

## INVOLUNTARILY COMMITTED PATIENTS AS PRISONERS

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### INTRODUCTION

Human subjects research has a shameful history of abuses committed against institutionalized people. Decades after the Nuremberg court condemned Nazi doctors to death for experimenting on prisoners in concentration camps, researchers in the United States continued to expose prisoners to measles, malaria, radioactive isotopes, and other painful and damaging interventions.<sup>1</sup> On his first visit to the Holmesburg prison in Pennsylvania, Dr. Albert Kligman reported seeing in this captive population “acres of skin” on which he could conduct dermatological experiments, including toxins that left prisoners scarred and blistered.<sup>2</sup>

The revelation of studies like these prompted public outcry and government action. A national commission tasked by Congress with examining the use of prisoners in research concluded that the conditions of their confinement render prisoners highly vulnerable to coercion and exploitation.<sup>3</sup> Federal agencies, including the Department of Health and Human Services (“HHS”) and the Bureau of Prisons, acted on these findings by imposing special rules designed to protect prisoners from research abuses.<sup>4</sup>

Yet both federal regulations and the research ethics literature have overlooked another captive population that requires special

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1. Keramet Reiter, Comment, *Experimentation on Prisoners: Persistent Dilemmas in Rights and Regulations*, 97 CAL. L. REV. 501, 510–12 (2009).

2. *Id.* at 501–02.

3. *See infra* Part I.

4. 45 C.F.R. §§ 46.301–306 (2015); U.S. DEP’T OF JUSTICE, FED. BUREAU OF PRISONS, PROGRAM STATEMENT NO. 6031.04, PATIENT CARE § 45 (2014); U.S. DEP’T OF JUSTICE, FED. BUREAU OF PRISONS, PROGRAM STATEMENT NO. 1070.07, RESEARCH § 10 (1999).

protections: involuntarily committed patients. The regulations that govern much federally funded research,<sup>5</sup> commonly called “the Common Rule,” exclude these patients by defining “prisoners” as encompassing only persons confined through the criminal justice system.<sup>6</sup> Yet these patients are similarly susceptible to unethical research practices. Like prisoners, involuntarily committed patients are confined against their will, rendering them isolated and dependent on institutional authorities. Moreover, the length of their confinement is largely determined by authorities who at least authorize, if not conduct, any research patients may be asked to join.

Properly applied, the general ethical principles governing human subjects research should bar the recruitment of involuntarily committed patients for most research. As with prisoners, these patients’ conditions of confinement present an overwhelming barrier to voluntary consent, and their recruitment will rarely be consistent with the interests of justice. However, the lack of express protections for this population in federal regulations governing human subjects research—together with the significant gaps in the applicability of those regulations—leaves these patients at risk.

A 2006 report by the Institute of Medicine recognized that the Common Rule’s narrow definition of “prisoner” improperly excludes some populations that are subject to the same pressures as inmates of correctional facilities.<sup>7</sup> The Institute recommended broadening that definition to extend the Common Rule’s special protections “to the fuller population of individuals who are under restricted liberty and, therefore, face potentially greater risks than the general population when participating in research.”<sup>8</sup> But while the Institute’s report emphasized that involuntarily committed patients face very similar circumstances as prisoners, and therefore require strong ethical safeguards, the authors did not include these patients in their proposed expanded definition. The

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5. 45 C.F.R. § 46 (2016).

6. *Id.* § 46.303(c).

7. INST. OF MED. OF THE NAT’L ACADS., ETHICAL CONSIDERATIONS FOR RESEARCH INVOLVING PRISONERS 4–5 (2007) [hereinafter IOM REPORT].

8. *Id.* at 101.

authors concluded that the special circumstances of patients under civil commitment orders were outside the scope of their charge and warranted separate consideration.<sup>9</sup>

This article takes up that task and argues that patients confined to government custody through the process of civil commitment should be afforded the same research protections as persons incarcerated through the criminal justice system. Applying the Common Rule's special protections for prisoners would reduce the risks to which these patients are exposed and would limit their participation to research that offers benefits directly to subjects or to involuntarily committed patients as a group.

Part I relates several stories of involuntarily committed patients who were recruited into studies posing serious risks. Part II draws on these cases to argue that the involuntary commitment of these patients leaves them vulnerable to unethical treatment by researchers. Their inherently coercive circumstances present an overwhelming obstacle to voluntary consent, and their captive status makes them attractive targets for research that could be performed using less vulnerable subjects.

Part III argues that most research on this patient population is improper under generally applicable principles of informed consent and fair subject selection. However, existing protections have proved insufficient to prevent unethical recruitment of these patients. Accordingly, Part IV builds on the Institute of Medicine's call for expanding the definition of "prisoner" in federal regulations, arguing that civilly committed patients should be included within its ambit and that the Common Rule's protections should be applied to all research involving involuntarily confined subjects.

#### I. RESEARCHERS HAVE SUBJECTED INVOLUNTARILY COMMITTED PATIENTS TO UNETHICAL TREATMENT

Involuntary commitment can take many forms. Every state has laws empowering law enforcement officers to temporarily detain people experiencing psychiatric crises on an emergency basis.<sup>10</sup>

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9. *Id.* at 26 n.1.

10. BRIAN STETTIN ET AL., TREATMENT ADVOCACY CTR., MENTAL HEALTH COMMITMENT LAWS: A SURVEY OF THE STATES 14 (2014) [hereinafter STETTIN ET AL., TAC

Most states allow such individuals to be detained without a court order for up to seventy-two hours (sometimes referred to as a “72-hour hold”) so that medical staff can seek to stabilize them and evaluate whether they require long-term commitment.<sup>11</sup>

State laws also empower courts to order an individual to be confined to a mental institution on a long-term basis. Standards for involuntary in-patient commitment vary considerably among the states. Thirty-three states have statutes that authorize courts to involuntarily commit adults for substance abuse.<sup>12</sup> Twenty states and the federal government have adopted statutes allowing sex offenders to be civilly committed after completing their criminal sentences.<sup>13</sup> All states have inpatient commitment statutes that empower courts to confine individuals on the basis of severe mental illness. The most permissive states, like Arizona, adopt a “need for treatment” standard under which courts may confine an individual upon “a finding that the person’s mental illness prevents him from seeking help on a voluntary basis and, if not treated, will cause him severe suffering and harm his health.”<sup>14</sup> At the other end of the spectrum, under the laws of states like Alabama, a court may only confine a mentally ill person who presents a “real and present threat of substantial harm to self and/or others.”<sup>15</sup>

As an alternative to inpatient commitment, forty-two states and the District of Columbia have outpatient commitment laws that allow courts to order certain mentally ill persons “to adhere to a specific program of outpatient treatment as a condition of remaining in the community.”<sup>16</sup> A variation on this practice is Minnesota’s “stay of commitment” option, under which a court

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SURVEY], <http://www.treatmentadvocacycenter.org/storage/documents/2014-state-survey-abridged.pdf>.

11. *Id.*

12. Paul P. Christopher et al., *Nature and Utilization of Civil Commitment for Substance Abuse in the United States*, 43 J. AM. ACAD. PSYCHIATRY L. 313, 315 (2015).

13. Fredrick E. Vars, *Delineating Sexual Dangerousness*, 50 HOUS. L. REV. 855, 857 (2013).

14. STETTIN ET AL., TAC SURVEY, *supra* note 10, at 7; ARIZ. REV. STAT. ANN. § 36-501 (2016).

15. ALA. CODE § 22-52-10.4 (2016).

16. STETTIN ET AL., TAC SURVEY, *supra* note 10, at 10; Candice T. Player, *Involuntary Outpatient Commitment: The Limits of Prevention*, 26 STAN. L. & POL’Y REV. 159, 161–62 (2015).

can decline to enforce an inpatient commitment order as long as the individual follows his treatment plan.<sup>17</sup> Under this procedure, the patient can avoid being confined to a mental institution as long he complies with the court's conditions regarding treatment.<sup>18</sup>

There is little data regarding how often institutionalized mental patients are used as research subjects.<sup>19</sup> What exists instead are scattered data points and anecdotal cases brought to light when an outside party becomes aware of abuses and has both the will and the resources to expose them. For example, a 1978 report by a national commission studying research protections determined that at that time the National Institute of Mental Health supported one hundred projects involving mentally ill inpatients, and the Veterans Administration supported an additional 230 such studies.<sup>20</sup> The report did not state how many of the subjects in these studies were involuntarily committed. In *T.D. v. New York State Office of Mental Health*, a disability rights group challenged regulations passed by the State of New York's Office of Mental Health ("OMH") governing research on incompetent patients residing at OMH-operated facilities.<sup>21</sup> The court's opinion noted that as of 1996 there were approximately 400 such studies involving "more than minimal risk."<sup>22</sup> Again, however, it is not clear how many of the subjects in those studies were involuntarily confined.<sup>23</sup>

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17. MINN. STAT. § 253B.095 (2009).

18. *Id.*

19. The Institute of Medicine observed a similar dearth of data for prisoners, noting "[t]here were no comprehensive reviews and no central repository of information about the amount and different types of research involving prisoners." IOM REPORT, *supra* note 7, at 59; see also Elyn R. Saks et al., *Proxy Consent to Research: The Legal Landscape*, 8 YALE J. HEALTH POL'Y L. & ETHICS 37, 40 (2008) ("There is no empirical data regarding the amount of research currently being conducted with decisionally impaired subjects.").

20. NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, U.S. DEPT' OF HEALTH, EDUC. & WELFARE, DHEW PUB. NO. (OS) 78-0006, RESEARCH INVOLVING THOSE INSTITUTIONALIZED AS MENTALLY INFIRM 36, 39 (1978) [hereinafter 1978 NAT'L COMM'N REP.].

21. 650 N.Y.S.2d 173, 175 (N.Y. App. Div. 1996).

22. *Id.* at 176 (citations omitted).

23. While the parties in that case agreed that the legal challenge would "directly and immediately affect only a very small percentage" of those studies, it is not clear whether that is because very few of those studies involved incompetent subjects, or few of those studies were federally funded, and therefore not within the scope of the legal challenge. *Id.*

This lack of information precludes systematic assessments of the extent to which involuntarily committed patients are being treated unethically by researchers or are being systematically targeted for inclusion in research because of their easy availability. However, specific examples of research abuses involving these patients illustrate how their circumstances can render them vulnerable to coercion and exploitation.

A. *Louis Smith, a.k.a. "John Doe"*

Until recently, the best-known example of the perils of using involuntarily committed patients in research was described in the case of *Kaimowitz v. Michigan Department of Mental Health*.<sup>24</sup> In 1972, the Michigan state legislature awarded two researchers funding to undertake a study using an experimental psychosurgery to address uncontrollable aggression.<sup>25</sup> The study protocol called for the recruitment of twenty-four involuntarily confined sexual psychopaths to serve as subjects in the study, which would compare the effect of brain surgery to the effect of the drug cyproterone acetate in altering the flow of male hormones.<sup>26</sup>

However, the researchers were only able to identify one inmate who met their criteria: Louis Smith. Identified in the Michigan Circuit Court opinion as "John Doe," Smith had been confined to the Ionia State Hospital for seventeen years.<sup>27</sup> Although the study was intended to compare two interventions, the researchers planned to proceed with brain surgery on Smith alone<sup>28</sup> until a lawyer discovered the proposed surgery and filed suit to stop it.<sup>29</sup> Although Smith insisted during his confinement that he consented voluntarily to the surgery, once released from confinement he withdrew his consent.<sup>30</sup> Testimony at trial revealed that he had consented to the procedure "partly because of his effort to show

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24. *Kaimowitz v. Dep't of Mental Health*, 13 CRIM. L. REP. (BNA) 2455, 13 CRL 2455 (Mich. 1973).

25. *Id.* at 2453.

26. *Id.*

27. *Id.*

28. *Id.*

29. Candace J. Fabri, *Constitutional Law—An Involuntarily Detained Mental Patient's Informed Consent Is Invalid for Experimental Psychosurgery*, 50 CHI.-KENT L. REV. 526, 529 (1973).

30. *Kaimowitz*, 13 CRIM. L. REP. (BNA), at 2453–54.

the doctors in the hospital that he was a cooperative patient.”<sup>31</sup> The Michigan court barred researchers from proceeding with the surgery, concluding that the “inherently coercive” institutional environment precluded voluntary consent to invasive procedures.<sup>32</sup>

### B. *Dan Markingson*

The case of Dan Markingson is worth relating in detail, both because it is recent and because it illustrates many facets of what makes the recruitment of involuntarily committed patients so problematic in today’s research environment. Markingson’s treatment has also been the subject of investigations by the State of Minnesota’s Legislative Auditor and the Association for the Accreditation of Human Research Protection Programs, both of which released damning reports in 2015.<sup>33</sup>

In 2003, Markingson was twenty-six years old and living in Los Angeles.<sup>34</sup> When Dan’s mother, Mary Weiss, came to visit him that summer, she discovered he was mentally disturbed. He made inscrutable comments and had “encircled his bed with wooden posts, salt, candles, and money, which he said would protect him from evil spirits. He showed her a spot on the carpet that he said the aliens had burned.”<sup>35</sup>

Mary eventually persuaded Markingson to come back to St. Paul, Minnesota, where his condition continued to deteriorate. He believed people could cast spells and read minds, and that some

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31. *Id.* at 2454.

32. *Id.*

33. OFFICE OF THE LEGIS. AUDITOR, STATE OF MINN., A CLINICAL DRUG STUDY AT THE UNIVERSITY OF MINNESOTA DEPARTMENT OF PSYCHIATRY: THE DAN MARKINGSON CASE 5 (2015) [hereinafter LEGIS. AUDITOR REP.], [www.auditor.leg.state.mn.us/sreview/Markingson.pdf](http://www.auditor.leg.state.mn.us/sreview/Markingson.pdf); ASS’N FOR THE ACCREDITATION OF HUMAN RESEARCH PROT. PROGRAMS, AN EXTERNAL REVIEW OF THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS AT THE UNIVERSITY OF MINNESOTA WITH SPECIAL ATTENTION TO RESEARCH WITH ADULTS WHO MAY LACK DECISION-MAKING CAPACITY 67 n.8 (2015) [hereinafter AAHRPP REP.], [http://research.umn.edu/advancehrp/documents/final\\_report.pdf](http://research.umn.edu/advancehrp/documents/final_report.pdf).

