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ORIGINAL PAPER

Ethical Practices and Legal Challenges in Mental Health Research

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Abstract

Considerations of justice and concern for well-being support conducting mental health research and addressing ethical concerns specific to mental health research are critical. We discuss these concerns, provide recommendations to enable the ethical conduct of mental health research, and argue that participants' interests should be given primary weight in resolving apparent dilemmas. We also comment on provisions of two legislative actions in India relevant to mental health research: Rights of Persons with Disability Act 2016 and the Mental Health Care Act 2017. Both conform to the 2006 United Nations Convention on Rights of Persons with Disabilities of which India is a signatory. Both provide protections and enumerate rights relevant to people with mental health conditions but with differing focus. The commonalities and differences between the three are discussed in the background of international literature on research in mental health conditions. Studies involving deception and future directions for ethical requirements regarding genetic research are discussed.

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Introduction

Conducting research on mental health conditions (MHCs) is ethically complicated, but of great clinical and indeed practical importance. Approximately 450 million people are likely to suffer from a mental or neurological disorder during their lifetime, across the world (World Health Organization 2013). The Indian National Mental Health Survey, 2015–2016 (Gururaj et al. 2016), estimated that among Indians above 18, prevalence of current "mental morbidity" was 10.6%. Although invisible, these conditions may be as debilitating and burdensome as serious somatic illnesses, compromising individuals' ability to flourish and affecting their families. Mental health conditions are among the most stigmatizing of diseases. There is heterogeneity in outcome for serious mental illnesses (psychoses) among different cultures: some Indian rural centers in a longitudinal study suggested better outcome than their western counterparts (Harrison et al. 2001). In Indian society, having a family member with an MHC marks out the individual and family, with resultant social and economic implications for both. Conducting mental health research is critical to understand and develop treatments (and preventive interventions) for MHCs to relieve the suffering they cause. Moreover, conducting mental health research is desirable from the perspective of equity with other disorders. Concern for patients' health and social well-being, as well as considerations of fairness, mandates a robust mental health research program in India.

Addressing ethical concerns specific to mental health research is critical. We discuss these concerns, provide recommendations to enable ethical conduct of mental health research, and also comment on provisions of two legislative actions in India relevant to mental health research: the Rights of Persons with Disability Act 2016 (RPWDA 2016) and the Mental Health Care Act 2017 (MHCA 2017). Both conform to the United Nations Convention on Rights of Persons with Disabilities (United Nations 2006) of which India is a signatory. Both laws provide protections and enumerate rights relevant to people with MHCs; for example, protections against exploitation, involuntary admission and treatment, and protection against prosecution for suicide (MHCA 2017). We focus on mental health research per se, rather than on the participation of people with MHCs in research on other disorders, although we recognize that the latter is necessary. People with mental health conditions are susceptible to physical disorders also and it is important to study them. We emphasize that those with MHCs should not be enrolled in studies of other health conditions merely as a convenience sample. There must be a sound scientific reason to enroll them in other research, especially if they are unable to provide informed consent. In addition, people with MHCs should not be excluded from research on other conditions just because of their MHC or the fact that special care must often be taken when enrolling them.

Ethical Overview: Mental Health, Vulnerability, and Special Protections

Like the *National Ethical Guidelines for Biomedical and Health Research Involving Human Participants* published by the Indian Council of Medical Research (ICMR 2017), we recognize that people with MHCs constitute a vulnerable population, which

warrants special safeguards when enrolling them in research. They may be especially vulnerable to burdens and harms associated with research participation for at least three reasons.

