

# WHAT SUBJECTS TEACH: THE EVERYDAY ETHICS OF HUMAN RESEARCH

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In *What Patients Teach: The Everyday Ethics of Health Care*, Larry R. Churchill, Joseph B. Fanning, and David Schenck describe how patients experience medical care.<sup>1</sup> Drawing on in-depth conversations with patients, Churchill and his coauthors develop a patient-centered medical ethics. They identify both “clinician traits that heal,” such as attentiveness, honesty, and empathy,<sup>2</sup> and clinician behaviors that harm, such as poor communication and treating the patient as an object or number rather than a valued individual.<sup>3</sup>

From the patient’s point of view, ethical care depends not only on how doctors and nurses handle dramatic life-and-death matters, but also on how they handle everyday clinical encounters.<sup>4</sup> *What Patients Teach* contends that medical ethics has neglected the ethics of routine care. Churchill and his coauthors argue that the conventional preoccupation with ethical principles “leads us away from the heart of the routine moral activity between clinicians and patients.”<sup>5</sup> In emphasizing abstract ethical principles, the authors say, conventional medical ethics “runs the risk of becoming irrelevant.”<sup>6</sup>

Besides neglecting the ethics of routine medical care, traditional ethics relies too heavily on what professionals, rather than patients, see as ethical care. Churchill and his coauthors criticize the “narcissism” of medical ethics codes.<sup>7</sup> Such codes “originate in the perceptions of the professionals themselves, with little or no influence from patients’ understanding of what is at stake in the

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1. LARRY R. CHURCHILL, JOSEPH B. FANNING & DAVID SCHENCK, *WHAT PATIENTS TEACH: THE EVERYDAY ETHICS OF HEALTH CARE* (2013).

2. *Id.* at 33.

3. *Id.* at 50–71.

4. *Id.* at xv.

5. *Id.* at 137.

6. *Id.*

7. *Id.* at 146–50.

therapeutic encounter.”<sup>8</sup> Similarly, lists of patients’ ethical responsibilities tend to reflect medical professionals’ moral judgments, excluding patients’ own views on the matter.<sup>9</sup>

I welcome this critique of conventional medical ethics; indeed, my ethicist coauthors and I make similar points in *Malignant: Medical Ethicists Confront Cancer*,<sup>10</sup> a book describing what we learned from personal experience as cancer patients and caregivers. In this Article, I seek to extend the critique. I believe that many of the points Churchill and his coauthors make about medical ethics apply equally to research ethics.

Based on this belief, I have begun writing a book that will consider research ethics from the perspectives of research subjects. A substantial body of work describes the perceptions and viewpoints of people who participate in research. This literature supplies the same sorts of insights and information that Churchill and his coauthors gleaned through interviewing patients. However, research ethics analysis too rarely considers this material.

A research ethics that neglects subjects’ perspectives has flaws resembling those of the principle-based medical ethics criticized in *What Patients Teach*. Conventional research ethics largely overlooks the everyday encounters that determine how subjects experience their participation. Existing research ethics codes and principles also reflect professional narcissism. For the most part, research ethics has developed without serious attention to the views of people who know what it is like to be a research subject.<sup>11</sup>

There are epistemic, ethical, and practical reasons to consider research subjects’ perspectives. A person participating in research can supply facts about the experience that are otherwise overlooked or downplayed by those who have never been in the participant’s position. The ethical judgments of study participants can also differ from those of researchers, ethicists, and the general public.<sup>12</sup> To

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8. *Id.* at 147. Perhaps reflecting differences between the two professions, the authors observe that codes developed by and for nurses are more attentive to patients’ perspectives than are physician codes of ethics. *Id.* at 149–50.

9. *Id.* at 149.

10. *MALIGNANT: MEDICAL ETHICISTS CONFRONT CANCER* (Rebecca Dresser ed., 2012).

11. See Norma Morris & Brian Balmer, *Are You Sitting Comfortably? Perspectives of the Researchers and the Researched on “Being Comfortable,”* 13 ACCOUNTABILITY RES. 111, 112 (2006), available at [http://www.academia.edu/7172965/Are\\_You\\_Sitting\\_Comfortably\\_Perspectives\\_of\\_the\\_Researchers\\_and\\_the\\_Researched\\_on\\_Being\\_Comfortable](http://www.academia.edu/7172965/Are_You_Sitting_Comfortably_Perspectives_of_the_Researchers_and_the_Researched_on_Being_Comfortable) (“[E]thical codes and guidelines, aimed at assuring the welfare of those taking part in research, need to take cognisance of the full range of the research subjects’ needs and interests, which go beyond the physical, but are inadequately reflected in much current guidance.”).

