

The “Vulnerability” of Psychiatric Research Participants: Why This Research Ethics Concept Needs to Be Revisited

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In March 2015, the US Presidential Commission for the Study of Bioethical Issues released a series of recommendations (*Gray Matters*, Volume 2) on contemporary topics at the intersection of neuroscience, ethics, and society.¹ The commission recognized at the outset a crucial tension facing neuroscience and psychiatric researchers today: rigorous research on psychiatric conditions is needed but is ethically challenging. Researchers, research ethics boards (REBs), and policy makers struggle to find a balance between the moral imperative to protect psychiatric research participants and the individual or group restrictions placed on their participation.¹ At worst, this tension may have led to restrictions on the development and conduct of psychiatric research, hindered the participation of individuals with psychiatric conditions, and encouraged suboptimal practices outside of research (e.g., off-label uses, medical innovation).^{2,3} This problem may be rooted, in part, in stereotypes and unfounded assumptions about the consent capacity (or lack thereof) of persons with psychiatric diagnoses that shape general attitudes about research participation. In consequence, these assumptions and stereotypes may further reinforce overprotective attitudes in research ethics because they suggest, erroneously, that psychiatric patients are uniquely vulnerable. Research ethics guidance and practice may thus ignore the full breadth of reasons other than decisional capacity that may render psychiatric patients vulnerable (e.g., suboptimal research designs). Even apart from their potential to affect the progress of psychiatric research, research ethics guidelines and practices that rely on unfounded assumptions about persons with psychiatric diagnoses constitute a challenge to the fundamental research ethics principle of respect for persons and require our critical attention. In this article, we argue for a need to revisit the concept of vulnerability in the context of psychiatric research. Currently, a narrow interpretation of research ethics inhibits discussion about the ethical inclusion of

persons with psychiatric diagnoses in research. Accordingly, a reconsideration of the vulnerability of psychiatric participants is an important step toward breaking down stereotypes in research ethics. Alongside the adoption of a participatory, evidence-based, and recovery-inspired approach to research ethics, revisiting what we mean by ‘vulnerability’ and who we designate as ‘vulnerable’ could empower patient and research communities and strengthen research ethics practices.

Vulnerability as a Key Concept in Research Ethics

The imperative for special research ethics protections for certain groups of ‘vulnerable’ persons can be explained, in part, by a history marred by the abuse and exploitation of persons with psychiatric diagnoses, neurological impairments, and behavioural disorders in research. This history includes Nazi-era experimentation and euthanasia of persons with psychiatric illness,⁴ the intentional infection with hepatitis of developmentally disabled children in the 1950s Willowbrook Study in the United States,⁵ and harmful research performed on unwitting subjects with psychiatric disorders at the Allen Memorial Institute in Montreal.⁶ More recently, troubling psychiatric research scandals have been brought to light at the University of Minnesota, including the CAFÉ study (Comparison of Atypicals in First-Episode

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Schizophrenia), in which Dan Markingson, a young participant with schizophrenia, took his life while enrolled in the trial.⁷ We would likely find widespread agreement within the research community about the vulnerability of research participants in the studies described above, including endorsement for their special protection. However, asking why or which factors rendered them vulnerable could result in more varied answers. For instance, while many would argue that their vulnerability may be characterized by the cognitive or psychiatric symptoms of their illness that affect decisional capacity, others might note that participants in these cases were institutionalized and lacked power or that situational factors in their environments and the research protocols involved the withholding of vital information from subjects. In the case of the CAFÉ study, bioethicist Carl Elliott emphasized that psychiatric researchers had financial incentives to enrol and keep participants in the study even when they were acutely psychotic and their symptoms were not improving and that the research protocol itself allowed for the recruitment of subjects who ought to have been treated by a standard of care.^{7,8}

Despite the variety of ways in which psychiatric research participants may be in positions of vulnerability, concerns around decisional capacity seem to dominate the discussion about the vulnerability of and need for research protections for participants with psychiatric disorders. For example, a 1998 report from the National Bioethics Advisory Commission proposed special provisions for the protection of all persons with mental and behavioral disorders, notably requiring independent capacity assessment for any participant enrolling in research involving more than minimal risk.⁹ The report perpetuated “subtle but pervasive stigmatization of persons with psychiatric disorders,”^{10(p689)} and while the proposed changes were never implemented, it captures the problematic (and unfounded) assumptions about psychiatric participants and psychiatric conditions in research ethics. Today, many research ethics guidelines, both implicitly and explicitly, reflect the assumption that persons with psychiatric disorders are vulnerable. International guidelines (such as the Council for International Organizations of Medical Sciences’ *International Ethical Guidelines for Biomedical Research Involving Human Subjects*) and national guidelines (such as the United Kingdom’s *Research Governance Framework for Health and Social Care*) label mental illness as a characteristic source of vulnerability without necessarily offering a more precise description of why or in what way participants might be vulnerable. When vulnerability is considered in the context of psychiatric research, it is often described as stemming from a lack of decisional capacity. When no explanation is provided in the guidance, we believe there are good reasons to think that researchers, REBs, and others fall back on overgeneralizations about lack of capacity. In addition, tools used to assess decisional capacity¹¹ (and also vulnerability based on decisional capacity) do not facilitate an examination of the relational and contextual