First, their conditions may impair their autonomy and decision-making ability, particularly their ability to act in their own interests. Second, their conditions may render them dependent on others for caregiving or result in their being institutionalized. Institutionalized individuals or individuals in states of extreme dependency may be (or may perceive themselves to be) subject to undue pressures. It is important to note, however, that many types of mental health research will involve also enrolling people without MHC, so-called "healthy controls." Third, because mental health conditions are stigmatizing conditions, individuals with these conditions may be especially vulnerable to harm of stigmatization and discrimination if their conditions become known. In Southeast Asian nations, especially in India, prejudice toward mentally ill people as being dangerous and aggressive is prevalent (Lauber and Rössler 2007; Mukherjee and Mukhopadhyay 2018; Zieger et al. 2016). In addition, factors such as religion and lower education are associated with a higher public desire for social distance from affected individuals and from their caregivers; there is also a perception that people with mental illness are unable to act in their own interests irrespective of their cognitive abilities (Zieger et al. 2016). Stigma is found to be higher in rural population than in urban population since the beginning as studied by Jadhav and others; they argued that rural population have punitive view and urban population has liberal view toward severe mental illness (Jadhav et al. 2007). In a recent stigma study in eight Asian countries, the causes of stigma were found to be similar across various nations (Kudva et al. 2020). In addition, some people with MHCs may experience additional vulnerabilities related to their age (e.g., children or the elderly), sex (e.g., female), or socioeconomic circumstances (e.g., poverty or illiteracy). The intersection of multiple sources of vulnerability may multiply the probability and magnitude of potential harm. Additionally, people, even healthy controls or mental health caregivers, may suffer stigmatization by virtue of enrolling in mental health research. Special protections must be observed during the recruitment and informed consent processes when enrolling people with MHCs, and special care must be taken to protect the privacy and confidentiality of those enrolled in mental health research. As discussed, research in mental conditions has several specific issues which need to be addressed, so researchers need to be specifically trained (Jain et al. 2017). The MHCA 2017 focuses mainly on the human rights of persons with mental illness but it is important for the lawmaker to account for the culture and newer scientific developments in the mental health field, and analyze the (un)met needs of the patients and families (Math et al. 2019).

Informed Consent

In research, the informed, voluntary consent of individual participants is required to respect the rights of individuals as self-determining persons and to enable them to protect their well-being. In order to be able to give their consent (or to refuse), people must have decisional capacity. Enrolling individuals with MHCs in research present special concerns about both the voluntariness of their decisions and their capacity to decide.

Voluntariness and the Situational Vulnerability of those with Mental Health Conditions

Although not all individuals with MHCs are dependent on others, those with more severe conditions are likely to be. Individuals with MHCs may be especially vulnerable to exploitation or to manipulation or undue pressure to participate in research and may be less able to protect themselves and to exercise their rights not to participate or to withdraw. They may feel intimidated and incapable of disagreeing with their caregivers, and thus may be subject to (at least perceived) undue pressure.

Therefore, special protections are appropriate when enrolling such individuals in research. Recommended protections include avoiding compensation-for-participation schemes that reward caregivers for encouraging the enrollment of their dependents and seeking the informed consent of dependent mentally ill individuals in the absence of their caregivers. Patients sometimes may not agree to use their tissue samples for new research, because they may have particular values or beliefs regarding particular types of research, for example about stem cell research, or research conducted by other research groups (Aalto-Setälä et al. 2009). Jesani (2009) in his commentary on ethics committees stated that Indian institutions, in the name of student research, asked patients to give written general consent saying that they have no objection to the use of their medical records—not only case papers but also all specimens of their body tissues and perhaps also X-rays, ultrasound scans, etc.—for use in any research. In another commentary, Desikan (2009) concluded that there is a scientific need to broaden the consent obtained. Research subjects, when well informed, have a right to participate even in broadly defined research giving blanket consent but they have the right to refuse consent at a later date.

Consent to participate in one aspect of a research project should not constitute consent to participate in all its aspects or procedures (such as interview, blood draw, or MRI). Rather, each part should be explained and separate consents obtained if it is likely that participants may have different values, beliefs, preferences, or concerns about the different procedures. Where appropriate, ethics committees can develop policies regarding "blanket consent" for use of samples in further studies, taking into account the local social and cultural norms, and the likely beliefs of persons with MHCs (Bhan 2010).

When institutionalized individuals with mental illness are asked to enroll in research, special care must be taken. In addition to the usual Institutional Ethics Committee (IEC) review of the research protocols, it may be advisable to require special review of research protocols seeking to enroll institutionalized individuals to ensure (a) that enrolling them is specifically pertinent to the study's research questions and is not merely a matter of convenience; (b) that it is genuinely possible for them to refuse to participate, and later to withdraw from the study, without any negative repercussions; and (c) that those being invited to enroll have decisional capacity to give informed consent (or to refuse). Mental illness does not mean that a person may not have decisional capacity, they have a right to participate or not participate in clinic or research (Lidz 2006; Deshpande et al. 2020). Their consent should be sought by investigators not affiliated with the institution and the process of investigators' seeking informed consent from residents of the institution should be overseen by a party neither affiliated with the research nor the institution. According to the MHCA 2017, if no such person is available to be appointed as a nominated representative, the Board shall

appoint the Director, Department of Social Welfare, or his designated representative, as the nominated representative of the person with mental illness.