12. See Susan M. Cox & Michael McDonald, *Ethics Is for Human Subjects Too: Participant Perspectives on Responsibility in Health Research*, 98 SOC. SCI. & MED. 224, 230 (2013) (criticizing the “very patronizing and paternalistic

apply ethical and regulatory standards governing informed consent and acceptable risk, researchers and oversight groups need input from those who have actually experienced study participation.<sup>13</sup>

People participating in research can contribute knowledge and ethical perspectives highly relevant to research decisions. But today's research enterprise often fails to elicit this information. Instead, researchers, ethicists, and others involved in research oversight try to imagine how people will experience and respond to study participation. For a variety of reasons, such speculative judgments can be inaccurate.

Research professionals and research subjects often occupy different social, cultural, educational, and economic positions. The same disparities can exist between subjects and members of the general public involved in research oversight. Moreover, many people considering whether to participate in research are coping with serious illnesses and life circumstances that those involved in oversight have never faced personally. These and other factors create a gap between hypothetical and actual research experiences.<sup>14</sup>

Rather than relying on speculation about the research participant's experience, ethics and oversight ought to rely on what actual participants say about their experiences. Research ethics, as well as regulations intended to promote ethical conduct, should be based on evidence. Ethical and regulatory decisions should take

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perspective" that assumes only researchers and ethics review committees think about research ethics).

13. For example, the Common Rule, a set of regulations adopted by federal agencies conducting and supporting human subject research, requires researchers to disclose information about their studies "in language understandable to the subject or the [subject's] representative." General Requirements for Informed Consent, 34 C.F.R. § 97.116 (2014). Another Common Rule provision requires that risks to subjects must be "reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result." Criteria for IRB Approval of Research, 34 C.F.R. § 97.111(a)(2). Experienced subjects can contribute information and opinions relevant to these and other regulatory provisions. Similarly, the *Belmont Report*, a highly influential research ethics statement, refers to the standard of "the reasonable volunteer" in discussing the information researchers should explain to prospective research participants. NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, U.S. DEPT OF HEALTH, EDUC., & WELFARE, PUB. NO. (OS) 78-0012, THE BELMONT REPORT 11 (1978). People with actual experience as subjects are highly qualified to represent the reasonable volunteer in research ethics deliberations.

14. I learned this when I faced a decision about participating in a cancer treatment study. See Rebecca Dresser, *Volunteering for Research*, in MALIGNANT: MEDICAL ETHICISTS CONFRONT CANCER, *supra* note 10, at 70, 70–71.

into account participants' knowledge, as well as their positions on ethical issues in research.<sup>15</sup>

Attention to subjects' perspectives makes sense from a broader policy standpoint, too. Today's researchers face serious problems in enlisting and retaining a sufficient number of human subjects.<sup>16</sup> A significant number of clinical trials are discontinued, most commonly because not enough people agree to participate.<sup>17</sup> Discontinued trials contribute nothing to the knowledge advances that justify the research enterprise. People enrolled in failed trials are also exposed to risk for no good reason. Finite resources are consumed by failed trials as well. And researchers and clinicians waste their time and energy on activities that have no useful outcome.<sup>18</sup>

The failure to incorporate subjects' viewpoints into study planning and oversight decisions contributes to the current enrollment problems. People will be reluctant to enroll in or

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15. See Cox & McDonald, *supra* note 12 (“[P]erspectives of human subjects are invaluable in reframing existing ethical issues in a more meaningful way, surfacing previously unidentified ethical issues, displaying divergent ethical priorities, re-evaluating the implications of research participation and restructuring researcher-participant relationships.”); Michelle L. Eder et al., *Improving Informed Consent: Suggestions from Parents of Children with Leukemia*, 119 PEDIATRICS e849, e850 (2007) (“Many have called for inclusion of participants’ views of the informed consent process, citing trial participants as an ‘underutilized resource’ whose ‘voice [is] largely ignored.’” (quoting Karen Cox, *Enhancing Cancer Clinical Trial Management: Recommendations from a Qualitative Study of Trial Participants’ Experiences*, 9 PSYCHO-ONCOLOGY 314, 315 (2000))); Morris & Balmer, *supra* note 11, at 130 (arguing that decisions about acceptable research should rely on a broad understanding of subjects’ concerns, not simply what researchers assume will concern subjects).