factors that could affect one’s understanding or appreciation of information.

Canadian research ethics guidance has initiated a shift towards a dynamic and context-dependent concept of vulnerability, emphasizing that certain groups, including those with mental illness, have historically been considered vulnerable but that participants’ individual circumstances must always be considered.^{12,13} Unfortunately, little evidence about how REBs understand or apply research ethics guidance (including the revised Canadian guidance) or how REB members are trained to apply this guidance to psychiatric research exists. Furthermore, the effectiveness of research ethics guidance itself is not routinely assessed. However, studies conducted in the United States have shown that REBs judge psychiatric research participants as having less decisional capacity, as being more vulnerable, and as needing special protections compared to other research participants, without clear justification.^{14,15} This is a problem not only because of the lack of respect these assumptions demonstrate and the widespread stigmatization they perpetuate towards persons with psychiatric disorders but also because of their practical implications on the ethics review process. As Kipnis¹⁶ argues, the terms *vulnerable* and *vulnerability* serve as “bioethical trump card[s],” stymieing rather than stimulating discussion about ethical inclusion in research and, often, leading to the exclusion of participants identified as vulnerable from research. A principle of or concern for vulnerability ought to be only one among many considered in the process of research ethics review, including, for example, the harms of systematically excluding a patient population from research or creating undue obstacles to their participation.

Vulnerability and Decisional Capacity

The view of psychiatric research participants as inherently vulnerable due to a lack of decisional capacity is not well supported by evidence. Research on the impact of psychiatric conditions (including psychotic, mood, and anxiety disorders) on the capacity to consent to research has established that most participants in these studies have decisional capacity.¹⁷⁻¹⁹ It has been found that the severity of illness, as measured through levels of social functioning, may have a negative impact on the ability to consent,¹⁷ but research consistently emphasizes that heterogeneity exists within diagnostic groups, and categorical assumptions of incapacity are untenable.^{17,20,21} Moreover, the contextual nature of decisional capacity calls into question the generalizability of any findings related to a particular group’s capacity to consent; at most, research may help us understand the factors that have the *potential* to impair capacity.

Those involved in the care and treatment of persons with psychiatric diagnoses are familiar with the heterogeneity of diagnostic groups and the complexity of testing and judging for capacity.²² Unfortunately, persons not involved in the day-to-day care of psychiatric patients, including some

members of REBs, may have diverging views about how, as well as to what extent, psychiatric symptoms may affect decisional capacity. As such it is essential to emphasize that, like other research participants, those with psychiatric conditions have strengths and weaknesses when it comes to understanding, appreciating, and consenting to research and that these capacities can fluctuate. The evidence does not support a categorical assumption of decisional incapacity in psychiatric research participants and ought not be the sole focus when assessing their vulnerability or ethical inclusion in research.

Reconsidering Vulnerability, Research Ethics, and Psychiatric Research

So where do we go from here? Perhaps discarding the concept of vulnerability entirely will eliminate the issues described so far. However, vulnerability is an important concept through which we can identify those research participants who would be best served by additional research protections. Moreover, the notion of vulnerability captures a history that has greatly informed the goals of research ethics governance; it is part of common language and is a concept with intuitive moral pull. For these reasons, we favor a reformulation of the concept that recognizes the relational factors that may create vulnerability in psychiatric research, of which decisional capacity is just one.

Recent literature underscores that vulnerability should not be viewed as an intrinsic property of the participant but rather as a dynamic, relational property describing an asymmetry between participants and those involved in the implementation and conduct of research that can be rendered more or less significant by situational factors.²³⁻²⁵ This view counters the rigid reliance of REBs on identifying sources of vulnerability that are static and located within participants themselves (e.g., a lack of capacity by virtue of a psychiatric diagnosis). Instead, vulnerability should be viewed as a situational feature that can arise from the relationships among participants, investigators, and sociocultural context. A static approach conceptualizes vulnerability as a characteristic of the research participant (e.g., by virtue of a diagnosis), but a relational approach considers vulnerability as stemming from both individual (i.e., intrinsic) and contextual (i.e., extrinsic) factors.