If individuals are involuntarily institutionalized and lack decisional capacity, it is generally inappropriate for a surrogate to consent to research participation on their behalf because of the involuntary nature of the placement that gives rise to the recruitment attempt. Surrogate consent on behalf of those who lack the decision-making ability necessary to give informed consent or refusal may be a suspect because surrogates may have competing loyalties to the individual and to the institution. Moreover, the involuntary nature of the individuals' confinement prevents them from simply "walking away" from the research interventions or from expressing dissent with impunity. For these reasons, only if research participation presents the opportunity for substantial therapeutic benefit that is otherwise not available may a surrogate enroll them in research. Thus, involuntarily committed psychiatric patients should not be enrolled in research unless research participation presents them with the only prospect- and a substantial prospect-of therapeutic benefit. There are no specific provisions on research on mentally ill admitted in mental health institutions under the MHCA 2017. Families can be involved in the care of and research on these institutionalized persons, while safeguarding their rights. However, that may also invoke conflict of interest and therefore additional legislation must be drafted to safeguard their safety and rights. There should be explicit provisions to safeguard such persons while including them in research which has no therapeutic benefit. India does not have explicit provisions as yet since there is paucity of research in such issues.

Decisional Capacity and Informed Consent of those with a Mental Health Condition

Having decisional capacity is a prerequisite for being able to give informed consent (or informed refusal) regarding research participation. An individual's capacity to consent or refuse is specific to a particular decision (e.g., a specific invitation to participate in research). An individual may have capacity to make one decision (e.g., to choose what to eat), but not another (e.g., to choose whom to marry). Similarly, an individual may have the capacity to give informed consent/refusal to a study that is very simple to understand and that involves low risk, not be capable of consenting to a complex study involving greater degree of risk.

According to Stanford Encyclopedia of Philosophy (Charland 2015), and Buchanan and Brock (1989), having decisional capacity means or requires having four of five abilities: being able (1) to understand and (2) to reason and deliberate about the nature, procedures, risks, and potential benefits of research participation (Buchanan and Brock 1989) and the other elements of informed consent (Berg et al. 2001); (3) to appreciate these risks and potential benefits; (4) to weigh them in light of one's own set of stable values; and (5) to communicate a decision (Buchanan and Brock 1989). It is the responsibility of investigators to ensure that prospective participants have decisional capacity to give informed consent when they are asked to participate in research. Then, the informed consent discussion may proceed. Having a psychiatric diagnosis or MHC does not necessarily mean that one lacks the capacity to make decisions, as noted in the MHCA 2017. It is important to recognize the wide range of conditions that fall under the label "psychiatric condition": depression, bipolar disorder, schizophrenia, pica, general anxiety disorder, kleptomania—all of these, for example, are psychiatric

conditions; however, not all of them undermine the decisional capacity necessary to give informed consent. Decisional capacity-impairing symptoms of some psychiatric conditions can be effectively treated so that they can participate in informed consent discussions and make decisions about research participation. Further, the impairment of decisional capacity associated with many MHCs is a matter of degree. Individuals with some degree of decisional capacity impairment may still be capable of giving informed consent/refusal, particularly if the process of informed consent is modified to facilitate their understanding (Deshpande et al. 2020; Dunn and Roberts 2005; Tharyan 2009). Comprehending information on consent is but one part of "health literacy". It includes the "ability to understand health information well enough to know what to do", as well as the "ability to actively engage with healthcare providers" (Friis et al. 2016).

The specific requirements for disclosure during the informed consent discussion are detailed in the Indian Council of Medical Research (2017) Guidelines. Investigators are responsible to ensure that appropriate disclosure is made and to try to ensure that prospective participants understand what is disclosed, perhaps by asking participants to explain back to them what has been disclosed. Further, investigators must answer any questions raised by prospective participants. We shall consider in the next section to what extent the Indian legislation makes for adequate provision for decision making in the context of research, both by persons with MHCs and by any surrogate decision makers.

