inevitably be questions about their capacity. Whether it is permissible to enroll people who cannot give informed consent into a study depends on several factors, including the availability of alternative study populations, the levels of risk involved, and the possible benefits to participants in comparison with alternative health care they could receive.

In research that expects to enroll people with questionable capacity to consent, it is wise to institute procedures for assessing the capacity of prospective participants. There are two general strategies for making these assessments. The first is to conduct tests that measure the general cognitive abilities of the person being assessed, as an IQ test does. If she has the ability to perform these sorts of mental operations sufficiently well, it is assumed that she also has the ability to make autonomous decisions about research participation. A Mini-Mental State Examination might be used to make this sort of assessment (Kim and Caine, 2002). The second capacity assessment strategy focuses on a prospective participant's understanding and reasoning with regard to the specific research project they are deciding about. If she understands that project and what it implies for her and is capable of articulating her reasoning about it, then it is clear that she is capable of consenting to participation, independent of her more general capacities. This sort of assessment requires questions that are tailored to each specific research project and cannot be properly carried out unless the assessor is familiar with that research.

Where someone lacks the capacity to give consent, sometimes a proxy decision maker can agree to trial participation on her behalf. In general, proxy consent is not equivalent to individual consent: unless the proxy was expressly designated to make research decisions by the patient while capacitated, the proxy lacks the power to exercise the patient's rights. As a result, the enrollment of people who lack capacity is only acceptable when the research poses a low net risk to participants or holds out the prospect of benefiting them. When someone has not designated a proxy decision maker for research, it is common to allow the person who has the power to make decisions about her medical care also to make decisions about research participation. However, because medical care is directed at the benefit of the patient, but research generally is not aimed at the benefit of participants, the basis for this assumption is unclear. Its legal basis may be weak, too. For example, in her discussion of research on South African stroke patients, Pope notes the confusion surrounding the legality of surrogate decision makers, given that the South African constitution forbids proxy decision making for adults (unless they have court-appointed curators), but local and international guidance documents seem to assume it.

Although it is natural to think of the capacity to give consent as an all-or-nothing phenomenon, it may be better conceptualized as domain-specific. Someone may be able to make decisions about some areas of her life, but not others. This fits with assumptions that

many people make in everyday life. For example, a 10-year-old child may be deemed capable of deciding what clothes she will wear but may not be capable of deciding whether to visit the dentist. The capacity to consent may admit of degrees in another way, too. Someone may have diminished capacity to consent but still be able to make decisions about their lives if given the appropriate assistance. For example, a patient with mild dementia might not be capable of deciding on his own whether he should move in with a caregiver, but his memory lapses during decision making could be compensated for by having his son present to remind him of details relevant to the decision. The concept of supported decision making has been much discussed in the literature on disability; however, its application to consent to research has received little attention (Herr, 2003; United Nations, 2007).

The ability to give valid informed consent is the aspect of autonomy that is most frequently discussed in the context of mental health research, but it is not the only important aspect. Several of the case studies in this collection also raise issues of voluntariness and coercion. For example, Douglas Wassenaar and Nicole Mamotte describe a study in which professors enrolled their students, which raises the question of the vulnerability of student subjects to pressure. Here, there is both the possibility of explicit coercion and the possibility that students will feel pressure even from well-meaning researchers. For various reasons, including dependence on caregivers or healthcare professionals and the stigma of their conditions, people with mental illnesses can be particularly vulnerable to coercion.

Post-Trial Obligations

The obligations of health researchers extend past the end of their study. Participants'data remain in the hands of researchers after their active involvement in a study is over, and patients with chronic conditions who enroll in clinical trials may leave them still in need of treatment.

Ongoing confidentiality is particularly important when studying stigmatized populations (such as men who have sex with men as discussed by Sana Loue) or people with stigmatizing conditions (such as bipolar disorder). In research on mental illnesses, as with many medical conditions, it is now commonplace for researchers to collect biological specimens and phenotypic data from participants to use in future research (such as genome-wide association studies). Additional challenges with regard to confidentiality are raised by the collection of data and biological specimens for future research because confidentiality must then be guaranteed in a long period of time and frequently with different research groups making use of the samples.