34. Carl Elliott, *The Deadly Corruption of Clinical Trials*, MOTHER JONES (Sept. 13, 2010, 5:00 AM), <http://www.motherjones.com/environment/2010/09/dan-markingson-drug-trial-astrazeneca>.

35. *Id.*

people might be “hybrids” who were not entirely human.<sup>36</sup> Even more alarming, he believed the Illuminati were planning a “storm” of mass murder in which he planned to participate, writing in an email “I’m especially eager to attend this storm and SLAY those who deserve slaying. I will choose victims immediately. . . I HAVE NO EMOTIONAL ATTACHMENTS. I KILL FOR FUN!”<sup>37</sup>

On November 12, Mary called the police after Markingson threatened to kill her.<sup>38</sup> The police took Markingson to Regions Medical Center in St. Paul, where the medical staff placed him under a “72 hour hold”—a procedure that allows medical staff to temporarily confine a patient who is determined to be mentally ill and to pose a danger to himself or others.<sup>39</sup> Regions then transferred Markingson to Fairview University Medical Center, a teaching hospital affiliated with the University of Minnesota.<sup>40</sup> There, Markingson was treated by an associate professor in the university’s psychiatry department named Dr. Stephen Olson.<sup>41</sup> On November 13, Dr. Olson examined Markingson and diagnosed him with paranoid schizophrenia, noting that he was at a high risk of acting on his violent delusions.<sup>42</sup> He prescribed Markingson the antipsychotic drug Risperdal (risperidone).<sup>43</sup>

Dr. Olson determined Markingson was psychotic and dangerous, and that he “lack[ed] the capacity to make decisions regarding his medical treatment.”<sup>44</sup> A court-appointed social worker shared that assessment, concluding that Markingson did not have “the capacity to make decisions regarding neuroleptic medications.”<sup>45</sup>

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36. *Id.*

37. *Id.*

38. LEGIS. AUDITOR REP., *supra* note 33, at 5.

39. *Id.*; MINN. STAT. § 253B.05 (2016).

40. LEGIS. AUDITOR REP., *supra* note 33, at 5.

41. *Id.*

42. JAMES L. JACOBSON, DAKOTA CTY., STATE OF MINN., REP. OF EXAMINER 3 (Nov. 19, 2003) [hereinafter JACOBSON, REP. OF EXAMINER], <https://www.scribd.com/document/49729697/Jacobson-Examiner-Report>.

43. LEGIS. AUDITOR REP., *supra* note 33, at 11.

44. *Id.*

45. *Id.*; Rep. of Pre-Petition Screening Team, *In re* Markingson, No. PX-03-10465 (Minn. Dist. Ct., 1st Jud. Dist. Nov. 17, 2003), <http://www.scribd.com/doc/49730113/Pre-petition-screening-report>.



On November 17, Fairview Hospital initiated proceedings to have Markingson committed to Anoka Metro Regional Treatment Center, a long-term state psychiatric facility.<sup>46</sup> A district court entered an initial commitment order confining Markingson to Fairview, pending a hearing scheduled for the following week.<sup>47</sup> On November 19, while the commitment proceedings were pending and Markingson was still in Fairview's custody, Dr. Olson approached Markingson about participating in a clinical trial of antipsychotic drugs called the CAFE study, for "Comparison of Atypicals in First Episode of Psychosis."<sup>48</sup> In addition to being Markingson's treating physician, Dr. Olson was a principal investigator for the CAFE study at the University of Minnesota trial site.<sup>49</sup>

On November 20, the district court entered an order committing Markingson to the Anoka facility, but "stayed" that commitment for six months on the condition that he "remain hospitalized, cooperate with the treatment plan at Fairview University Medical Center until medically discharged, and follow all of the aftercare recommendations of the treatment team."<sup>50</sup> Although Dr. Olson, a social worker, and a clinical psychologist had each determined that Markingson lacked the capacity to make decisions regarding his own care, the court did not appoint a legal guardian to make decisions on Markingson's behalf.<sup>51</sup>

The following day, Markingson's decision-making capacity was again assessed by Jean Kenney, the study coordinator for the CAFE study.<sup>52</sup> Although a court-appointed psychologist had ex-

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46. LEGIS. AUDITOR REP., *supra* note 33, at 5.

47. *Id.*; Order to Confine, to Transport for Examination, Hearing, Appointment of Attorney, Examiner and Notice, *In re* Markingson, No. PX-03-10465 (Minn. Dist. Ct., 1st Jud. Dist. Nov. 17, 2003), <https://www.scribd.com/document/49672066/Commitment-Order>.

48. LEGIS. AUDITOR REP., *supra* note 33, at 5–6; *CAFE Comparison of Atypicals in First Episode of Psychosis*, CLINICALTRIALS.GOV, <https://clinicaltrials.gov/ct2/show/NCT00034892> (last updated Jan. 3, 2013).

49. LEGIS. AUDITOR REP., *supra* note 33, at 6.

50. Findings of Fact, Conclusions of Law and Order for Stayed Commitment at 2, *In re* Markingson, No. PX-03-10465 (Minn. Dist. Ct., 1st Jud. Dist. Nov. 20, 2003) [hereinafter Order for Stayed Commitment], <https://www.scribd.com/document/113945040/Stay-of-Commitment-for-Dan-Markingson>; LEGIS. AUDITOR REP., *supra* note 33, at 11.

51. LEGIS. AUDITOR REP., *supra* note 33, at 5, 11.

52. *Id.* at 11.

amined Markingson two days earlier and determined that he had “a substantial disorder of thought” and a “gross impairment of judgment, behavior, [and] capacity to recognize reality, [or] capacity to reason or understand,”<sup>53</sup> Kenney concluded that he had sufficient decision-making capacity to consent to research participation.<sup>54</sup> Under a court order to follow the recommendations of his caregivers, and threatened with involuntary confinement for non-compliance, Markingson signed the ten-page informed consent document and was enrolled in the study.<sup>55</sup>

The CAFE study was sponsored by AstraZeneca, and was designed to compare the efficacy of its antipsychotic drug, Seroquel, against two competing drugs in treating first episode psychosis.<sup>56</sup> AstraZeneca had outsourced management of the study to a contract research organization called Quintiles. The University of Minnesota was one of twenty-six sites enlisted by Quintiles to recruit 400 subjects experiencing their first psychotic episode to take one of the three study drugs for a year.<sup>57</sup>

Markingson’s recruitment into the CAFE study had several implications for his treatment. The study was double-blinded and randomized, meaning Markingson was randomly assigned to one of the three medications, and neither he nor the researchers knew which drug he was taking.<sup>58</sup> The study protocol

barred subjects from being taken off their assigned drug; it didn’t allow them to be switched to another drug if their assigned drug was not working; and it restricted the number of additional drugs subjects could be given to manage side effects and symptoms such as depression, anxiety, or agitation. . . . These restrictions meant that subjects in the CAFE study had fewer therapeutic options than they would have had outside the study.<sup>59</sup>

Enrollment in the study also meant that Markingson’s treating physician, Dr. Olson, was no longer concerned solely with his

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53. JACOBSON, REP. OF EXAMINER, *supra* note 42, at 1, 3; LEGIS. AUDITOR REP., *supra* note 33, at 11.

54. LEGIS. AUDITOR REP., *supra* note 33, at 11.

55. *Id.*

56. *Id.* at 5–6; *CAFE Comparison of Atypicals in First Episode of Psychosis*, *supra* note 48.

57. Elliott, *supra* note 34.

58. LEGIS. AUDITOR REP., *supra* note 33, at 5–6.

59. Elliott, *supra* note 34.

treatment, but also with his obligations as a principal investigator.<sup>60</sup>

Patients experiencing their first episode of psychosis are known to present a higher risk of killing themselves or others.<sup>61</sup> Accordingly, studies of antipsychotic drugs commonly prohibit recruitment of patients who pose a risk of suicide or violence.<sup>62</sup> However, the CAFE study protocol barred recruitment only of subjects who were deemed to be at risk of suicide, not homicide.<sup>63</sup> Thus notwithstanding Markingson's threat to kill his mother, he was eligible for the study because he had not threatened to harm himself.<sup>64</sup>

Although Dr. Olson had prescribed Risperdal to Markingson upon his admission to Fairview Hospital on December 5, Markingson was switched to his randomly assigned CAFE study drug, which was later determined to be Seroquel.<sup>65</sup> Three days after changing Markingson's medication, Dr. Olson discharged him to a halfway house for people with mental illness.<sup>66</sup> Upon his discharge, Markingson was required to sign an aftercare agreement that required him to keep his CAFE study appointments and to continue taking his medications.<sup>67</sup> The document warned Markingson that "[c]onsequences for not following this plan could result in court commitment to the hospital."<sup>68</sup>

Markingson's mother, Mary, was not present when he agreed to be enrolled in the CAFE study.<sup>69</sup> When she learned of his re-

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60. LEGIS. AUDITOR REP., *supra* note 33, at 6.

61. Olav Nielssen & Matthew Large, *Rates of Homicide During the First Episode of Psychosis and After Treatment: A Systematic Review and Meta-Analysis*, 36 SCHIZOPHRENIA BULL. 702, 702 (2010); Maurizio Pompili et al., *Suicide Risk in First Episode Psychosis: A Selective Review of the Current Literature*, 129 SCHIZOPHRENIA RES. 1, 1 (2011).

62. Elliott, *supra* note 34; T. Scott Stroup & John R. Geddes, *Randomized Controlled Trials for Schizophrenia: Study Designs Targeted to Distinct Goals*, 34 SCHIZOPHRENIA BULL. 266, 269 (2008).

63. Elliott, *supra* note 34.

64. *Id.*

65. LEGIS. AUDITOR REP., *supra* note 33, at 6–7.

66. *Id.* at 6.

67. Aftercare Agreement, *In re Markingson*, No. PX-03-10465 (Minn. Dist. Ct., 1st Jud. Dist. Nov. 20, 2008), <https://www.scribd.com/doc/54233449/Markings-On-Discharge-Plan> (signed on Dec. 8, 2003).

68. *Id.*

69. Elliott, *supra* note 34.

cruitment, she objected to Dr. Olson.<sup>70</sup> However, because Markingson was an adult and the court had not given her any legal authority to make decisions on his behalf, she had no power to have her son dismissed from the study.<sup>71</sup> She repeatedly pleaded with Dr. Olson and Dr. Charles Schulz—another principal investigator in the CAFE study, as well as the chairman of the university’s psychiatry department—to release him from the study, but they refused.<sup>72</sup> Her pleas became more urgent as she watched Markingson’s condition deteriorate at the halfway house.<sup>73</sup> She was alarmed at his agitation, noting “[h]e was so tense, with this ready-to-explode quality.”<sup>74</sup> Although she repeatedly contacted Markingson’s treatment team by phone and by mail, “there is little documented evidence that the study team followed up with her, particularly in a timely way.”<sup>75</sup>

Although Dr. Olson saw Markingson only six times in the six months between his admission to Fairview Hospital and his death, he dismissed Mary’s concerns.<sup>76</sup> And while he insisted that Markingson was doing well on his study drug, as Markingson’s “stay of commitment was about to expire, [Dr.] Olson recommended extending it for another six months—the duration of the CAFE study.”<sup>77</sup> In support of that recommendation, Dr. Olson argued Markingson still had “little insight into his mental disorder” and might “place himself at risk of harm if he were to terminate his treatment.”<sup>78</sup>

On April 11, 2004, Mary visited Markingson and found him “out of control.”<sup>79</sup> Alarmed, she left a telephone message with Jean Kenney, the CAFE study coordinator, asking “Do we have to wait until he kills himself or anyone else before anyone does anything?”<sup>80</sup> According to the Legislative Auditor’s report, “Weiss’s

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70. *Id.*

71. *See id.*

72. *Id.*

73. *See id.*

74. *Id.*

75. LEGIS. AUDITOR REP., *supra* note 33, at 17.

76. Elliott, *supra* note 34.

77. *Id.*

78. *Id.*

79. LEGIS. AUDITOR REP., *supra* note 33, at 17.

80. *Id.*

call on April 11 is not documented in Markingson's progress notes until four days later, April 15.<sup>81</sup> There is no documented evidence that anyone on the treatment team followed up with her until at least a week later."<sup>82</sup>

On the morning of May 8, 2004, a halfway-house worker found Markingson's corpse in a bathroom.<sup>83</sup> He had used a box cutter to slash open his abdomen and slice his neck, nearly decapitating himself.<sup>84</sup> He had left a note on his nightstand that read "I left this experience smiling!"<sup>85</sup>

### C. Robert Huber

Three years after Markingson's death, Dr. Olson again recruited an involuntarily confined patient into a drug study for which he was a principal investigator. In 2007, Robert Huber reported to an emergency room complaining of ringing in his ears, hearing voices, and anxiety.<sup>86</sup> He was transferred to Fairview Riverside Hospital's psychiatric unit, where the medical team diagnosed him with paranoid schizophrenia.<sup>87</sup> Huber was confined at Fairview Riverside for two weeks, during which time he claims "he received daily requests from Dr. Stephen Olson and others in the [University of Minnesota's] Psychiatry Department to volunteer for a drug trial involving an experimental medication called bifeprunox."<sup>88</sup> Huber claims he felt coerced to consent to the study "because he thought Olson would keep him in the hospital until he did."<sup>89</sup> He also claims that Fairview staff used his lack of insurance to pressure him to participate, telling Huber "you have a giant medical bill and if you do the research, you won't have this

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81. *Id.*

82. *Id.*

83. Elliott, *supra* note 34.

84. *Id.*

85. *Id.*

86. Jeff Baillon, *Investigators: U of M Drug Study Criticism Grows*, FOX 9 (May 19, 2014), <http://www.fox9.com/health/1647039-story>.