Surrogate Consent for Research Participation

In the context of clinical care, designed solely for the patient's benefit, when a patient's decision-making ability is impaired, informed consent for treatment must be sought from the patient's designated surrogate, next-of-kin, or legally authorized representative sometimes called a legally acceptable representative (World Medical Association 1964; 2009, clause 27, 29) or the "nominated representative" (NR) (MHCA 2017). Similarly, in research, a surrogate may be someone specifically designated by the person during a period when the person had decision-making capacity (Advance Directive, MHCA 2017), or may be the next-of-kin, a legally appointed/authorized representative (LAR), or nominated representative (NR). If not specifically designated by the person, the surrogate or LAR/NR may be a relative or friend of the person. While the RPWDA 2016 states that "no person with disability shall be a subject of any research without his or her free and informed consent obtained through accessible modes, means and formats of communication" the MHCA 2017 opens the door for enrolling individuals with MHCs who lack decisional capacity to provide their own informed consent. The MHCA 2017 provides some guidance regarding how a person may name his/her own nominated representative (NR), as well as how to proceed to identify and appoint an NR on a person's behalf if the person with a MHC has not done so him/herself and provides guidance for NRs regarding what they should consider when making healthcare decisions on the person's behalf. The duties of a NR include providing support to a person with a MHC so that the person him/herself can make the medical decisions.

The MHCA 2017 does not provide, however, for the NR alone to enroll in research, even research with potential therapeutic benefit for the individual, an individual with a MHC who lacks decisional capacity. Instead, it states that "in case of research

involving any psychological, physical, chemical or medicinal interventions to be conducted on person who is unable to give free and informed consent but does not resist participation in such research, permission to conduct such research shall be obtained from concerned State Authority" (Section 99.2). The State Authority may then allow the individual to be enrolled in the research study, if the NR provides (surrogate) informed consent, provided that the State Authority ascertains that: "(a) the proposed research cannot be performed on persons who are capable of giving free and informed consent" i.e., enrolling those with MHCs is not a mere matter of convenience but scientific necessity; "(b) the proposed research is necessary to promote the mental health of the population represented by the person; (c) the purpose of the proposed research is to obtain knowledge relevant to the particular mental health needs of persons with mental illness; and (d) a full disclosure of the interests of persons and organizations conducting the proposed research is made and there is no conflict of interest involved; and (e) the proposed research follows all the national and international guidelines and regulations concerning the conduct of such research and ethical approval has been obtained from the Institutional Ethics Committee where such research is to be conducted" (Section 99.3).

The MHCA 2017 and this article are thus in accord, and both concur with the US National Bioethics Advisory Commission (1998) Report that provided extensive consideration of these issues. In this regard, the MHCA 2017 seems to offer ethically relevant guidance to the State Authority. In contrast, the RPWDA 2016 not only requires that the research enrollee be capable of giving informed consent, but also that "prior permission of a Committee for Research on Disability" be obtained, and that this Committee be "constituted in the prescribed manner for the purpose by the appropriate Government in which not less than half of the Members shall themselves be either persons with disabilities or Members of the registered organization," without providing any guidance on how the Committee should evaluate the proposed research (RPWDA 2016, Section 6.2). The MHCA 2017 also has described that ethics approval is to be obtained for any research (section 99.1e). It has also mentioned that the proposed research must follow all the national and international guidelines and regulations concerning the conduct of such research.

The MHCA 2017, however, imposes a provision that may unduly impede mental health research. Because only the State Authority can permit a NR to provide consent for a person with a MHC to participate in the research (Duffy and Kelly 2019), many people may be excluded from research because it is unclear who will undertake the process of applying to the State Authority, Mental Health Review Board, or the Social Welfare Officer, to review the research and grant the NR permission to provide the necessary informed consent. We suggest that the Institutional Ethics Committee (IEC), which is the nodal Committee for research at the local level, should be tasked with appealing to the appropriate State Authority, and perhaps should be allowed the powers of review that the MHCA 2017 reserves for the State Authority. Given the size of Indian States and the administrative burdens faced by State Authorities, some allocation of this responsibility to IECs may be necessary to avoid, in effect, excluding people with MHCs from research when they cannot consent to enrollment themselves.