16. INST. OF MED., PUBLIC ENGAGEMENT AND CLINICAL TRIALS: NEW MODELS AND DISRUPTIVE TECHNOLOGIES: WORKSHOP SUMMARY 2 (2011).

17. See Benjamin Kasenda et al., *Prevalence, Characteristics, and Publication of Discontinued Randomized Trials*, 311 JAMA 1045, 1046–50 (2014); see also Ricki Carroll et al., *Motivations of Patients with Pulmonary Arterial Hypertension to Participate in Randomized Clinical Trials*, 9 CLINICAL TRIALS 348, 349 (2012) (describing problems in enrolling subjects “either in large enough numbers to meet sample size targets or sufficiently quickly to make the costs of trial conduct manageable”); Gregory A. Curt & Bruce A. Chabner, *One in Five Cancer Clinical Trials Is Published: A Terrible Symptom—What’s the Diagnosis?*, 13 ONCOLOGIST 923, 923 (2008) (explaining that at least one of five trials at four National Cancer Institute Comprehensive Cancer Centers failed to enroll any subjects and that only fifty to sixty percent of trials at those centers met enrollment requirements); Peter Korn, *Clinical Trials Stymied as Patients Balk at “Experiments,”* PORTLANDTRIBUNE (Jan. 16, 2014, 6:00 AM), <http://portlandtribune.com/pt/9-news/207447-63461-clinical-trials-stymied-as-patients-balk-at-experiments> (describing Oregon Health & Science University’s finding that the school was annually consuming one million dollars in attempting to conduct trials that were later cancelled or fell short of adequate enrollment).

18. See Alex John London et al., *Beyond Access vs. Protection in Trials of Innovative Therapies*, 328 SCIENCE 829, 829–30 (2010).

complete studies that do not adequately address their concerns. They will be reluctant to participate in studies they consider overly burdensome or demanding.<sup>19</sup> Information about subjects' perspectives is needed to determine when and why trials are likely to have difficulties recruiting and retaining subjects.

This Article examines subjects' perspectives on study participation. Part I presents material describing how healthy volunteers and patients perceive the potential benefits and harms of participation and how they decide whether or not to enroll in trials. This Part also describes experiences of parents and surrogates making decisions regarding participation for children and adults incapable of making their own research choices. Part II considers how to incorporate subjects' viewpoints into ethical and regulatory decision making about human research. In this Part, I argue that experienced subjects should participate in human research oversight activities, study planning and implementation, and research ethics and policy formation.

To explore the world of research subjects, I turn to a variety of sources: empirical research on subjects' perceptions and viewpoints, subjects' personal accounts of participation, and media stories reporting on subjects' experiences. Whenever possible, I draw on reports of open-ended interviews and other qualitative inquiries that allow subjects to bring up the concerns and experiences they consider relevant and important. Such inquiries offer different insights than do questionnaires and surveys, which are shaped by the interests and awareness of the research team creating them.<sup>20</sup> My objectives are to highlight subjects' voices, describe "how it actually feels . . . to be the subject of clinical research,"<sup>21</sup> and

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19. See Korn, *supra* note 17 (explaining that Dr. Harlan Krumholz attributes enrollment problems to "doctors and hospitals who have never considered how participation in a clinical trial feels to patients").

20. See C. Behrendt et al., *What Do Our Patients Understand About Their Trial Participation? Assessing Patients' Understanding of Their Informed Consent Consultation About Randomised Clinical Trials*, 37 J. MED. ETHICS 74, 74 (2011) (noting that few studies exist on patients' perspectives of informed consent and that most existing studies used questionnaires that failed to elicit patients' independent perspectives); Eder et al., *supra* note 15 (explaining that studies using close-ended questions do not let people present what is relevant to them, and, as a result, recommendations that follow "may reflect the views and interests of the researchers rather than aspects of the informed consent process that parents consider most important and in need of improvement").