87. *Id.*

88. Jeremy Olson, *University of Minnesota Admits Missteps In Second Schizophrenia Drug Study*, STAR TRIB. (Minn.) (May 9, 2015, 6:22 PM), <http://www.startribune.com/u-admits-missteps-in-2nd-schizophrenia-drug-study/303143181/>.

89. *Id.*

giant medical bill.”<sup>90</sup> That claim appears corroborated by Dr. Olson’s own records, which indicate that Huber was “‘very interested’ in the opportunity to have his medical expenses covered by the study because of a lack of insurance.”<sup>91</sup>

Dr. Olson’s clinical records indicate Huber expressed concerns about the safety of the study drug, and that Olson reassured him that “‘enough patients have been treated to be more sure of its safety.’”<sup>92</sup> In truth, bifeprunox had not been proven safe—part of the purpose of the study was to establish its safety.<sup>93</sup> In fact, the following month, the Food and Drug Administration (“FDA”) announced that it would not approve the drug following the death of another study subject due to severe liver complications.<sup>94</sup> However, Huber was not informed of these facts, and continued taking the study drug for two more months.<sup>95</sup> During that time, “‘he experienced abdominal pains so severe that he required at least two visits to hospital emergency rooms.’”<sup>96</sup> Rather than reporting these complaints as adverse events, Dr. Olson recorded them as “‘psychosomatic’” side effects that were “‘unlikely’” to be related to the study drug.<sup>97</sup> Huber says eventually his distress became so pronounced that he considered suicide to make the pain stop.<sup>98</sup> Dr. Olson wrote that Huber “‘decided to quit the study due to these psychosomatic Sx [side effects].’”<sup>99</sup>

## II. RESEARCH RECRUITMENT OF INVOLUNTARILY COMMITTED PATIENTS RAISES SERIOUS RISKS OF ABUSES

While the Markingson and Huber cases show that involuntarily confined patients continue to be used as research subjects, they give no indication of how many other such patients may be at other facilities around the country. Indeed, even after multiple investigations into the University of Minnesota’s recruitment

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90. Baillon, *supra* note 86.

91. *Id.*

92. *Id.*

93. *See* Olson, *supra* note 88.

94. *Id.*

95. *Id.*

96. *Id.*

97. Baillon, *supra* note 86.

98. Olson, *supra* note 88.

99. Baillon, *supra* note 86.

practices, it is still not known how many other involuntarily confined patients university researchers have recruited into the CAFE study or other research.

However, there is no reason to believe these cases are aberrations involving rogue researchers. In each of these cases, the treatment of these subjects found defenders. The study in the *Kaimowitz* case was authorized and funded by Michigan's legislature, and researchers defended the study in the courts. Officials at the University of Minnesota—including senior Institutional Review Board ("IRB") officials—repeatedly insisted that Markingson's recruitment was consistent with ethical guidelines and entirely beyond reproach.<sup>100</sup> The University's IRB likewise concluded Robert Huber's consent was voluntary and a consultant hired by the University agreed.<sup>101</sup>

Although it would be preferable to have empirical data regarding involuntarily committed patients' participation in research, the incidents that have come to light highlight the power disparities between these patients and researchers and the resulting danger of mistreatment. With respect to research recruitment, patients under commitment orders are similarly situated to prisoners, who are widely recognized as being vulnerable to coercion and exploitation.<sup>102</sup> Like prisoners, these patients' circumstances

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100. See, e.g., Aaron Friedman, *University of Minnesota Research Case Is Not a Scandal*, STAR TRIB. (Minn.) (May 16, 2013, 6:32 PM), <http://www.startribune.com/university-of-minnesota-research-case-is-not-a-scandal/207795501/> (noting that Dr. Aaron Friedman, who was then the University of Minnesota's president for health sciences and dean of the Medical School, wrote "Mr. Markingson's suicide was a tragedy, but it is not a scandal. Nine years later, it is time to stop blaming our university and our researchers."); Andy Mannix, *Dan Markingson's 2004 Suicide: 'Corrective Action' Issued to Former U of M Employee*, CITYPAGES (Minn.) (Nov. 13, 2012), <http://www.citypages.com/news/dan-markingsons-2004-suicide-corrective-action-issued-to-former-u-of-m-employee-6558956> ("The college has repeatedly denied any wrongdoing, pointing to a number of state and federal entities that have investigated the case and cleared those who worked on the study."); LEGIS. AUDITOR REP., *supra* note 33 (noting that university leaders have been "consistently unwilling to discuss or even acknowledge that serious ethical issues and conflicts are involved").

101. FTI CONSULTING, INDEPENDENT ASSESSMENT OF A UNIVERSITY OF MINNESOTA INSTITUTIONAL REVIEW BOARD NON-COMPLIANCE DETERMINATION 16 (2015), <http://www.health.umn.edu/sites/default/files/FTI-Release.pdf>. However, the key findings supporting the consultant's conclusion are redacted from the publicly available copy of the report. *Id.* In addition, the consultant never interviewed Huber, relying instead on an absence of "documented evidence" of coercion. *Id.* at 16, Appendix B. It is not clear what kind of documentation would have shown coercion or why one should expect such documentation to exist.

102. IOM REPORT, *supra* note 7, at 21 ("Prisoners are an especially vulnerable class of

raise serious concerns about the feasibility of obtaining voluntary informed consent to research participation. Precisely because of their vulnerability, these patients are also at risk of being targeted for research recruitment because of their easy availability.

*A. Involuntary Commitment Presents an Overwhelming Barrier to Voluntary Informed Consent to Research*

Ethical guidelines generally require that subjects give their informed consent to participation.<sup>103</sup> Among other elements, informed consent requires that subjects are competent to make decisions regarding whether to participate in research and that their consent is given voluntarily.<sup>104</sup> It is difficult, if not impossible, to meet these requirements with patients under commitment orders.

1. Impaired Decision-Making Capacity

As an initial matter, recruiting involuntarily committed patients raises obvious concerns about the decision-making capacity of these subjects.<sup>105</sup> By definition, mentally ill patients who have

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potential research participants who historically have been exploited by physicians and researchers seeking expedient solutions to complex research problems[ ]. They are the classic ‘captive population.’”); NAT’L COMM’N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, U.S. DEP’T OF HEALTH, EDUC. & WELFARE, DHEW PUB. NO. OS 76-131, RESEARCH INVOLVING PRISONERS 5 (1976) [hereinafter 1976 NAT’L COMM’N REP.] (“There are two basic ethical dilemmas concerning the use of prisoners as research subjects: (1) whether prisoners bear a fair share of the burdens and receive a fair share of the benefits of research; and (2) whether prisoners are, in the words of the Nuremberg Code, ‘so situated as to be able to exercise free power of choice’—that is, whether prisoners can give truly voluntary consent to participate in research.”); 45 C.F.R. § 46.302 (2015) (“[P]risoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research.”).

103. Ezekiel J. Emanuel et al., *What Makes Clinical Research Ethical?*, 283 JAMA 2701, 2706 (2000); 45 C.F.R. § 46.111(a)(4) (2015).

104. NAT’L COMM’N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, U.S. DEP’T OF HEALTH, EDUC., & WELFARE, DHEW PUB. NO. (OS) 78-0014, THE BELMONT REPORT 6-8 (1979) [hereinafter BELMONT REP.], [http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b\\_09\\_02\\_Belmont%20Report.pdf](http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b_09_02_Belmont%20Report.pdf).

105. OFFICE FOR HUMAN RESEARCH PROTECTIONS, U.S. DEP’T OF HEALTH AND HUMAN SERVS., INSTITUTIONAL REVIEW BOARD GUIDEBOOK ch. 6(D) (1993) [hereinafter IRB GUIDEBOOK], [http://wayback.archive-it.org/org-745/20150930182815/http://www.hhs.gov/ohrp/archive/irb/irb\\_chapter6.htm#g5](http://wayback.archive-it.org/org-745/20150930182815/http://www.hhs.gov/ohrp/archive/irb/irb_chapter6.htm#g5) (“The predominant ethical concern in research involving individuals with psychiatric, cognitive, or developmental disorders, or who are substance abusers is that their disorders may compromise their capacity to understand



been involuntarily committed are ill-equipped to make judgments regarding their own care. Under even the most permissive “need for treatment” commitment standard, a person may not be involuntarily confined unless a court has determined that she suffers from a mental illness that “[s]ubstantially impairs the person’s capacity to make an informed decision regarding treatment.”<sup>106</sup>

The most relevant studies of committed patients’ competence come from the United Kingdom. A study conducted on the inpatient units of London’s Maudsley Hospital found that 86 percent of patients detained under the Mental Health Act did not have the capacity to consent to treatment, as measured by the MacArthur competence assessment tool.<sup>107</sup> This figure is consistent with a smaller 2005 British study, which found that that 83 percent (thirty of thirty-six patients) did not have the capacity to consent.<sup>108</sup> It is worth mentioning that these studies measured capacity to consent to treatment, not research. However, arguably the threshold for capacity to consent to research should be even higher than the standard for treatment, at least when the research has the potential for significant risk.

Although many involuntarily committed patients may lack adequate decision-making capacity to consent to research, the lack of explicit protections for these patients gives researchers broad latitude in assessing their capacity. For example, Dan Markingson was involuntarily committed because he was suffering from profound psychosis and threatening mass murder. A week before his commitment proceedings began, he believed that Angelina Jolie was his sister and that his mother was a lizard.<sup>109</sup> In the days prior to his recruitment into the CAFE study, his treating physician, a psychologist, and a social worker each judged him to be incapable of making his own decisions regarding medications.<sup>110</sup>

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the information presented and their ability to make a reasoned decision about participation.”).

106. ARIZ. REV. STAT. ANN. § 36-501(31)(b) (2016); TAC SURVEY, *supra* note 10, at 7–8.

107. GARETH S. OWEN ET AL., BMJ, MENTAL CAPACITY TO MAKE DECISIONS ON TREATMENT IN PEOPLE ADMITTED TO PSYCHIATRIC HOSPITALS 1–3 (2008), [www.bmj.com/content/337/bmj.39580.546597.BE.full.pdf](http://www.bmj.com/content/337/bmj.39580.546597.BE.full.pdf).

108. Ruth Cairns et al., *Prevalence and Predictors of Mental Incapacity in Psychiatric in-Patients*, 187 BR. J. PSYCHIATRY 379, 379 (2005).

109. Rep. of Pre-Petition Screening Team, *supra* note 45.

110. On November 14, Dr. Olson determined that Dan was psychotic and dangerous and that he “lack[ed] the capacity to make decisions regarding [his] treatment.” Exam’r’s

Yet these assessments did not prevent Markingson from being asked to consent to research. In fact, Dr. Olson first discussed the CAFE study with Markingson on November 19—the same day a court-appointed psychologist examined Markingson and determined he had “a substantial Disorder of Thought” and a “Gross Impairment of Judgment, Behavior, Capacity to Recognize Reality [or] to Reason or Understand.”<sup>111</sup> Yet when Markingson was evaluated by CAFE study coordinator Jean Kenney on November 21, she determined that he was competent to comprehend and rationally weigh the risks and benefits of participating in a randomized, double-blinded drug trial.<sup>112</sup>

There is no doubt some involuntarily committed patients are competent to make decisions regarding research participation. Nevertheless, the high prevalence of impaired capacity among these patients renders the population especially vulnerable and weighs in favor of special protections for this group.

## 2. Inherently Coercive Circumstances

Even among involuntarily committed patients who have adequate capacity to consent to research participation, the more fundamental problem is that their circumstances render it impossible to ensure that their consent to participate is given voluntarily.<sup>113</sup> Voluntariness is a core requirement of research ethics.<sup>114</sup> Accordingly, Subpart A of the Common Rule requires

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Statement in Support of Petition for Commitment, *In re Markingson*, No. PX-03-10465 (Minn. Dist. Ct., 1st Jud. Dist. Nov. 17, 2003), <https://www.scribd.com/doc/49742149/Olson-Examiner-Statement-Commitment>. On November 17, a court-appointed social worker shared that assessment, concluding that Markingson did not have “the capacity to make decisions regarding neuroleptic medications.” LEGIS. AUDITOR REP., *supra* note 33, at 11; Rep. of Pre-Petition Screening Team, *supra* note 45.

111. REP. OF EXAMINER, *supra* note 42, at 3; LEGIS. AUDITOR REP., *supra* note 33, at 11.

112. LEGIS. AUDITOR REP., *supra* note 33, at 11.

113. See *Kaimowitz v. Dep’t of Mental Health*, 1 MENTAL DISABILITY L. REP. (ABA) 147, 150 (Mich. Cir. Ct., Wayne Cty. July 10, 1973) (“Although an involuntarily detained mental patient may have a sufficient I.Q. to intellectually comprehend his circumstances (in Dr. Rodin’s experiment, a person was required to have at least an I.Q. of 80), the very nature of his incarceration diminishes the capacity to consent to psychosurgery. He is particularly vulnerable as a result of his mental condition, the deprivation stemming from involuntary confinement, and the effects of the phenomenon of ‘institutionalization.’”).