Thus, the MHCA 2017 seems to have fulfilled some but not all of what had been expected of it (Thippeswamy et al. 2012; Kar and Tiwari 2014). For example, it defines in the context of mental healthcare hitherto undefined terms, including "caregiver,"

"nominated representative," "consent," "support" for decision making, and "advance directive" for research. But it was open to criticism for "over-legalizing and complicating mental healthcare delivery" (Kar and Tiwari 2014).

It is important to recognize the reason for these special provisions—namely that in contrast to clinical care, research is not designed primarily for the benefit of research participants. Therefore, if those lacking decisional capacity who cannot exercise the right of informed consent to protect themselves are to be enrolled in research, then they must receive special protections when they are asked to enroll. This rule must be applied in designating a surrogate decision maker and when the surrogate makes the enrollment decision (Emanuel et al. 2000; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979). Some of these protections focus on the research study itself, others on the surrogate who makes decisions on the individual's behalf. Our view is that an appropriately trained ethics body—such as a nodal committee—is best placed to deliberate on and decide such delicate ethical issues.

Surrogate Decision Makers Appointed by the Person with a Mental Health Condition

Because many mental illnesses impair decision-making capacity only intermittently, in India, it is legally possible for a person with a MHC to identify a surrogate (Nominated Representative, MHCA 2017) in advance of a period of decision-making incapacity. When a surrogate has enrolled a participant, unable to consent of his or her own behalf, and s/he subsequently regains decision-making ability and is competent to give or refuse consent, re-consent must be sought from the participant (Indian Council of Medical Research 2017).

As recognized by the MHCA 2017, a person with a MHC may be able to express preferences regarding research participation—including the type of research in which he/she would be willing to participate, or views regarding a personally acceptable balance of risks and benefits—during periods of decision-making capacity. The surrogate should consider these preferences and views when deciding on the person's behalf, based upon the best understanding of what the person would have decided if competent to do so. Perhaps in some contexts and jurisdictions, a "research advance directive," modeled on an advance directive in the context of treatment preferences in the MHCA 2017, may be recognized as a valid way for a person to express preferences regarding research participation should s/he lose decision-making capacity in the future. Roberts and Kim conducted a study to evaluate whether preferences and decisions of mentally ill patients were aligned with and attuned to their chosen surrogates, and found that the preferences and decisions of the patient-surrogate pairs were quite similar. Thus, substituted judgment standard for decision making when employed by a surrogate protects the autonomy and well-being of the patient by best approximating what the patient would choose if competent to do so (Roberts and Kim 2016).

Within the following limits related to the risks and potential benefits of the study, and constrained by the individual's preferences, views, and values, the surrogate could make decisions regarding research participation on behalf of the person lacking decision-making capacity. These criteria are designed to ensure that no person lacking decision-making capacity is enrolled in a study that competent persons would refuse to enroll in and that the participation of such persons is truly necessary to attempt to achieve important knowledge that may provide substantial benefit to similarly situated individuals in the future (World Medical Association 1964; 2009).

First, if a study presents only minimal risk to participants, or if a study presents greater than minimal risk but offers the prospect of *direct* medical benefit to participants, a person lacking the capacity to consent could be enrolled in the study if the surrogate or LAR gives permission and the prospective participant does not dissent (World Medical Association 2009; clause 27, 28). Minimal risk research may be characterized as research in which the "probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" (Office for Human Research Protections 2009; Roberts et al. 2006). Direct benefits of research are understood to be benefits to the participant that result from receiving the study intervention (e.g., an experimental drug, a behavioral intervention under study). Direct benefits are contrasted with indirect benefits that result from mere participation in the study, such as a participant's feeling of increased self-worth or altruism, increased medical attention, or payment for participation.

Second, if a study presents greater than minimal risk and does not offer the prospect of direct medical benefit to participants, then both the surrogate and the IEC reviewing the study protocol should be exceedingly careful to ensure that it is absolutely necessary to enroll participants lacking decision-making capacity, that the research presents the possibility of substantial benefit to the population being studied, and that risks are reasonable in relation to this possible benefit. These criteria are designed to ensure that no person lacking decision-making capacity is enrolled in a study that competent persons would refuse to enroll in and that the participation of persons lacking decision-making capacity is truly necessary to attempt to achieve important knowledge that may provide substantial benefit to similarly situated individuals in the future (World Medical Association 2009).