Relational sources of vulnerability include participants' education level or health literacy, as well as suboptimal study designs, researcher biases, or a lack of support for research participants who need it (e.g., the provision of participant advocates in environments where asymmetries of power are likely). All these factors could lead to inappropriate or exploitative enrollment of research participants in clinical trials. For example, when researchers have financial incentives to enrol and keep participants in a study, this creates a situation of vulnerability for those enrolled. Importantly, the relational view of vulnerability also takes into account that vulnerability is dynamic and exists on a

continuum, rather than being an all-or-none property. Protections for psychiatric research participants in situations of vulnerability should be broadened to include more than strategies to improve consent or decisional capacity—because this may not be the root of vulnerability. Instead, on a relational view, vulnerability can be remediated through measures that address its sources, including augmenting participants' understanding and decision-making literacy or identifying and eliminating investigator-driven biases.²³

The deployment of participatory and evidence-based processes in research ethics could support a reconsideration of the notion of vulnerability, amplify its positive effects, and have beneficial impacts on other aspects of research ethics. A participatory model of research ethics shares similar core principles to the philosophy of recovery in mental health. Just as a philosophy of recovery recognizes the uniqueness of the individual and places value on experiential knowledge,²⁶ a participatory research ethics entails soliciting the perspectives and experiences of research participants and taking them meaningfully into account in the revision and development of policies aimed at their protection. Genuinely engaging those who have been overwhelmingly excluded from research and policy development is a practical mechanism for redistributing power. In the context of vulnerability where a lack of power can itself be a source of vulnerability, engaging potentially vulnerable research participants in the development of the policies and protections applied to them could ultimately remediate some aspects of their vulnerability (e.g., asymmetries of power compounded by the research environment). Furthermore, a recovery-inspired and participant-focused approach to research ethics also calls on us to critically examine research processes and recognize that a one-size-fits-all approach may not be appropriate in the context of mental health. For example, informed consent practices could be altered to reflect the individual capacities of persons with psychiatric diagnoses.²⁷

In addition to emphasizing participant engagement and evidence-based practices, the approach we describe has the potential to positively affect research ethics more broadly, emphasizing the need to assess the outcomes of research ethics governance. Currently, there exists no mechanism or systematic effort to assess the effectiveness of research ethics guidelines or review boards in ensuring the appropriate inclusion, informing of, and protection of research participants.²⁸ Creating an open and collaborative model of policy development and refinement would allow for increased responsiveness to the needs of research participants and greater opportunity for the incorporation of evidence- and experience-based guidance.

Summary

The concept of vulnerability arose to protect those deemed susceptible to being harmed or exploited in research. The application of this concept in psychiatric research seems to

have narrowed to a view that equates vulnerability with compromised decisional capacity and understand it as an intrinsic characteristic of research participants. In the absence of evidence about outcomes and participants' experiences, research ethics oversight may nurture an over-protective approach. Revisiting the pivotal concept of vulnerability and supporting concrete changes in the governance of research ethics is an essential component of a new approach that has the potential to significantly and positively affect the participation of psychiatric participants in research.