114. *The Nuremberg Code (1947)*, 313 BMJ 1448, 1448 (1996), [www.bmj.com/content/313/7070/1448.1](http://www.bmj.com/content/313/7070/1448.1) (“The voluntary consent of the human subject is absolutely essential. This means that the person involved . . . should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress,

that researchers seek participants' consent "only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence."<sup>115</sup>

However, in the context of prisoners it has long been recognized that institutional confinement can preclude voluntary consent. In its 1976 report, *Research Involving Prisoners*, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research found that "prisoners are, as a consequence of being prisoners, more subject to coerced choice and more readily available for the imposition of burdens which others will not willingly bear."<sup>116</sup> Because "the Commission did not find in prisons the conditions requisite for a sufficiently high degree of voluntariness and openness," it recommended imposing strict limits on the types of research that could be performed using prisoners and implementing a raft of procedural safeguards to protect against coercion and exploitation.<sup>117</sup> Recognizing that "prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research," the Department of Health and Human Services acted on these recommendations by implementing special protections for prisoners in certain federally funded research.<sup>118</sup>

These concerns apply with even greater force to institutionalized mental patients. As an initial matter, like prisoners, these patients can be vulnerable to coercive influences by virtue of their physical isolation from the rest of society, as well as by potential estrangement from family members and other trusted sources of

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overreaching, or other ulterior form of constraint or coercion"); *WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects*, WORLD MED. ASS'N ¶ 25 [hereinafter *Declaration of Helsinki*], <http://www.wma.net/en/30publications/10policies/b3/> (last visited Apr. 5, 2017) ("Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. . . . [N]o individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees."); BELMONT REP. *supra* note 104, at 7–8 ("An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence.").

115. 45 C.F.R. § 46.116 (2016).

116. 1976 NAT'L COMM'N REP., *supra* note 102, at 8.

117. *Id.* at 12, 14–16, 20–21.

118. 45 C.F.R. § 46.302 (2016).

independent advice.<sup>119</sup> For example, when Markingson was recruited into the CAFE study, he was in a locked ward at Fairview Hospital. He did not have access to his mother or to a social worker appointed by the court to help protect his interests.<sup>120</sup> As the Legislative Auditor determined, “given his confinement and isolation at FUMC, Markingson had no one to provide him with independent advice about agreeing to participate in the drug study; all of the information and advice he was given came from Dr. Olson [, the principal investigator,] and Jean Kenney [, the study coordinator].”<sup>121</sup>

The potential for coercion is further heightened by the enormous power disparities between institutionalized individuals and the institution’s authorities.<sup>122</sup> While the requirement of voluntariness is rooted in respect for autonomous individuals’ right to make decisions in accordance with their own values and priorities, confinement to an institution—particularly for extended periods—can profoundly erode an individual’s sense of identity and capacity for self-determination. As Erving Goffman explored in his seminal work, *Asylums*, “total institutions,” such as prisons and mental hospitals, “disrupt or defile precisely those actions that in civil society have the role of attesting to the actor and those in his presence that he has some command over his world—that he is a person with ‘adult’ self-determination, autonomy, and freedom of action.”<sup>123</sup> In these environments, authorities dominate every aspect of an inmate’s existence, setting daily schedules, controlling access to both the necessities of living and other comforts, and exercising power to reward compliance and punish non-

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119. ERVING GOFFMAN, *ASYLUMS: ESSAYS ON THE SOCIAL SITUATION OF MENTAL PATIENTS AND OTHER INMATES* 136–41 (First Anchor Books ed., 1961).

120. LEGIS. AUDITOR REP., *supra* note 33, at 15.

121. *Id.*

122. *Kaimowitz v. Dep’t of Mental Health*, 1 MENTAL DISABILITY L. REP. (ABA) 147, 151 (Mich. Cir. Ct., Wayne Cty. July 10, 1973) (“Involuntarily confined mental patients live in an inherently coercive institutional environment. Indirect and subtle psychological coercion has profound effect upon the patient population. Involuntarily confined patients cannot reason as equals with the doctors and administrators . . . . They are not able to voluntarily give informed consent because of the inherent inequality in their position.”).

123. GOFFMAN, *supra* note 119, at 43; *see also Kaimowitz*, 1 MENTAL DISABILITY L. REP. at 150 (“Institutionalization tends to strip the individual of the support which permits him to maintain his sense of self-worth and the value of his own physical and mental integrity.”).

compliance.<sup>124</sup> As Paul Appelbaum observed, people who live in these circumstances become accustomed to deferring to the will of institutional authorities—and may continue to “assume that behaving contrary to the wishes of those in power will result in adverse sanctions” even when they are told otherwise.<sup>125</sup>

In the *Kaimowitz* case, for example, the court highlighted Doe’s testimony that he needed authorities’ approval for “such minor things as the right to have a lamp in his room, or the right to have ground privileges to go for a picnic with his family.”<sup>126</sup> “For 17 years he lived completely under the control of the hospital. Nearly every important aspect of his life was decided without any opportunity on his part to participate in the decision-making process.”<sup>127</sup> Given this backdrop of nearly total control over inmates, the court concluded “[t]he involuntarily detained mental patient is in an inherently coercive atmosphere even though no direct pressures may be placed upon him.”<sup>128</sup>

Perhaps the most important power institutional authorities hold over involuntarily confined individuals is determining when they are ready to be released.<sup>129</sup> The 1976 National Commission report on research with prisoners identified “indeterminate release dates with nonobjective or unknown conditions for leaving the prison” as a critical barrier to voluntary consent.<sup>130</sup> This concern is even more salient in the context of civil commitment. Unlike criminals, who are sentenced to prison for specified periods of time (admittedly subject to some adjustments), involuntarily committed patients are confined for indeterminate periods.<sup>131</sup>

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124. See GOFFMAN, *supra* note 119, at 48–54; see also *Kaimowitz*, 1 MENTAL DISABILITY L. REP. at 147, 150–51 (discussing the highly regulated and heavily restricted environment experienced by institutionalized inmates).

125. Paul S. Appelbaum, *Consent and Coercion: Research with Involuntarily Treated Persons with Mental Illness or Substance Abuse*, 4 ACCOUNTABILITY IN RES. 69, 76 (1995).

126. *Kaimowitz*, 1 MENTAL DISABILITY L. REP. at 151.

127. *Id.*

128. *Id.*

129. *Id.* (“It is obvious that the most important thing to a large number of involuntarily detained mental patients incarcerated for an unknown length of time, is freedom.”); 1976 NAT’L COMM’N REP., *supra* note 102, at 62.

130. 1976 NAT’L COMM’N REP., *supra* note 102, at 50.

131. Stephen J. Schulhofer, *Two Systems of Social Protection: Comments on the Civil-Criminal Distinction, with Particular Reference to Sexually Violent Predator Laws*, 7 J. CONTEMP. LEGAL ISSUES 69, 70 (1996) (“All states have statutes permitting the indefinite

Their freedom depends on institutional authorities determining that the patient is fit for release.

This creates strong incentives for confined patients to seek these authorities' approval. The Office for Human Research Protections' Institutional Review Board Guidebook advises that "[t]he eagerness for release may induce an institutionalized person, especially one who is involuntarily confined, to participate in research out of a desire to appear 'rational' and 'cooperative' to those who will make decisions about his or her release."<sup>132</sup> The *Kaimowitz* court went further, concluding "[i]t is impossible for an involuntarily detained mental patient to be free of ulterior forms of restraint or coercion when his very release from the institution may depend upon his cooperating with the institutional authorities and giving consent to experimental surgery."<sup>133</sup>

The Markingson case illustrates this potential for coercion.<sup>134</sup> Markingson faced involuntary commitment to a long-term state mental facility when Dr. Olson, his treating physician, first approached him about participating in the CAFE study. On November 20, a court issued an order that stayed Markingson's commitment on the condition that he "cooperate with the treatment plan at Fairview University Medical Center until medically discharged, and follow all of the aftercare recommendations of the treatment team[.]"<sup>135</sup> The next day, Dr. Olson's subordinate, Jean Kenney, sought and obtained Markingson's consent to participate in the CAFE study.<sup>136</sup>

Although ethical guidelines require that subjects understand that they are free to terminate their participation at any time

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civil commitment of persons who are mentally ill and dangerous to themselves or others.").

132. IRB GUIDEBOOK, *supra* note 105, at ch. 6(D); *see also* BELMONT REP., *supra* note 104, at 8 (noting that "[u]njustifiable pressures usually occur when persons in positions of authority or commanding influence—especially where possible sanctions are involved—urge a course of action for a subject").

133. *Kaimowitz*, 1 MENTAL DISABILITY L. REP. at 151.

134. LEGIS. AUDITOR REP., *supra* note 33, at 10 ("Dan Markingson was extraordinarily vulnerable when Dr. Olson recruited him into a drug study; Markingson was mentally ill and faced commitment to a state psychiatric hospital if he did not cooperate with the Fairview University Medical Center treatment plan and his treatment team's aftercare recommendations following discharge.").

135. Order for Stayed Commitment, *supra* note 50, at 2; LEGIS. AUDITOR REP., *supra* note 33, at 11.

136. LEGIS. AUDITOR REP., *supra* note 33, at 6.

without suffering adverse consequences,<sup>137</sup> when Markingson was discharged from the hospital to a halfway house he was required to sign an agreement that required him to keep his CAFE study appointments and continue taking his medications.<sup>138</sup> The document again warned Markingson that “[c]onsequences for not following this plan could result in court commitment to the hospital.”<sup>139</sup> Minnesota’s Legislative Auditor observed that although Dr. Olson repeatedly claimed that “Markingson was told that he did not have to participate in the drug study and that he had a right to alternative treatment[,]” it was not clear “what Dr. Olson or Ms. Kenney said or implied about what that alternative might be.”<sup>140</sup> A review of the Markingson case by the Association for the Accreditation of Human Research Protection Programs concluded, “the fear of being subjected to an involuntary legal process for perceived noncooperation, even if there is no *direct* threat of such legal compulsion, is an overwhelming barrier to voluntariness.”<sup>141</sup>

Similarly, in the *Kaimowitz* case, the doctor who sought to perform psychosurgery on a mental patient testified that “involuntarily confined patients tend to tell their doctors what the patient thinks these people want to hear.”<sup>142</sup> The patient’s testimony bore out this contention. While he was confined, Smith steadfastly insisted that his consent to experimental brain surgery was entirely voluntary and that he would have consented to the surgery even if he were not confined in an institution.<sup>143</sup> Yet once he was released from confinement, he withdrew his consent.<sup>144</sup> The testimony at trial indicated that Smith had in fact consented to this surgery “partly because of his effort to show the doctors in the hospital that he was a cooperative patient.”<sup>145</sup> Smith was willing to accept the extremely serious risks of experimental brain sur-

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137. 45 C.F.R. § 46.116(a)(8) (2016).

138. Aftercare Agreement, *supra* note 67.

139. *Id.*

140. LEGIS. AUDITOR REP., *supra* note 33, at 15.

141. AAHRPP REP., *supra* note 33, at 67; *see also* TAC SURVEY, *supra* note 10, at 11 (noting that outpatient commitment “motivates patients by impressing upon them, through the symbolic power of the judge as an authority figure, the seriousness of their need to comply with treatment. (This is sometimes called ‘the black robe effect.’)”).

142. *Kaimowitz v. Dep’t of Mental Health*, 1 MENTAL DISABILITY L. REP. 141, 150 (Mich. Cir. Ct., Wayne Cty. July 10, 1973).

143. *Id.* at 147.

144. *Id.* at 154 n.23.

145. *Id.* at 151.

gery—which included the possibility of brain damage or death—because he believed it would help him gain his liberty.

The Common Rule seeks to protect voluntariness by requiring that subjects be informed “that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.”<sup>146</sup> For prisoners, the rules further require that “each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.”<sup>147</sup>

But the inherent coerciveness of the institutional environment cannot be remedied simply by explaining to patients that they are free to refuse participation without suffering adverse consequences—even when patients have sufficient decision-making capacity to comprehend this information. First, stating this in a consent form does not make it true. While institutional authorities may have no intention of punishing patients for declining to participate, they may nevertheless draw adverse inferences from a patient’s refusal. If authorities believe participation is in the patient’s interest, they may take the patient’s refusal as an indication that the patient is not capable of making decisions regarding his or her own care, and may take that into account—consciously or subconsciously—when making assessments about the patient’s progress and suitability for release.

Second, even when authorities would draw no adverse inferences from a patient’s refusal to participate in research, merely informing a patient of this may do little to counteract the effects of a patient’s routine, forced acquiescence to authorities’ imperatives.<sup>148</sup> As Thomas Grisso asks,

When a member has adapted to a system of few choices, substantial dependence on official-controlled rewards, and functional regimentation, what does it mean to him or her when an official (or a profes-

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146. 45 C.F.R. § 46.116(a)(8) (2016).

147. *Id.* § 46.305(a)(6).

148. Thomas Grisso, *Voluntary Consent to Research Participation in the Institutional Context*, in RESEARCH ETHICS: A PSYCHOLOGICAL APPROACH 203, 212 (Barbara H. Stanley et al. eds., 1996) (“[R]esidents’ expectancies based on their socialization to the power and control of institutional officials are not always easily undermined by providing contradictory information.”).



sional from outside the system) walks up and says: ‘Here’s something I’d like you to do—but it’s up to you; do you want to do it or not?’ What would it take to convince the institutionally socialized member to shed member identity and to resume personal identity as an autonomous individual for this one specific purpose?<sup>149</sup>

This concern is amplified when the researcher seeking the patient’s consent is also the treating physician.<sup>150</sup> The Declaration of Helsinki advises that “[w]hen seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress.”<sup>151</sup> In those situations, the Declaration advises that “informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.”<sup>152</sup>

However, even when researchers are independent from institutional authorities, involuntarily committed patients may not appreciate that distinction.<sup>153</sup> And they may be so inured to deferring to authorities that the distinction may have little impact on their beliefs regarding their freedom to choose or their ability to exercise agency. For example, in a study of fifteen and sixteen-year-olds confined to a juvenile detention center, Grisso engaged in an extensive pre-experimental consent session with 192 subjects. Subjects were informed at least twice that they were free to refuse participation without suffering adverse consequences, that they could discontinue their participation at any time, and that the researcher was independent from the court and police and would not share with these authorities any information obtained in the research.<sup>154</sup> Quizzed afterwards, however, 46 percent of the subjects did not recall that the researcher was independent and

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149. *Id.* at 206.

150. *See id.* at 205 (stating that institutionalized patients’ “power deficiency” vis a vis researchers “may be especially salient when institutional residents’ research participation is sought by an investigator with institutionally sanctioned authority.”).

151. *Declaration of Helsinki, supra* note 114, ¶ 27.