Third, the dissent of any individual—including those lacking decisional capacity—must be respected. Any person's objection to research participation—whether informed or not, whether the result of competent decision making or not—must be respected. For example, the utterance of a patient with psychosis who says "no, no, no"—when asked to participate in research, or in response to research questions, or when being given an experimental intervention—should be respected as a valid refusal to participate. Similarly, a participant's physical resistance to study interventions should be regarded as an objection to participation and should be respected. If a surrogate has given permission for a participant to participate, but the participant refuses, objects, or dissents, the participant may be approached at a future time to learn whether he/she has had a change of mind. Care should be taken to ensure that this re-approaching cannot be construed as pressure to participate.

Finally, the surrogate should monitor the participant's participation in the study at all stages and be prepared to withdraw the participant from the study if conditions warrant withdrawal, for example, if the balance of risks and potential benefits changes, if adverse events arise that warrant withdrawal for the participant's protection, if other treatment options emerge that would promote the participant's welfare to a greater extent than study participation, or if other information emerges suggesting that continued participation presents an increased level of risk or burden to the participant.

Conflicting Interests of Surrogates and Caregiver Burden

Indian surrogates should follow these internationally accepted parameters. The surrogate has to act in a manner as far as possible similar to the patient's own decisions, as if the

patient was competent. This warrants that the surrogate should be in tune with patient's choice as suggested by Roberts and Kim (Roberts and Kim 2016). If the patient's preferences cannot be constructed based on what the surrogate knows about the patient's values and preferences, the surrogate should act insofar as possible, as the patient would were the patient competent to do so. And secondly, if the patient's preferences cannot be constructed based on what the surrogate knows about the patient's values and preferences, the surrogate should act to promote the patient's well-being and consider the potential for benefit from research participation. In totality, the surrogate needs to promote the patient's well-being and consider the potential for benefit from research participation. In India, family is an integral part of patient treatment. They accompany patients and act as surrogates and are expected to know the patient's preferences, but some family members may have their own interests and may not act as ideal surrogates. For the researcher, it is important to always keep the participants' best interests in mind.

Nevertheless, within families of individuals with MHCs, the interests of those with MHCs and those providing their care may diverge or even conflict. Caregivers, for example, might benefit from a respite from caregiving by being able to leave their ill family member with investigators for some period of time, while the person with the MHC finds the time away from home disruptive or frightening. The caregiver might, therefore, have an incentive to enroll their ill family member in a study while the ill person actually objects to participating.

Investigators should therefore endeavor to ensure surrogates enroll participants in studies based on an estimation of what the participants would choose for themselves, as well as the prospect of direct benefit to the participants or to the population of those similarly situated (future patients). Self-interest or the possibility of payment for participation should not be permitted to prompt surrogates to enroll participants lacking decision-making capacity in research. In addition, any indirect benefits of research participation, including any financial payment, should be designed to benefit the study participant, the person with a MHC, not the surrogate or LAR.

Informed consent from surrogates who are apparently not acting in the interest of the prospective participant should not be accepted. Investigators should be cognizant of the possibility of conflicting interests between the prospective participant and the surrogate. The IEC may be appealed to by an investigator, or by the surrogate, to help resolve any conflicts in order to protect the interests of the participant being enrolled in research. This would be more efficient and cost effective than approaching a busy State Authority (MHCA 2017). In case of research involving any psychological, physical, chemical, or medicinal interventions to be conducted on person who is unable to give free and informed consent but does not resist participation in such research, permission to conduct such research shall be obtained from concerned State Authority and State Authority should ascertain that the surrogate does not have conflict of interest. Giving some power to ethics committee may reduce burden and speed up the process.