21. S. M. Madsen et al., *Participating in a Cancer Clinical Trial? The Balancing of Options in the Loneliness of Autonomy: A Grounded Theory Interview Study*, 46 ACTA ONCOLOGICA 49, 49 (2007). Unfortunately, the literature contains much less information about people who decline study participation than about those who consent to participate. There is also a dearth of information on the views of patients who participate in research and have poor health outcomes. Indeed, one team reported that the ethics committee reviewing their study refused to allow interviews with cancer patients whose disease failed to respond to the treatment regimen they received

determine how subjects “make sense of the total experience of trial participation, from recruitment through to follow-up.”<sup>22</sup>

## I. RESEARCH PARTICIPATION: SUBJECTS’ PERSPECTIVES

There are two general categories of human research: studies involving healthy or “normal” volunteers and studies involving people with medical conditions, who are often referred to as patient-subjects.<sup>23</sup> Below I describe how healthy volunteers and patient-subjects evaluate research benefits and burdens in making research decisions.

### A. *Healthy Volunteers*

#### 1. *Benefits*

Compensation is a major benefit of study participation for healthy volunteers. In interviews and questionnaires, many volunteers name financial benefits as the main reason they consider study participation.<sup>24</sup> Some healthy people say they are willing to

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in a trial. *Id.* at 50. Yet data about trial decliners and trial participants with bad outcomes would be quite valuable in ethical and policy deliberations about human research. See Claire Snowdon et al., *Making Sense of Randomization: Responses of Parents of Critically Ill Babies to Random Allocation of Treatment in a Clinical Trial*, 45 SOC. SCI. & MED. 1337, 1350 (1997) (citing the need to include patient-subjects with poor outcomes “to more fully represent perceptions and understandings” of trial participation).

22. Cox, *supra* note 15. In this Article, I use the terms “subject” and “participant” to refer to someone involved in any stage of the research process, from study recruitment to completion.

23. See Advisory Comm. on Human Radiation Experiments, *Research Ethics and the Medical Profession*, 276 JAMA 403, 403–04 (1996).

24. See, e.g., Kirsten Bell & Amy Salmon, *What Women Who Use Drugs Have to Say About Ethical Research: Findings of an Exploratory Qualitative Study*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Dec. 2011, at 84, 92 (noting that women who had participated in studies endorsed financial incentives); Carmen Radecki Breitkopf et al., *Perceptions of Reimbursement for Clinical Trial Participation*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Sept. 2011, at 31, 31, 35 (describing interviews in which healthy volunteers viewed compensation as a benefit of trial participation and doubted that people would enroll in the absence of compensation); R. Hermann et al., *Adverse Events and Discomfort in Studies on Healthy Subjects: The Volunteer’s Perspective*, 53 EUR. J. CLINICAL PHARMACOLOGY 207, 209 (1997) (noting that seventy-six percent of 440 healthy study volunteers who responded to a questionnaire said that monetary reward was important); Leanne Stunkel & Christine Grady, *More than the Money: A Review of the Literature Examining Healthy Volunteer Motivations*, 32 CONTEMP. CLINICAL TRIALS 342, 342 (2011) (reviewing studies finding that financial reward is the most important, though not the sole, factor motivating healthy volunteer participation). Although subjects consider payment a benefit of participation, the U.S. Food and Drug Administration rejects this characterization. An agency document says, “Payment to research subjects for participation in studies is not considered a benefit, it is a recruitment incentive.” *Payment to Research Subjects—Information Sheet*, U.S. FOOD &

participate in studies offering no payment, but usually this response addresses hypothetical, not actual, participation.<sup>25</sup>

Compensation is most important to people participating in studies on a regular basis.<sup>26</sup> For many of these repeat volunteers, study participation is an important source of income.<sup>27</sup>

In seeking payment, these “professional guinea pigs” see themselves as motivated by the same considerations as the researchers who make a living from their study involvement.<sup>28</sup> Volunteers in this group also tend to think that study payment should be higher than it is, dismissing ethicists’ concerns about undue financial inducement to enroll in studies.<sup>29</sup>

Although many healthy volunteers see compensation as the major benefit of study participation, they cite other benefits, too. Some say they want to contribute to scientific knowledge and healthcare improvements.<sup>30</sup> Some are attracted by the health examinations and tests that subjects receive in many studies.<sup>31</sup> Repeat volunteers say that participation is an attractive alternative to other employment options.<sup>32</sup> Additional motivating factors

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DRUG ADMIN., <http://www.fda.gov/regulatoryinformation/guidances/ucm126429.htm> (last updated June 25, 2014).