152. *Id.*

153. Grisso, *supra* note 148, at 209 (“[T]he potential volunteer brings to the situation certain expectancies about members’ interactions with institutional officials. These expectancies may generalize to other persons (such as the researcher) whose status may be perceived to be more nearly that of an institutional official than that of an institutional member.”).

154. *Id.* at 211.

61 percent expressed doubts about the truthfulness of that claim.<sup>155</sup> Given their profound mental illnesses, involuntarily committed patients may be even less capable of distinguishing between researchers and institutional authorities.

B. *Recruiting Involuntarily Confined Psychiatric Patients Targets a Vulnerable Population*

As the history of human subjects research has shown, many subjects are vulnerable to exploitation or mistreatment by virtue of their condition or situation. For this reason, the Common Rule extends special protections to certain “vulnerable populations.”<sup>156</sup> The relevant passage of the Common Rule does not provide an exhaustive list of vulnerable populations, but as examples it names “children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.”<sup>157</sup> If, as many have argued, vulnerability is characterized by a diminished capacity to protect one’s own interests,<sup>158</sup> then involuntarily confined, mentally ill patients are clearly as vulnerable as many of the listed populations.

Justice requires that vulnerable populations should not be targeted for participation in research because of their easy availability or manipulability.<sup>159</sup> Moreover, vulnerable populations should not bear the burdens of research that they are unlikely to benefit from, either individually or as a group.<sup>160</sup> Accordingly, Subpart A of the Common Rule provides that IRBs may only approve a re-

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155. *Id.* at 211–12.

156. 45 C.F.R. § 46.111(a)(3) (2016).

157. *Id.*

158. COUNCIL FOR INT’L ORGS. OF MED. SCIS. (CIOMS), INTERNATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS 64 (2002) [hereinafter CIOMS GUIDELINES]; Doris Schroeder & Eugenijus Gefenas, *Vulnerability: Too Vague and Too Broad?*, 18 CAMBRIDGE Q. HEALTHCARE ETHICS 113, 113–14 (2009).

159. Emanuel et al., *supra* note 103, at 2704 (“[F]air subject selection requires that the scientific goals of the study, not vulnerability, privilege, or other factors unrelated to the purposes of the research, be the primary basis for determining the groups and individuals that will be recruited and enrolled.”).

160. *Declaration of Helsinki*, *supra* note 114, ¶ 20 (“Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.”).

search protocol after finding that selection of subjects is equitable.<sup>161</sup>

However, market pressures can work against this goal by creating incentives to quickly recruit subjects for participation in research that may be unattractive to more advantaged populations. Within the pharmaceutical industry in particular, subject recruitment is one of the biggest impediments to the success of clinical trials.<sup>162</sup> Several studies have found that most randomized controlled trials fail to achieve their recruitment targets, while others must be delayed in order to recruit sufficient subjects.<sup>163</sup> As a result, pharmaceutical researchers are under immense pressure to quickly enroll willing subjects. A report on research recruitment by HHS's Office of the Inspector General reported that when asked what sponsors are looking for from research sites, one investigator replied, "Number one—rapid enrollment. Number two—rapid enrollment. Number three—rapid enrollment."<sup>164</sup>

This pressure has sometimes led researchers to target institutionalized persons for research participation. As the Belmont Report warned:

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161. 45 C.F.R. § 46.111(a)(3) (2016).

162. See, e.g., Kathleen B. Drennan, *Patient Recruitment: The Costly and Growing Bottleneck in Drug Development*, 7 DRUG DISCOVERY TODAY 3 (2002) ("Within the clinical trials industry, it is a well-known fact that at least 80% of trials fail to meet their enrollment deadlines."); Taren Grom, *Unclogging the Patient Recruitment Bottleneck*, PHARMAVOICE (Feb. 2011), <http://www.pharmavoices.com/article/2182/> ("Patient recruitment remains to be one of the biggest, and most costly, bottlenecks in clinical development. . . . [I]ndustry averages reveal that more than 80% of clinical trials are delayed because of poor enrollment.").

163. Alison M. McDonald et al., *What Influences Recruitment to Randomised Controlled Trials? A Review of Trials Funded By Two UK Funding Agencies*, 7 TRIALS 9, 9 (2006) (study of 114 multisite trials found that fewer than one-third of these studies achieved their original target for subject recruitment); Shaun Treweek et al., *Methods To Improve Recruitment to Randomised Controlled Trials: Cochrane Systematic Review and Meta-Analysis*, 3 BMJ OPEN 24, 25 (2013) (in a study of trials in the U.S. National Institute of Health inventory, 66 percent failed to meet recruitment targets, and 24 percent failed to meet even half of the recruitment targets); Judith M. Watson & David J. Torgerson, *Increasing Recruitment To Randomised Trials: A Review Of Randomised Controlled Trials*, 6 BMC MED. RES. METHODOLOGY 34, 34 (2006) ("Recruitment to randomised trials can be very poor. A recent survey of corresponding authors of randomised trials published between the years 2000 and 2001 in the Lancet or BMJ found that nearly 60% had either failed to meet their recruitment target or required an extended recruitment period.").

164. U.S. DEP'T OF HEALTH AND HUMAN SERVS., OFFICE OF THE INSPECTOR GENERAL, OEI-01-97-00195, RECRUITING HUMAN SUBJECTS: PRESSURES IN INDUSTRY-SPONSORED CLINICAL RESEARCH 13 (2000).

[T]he institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.<sup>165</sup>

For example, in the 1960s, new regulations requiring safety testing of pharmaceuticals as a condition of FDA approval drove drug companies to seek out prisoners as test subjects.<sup>166</sup> The National Commission's 1976 report concluded that this practice was often exploitative.<sup>167</sup> Noting a "paucity of evidence of any necessity to conduct research in prisons,"<sup>168</sup> the Commission recommended that research on prisoners be strictly curtailed in order "to ensure that this burden not be unduly visited upon prisoners simply because of their captive status and administrative availability."<sup>169</sup> Consistent with that recommendation, Subpart C of the Common Rule bars research on prisoners, with limited exceptions.<sup>170</sup>

Although these provisions all but ended recruitment of prisoners in federally funded research, they impose no restrictions on the use of involuntarily committed patients, who may be attractive subjects in current market conditions. Medications to treat psychiatric illnesses are among the most highly prescribed drugs in the world, generating tens of billions in revenues annually.<sup>171</sup> These medications must be tested on mentally ill subjects, both as part of the FDA approval process and (as in the CAFE study) in postmarketing studies.<sup>172</sup>

The *Markingson* case illustrates the potential for involuntarily confined mental patients to be targeted for inclusion in research because of their easy availability and manipulability. As a principal investigator for the CAFE study, Dr. Olson was under signifi-

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165. BELMONT REP., *supra* note 104, at 10.

166. 1976 NAT'L COMM'N REP., *supra* note 102, at 24; Reiter, *supra* note 1, at 515.

167. 1976 NAT'L COMM'N REP., *supra* note 102, at 7.

168. *Id.* at 12.

169. *Id.* at 7.

170. 45 C.F.R. § 306(b) (2016).

171. Michael Bartholow, *Top 200 Drugs of 2012*, PHARMACY TIMES (July 17, 2013), <http://www.pharmacytimes.com/publications/issue/2013/July2013/Top-200-Drugs-of-2012> (reporting \$23.5 billion in U.S. health care expenditures on mental health drugs in 2012).

172. See 21 U.S.C. § 355(a)–(b) (2012 & Supp. II 2015); see also Elliott, *supra* note 34.

cant pressure to recruit subjects. His agreement with AstraZeneca called for him to enroll thirty participants at the University of Minnesota trial site, with the university earning \$15,648 for each subject who completed the study.<sup>173</sup> But at the outset he and his team struggled badly to meet that target, recruiting only one subject in the first six months of the study.<sup>174</sup> This performance was so poor that Quintiles, the contract research organization managing the trial, placed the University of Minnesota trial site on “probation” for its lackluster recruitment.<sup>175</sup> Study coordinator Jean Kenney expressed particular frustration about parents intervening to dissuade their children from enrolling in the CAFE study.<sup>176</sup> In a January 2003 email to Quintiles, Kenney wrote:

Have had another person show interest from inpatient and then the parent put the pressure on and said, “NO.” (3rd time this has happened) Have tried to ask about concerns, etc. but usually just get a NO. So, some frustration here b/c we really need to get more enrollees. We’ve had none for January and that concerns me a lot.<sup>177</sup>

To bolster its recruitment efforts, in April 2003, the University’s psychiatry department set up an inpatient unit at Fairview Hospital where they could get better access to patients.<sup>178</sup> Under this new arrangement, every patient who reported to Fairview with symptoms of psychosis would be evaluated as a potential research subject for the CAFE study.<sup>179</sup> After recruiting only one subject in the first six months of the trial, under this arrangement, Dr. Olson recruited twelve more subjects in the next eight months, including Markingson.<sup>180</sup>

Under these conditions, Markingson may have been an attractive target for recruitment precisely because he was involuntarily

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173. LEGIS. AUDITOR REP., *supra* note 33, at 15.

174. Jeremy Olson & Paul Tosto, *The Death of Subject 13*, ST. PAUL PIONEER PRESS, May 18, 2008, at A1.

175. Deposition of Charles Schulz at 200, *Weiss v. Bd. of Regents for the Univ. of Minn.*, No. 27-CV-07-1679, 2008 WL 4103146 (Minn. Dist. Ct., 4th Jud. Dist. June 22, 2007), <https://www.scribd.com/document/50047611/Schulz-Deposition>.

176. LEGIS. AUDITOR REP., *supra* note 33, at 15–16.

177. *Id.* at 16.

178. Olson & Tosto, *supra* note 174.

179. *Id.*

180. Alexandros Stamatoglou, *The Physician Payment Sunshine Act: An Important First Step in Mitigating Financial Conflicts of Interest in Medical and Clinical Practice*, 45 MARSHALL L. REV. 963, 964 n.10 (2012).

confined, isolated from his mother, and facing long-term commitment to a mental institution if Dr. Olson deemed him unfit for release. As the Legislative Auditor concluded:

Even though payments from AstraZeneca did not go directly to Dr. Olson or Jean Kenney, University officials told us—and have said publicly many times—that the University’s budget depends on faculty bringing in outside revenue from research grants. Nevertheless, we cannot be certain what role obtaining outside revenue played in Dan Markingson’s recruitment and retention in the CAFÉ study. But we do know that AstraZeneca set a goal for Dr. Olson and prorated its payments to the University in a way that clearly created an incentive to enroll and keep subjects enrolled in the CAFÉ study. We also know that Dr. Olson kept Markingson in the study despite Mary Weiss’ repeated warnings<sup>181</sup> that Dan was not well and the study medication was not working.

As a captive population whose autonomy is strictly circumscribed, involuntarily committed patients may be tempting targets for “types of research which persons better situated would ordinarily refuse.”<sup>182</sup> Yet the Common Rule does not list mental illness as a specific example of vulnerability apart from the general category of “mentally disabled persons,” nor does it provide any concrete guidance for dealing with the problems characteristic of studies with mentally ill research subjects. As Bonnie writes: “The regulations are altogether silent on impairment of decision-making capacity, the consequences of decisional impairment, the designation and duties of proxy decision makers, and the nature of safeguards that IRBs are expected to consider.”<sup>183</sup>

In fact, the additional layer of protections that the Common Rule supposedly afforded to vulnerable populations is very thin indeed. The Common Rule simply instructs IRBs to make sure that “additional safeguards have been included in the study to protect the rights and welfare of these subjects.”<sup>184</sup> In addition, if an IRB regularly reviews protocols involving vulnerable populations, the Common Rule advises it to include “one or more indi-

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181. LEGIS. AUDITOR REP., *supra* note 33, at 16–17.

182. 1976 NAT’L COMM’N REP., *supra* note 102, at 8.

183. Richard J. Bonnie, *Research with Cognitively Impaired Subjects*, 54 ARCHIVES GEN. PSYCHOL. 105, 109 (1997).

184. 45 C.F.R. § 46.111 (2016).

viduals who are knowledgeable about and experienced in working with these subjects.”<sup>185</sup>

The inadequacy of the Common Rule to sufficiently address the problems of research with mentally ill subjects was noted by the National Bioethics Advisory Commission in its 1998 report, *Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity*.<sup>186</sup> The Commission observed that “persons with mental disorders who may have impaired capacity[ ] to make decisions, and therefore to give voluntary informed consent, have not received any such special protections,” and that federal research guidelines “provide no specific guidance for IRBs and investigators.”<sup>187</sup> It concluded, “[t]he National Bioethics Advisory Commission [ ] believes this state of affairs is not satisfactory.”<sup>188</sup>

Other official bodies have attempted to fill this gap. For example, the International Ethical Guidelines for Biomedical Research Involving Human Subjects produced by the Council for International Organizations of Medical Sciences (“CIOMS”) count as vulnerable all individuals “who by reason of mental or behavioural disorders are not capable of giving adequately informed consent.”<sup>189</sup> Among the special protections the CIOMS guidelines recommend are consent from a responsible family member or legally authorized representative, consent of the subject insofar as it is possible, and assurance that the research is to obtain knowledge relevant to the health needs of persons with mental or behavioral disorders.<sup>190</sup> Most importantly, investigators must ensure that research is not done on such persons if the research “might equally well be carried out on persons whose capacity to give adequately informed consent is not impaired.”<sup>191</sup>

This last requirement is critical, as the notorious Willowbrook hepatitis study made clear. From 1958 to 1964, at the Willowbrook State School on Staten Island, New York University pediatrician Saul Krugman deliberately infected mentally disabled, in-

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185. *Id.* § 46.107.

186. NAT’L BIOETHICS ADVISORY COMM’N, RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISIONMAKING CAPACITY 1–2 (1998).

187. *Id.* at 2 (citation omitted).