Privacy and Confidentiality, and the Stigma of Mental Health Conditions

Participation in mental health research may make a person vulnerable to stigmatization and discrimination. Even if the person is a healthy control, other people may mistakenly

believe that the person has a MHC. Because of the magnitude and probability of harm resulting from being associated with a stigmatizing condition, special protections should be undertaken to ensure their privacy and confidentiality. In some cases, these special protections involve being especially meticulous in taking usual measures pursued to protect confidentiality of participants' identity and data. These include not using a consent form if such documentation presents the primary risk of confidentiality breach (Department of Health and Human Services) (FDA 1996), deidentifying or anonymizing any individualized data, storing data securely, reporting only aggregate results, being vague about identifying details (e.g., locations of clinics, demographics of participants) in any publications or reports, being discrete in communication about the study or with participants, and contesting any disclosure of research data or participant identity (e.g., in response to court request). Confidentiality in research is not included in the MHCA 2017 but informed consent of Legal Representative is mandatory. A detailed confidentiality clause, approved by the supervising Ethics Committee, should be added too.

It is important to note two additional issues about protecting research participants from stigma. First, although such special protections are important, they also serve to reinforce the special and thus stigmatizing nature of the condition or population being studied. This reinforcement is the lesser of two evils: it is better to protect current participants even at the risk of reinforcing the stigma of mental illness by not treating it exactly like other diseases under study. Second, there may be greater risks of stigmatizing someone through research participation when that person is recruited from the general population rather than from a clinical psychiatric population (Tharyan 2009).

For some persons already under treatment for a psychiatric condition, research participation might not present a substantially greater burden of stigma. On the other hand, if the person is not symptomatic, diagnosed, or under treatment, research participation may be the primary source of labeling him/her as having a MHC (and may even be the occasion or context of his diagnosis). In this latter case, research participation itself imposes the risks of stigma and its potential consequences, like discrimination. These potentially greater risks of stigmatization should not prohibit recruitment of participants from the general, nonclinical population; instead, awareness of the risks imposed by research should prompt investigators to plan to minimize them.

Special Protections when Studying Mental Health Conditions

In the course of any research study, if a participant reveals a credible plan to seriously harm him/herself (e.g., suicidal ideation) or others, investigators have a responsibility to intervene and to report to the relevant parties. To maintain a relationship of trust between investigators and participants, however, prospective participants must be informed during the informed consent process how suicidal ideation or other risks of harm to self or others will be addressed (Indian Council of Medical Research 2017, chapters on General Principles section 1.1.5, Vulnerability section 6.8.1, Social and Behavioral Sciences Research for Health Box 9.1 and section 9.2.8). If participants' confidentiality may be breached or they may be committed to hospitals upon expression of such thoughts, this possibility must be disclosed to them. If they may be reported to their family members, police, or other authorities upon expression of such thoughts, this too must be disclosed. While some interventions—like hospitalization

and treatment for suicidality—may be primarily for the participants' own benefit, they may not perceive it as such and may want to refuse to participate in a study. Other interventions are primarily for the protection of others, as when a participant is detained and hospitalized because of the expression of homicidal ideas, and prospective participants may not want to participate in research if such hospitalization is possible.

Such interventions should be invoked only when necessary, should be of duration as short and as least restrictive as possible, and must be in accordance with relevant laws. It may be objected that participants will hide their suicidal thoughts or thoughts of harming others if they are aware that they will be reported and hospitalized. Nevertheless, they have a right to such information, and its disclosure may help forge a more collaborative relationship between investigator and participant, if the participant realizes that the investigator will act to protect the participant from causing harm self or others. Suicide attempt is described in the MHCA 2017 (section 115) (1) Notwithstanding anything contained in section 309 of the Indian Penal Code any person who attempts to commit suicide shall be presumed, unless proved otherwise, to have severe stress and shall not be tried and punished under the said Code. (2) The appropriate Government shall have a duty to provide care, treatment, and rehabilitation to a person, having severe stress and who attempted to commit suicide, to reduce the risk of recurrence of attempt to commit suicide. Still retaining Sec 309 IPC is not appropriate any more. It is important that citizens be made aware of the relevant provisions of the MHCA 2017, it needs to be mandatorily implemented (Sneha et al. 2018).

Ethical Issues in Specific Types of Mental Health Research

Mental health research includes many study designs, approaches, and types. Some types of mental health research present specific constellations of ethical concerns.