Authors' Note

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References

1. Presidential Commission for the Study of Bioethical Issues. Gray matters: topics at the intersection of neuroscience, ethics, and society. Vol 2. Washington (DC): Presidential Commission for the Study of Bioethical Issues; 2015.
2. Di Pietro N, Illes J. Rising antipsychotic prescriptions for children and youth: cross-sectoral solutions for a multimodal problem. *Can Med Assoc J*. 2014;186(9):653-654.
3. Hyman SE. Revolution stalled. *Sci Transl Med*. 2012;4(155):155cm11.
4. Torrey EF, Yolken RH. Psychiatric genocide: Nazi attempts to eradicate schizophrenia. *Schizophrenia Bull*. 2010;36(1):26-32.
5. Beecher HK. Ethics and clinical research. 1966. *Bull World Health Organ*. 2001;79(4):367-372.
6. Ross CA. The C.I.A. doctors: human rights violations by American psychiatrists. Richardson (TX): Manitou Communications; 2006.
7. Elliott C. The deadly corruption of clinical trials. *MotherJones*. 2010 September/October. Available from: <http://www.motherjones.com/environment/2010/09/dan-markinson-drug-trial-astrazeneca>
8. Elliott C. The University of Minnesota's medical research mess. *New York Times*. 2015 May 26. Available from: http://www.nytimes.com/2015/05/26/opinion/the-university-of-minnesotas-medical-research-mess.html?_r=0.
9. National Bioethics Advisory Commission. Research involving persons with mental disorders that may affect decision-making capacity. Vol I. Rockville (MD): National Bioethics Advisory Commission; 1998.
10. Oldham JM, Haimowitz S, Delano SJ. Protection of persons with mental disorders from research risk: a response to the report of the National Bioethics Advisory Commission. *Arch Gen Psychiatry*. 1999;56(8):688-693.
11. Grisso T, Appelbaum PS, Hill-Fotouhi C. The MacCAT-T: a clinical tool to assess patients' capacities to make treatment decisions. *Psychiatr Serv*. 1997;48(11):1415-1419.
12. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. Tri-Council policy statement: ethical conduct for research involving humans [Internet]. 2014 December. Available from: http://www.pre.ethics.gc.ca/pdf/eng/tcps2-2014/TCPS_2_FINAL_Web.pdf.
13. Subgroup on Procedural Issues for the TCPS (ProGroup): A Working Committee of the Interagency Advisory Panel on Research Ethics (PRE). Proportionate approach to research ethics review in the TCPS: proposed textual changes for the concept of vulnerability in the TCPS [Internet]. 2008 January. Available from: http://www.pre.ethics.gc.ca/policy-politique/initiatives/docs/Vulnerability_in_the_TCPS_-_ProGroup_Jan_2008_-_EN.pdf.
14. Tait RC, Chibnall JT, Iltis A, et al. Assessment of consent capability in psychiatric and medical studies. *J Empir Res Hum Res Ethics*. 2013;6(1):39-50.
15. Luebbert R, Tait RC, Chibnall JT, et al. IRB member judgments of decisional capacity, coercion, and risk in medical and psychiatric studies. *J Empir Res Hum Res Ethics*. 2008;3(1):15-24.
16. Kipnis K. Vulnerability in research subjects: a bioethical taxonomy. In: National Bioethics Advisory Commission, editor. Report on ethical and policy issues in research involving human participants: Volume II. Commissioned papers and staff analysis. Bethesda (MD): National Bioethics Advisory Commission; 2001.
17. Moran-Sanchez I, Luna A, Perez-Carceles MD. Assessment of capacity to consent to research among psychiatric outpatients: prevalence and associated factors [Epub ahead of print]. *Psychiatr Q*. [2015 May 8; cited 2015 Aug 7]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25952945>.
18. Appelbaum PS, Grisso T, Frank E, et al. Competence of depressed patients for consent to research. *Am J Psychiatry*. 1999;156(9):1380-1384.
19. Cohen BJ, McGarvey EL, Pinkerton RC, et al. Willingness and competence of depressed and schizophrenic inpatients to consent to research. *J Am Acad Psychiatry*. 2004;32(2):134-143.
20. Palmer BW, Dunn LB, Appelbaum PS, et al. Assessment of capacity to consent to research among older persons with schizophrenia, Alzheimer disease, or diabetes mellitus: comparison of a 3-item questionnaire with a comprehensive standardized capacity instrument. *Arch Gen Psychiatry*. 2005;62(7):726-733.

21. Dunn LB, Roberts LW. Emerging findings in ethics of schizophrenia research. *Curr Opin Psychiatr.* 2005;18(2):111-119.
22. Okai D, Owen G, McGuire H, et al. Mental capacity in psychiatric patients: systematic review. *Br J Psychiatr.* 2007;191:291-297.
23. Bell E, Racine E, Chiasson P, et al. Beyond consent in research: revisiting vulnerability in deep brain stimulation for psychiatric disorders. *Camb Q Healthc Ethics.* 2014;23:361-368.
24. Luna F, Vanderpoel S. Not the usual suspects: addressing layers of vulnerability. *Bioethics.* 2013;27(6):325-332.
25. Mackenzie C, Rogers W, Dodds S, editors. *Vulnerability: new essays in ethics and feminist philosophy.* New York: Oxford University Press; 2013.
26. Whitley R, Palmer V, Gunn J. Recovery from severe mental illness. *CMAJ.* 2015;187(13):951-952.
27. Bell E. Young persons in research: a call for the engagement of youth in mental health research. *Am J Bioeth.* 2015;15(11):28-30.
28. McDonald M. Canadian governance of health research involving human subjects: is anybody minding the store? *Health Law J.* 2001;9:1-21.