25. See Stunkel & Grady, *supra* note 24, at 344–45. An exception was a survey finding that healthy volunteers who had participated in research at leading academic centers did not rank payment as the top reason for their participation. Rhonda G. Kost et al., *Research Participant-Centered Outcomes at NIH-Supported Clinical Research Centers*, 7 *CLINICAL & TRANSLATIONAL SCI.* 430, 430–33, 436 (2014).

26. See Stunkel & Grady, *supra* note 24, at 351. One volunteer told a reporter that he ranked studies according to the cash per study day that participants would receive; for example, he said that a study paying five hundred dollars for four weekends was “terrible.” Barbara Solow, *The Secret Lives of Guinea Pigs*, *INDY WK.* (Feb. 9, 2000), <http://www.indyweek.com/gyrobase/Content?oid=13968>.

27. See Carl Elliott, *Guinea-Pigging*, *NEW YORKER*, Jan. 7, 2008, at 36, 36 (“In some cities . . . the drug-testing economy has produced a community of semi-professional research subjects, who enroll in one study after another. Some of them do nothing else. For them, ‘guinea-pigging,’ as they call it, has become a job.”).

28. *Id.* at 37; see also Bell & Salmon, *supra* note 24, at 90 (quoting one participant, who commented that researchers are “getting paid to do the fucking research. Why can’t we get paid to give them what they want!”).

29. See Elliott, *supra* note 27, at 40.

30. See, e.g., Hermann et al., *supra* note 24; Stunkel & Grady, *supra* note 24, at 344, 348–49.

31. See Stunkel & Grady, *supra* note 24, at 344, 348–49.

32. See Kate Mandeville, *My Life as a Guinea Pig*, 332 *BMJ* 735, 735 (2006) (stating that “trial participation is considerably more interesting than a supermarket job”); Josh McHugh, *Drug Test Cowboys: The Secret World of Pharmaceutical Trial Subjects*, *WIRED* (Apr. 24, 2007, 2:00 AM), [http://www.wired.com/wired/archive/15.05/feat\\_drugtest.html](http://www.wired.com/wired/archive/15.05/feat_drugtest.html) (“I’ve worked as an electrician and seen guys get electrocuted. Being a lab rat is the only work situation where you’ve got around-the-clock medical attention. It’s the safest job I’ve ever been in.”).

include curiosity, a desire to meet people or take a break from the routine,<sup>33</sup> and an interest in learning “what’s new in the medical field.”<sup>34</sup>

Volunteers want to participate in studies that produce useful information and real benefits to others.<sup>35</sup> Many volunteers see themselves as essential contributors to research. Because they believe they have a stake in the study product, they believe they should have an opportunity to learn about study results.<sup>36</sup> Many also see compensation as recognition of their necessary role. For them, compensation, rather than being exploitative, “in some respects serve[s] to equalize an otherwise highly imbalanced exchange.”<sup>37</sup>

Experienced volunteers look for studies conducted by people they can trust, people who treat them with respect and understanding. They value courteous and skilled research staff members who appreciate what subjects do and pay attention to their well-being.<sup>38</sup> For example, one volunteer wrote about how delighted she was when a nurse praised her commitment to study requirements.<sup>39</sup> Another volunteer advised researchers: “Be approachable. Don’t be judgmental. Hear what we have to say. Honestly listen to it.”<sup>40</sup> Volunteers participating in studies that require them to live in research facilities for weeks or even months value comfortable quarters, decent food, and entertaining pastimes.<sup>41</sup> Although matters like these may seem mundane to the outsider, subjects see them as expressions of researchers’ respect and concern for their welfare.

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33. Stunkel & Grady, *supra* note 24, at 344, 348–49.