188. *Id.*

189. CIOMS GUIDELINES, *supra* note 158, at 70.

190. *Id.*

191. *Id.*

stitutionalized children with hepatitis A in order to study the course of the disease.<sup>192</sup> After Henry Beecher's famous article in the *New England Journal of Medicine* made the Willowbrook study an issue of public controversy,<sup>193</sup> Krugman defended it in part by arguing that hepatitis A was already endemic at Willowbrook, a notoriously filthy, overcrowded, poorly funded institution.<sup>194</sup> He also pointed out that he had asked the children's parents for proxy consent.<sup>195</sup> But as Paul Ramsey argued in response, there was nothing about Krugman's study that required it to be done on children, much less disabled, institutionalized children.<sup>196</sup> The study could just as well have been done on competent adults who were capable of giving voluntary consent.

A 1978 national commission made the same point about institutionalized populations in general. In a report entitled *Research Involving Those Institutionalized as Mentally Infirm*, the commission wrote:

If there are two classes of subjects, one of which is already severely burdened and the other of which is much less burdened, then in order to equalize the distribution of burdens, the latter class ought to accept any additional risks. Because those institutionalized as mentally infirm are already burdened by their disabilities, other less burdened classes of persons should accept the risks of research.<sup>197</sup>

The same point applies to involuntarily confined mental patients. Very few psychiatric research studies must be conducted on involuntarily confined patients rather than outpatients or inpatients who have been admitted on a voluntary basis. While arguably some studies may be very difficult to conduct on populations other than involuntary patients (studies of physical restraints, for instance), these rare exceptions should not be permitted to guide policy. In general, given a choice, researchers should be required to conduct studies on the least vulnerable population.

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192. Doriane Lambelet Coleman, *The Legal Ethics of Pediatric Research*, 57 DUKE L.J. 517, 531 (2007).

193. See generally Henry K. Beecher, *Ethics and Clinical Research*, 274 NEW ENG. J. MED. 1354 (1966) (discussing the ethics of the Willowbrook study).

194. Saul Krugman, Letter to the Editor, *Experiments at the Willowbrook State School*, THE LANCET, May 8, 1971, at 966.

195. *Id.*

196. PAUL RAMSEY, THE PATIENT AS PERSON: EXPLORATIONS IN MEDICAL ETHICS 48-49 (2d ed. 1970).

197. 1978 NAT'L COMM'N REP., *supra* note 20, at 60.



### III. EXISTING RESEARCH PROTECTIONS ARE INSUFFICIENT TO PROTECT INVOLUNTARILY COMMITTED PATIENTS

As described above, involuntarily committed patients are not suitable candidates for most research under the general provisions of the Common Rule. Nevertheless, existing research guidelines are inadequate to protect these patients from coercion and exploitation. Federal rules apply only to a limited range of research, while state law protections vary widely. Current rules also offer insufficient guidance regarding ethical recruitment of these patients and lack meaningful oversight and enforcement mechanisms.

#### A. *Existing Rules Have Enormous Gaps in Coverage*

There is no uniform set of guidelines that apply to all human subjects research in the United States. The vast majority of human subjects research is not covered by the Common Rule, which generally applies only to research conducted or supported by a federal agency that has adopted the rule.<sup>198</sup> Organizations conducting federally funded research must submit a Federalwide Assurance to the Office of Human Research Protections, which gives them the option of extending the Common Rule to all of their human subjects research, including studies without federal funding.<sup>199</sup> However, a diminishing number of institutions are choosing to do so. According to the Association for the Accreditation of Human Research Protection Programs, only 32 percent of academic institutions with accredited human research protections

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198. 45 C.F.R. § 46.101(a) (2016) (“Except as provided in paragraph (b) of this section, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research.”). Proposed changes call for expanding the rule’s coverage to encompass “all studies, regardless of funding source, that are conducted by a U.S. institution that receives some federal funding for human subjects research from a Common Rule agency.” *Regulatory Changes in ANPRM: Comparison of Existing Rules with Some of the Changes Being Considered*, DEPT OF HEALTH AND HUM. SERVS., <http://www.hhs.gov/ohrp/regulations-and-policy/regulations/regulatory-changes-in-anprm/index.html> (last visited Apr. 5, 2017). Even with this change, however, the rules would not apply to institutions that do not receive federal funding, including privately funded research. *See id.*

199. *Federalwide Assurance Instructions*, DEPT OF HEALTH AND HUM. SERVS., <http://www.hhs.gov/ohrp/register-irbs-and-obtain-fwass/forms/fwa-instructions/index.html> (last visited Apr. 5, 2017).

programs chose to apply the Common Rule to non-federally funded studies in 2014.<sup>200</sup>

Had the Common Rule been in effect at the time of the *Kaimowitz* case, the proposed psychosurgery research would not have been subject to its provisions because it was funded by the State of Michigan. Similarly, the CAFE trial in which Markingson was enrolled was not governed by federal regulations because the study was funded by a pharmaceutical company.<sup>201</sup> Although the FDA has adopted regulations similar to the provisions of Subpart A of the Common Rule, these rules only apply to clinical investigations regulated by the FDA and research supporting applications for FDA approval of drugs and devices.<sup>202</sup> Because the CAFE trial was a post-marketing study of FDA-approved drugs, these regulations also did not apply to the trial.

State laws governing research vary dramatically in the protections they afford involuntarily committed patients. Missouri law bars all biomedical and pharmacological research in mental health facilities housing civilly detained patients “unless such research is intended to alleviate or prevent the disabling conditions or is reasonably expected to be of direct therapeutic benefit to the participants.”<sup>203</sup> The statute further provides that no involuntary patient may consent to participate in any such research without a court order.<sup>204</sup> In response to the *Markingson* case, Minnesota’s legislature passed “Dan’s Law,” which prohibits recruitment of patients under a stay of commitment order, with limited exceptions.<sup>205</sup> Other jurisdictions require that research involving involuntarily committed patients must satisfy the requirements of the

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200. Theresa Defino, *AAHRPP Metrics Report Shows Slightly Fewer ‘Unchecked Boxes’*, 12 REP. ON RES. COMPLIANCE 6–7 (2015).

201. Although the FDA has adopted regulations similar to the provisions of Subpart A, these rules apply only to “clinical investigations regulated by the [FDA] . . . as well as clinical investigations that support applications for research or marketing permits for products regulated by the [FDA],” including drugs and medical devices. 21 C.F.R. § 50.1(a) (2016). Because the CAFE trial was a post-marketing study of FDA-approved drugs, these regulations did not apply to the trial. It is possible the University of Minnesota voluntarily committed to apply the Common Rule to all of its research during this period, but we have been unable to confirm this.

202. *Id.*

203. MO. ANN. STAT. § 630.192 (2016).

204. *Id.*

205. MINN. STAT. ANN. § 253B.095 (2016).

Common Rule.<sup>206</sup> Still, others merely provide that no such research should be conducted without patients' informed consent.<sup>207</sup>

The potential for state laws to leave involuntarily confined patients at risk of mistreatment is illustrated by regulations promulgated by the State of New York's Office of Mental Health ("OMH") in the 1990s, ostensibly "to ensure the protection of patients who participate in research while, at the same time, facilitating research into the very disorders from which they suffer and which underlie their impairment."<sup>208</sup> However, in response to a legal challenge filed by a disabilities rights group, a court found the regulations grossly inadequate to protect patients in the state's care.

Among other defects,<sup>209</sup> OMH's standards for enrolling incompetent, involuntarily committed patients in clinical trials were lower than the standards the United States Supreme Court has determined are required for involuntarily medicating convicted criminals. Due process allows prison officials to give inmates psychotropic medications against their will only "if the inmate is dangerous to himself or others and the treatment is in the inmate's medical interest."<sup>210</sup> Prisoners "must receive notice of the tentative diagnosis, the factual basis for the diagnosis, and why the staff believes medication is necessary," and they have a right to hearings within the institution as well as review by a court.<sup>211</sup>

By contrast, the OMH regulations permitted researchers to subject involuntarily committed patients to interventions that not only were medically unnecessary, but that offered them either no benefit or minimal benefits.<sup>212</sup> Moreover, the OMH rules did not require that patients or their representatives even be notified

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206. See, e.g., MONT. CODE ANN. §§ 53-20-147, 53-21-147 (2017); see TENN. CODE ANN. § 41-21-601 (2016); WIS. STAT. ANN. § 51.61(j) (2016).

207. See CAL. CODE REGS. tit. 9, § 778 (2017); NEV. REV. STAT. § 433.484 (2016); S.D. CODIFIED LAWS § 27A-12-3.12 (2016).

208. *T.D. v. New York State Office of Mental Health*, 650 N.Y.S.2d 173, 175 (N.Y. App. Div. 1996).

209. The rules did not specify the minimum qualifications of individuals who were responsible for assessing subjects' decision-making capacity. *Id.* at 189. Moreover, although OMH argued it voluntarily complied with federal regulations, the court determined the office had actually "exempted themselves from important reporting requirements and instead [had] elected to report to themselves." *Id.* at 184.

210. *Washington v. Harper*, 494 U.S. 210, 227 (1990).

211. *Id.* at 216.

212. *T.D.*, 650 N.Y.S.2d at 185.

that they had been found incompetent, or that a surrogate had determined they should participate in research.<sup>213</sup> Accordingly, patients had no way to challenge or seek review of those determinations. Indeed, “given the lack of a notice requirement, the patient . . . may not even be aware he or she is involved in research.”<sup>214</sup> If incompetent patients declined to participate in research, that refusal could be overridden without notice to the patient or her representative, forcibly subjecting these patients to “invasive and painful procedures and/or the administration of psychotropic drugs” to advance research that offered them no benefit.<sup>215</sup> In sum, under the OMH regulations *convicted criminals* had greater rights to refuse *treatment* than involuntarily committed patients had rights to refuse participation in non-therapeutic research.

The lack of uniform federal standards applicable to all human subjects research leaves involuntarily committed patients subject to varying levels of protection. In many cases, those protections are grossly deficient.

#### B. *IRB Oversight Is Insufficient to Protect Involuntarily Committed Patients*

Even if the Common Rule applied to all research involving involuntarily committed patients, the oversight required by Subpart A is not robust enough to prevent abuses, particularly in the context of research using involuntarily confined subjects.<sup>216</sup> The lynchpin of the system for protecting research subjects is review by Institutional Review Boards, or IRBs.<sup>217</sup> The federal rules place these panels of volunteers in the role of gatekeepers, requiring researchers to obtain an IRB’s approval before recruiting subjects. These boards prospectively evaluate researchers’ study pro-

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213. *Id.* at 189, 193.

214. *Id.* at 190.

215. *Id.* at 185.

216. See IOM REPORT, *supra* note 7, at 12 (“Approval of research by the IRB is a critical step, but it is not sufficient. Research involving prisoners must be monitored throughout the course of the study to verify that procedures are being conducted as approved and to detect adverse events or unanticipated problems in a timely manner.”).

217. See IRB GUIDEBOOK, *supra* note 105, at ch. 1(A) (explaining that IRBs are “established to protect the rights and welfare of human research subjects recruited to participate in research activities”).

protocols, which describe how they propose to run the study and the protections they will provide to subjects.<sup>218</sup> IRBs can reject studies or require changes to protocols to ensure that research conforms to federal rules.<sup>219</sup>

Critics have raised serious concerns about the ability of IRBs to protect subjects in the multi-billion dollar clinical trials industry.<sup>220</sup> First, although the Common Rule has some requirements regarding the constitution of IRB membership,<sup>221</sup> “[a]nyone who can bring together five people, including a community representative, a physician, a lawyer and an ‘ethicist,’ can set up shop and start competing for business.”<sup>222</sup> Although HHS has a process for registering IRBs, registration generally is not required.<sup>223</sup> Even when IRBs register, it is not clear that HHS monitors these registrations to ensure the legitimacy and quality of IRBs. As part of a 2009 investigation, the Government Accountability Office registered a fake IRB whose CEO was listed as Truper Dawg, named after a staff member’s three-legged dog.<sup>224</sup> Other names in the registration application included “April Phuls” and “Timothy Wittless.”<sup>225</sup> Nevertheless, HHS registered the IRB. The Government Accountability Office (“GAO”) then created a website for the fake IRB and quickly began receiving study protocols for ethical review—including one from a research company that wanted to do human trials involving invasive surgery.<sup>226</sup>

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218. 45 C.F.R. § 46.109 (2016).

219. *Id.*

220. See Osagie K. Obasogie, *Prisoners as Human Subjects: A Closer Look at the Institute of Medicine’s Recommendations to Loosen Current Restrictions on Using Prisoners in Scientific Research*, 6 STAN. J. C.R. & C.L. 41, 75–77 (2010); Ezekiel J. Emanuel et al., *Should Society Allow Research Ethics Boards to Be Run As For-Profit Enterprises?*, 3 PLOS MED. 0941, 0942–0944 (2006); David Evans et al., *Big Pharma’s Shameful Secret*, BLOOMBERG MARKETS, Dec. 2005, at 39.

221. 45 C.F.R. § 46.107 (2016).

222. Emanuel et al., *supra* note 220, at 0942.

223. 45 C.F.R. § 46.501 requires IRBs to register with HHS only “if they will review human subjects research conducted or supported by HHS and are to be designated under an assurance of compliance approved for federalwide use (i.e., an FWA) by OHRP.” *IRB Registration Process FAQs*, DEP’T OF HEALTH & HUM. SERVS., <http://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/irb-registration-process/index.html> (last visited Apr. 5, 2017).

224. Alicia Mundy, *Sting Operation Exposes Gaps in Oversight of Human Experiments*, WALL ST. J. (Mar. 26, 2009, 8:36 PM), <http://www.wsj.com/articles/SB123811179572353181>.