Biobanking also generates some distinctive ethical problems of its own. One concerns how consent to the future use of biological specimens should be obtained. Can participants simply give away their samples for use in whatever future research may be proposed, or do they need to have some idea of what this research might involve in order to give valid consent? A second problem, which arises particularly in transnational research, concerns who should control the ongoing use of the biobank. Many researchers think that biological samples should not leave the country in which they were collected, and developing country researchers worry that they will not be allowed to do research on the biobanks that end up in

developed countries. This was another key concern with the proposed study in Latin America.

In international collaborative research, further questions arise as a result of the disparities between developing country participants and researchers and developed country sponsors and researchers. For example, when clinical trials test novel therapies, should successful therapies be made available after the trial? If they should, who is responsible for ensuring their provision, to whom should they be provided, and in what does providing them consist? In the case of chronic mental illnesses like depression or bipolar disorder, patient-participants may need maintenance treatment for the rest of their lives and may be at risk if treatment is stopped. This suggests that the question of what happens to them after the trial must at least be considered by those who sponsor and conduct the trial and the regulatory bodies that oversee it. Exactly on whom obligations fall remains a matter of debate (Millum, 2011).

Ethics Guidelines

A number of important policy documents are relevant to the ethics of research into mental disorders. The WMA's *Declaration of Helsinki* and the CIOMS' *Ethical Guidelines for Biomedical Research* both consider research on individuals whose capacity and/or competence to consent is impaired. They agree on three conditions: a) research on these people is justified only if it cannot be carried out on individuals who can give adequate informed consent, b) consent to such research should be obtained from a proxy representative, and c) the goal of such research should be the promotion of the health of the population that the research participants represent (Council for International Organizations of Medical Sciences, 2002; World Medical Association, 2008). In addition, with regard to individuals who are incapable of giving consent, Guideline 9 of CIOMS states that interventions that do not “hold out the prospect of direct benefit for the individual subject” should generally involve no more risk than their “routine medical or psychological examination.”

In 1998, the US National Bioethics Advisory Commission (NBAC) published a report entitled *Research Involving Persons with Mental Disorders That May Affect Decision-making Capacity* (National Bioethics Advisory Commission, 1998). As the title suggests, this report concentrates on issues related to the capacity or competence of research participants to give informed consent. Its recommendations are largely consistent with those made in the Declaration of Helsinki and CIOMS, although it is able to devote much more space to detailed policy questions (at least in the United States context). Two domains of more specific guidance are of particular interest. First, the NBAC report considers the conditions under which individuals who lack the capacity to consent may be enrolled in research posing different levels of risk and supplying different levels of expected benefits to participants. Second, it provides some analysis of who should be recognized as an appropriate proxy decision maker (or “legally authorized representative”) for participation in clinical trials.

Finally, the World Psychiatric Association's *Madrid Declaration* gives guidelines on the ethics of psychiatric practice. This declaration may have implications for what is permissible

in psychiatric research, insofar as the duties of psychiatrists as personal physicians are also duties of psychiatrists as medical researchers. It also briefly considers the ethics of psychiatric research, although it notes only the special vulnerability of psychiatric patients as a concern distinctive of mental health research (World Psychiatric Association, 2002).

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Table 1
Case Studies in the Ethics of Mental Health Research

Contributor	Case	Location	Central Issues
Douglas Wassenaar and Nicole Mamotte *Commentary* by Robert Michels *Commentary* by Samantha Copeland	The use of students as participants in mental health research: Eating disorders in developing countries	South Africa	Coercion, consent, researcher-participant relationship
Shimon Tashiro, Maki M. Yamada, and Kenji Matsui	Ethical issues of placebo-controlled studies in depression: The case of a randomized withdrawal trial in Japan	Japan	Comparative risks and benefits of different trial designs
Virginia Rodriguez	Genetic screening for antisocial personality disorder	Latin America	Fair subject selection, control of samples/data, capacity building
Anne Pope	Qualitative research with adult stroke patients	South Africa	Legal vagueness, capacity to consent
Charles H. Zeanah *Commentary* by Annette Rid	The Bucharest early intervention project: A randomized controlled trial comparing foster care and institutionalization	Romania	Fair subject selection, scientific value, equipoise, risk
Sana Loue *Commentary* by Douglas Brugge	The co-occurrence of bipolar disorder and human immunodeficiency virus risk among African-American men who have sex with men	United States	Stigma, confidentiality, community consultation, institutional review board review