34. Solow, *supra* note 26.

35. Bell & Salmon, *supra* note 24, at 88.

36. Stunkel & Grady, *supra* note 24, at 347 tbl.3.

37. Bell & Salmon, *supra* note 24.

38. Stunkel & Grady, *supra* note 24, at 350.

39. *22 Nights and 23 Days: Diary of #1J, Drug Study Subject*, GUINEA PIG ZERO, <http://www.guineapigzero.com/23days.html> (last visited Mar. 3, 2015) (explaining that the subject was “not thrilled” about all of the study procedures but felt complimented when a study nurse said she would “love to have” the subject in another study).

40. Bell & Salmon, *supra* note 24, at 88.

41. See, e.g., Donno, *Awake with a Vengeance*, in GUINEA PIG ZERO: AN ANTHOLOGY OF THE JOURNAL FOR HUMAN RESEARCH SUBJECTS 22, 26 (Robert Helms ed., 2002) (commending staff that “bent over backward to get us anything we wanted, from books and hard-to-find movies to hoagie sandwiches from my favorite deli for super bowl Sunday and a bulb of raw garlic when I felt a cold coming on”); Theresa Dulce, *Spanish Fly Guinea Pig: PPD Pharmaco, Where Slackers Refuel*, in GUINEA PIG ZERO: AN ANTHOLOGY OF THE JOURNAL FOR HUMAN RESEARCH SUBJECTS, *supra*, at 34, 36 (“Going to the cafeteria was something I lived for.”).



## 2. Harms

Certain study features attract healthy individuals to research participation, but other aspects of participation are not so appealing. Studies expose participants to physical and psychological risks. Conventional approaches to research ethics and regulations take into account many of these hazards, but experienced volunteers point to difficulties that others in the research enterprise rarely acknowledge.<sup>42</sup>

Some volunteers have written vivid accounts highlighting overlooked study burdens. One example involves a science journalist's story about her participation in a weeklong study of the brain's response to temporary blindness. Before she began the trial, she wrote, a researcher ridiculed her worry that the study could leave her permanently blind.<sup>43</sup> Other disturbing incidents occurred during the study. A broken scanner delayed an MRI and, after it was partially repaired, continued to overheat, requiring her to "lie still for what [felt] like hours."<sup>44</sup> Contrary to researchers' assurances, study procedures were far from "quick and easy."<sup>45</sup> Adjusting to sightlessness was difficult, too; she cut her lip while trying to walk and "saw" unsettling images while wearing the blindfold.<sup>46</sup> Other incidents left her anxious, alarmed, and feeling vulnerable; after a few days, she was "so ready for [the study] to end."<sup>47</sup> After the blindfold was removed, it took time for her vision to return; when it did, she started "to cry with relief."<sup>48</sup>

This personal account is one among many showing that study requirements that appear on paper as undemanding can in fact be quite burdensome to participants. Another healthy volunteer made this point about the yearly memory tests he was given in a study of potential Alzheimer's disease biomarkers.<sup>49</sup> Such tests are usually considered low-burden research procedures. But this volunteer found the tests unexpectedly stressful. During the tests, he kept

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42. After conducting an in-depth study of research participant experiences, one team suggested that the term "impact" is a better way to refer to study burdens than the standard term "risk." Michael McDonald et al., *Toward Human Research Protection That Is Evidence Based and Participant Centered*, in HUMAN SUBJECTS RESEARCH REGULATION: PERSPECTIVES ON THE FUTURE 113, 117 (I. Glenn Cohen & Holly Fernandez Lynch eds., 2014).

43. Alison Motluk, *Diary of a Lab Rat*, 196 NEW SCIENTIST 38, 39 (2007).

44. *Id.* at 40.

45. *Id.*

46. *Id.* (describing "[j]agged shapes, vertical lightning strikes, symmetrical patterns, strings that quiver in time to the music on my CD").

47. *Id.* at 41.