225. *Id.*

226. U.S. GOV’T ACCOUNTABILITY OFFICE, GAO-09-448T, HUMAN SUBJECTS RESEARCH:

Nothing in the federal rules prevents research organizations “from selecting the IRB least likely to reject the trial or delay approval by imposing too many restrictions. If one IRB is too stringent, they can simply go to the one next door.”<sup>227</sup> Accordingly private, for-profit IRBs have sprung up to compete for business from entities conducting research—a practice so common that a majority of research supporting new drug submissions to the FDA is now approved by for-profit IRBs.<sup>228</sup> This arrangement presents a fundamental conflict of interest, as IRBs are paid by the same entities they are entrusted with policing.<sup>229</sup> This system incentivizes quick approvals, rather than thorough, exacting analysis.

GAO investigators demonstrated the seriousness of this problem by setting up a fake medical device company and submitting a research proposal to various for-profit IRBs.<sup>230</sup> The protocol called for researchers to pour a liter of a liquid—previously rejected by the FDA as unsafe—into women’s abdominal cavities after surgery.<sup>231</sup> Two IRBs rejected the proposal, with a member of one describing the study as “a terrible risk for the patient . . . It is the worst thing I have ever seen.”<sup>232</sup> Yet the study was approved by another review board called Coast IRB, which encouraged research entities to “[r]elax and Coast through your next IRB experience with us!”<sup>233</sup> The GAO determined that in the previous five years, Coast had reviewed 356 protocols for research on human subjects and had approved all of them.<sup>234</sup> The company had earned \$9.3 million in revenue in the previous four years.<sup>235</sup>

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UNDERCOVER TESTS SHOW THE INSTITUTIONAL REVIEW BOARD SYSTEM IS VULNERABLE TO UNETHICAL MANIPULATION (2009).

227. Emanuel et al., *supra* note 220, at 0942.

228. Carl Elliott & Trudo Lemmens, *Ethics for Sale*, SLATE (Dec. 13, 2005, 1:01 PM), [http://www.slate.com/articles/health\\_and\\_science/medical\\_examiner/2005/12/ethics\\_for\\_sale.html](http://www.slate.com/articles/health_and_science/medical_examiner/2005/12/ethics_for_sale.html).

229. Emanuel et al., *supra* note 220, at 0942.

230. Mundy, *supra* note 224.

231. Heidi Ledford, *U.S. Government Investigates Human Research Protections*, NATURE (Mar. 27, 2009, 2:40 PM), [http://blogs.nature.com/news/2009/03/us\\_government\\_investigates\\_hum.html](http://blogs.nature.com/news/2009/03/us_government_investigates_hum.html).

232. Mundy, *supra* note 224.

233. *See What Is Your Experience with Your IRB?*, COAST IRB (July 11, 2008), <http://coastirb.blogspot.com/2008/07/coast-irb-what-is-your-experience-with.html>.

234. Editorial, *How Ethical Are For-Profit Institutional Review Boards?*, 373 LANCET 1400, 1400 (2009).

235. *Id.*

University IRBs face serious conflicts of interest of their own. As Ezekiel Emanuel has observed:

Both commercial and academic IRBs have a financial conflict of interest, especially since increasingly academic IRBs are charging competitive prices for their services, making them indistinguishable from commercial IRBs. Academic IRBs have the additional conflict that the researchers being reviewed are colleagues of the IRB members. And they have yet a further conflict since the institution wants and needs the commercial research in order to gain access to new drugs and devices to enhance its reputation as innovative.<sup>236</sup>

These conflicts were on display in the Markingson case, in which the IRB panel overseeing the CAFE study was chaired by a doctor with substantial personal, professional, and financial conflicts of interest.<sup>237</sup> The IRB panel was chaired by Dr. David Adson, a faculty member in the Department of Psychiatry.<sup>238</sup> In that role, Dr. Adson was responsible for reviewing a study whose principal investigators were two of his colleagues, one of whom was the chair of his department.<sup>239</sup> He was also the director of the research center in which the CAFE study was housed.<sup>240</sup> Dr. Adson had also received some \$650,000 in payments from drug companies over an eight-year period, with around \$150,000 coming from Astra-Zeneca, the sponsor of the CAFE trial.<sup>241</sup>

Even when IRBs rigorously review research protocols, their work is almost entirely prospective—they exercise very little oversight of research on an ongoing basis.<sup>242</sup> Rather than directly observing the conduct of research or interacting with subjects, IRBs trust researchers to follow the protocols they submitted and to report any problems they encounter. For example, the chair of the University of Minnesota's IRB told the Legislative Auditor

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236. Emanuel et al., *supra* note 220, at 0943.

237. See LEGIS. AUDITOR REP., *supra* note 33, at 21.

238. Carl Elliott, *Getting By with a Little Help from Your Friends*, THE HASTINGS CTR. (Oct. 18, 2013, 10:48 AM), <http://www.thehastingscenter.org/getting-by-with-a-little-help-from-your-friends/>.

239. *Id.*

240. *Id.*

241. *Id.*

242. In the *T.D.* case, the appellate court rejected OMH's argument that the deficiencies in its own regulations were not of concern because subjects would still be protected by IRBs. The appellate court rejected that argument, noting that "in practice, the IRBs do not conduct in-depth evaluations" and "do not review the work of the researchers on a day-to-day or even monthly basis." *T.D. v. N.Y. State Office of Mental Health*, 650 N.Y.S.2d 173, 189 n.9, 190 (N.Y. App. Div. 1996).

that “the IRB pays close attention to research policies, procedures, and guidance but cannot ensure that a researcher is following the strict letter of the law or ethical principles.”<sup>243</sup> Instead, she indicated that the IRB trusts researchers to follow the rules, rejecting even the notion of “trust but verify” as impractical and inconsistent with common practice.<sup>244</sup>

This is something of a paradox, since the very purpose of IRBs is to protect subjects from unethical conduct by researchers.<sup>245</sup> But many IRBs do not exercise any meaningful oversight to ensure that researchers are actually following their protocols. Again, the *Markingson* case illustrates this problem. Dr. Olson told the IRB that “[s]ubjects will have an advocate. This person will typically be a case manager, nurse, family member or friend . . . .”<sup>246</sup> The Legislative Auditor noted that “[i]n Markingson’s case, an advocate could have considered his special circumstances—including the potential coerciveness of being under a stay of commitment—and discussed those issues with Markingson *before* he signed the consent form.”<sup>247</sup> However, Markingson was not provided with an advocate at any time prior to his enrollment in the CAFE study.<sup>248</sup>

The inadequacy of IRBs to protect research subjects is exacerbated when subjects are involuntarily confined. It is especially difficult to exercise effective oversight of research that is undertaken on populations who are isolated from society, under constant surveillance by authorities, and subject to potential retaliation for reporting problems.<sup>249</sup> Involuntarily committed mental patients are not well-positioned to recognize or report mistreatment, particularly while they are confined. In the *Kaimowitz* case, for example, it was not Louis Smith who challenged re-

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243. LEGIS. AUDITOR REP., *supra* note 33, at 22.

244. *Id.* The previous director of the University of Minnesota’s IRB likewise testified in a deposition that the purpose of an IRB is not to protect research subjects, but simply to ensure that researchers have an adequate plan in place to protect subjects. Elliott, *supra* note 34.

245. Elliott, *supra* note 34 (quoting Dr. Olson’s application to the IRB).

246. LEGIS. AUDITOR REP., *supra* note 33, at 19.

247. *Id.* (emphasis in original).

248. *Id.*

249. See IOM REPORT, *supra* note 7, at 120–21 (quoting Allen Hornblum, “It is so much easier for indiscretions or bad intentions to take place behind those prison walls and razor wire. I have seen it in so many cases, where doctors who were sworn to save lives and do good have become so consumed by that intellectual scientific quest that they forget about the test subject. It is just so easy to abuse the situation.”).



searchers' proposal to subject him to experimental psychosurgery.<sup>250</sup> Rather, a lawyer learned of the impending experiment and filed suit to stop it.<sup>251</sup> In Robert Huber's case, no one intervened.<sup>252</sup> He complained repeatedly about severe abdominal pain, but Dr. Olson dismissed his complaints as "psychosomatic," and not related to the study drug—which had already been denied FDA approval after another patient died of severe liver complications.<sup>253</sup> Huber withdrew from the study only after he had been released from confinement and had contemplated suicide to end his pain.<sup>254</sup>

Even when subjects have someone who is interested in their care and willing to advocate for them, there is no guarantee they will be able to effectively address problems with their treatment. Markingson's mother, Mary Weiss, repeatedly reached out to members of his treatment team, expressing grave concerns about his care and his deteriorating condition.<sup>255</sup> Yet the Legislative Auditor found "little evidence that the study team adequately followed up with her about her concerns."<sup>256</sup> The study team did not even record Weiss's warning that her son was in danger of killing himself or someone else for more than four days and did not follow up with her until at least a week after her desperate message.<sup>257</sup> "Weiss ultimately reached the conclusion no one could help her or her son. She said, 'I was watching my son deteriorate and there was absolutely no one that I could go to.'"<sup>258</sup>

#### IV. RESEARCH INVOLVING INVOLUNTARILY COMMITTED PATIENTS SHOULD BE SUBJECT TO UNIFORM SPECIAL PROTECTIONS

Although IRBs generally do little to protect subjects while research is in progress, they can play an important role in protect-

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250. See Fabri, *supra* note 29, at 529.

251. *Id.*

252. See Susan Du, *Patient Claims He Too Was Abused in University of Minnesota Study*, CITYPAGES (Minn.) (May 8, 2015), <http://www.citypages.com/news/patient-claims-he-too-was-abused-in-university-of-minnesota-study-6550205>.

253. Baillon, *supra* note 86.

254. *Id.*

255. LEGIS. AUDITOR REP., *supra* note 33, at 17.

256. *Id.*

257. *Id.*

258. *Id.* at 18.

ing involuntarily committed patients at the protocol approval stage by sharply limiting their recruitment. As discussed above, review boards should restrict the use of these patients under the generally applicable principles of informed consent and fair subject selection found in Subpart A of the Common Rule. But even when federal rules apply—or when research entities voluntarily commit to following them—these broad general principles give researchers and IRBs too little guidance and too much latitude regarding what protections are required for involuntarily committed patients. This leaves researchers free to argue that it is ethically acceptable to include these patients in a wide range of research, citing the lack of express prohibitions of this recruitment.

Indeed, in the *T.D.* case, the Office of Mental Health defended its grossly inadequate rules all the way to the state's highest court, and a slew of research organizations also filed amicus briefs defending these regulations.<sup>259</sup> The University of Minnesota likewise vigorously defended Dr. Olson's recruitment of Markingson for more than a decade, both in court and in the press.<sup>260</sup> University officials only acknowledged the impropriety of Markingson's recruitment after two independent investigations issued scathing reports condemning the researchers' conduct.<sup>261</sup> Even after one of those reports stated flatly that "the fear of being subjected to an involuntary legal process for perceived noncooperation . . . is an overwhelming barrier to voluntariness."<sup>262</sup> The university's Associate Vice President for Research continues to defend its treatment of Robert Huber, who was recruited while involuntarily confined under a seventy-two-hour hold, writing:

[T]he enrollment of the participant [Huber] in the trial took place in 2007, before the passing of the 2009 legislation by the State of Minnesota relative to the practice of recruiting patients undergoing a

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259. *T.D. v. N.Y. State Office of Mental Health*, 650 N.Y.S.2d 173, 177 (N.Y. App. Div. 1996) (noting the amicus briefs defending these regulations).

260. See, e.g., Friedman, *supra* note 100.

261. Susan Du, *U of M's Tone on Dan Markingson Changes Drastically After Legislative Auditor's Report*, CITYPAGES (Minn.) (Mar. 25, 2015), <http://www.citypages.com/news/u-of-ms-tone-on-dan-markingson-changes-drastically-after-legislative-auditors-report-6533046>.

262. AAHRPP REP., *supra* note 33, at 67. The report further noted that the risk of coercion is heightened when, as in the recruitment of Robert Huber, "the principal investigator is also the treating physician and thus has the power to initiate the individual's involuntary confinement." *Id.*

stay of commitment. There also was not (and still is not) a national regulation in 2007 relative to this practice. This practice, therefore, was considered acceptable at the time of the participant's enrollment in this trial and appears to remain allowable under Minnesota law.<sup>263</sup>

Both the Department of Health and Human Services and the Federal Bureau of Prisons have long recognized that prisoners require additional, explicit protections against coercion and exploitation, which these agencies have implemented through regulations that restrict their recruitment.<sup>264</sup> Although involuntarily committed patients are similarly situated to prisoners, they do not have the same explicit protections, leaving them vulnerable to abuses. Accordingly, the Common Rule's protections for prisoners should be extended to these patients, and the expanded rule's reach should cover all human subjects research.

A. *The Common Rule's Definition of Prisoner Should Be Expanded To Include Involuntarily Committed Patients*

The Common Rule recognizes that prisoners need additional safeguards because they "may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research."<sup>265</sup> Accordingly, Subpart C of the Common Rule extends special research protections to prisoners, sharply restricting the types of studies for which they may be recruited as subjects and providing additional procedural requirements.<sup>266</sup> However, the rule defines "prisoner" narrowly, as "[a]ny individual involuntarily confined or detained *in a penal institution*."<sup>267</sup> Thus, because patients confined by civil commitment orders are

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263. Letter from Pamela Webb to Carl Elliott (Jan. 27, 2016), <https://www.scribd.com/document/297005044/Pamela-Webb-Research-Compliance-Office-Response-to-Carl-Elliott-Regarding-Robert-Huber-and-Bifeprunox-Study>. This defense is all the more striking given that the university has implicitly recognized the impropriety of recruiting patients under 72-hour holds by voluntarily suspending this practice. *Id.*

264. See 45 C.F.R. §§ 46.300–306 (2016); U.S. DEP'T OF JUSTICE, FED. BUREAU OF PRISONS, PROGRAM STATEMENT NO. 6031.04, PATIENT CARE § 45 (2014). See generally U.S. DEP'T OF JUSTICE, FED. BUREAU OF PRISONS, PROGRAM STATEMENT NO. 1070.07, SUBMISSION AND PROCESSING OF PROPOSAL § 10 (1999) (discussing the general procedure for acceptance of a research proposal).

265. 45 C.F.R. § 46.302 (2016).