Research Involving Deception

Some study designs employed in mental health research appear to reduce or violate human subjects' protections or specific requirements of informed consent. An example is studies involving deception either in recruiting participants or in the study intervention, or both. Deception—the intentional creation or maintenance of a false belief by supplying or omitting information—is contrary to the values and norms underlying informed consent. Deceiving people undermines their ability to be self-determining and usually fails to display respect for them as persons.

Nevertheless, because beliefs influence behavior and because mental health research is often concerned either to observe behavior or to study the effects of interventions on behavior, it may be desirable to control the influences on participants' behavior. This may involve temporarily limiting their beliefs so that the beliefs do not influence their behaviors that are under observation. An example is the use of placebo. If participants know that they are receiving an inactive substance (e.g., a sugar pill), it will be impossible for them to serve as controls for the evaluation of the effect of an active substance in a second group of participants. Another example would be an observational study of compulsive behaviors, in which informing participants that their behaviors are being monitored may affect the frequency or duration of the behaviors. In some

studies, a degree of deception—usually a matter of omitting to inform fully—is necessary if the studies are to be accomplished at all. It is critical, however, to distinguish studies in which full disclosure would invalidate the study or render it impossible, from those in which full disclosure is merely inconvenient or makes it more difficult to recruit participants. The former are permissible; the latter are not.

When informing participants of some pertinent aspect of the study would impair the validity of the research, it may be possible to justify less than full disclosure during informed consent. IEC approval of withholding information should be required, and participants should be informed that they are being asked to participate in research about which some features will not be disclosed until the study (or their participation) has concluded. According to the *Belmont Report* (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979), "in all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to participants that are more than minimal, and (3) there is an adequate plan for debriefing participants, when appropriate, and for dissemination of research results to them." In all studies, participants' questions must be answered truthfully without withholding information to increase study enrollment or cooperation. As soon as practicable, and no later than the conclusion of a study involving less than full disclosure, participants must be "debriefed," about true nature of the study.

In the ICMR Guidelines, a section is devoted to circumstances of "deceptive" research or research where full disclosure is not possible due to the nature of the research (Indian Council of Medical Research 2017, chapter on Informed Consent section 5.11).

Genetic Studies of Mental Health Conditions

Genetic research and genomic research on MHCs present not only the previously discussed ethical issues associated with mental health research, but also concerns associated with genetic/genomic research. Many of these arise from the familial nature of genetic conditions—genetic information about one family member may have implications for other members, including for reproductive planning. Heightening concerns about genetic research is the profound significance some people attribute to genes as the so-called blueprint of human life, or the possibility that genetic information reveals information about a person's recent or distant ancestors. Other issues arise from the predictive or risk assessment nature of genetics; in other words, a genetic finding may not be associated with current symptomatology, but may indicate an increased risk for future expression of a condition (sometimes a condition for which no prevention or treatment is yet possible). Finally, like other research, genetic research yields incidental findings, "a finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study" (Wolf and Wertenschlag 1988). Investigators must develop a plan to manage such incidental findings, for example, deciding whether to offer to return such findings to participants. For the relevant process on informed consent seeking, see ICMR Guidelines, see Chapter on Informed Consent Process section 5.4.8.

The ICMR Guidelines, see Chapter on Informed Consent Process section 5.4.8, state that in genetic research, other members of a family may become inadvertently involved

as participants if their details are recorded as a part of the family history. If information about the secondary participants is identifiable then their informed consent will also be required. In addition, if there is a possibility that the research could lead to any stigmatizing condition like genetic disorders, there should be provision for pretest and posttest counseling (Ali et al. 2019). Illiteracy and lack of awareness of genetics may pose more problems in Indian studies.

Conclusion

Ethical concerns about involving person with compromised consent will continue to arise in the context of biotechnological advances. Dilemmas should be resolved expeditiously within the context of legal and ethical guidelines; the interests of the participant should be the foremost consideration. The main aim of mental health research should be to protect the welfare of research participants with MHCs in order to facilitate the ethical conduct of research that will potentially benefit future populations of the human race. The MHCA 2017 mandates the scientist/researcher to adhere to the "National Ethical Guidelines for Biomedical and Health Research Involving Human Participant," laid down by the Indian Council of Medical Research 2017); Ali et al. 2019). These ICMR Guidelines provide in detail how to protect research subjects including mentally ill complementing each other.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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