266. *Id.* §§ 46.301–306.

267. *Id.* § 46.303(c) (emphasis added).

not detained in penal institutions, they are not considered prisoners under the Common Rule.

In its 2007 report, the Institute of Medicine recognized that the Common Rule's definition of "prisoner" excludes some populations that are subject to the same pressures as inmates of correctional facilities. The Institute recommended expanding Subpart C's protections "to the fuller population of individuals who are under restricted liberty and, therefore, face potentially greater risks than the general population when participating in research."<sup>268</sup> However, the Institute stopped short of including civilly committed mental patients in its proposed expanded definition. Although the authors emphasized that "these groups face very similar circumstances and that very strong ethical safeguards are required" for both populations, they concluded that the special circumstances of patients under civil commitment orders were outside the scope of their charge and warranted separate consideration.<sup>269</sup>

Patients confined to the state's custody through civil commitment proceedings merit the same protections as persons incarcerated through the criminal justice system. As described above, these patients are vulnerable in the same ways as prisoners. The fact that they are confined through a civil process rather than through the criminal justice system has no bearing on their susceptibility to unethical treatment.

Extending the protections of Subpart C to civilly committed patients would substantially mitigate their vulnerability to coercion and exploitation. Subpart C sets a default rule that research on prisoners is not permitted unless it involves (1) "the possible causes, effects, and processes of incarceration and of criminal behavior," (2) "prisons as institutional structures or of prisoners as incarcerated persons," (3) "conditions particularly affecting prisoners as a class," or (4) "practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subjects."<sup>270</sup> The first two categories of research are only permitted if "the study presents no more than minimal risk and no more than inconvenience to the sub-

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268. IOM REPORT, *supra* note 7, at 101.

269. *Id.* at 26 n.1.

270. 45 C.F.R. § 46.306 (2016).

jects.”<sup>271</sup> Research on conditions particularly affecting prisoners as a class “may proceed only after the Secretary [of HHS] has consulted with appropriate experts, including experts in penology medicine and ethics, and published notice, in the Federal Register, of his intent to approve such research.”<sup>272</sup>

Subpart C also contains special requirements regarding IRB membership and approval. In addition to requiring that IRBs approve each research project involving prisoners individually, IRBs for prisoner research must include at least one member that is either a prisoner or “a prisoner representative with appropriate background and experience to serve in that capacity.”<sup>273</sup> To approve a study on prisoners, the IRB must conclude that the research proposal not only meets the generally applicable Common Rule requirements, but several additional criteria as well.<sup>274</sup> For example, IRBs must be assured that parole boards will not consider prisoners’ consent or refusal to participate in research when making parole decisions and that each prisoner is clearly informed of this in advance.<sup>275</sup> To protect against exploitation, IRBs must also find that “[t]he risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers.”<sup>276</sup> In addition to obtaining IRB approval for research protocols involving prisoners, researchers must also obtain certification from the Office of Human Research Protections that the proposed study fits one of the categories of permitted research and the ethical requirements have been met.<sup>277</sup>

Limiting research on involuntarily committed patients to studies involving minimal risks would substantially allay concerns about the voluntariness of these patients’ consent. Researchers must still take pains to ensure that patients understand they have the right to refuse to participate in the research without facing adverse consequences.<sup>278</sup> But if some patients still feel pressured to consent—e.g., out of a desire to appear reasonable to au-

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271. *Id.*

272. *Id.*

273. *Id.* § 46.304(b).

274. *Id.* § 46.305(a).

275. *Id.* § 46.305(a)(6).

276. *Id.* § 46.305(a)(3).

277. *Id.* § 46.306(a); IOM REPORT, *supra* note 7, at 81 (“This certification step adds an average of 3–4 weeks to the review process.”).

278. *See* 45 C.F.R. § 46.116(a)(8) (2016).

thorities or otherwise curry their favor—at least they would not be subjected to serious risks. In addition, Subpart C addresses concerns about exploitation and fair subject selection by limiting the inclusion of prisoners to research that seeks to benefit them, either individually or as a group. The rules seek to ensure that prisoners are not targeted merely because they are an available, captive population, but instead because the research aims at addressing their conditions.

Although we endorse and expand on the Institute of Medicine's recommendation to expand the definition of prisoner in the Common Rule, we reject the Institute's proposal to abandon Subpart C's "categorical" approach to prisoner research.<sup>279</sup> Subpart C sets a default rule that bars all studies involving prisoners, with exceptions for specific categories of research. The Institute of Medicine advocated replacing this approach with a "risk-benefit framework" in which IRBs would make case-by-case assessments of each protocol's potential benefits and harms and would "identify the particular ethical issues that each protocol raises in the specific context of the correctional setting."<sup>280</sup> This approach would give IRBs broad discretion to permit research on prisoners whenever they determine the risks of a study are outweighed by its potential benefits—even "where the benefit to prisoners is indirect and/or temporally distant."<sup>281</sup> Similarly, with respect to promoting justice in the selection of research subjects, the Institute recommended abandoning Subpart C's limitation of research on prisoners to studies that are particularly applicable to their plight, such as studies on the effects of incarceration.<sup>282</sup> Rather, under the Institute's proposal, "[i]t will be up to IRBs to determine whether there is a convincing affirmative reason for conducting research in a prison setting."<sup>283</sup>

The profound inadequacies of IRB review argue strongly against giving them broad discretion to permit research that may involve more serious risks and that may not be aimed at benefiting prisoners either individually or as a group. Even under the

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279. See IOM Report, *supra* note 7, at 123. See generally Reiter, *supra* note 1 (arguing against the cost-benefit analysis recommended by the Institute).

280. IOM REPORT, *supra* note 7, at 123.

281. *Id.* at 124.

282. *Id.* at 143; 45 C.F.R. § 46.306 (2016).

283. IOM REPORT, *supra* note 7, at 124.

more limited categorical approach currently in place, IRBs have too often failed to protect prisoners from abuses.<sup>284</sup> Expanding review boards' discretion to allow more research on these populations would put prisoners at an even greater risk. The most effective way IRBs can protect these subjects is by limiting their recruitment to low-risk research that is particularly relevant to prisoners.

Notably, the Institute itself recommended maintaining categorical restrictions on the use of prisoners in biomedical studies.<sup>285</sup> The authors appear to single out these studies for special restrictions based on an assumption that biomedical research entails greater risks for prisoners than other types of studies, such as behavioral or epidemiological research.<sup>286</sup> In fact, behavioral research can include interventions posing serious risks to subjects, such as studies involving "segregation or other isolated settings and its effects."<sup>287</sup> As Keramet Reiter observed, "behavioral modification 'experiments' can be difficult to distinguish from punishment and from everyday prison policies. The difficulty of detecting and defining behavioral modification experiments makes this category of experiments ripe for abuse."<sup>288</sup>

If strict categorical restrictions are justified when research may pose serious risks to prisoners, then there is no reason to limit this approach to biomedical studies. Given the difficulty of ensuring voluntary consent from involuntarily confined persons, it makes sense to limit their participation to studies involving minimal risks of harm. And, because these individuals are a vulnerable population whose inclusion is not necessary for most studies, it is in the interest of justice to limit their participation to studies that require their inclusion and hold out the prospect of benefit to this population.

We are also not persuaded by the Institute of Medicine's claim that limiting prisoners' research participation in this way impermissibly violates their autonomy by denying them the opportuni-

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284. See Reiter, *supra* note 1, at 527–28.

285. See IOM REPORT, *supra* note 7, at 125.

286. See *id.* at 125–26.

287. *Id.* at 168.

288. Reiter, *supra* note 1, at 510.

ty to share in the benefits of research.<sup>289</sup> Although the categorical approach might deprive some of these individuals of opportunities they would welcome, that tells us nothing about the propriety of these restrictions. Research protections are premised on the idea that some paternalism is warranted in the context of medical research because of the disparities of knowledge and power between researchers and subjects and the history of grotesque abuses of vulnerable people in research. Accordingly, the rules governing human subjects research are replete with protections that limit the circumstances under which individuals may participate in research.

For example, under the Common Rule, a study cannot be approved unless an IRB determines that risks to subjects are minimized and “are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.”<sup>290</sup> Although this rule effectively bars prospective subjects from participating in some high-risk research, it does not violate these individuals’ autonomy. As the Belmont Report notes, “[t]o show lack of respect for an autonomous agent is . . . to deny an individual the freedom to act on [her] considered judgments . . . *when there are no compelling reasons to do so.*”<sup>291</sup> As the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research concluded—following a much more extensive investigation than the Institute of Medicine’s<sup>292</sup>—prisoners’ vulnerability and the history of research abuses against this population supply compelling reasons to limit their recruitment.<sup>293</sup>

This is doubly true for involuntarily committed patients, whose autonomy is severely limited in multiple ways precisely because they have been judged unfit to make important decisions regarding their own welfare.<sup>294</sup> The vulnerability of these patients to coercion and exploitation provides compelling reasons to limit their research participation to low-risk studies that are highly relevant to their conditions.

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289. See IOM REPORT, *supra* note 7, at 119–22.

290. 45 C.F.R. § 46.111(a)(2) (2016).

291. BELMONT REP., *supra* note 104, at 4 (emphasis added).

292. See Reiter, *supra* note 1, at 536–40.

293. See 1976 NAT’L COMM’N REP., *supra* note 102, at 6–7.

294. See *supra* notes 9–14 and accompanying text.



B. *The Common Rule Should Be Expanded to Cover All Human Subjects Research*

Although expanding the Common Rule's definition of "prisoner" to include involuntarily committed patients is an important first step, it is not sufficient. Federal rules apply to only a limited subset of research on prisoners, leaving many vulnerable to unethical treatment.

The Common Rule applies only to research supported by a federal agency that has adopted the Rule and institutions that have voluntarily committed to adhering to the Rule.<sup>295</sup> While many agencies have adopted portions of the Common Rule, only three have adopted Subpart C's rules regarding prisoners.<sup>296</sup> Despite the "history and controversy surrounding medical and pharmacological studies in prisons"<sup>297</sup> that motivated the enactment of these protections, the FDA has not adopted any similar provisions.<sup>298</sup> While the Federal Bureau of Prisons has adopted regulations that govern all research on prisoners in federal prisons, these rules do not apply to individuals incarcerated in state prisons, who comprise the vast majority of prisoners in the United States.<sup>299</sup>

Because of these limitations, no federal rules govern research on prisoners in state facilities that is not either supported by the federal government or used to obtain FDA approval. Any research outside that scope is governed by state laws and policies, which are highly variable. For example, thirty-three states prohibit using prisoners in therapeutic biomedical research, while fifteen permit this practice.<sup>300</sup> Forty-five states prohibit the use of prisoners for nontherapeutic biomedical studies, while three permit such research.<sup>301</sup> Forty-three states prohibit using prisoners in nontherapeutic social or behavioral studies involving greater than minimal risk, while five states permit this research.<sup>302</sup>

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295. *See supra* notes 187–89 and accompanying text.

296. IOM REPORT, *supra* note 7, at 6.

297. *Id.* at 125.

298. *Id.* at 74.

299. *Id.* at 89, 91.

300. *Id.* at 60.

301. *Id.*

302. *Id.*

Noting these serious deficiencies in existing regulations, in its 2007 report the Institute of Medicine urged that “[a]ll human subjects research involving prisoners should be regulated by the same ethical standards irrespective of source of funding, supporting agency, or type of correctional facility (federal, state, local, or private) or program that houses the prisoner.”<sup>303</sup> The report called on Congress to “mandate a uniform set of guidelines for human research participant protection programs for research involving prisoners.”<sup>304</sup>

The same is true with respect to involuntarily committed mental patients.<sup>305</sup> The vulnerability of these patients as research subjects does not depend on a study’s source of funding. Accordingly, in addition to expanding the Common Rule’s definition of “prisoner” to include civilly committed mental patients, Congress should act on the Institute of Medicine’s call to extend the rule’s protections to all research involving involuntarily confined subjects.

#### CONCLUSION

Recognizing prisoners’ vulnerability to coercion and exploitation, federal rules sharply limit the types of studies for which prisoners may be recruited and mandate extensive procedural protections for research involving this population. However, as the Institute of Medicine has previously acknowledged, the federal rules’ narrow definition of “prisoner” excludes other groups who are similarly vulnerable, including involuntarily committed patients. Like prisoners, these patients’ autonomy may be undermined by routinely having to defer to authorities’ decisions in order to avoid punishment and gain privileges. They may also be isolated and have little ability to report mistreatment or advocate for their own interests. The fact that these patients’ liberty is restricted through civil commitment rather than criminal sentencing is irrelevant to their need for protection from unethical research practices. Accordingly, federal rules should identify these

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303. *Id.* at 6.

304. *Id.* at 94.

305. The Institute of Medicine Report recognized that “persons under restricted liberty due to mental illness . . . face very similar circumstances [to prisoners] and that very strong ethical safeguards are required.” *Id.* at 26 n.1. However, the Institute did not advocate expanding the definition of “prisoner” to include these patients, noting that these populations have special needs that warranted separate consideration. *Id.*

patients as a species of prisoner, entitled to the same explicit protections.

Like other prisoners, involuntarily committed patients are also threatened by the lack of uniform federal rules governing research. The protections subjects receive across studies should not vary according to factors that have no bearing on their need for protection, such as the study's source of funding or the state in which the research is conducted. Thus, in addition to extending federal protections for prisoners to involuntarily committed patients, these rules should be amended to apply to all human subjects research.

We recognize that these changes are unlikely to be implemented in the near future. In the nine years since the Institute of Medicine urged expanding the definition of "prisoner" and broadening the application of federal rules, neither Congress nor the Department of Health and Human Services has moved toward adopting these recommendations. Nevertheless, even in the absence of explicit federal rules, ethical principles of informed consent and fair subject selection require IRBs to protect vulnerable subjects from coercive and exploitative recruitment practices. Regardless of federal intransigence, IRBs should extend to involuntarily committed patients the same protections afforded to prisoners.