48. *Id.*

49. Video: Living Room Conversation—In Their Own Voices: A Discussion with Research Subjects Who Also Work in the Field of Subject Protections (Public Responsibility in Medicine and Research 2010) [hereinafter Research Subjects Who Also Work in the Field of Subject Protections], available at <http://www.meetingproceedings.us/2010/aerc/contents/video/lrc1.htm>.

wondering whether his performance was satisfactory,<sup>50</sup> and this negative reaction made him realize that the tests could be even more upsetting to someone with memory problems.<sup>51</sup> A volunteer in a study of potential schizophrenia biomarkers made a similar observation, describing the eighteen hours of neuropsychological testing he underwent as “anything but ‘noninvasive.’ Instead it was invasive in a way that was more insidious than if someone had stuck a tube down his throat.”<sup>52</sup>

Volunteers also point to personal hardships imposed by outwardly insignificant study demands. Volunteers call attention to the “nontrivial” time required to participate in studies and the need to arrange childcare and transportation.<sup>53</sup> Studies may also involve embarrassing examinations and procedures and restrictions on ordinary activities.<sup>54</sup> Study schedule changes are also a major inconvenience for volunteers.<sup>55</sup> And when the side effects of study drugs leave subjects unable to go to work, they may lose income as a result of their participation.<sup>56</sup>

Repeat volunteers complain about the tedium of studies requiring overnight stays, too. One participant in a two-week study wrote that the study unit “had this desperate, Flowers in the Attic feel to it.”<sup>57</sup> She and the other volunteers would “look out the window and watch people do their normal, everyday errands.”<sup>58</sup> Another described his state of mind:

I feel that I am a worker[,] but it is not work, it's like a security guard that does not produce nothing [sic], just watches stuff. A security guard just gets paid to be bored, it's

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50. *Id.*

51. *Id.*

52. ALEX O'MEARA, CHASING MEDICAL MIRACLES: THE PROMISE AND PERILS OF CLINICAL TRIALS 115 (2009).

53. See Breitkopf et al., *supra* note 24, at 34 (explaining that “participants focused on the time involved and various aspects of the study procedures[,] . . . including physical and emotional aspects of participation,” and also noted time away from work, travel time, and time performing study-related procedures at home); Margaret L. Russell et al., *Paying Research Subjects: Participants' Perspectives*, 26 J. MED. ETHICS 126, 127 (2000) (discussing comments by vaccine study subjects).

54. Breitkopf et al., *supra* note 24, at 34 (discussing comments of women in a study involving gynecological examinations, which included an abstinence requirement).

55. ROBERTO ABADIE, THE PROFESSIONAL GUINEA PIG: BIG PHARMA AND THE RISKY WORLD OF HUMAN SUBJECTS 57 (2010).

56. See Research Subjects Who Also Work in the Field of Subject Protections, *supra* note 49 (discussing suffering serious side effects from a study drug, forcing the subject to stay home from work, and also noting that many people in that situation could lose wages).

57. Dulce, *supra* note 41, at 35.

58. *Id.*

about how much you can deal with being bored, that's the real hard part of it, the time and discomfort of being there.<sup>59</sup>

Just as courteous treatment and pleasant surroundings improve things for study volunteers, rudeness and unpleasant surroundings make things worse. The study environment has a significant impact on a subject's well-being.<sup>60</sup> Volunteers complain of things like cold waiting rooms and inedible food.<sup>61</sup> Rude behavior by people conducting research is a common theme in volunteer complaints. In one focus group, for example, a group of women criticized researchers for "acting superior" and "talking down and being condescending."<sup>62</sup> Other volunteers report that they were treated as data sources rather than people. As one put it, "[T]hey don't care about what you are thinking and they don't want to be talked about, they just want your body to do something and react to the drug so they can watch it."<sup>63</sup>

Disorganized and inattentive research staffs add burdens beyond those imposed by study requirements. One volunteer in a drug study wrote of her extreme anxiety, racing thoughts, and sleeplessness while taking a study drug.<sup>64</sup> She tried to reach someone on the research team but had to leave several messages and wait a week for her call to be returned.<sup>65</sup> Later, a staff member apologized, explaining that she had been on vacation and her substitute contact had turned off her pager.<sup>66</sup> At that point, the volunteer wrote, "I knew exactly what was going on—nobody cared."<sup>67</sup> Eventually she received a phone call from a study doctor, who said that symptoms like hers "sometimes" diminished over time and then ended the call without offering any follow-up plan.<sup>68</sup>

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59. ABADIE, *supra* note 55, at 2–3.

60. *See, e.g.*, Hermann et al., *supra* note 24, at 210 (stating that from the subject's perspective, positive or negative "environmental study conditions appeared to have the most relevant impact on their personal well-being").

61. *See, e.g.*, Emily Elliot, *Panic at Penn*, in GUINEA PIG ZERO: AN ANTHOLOGY OF THE JOURNAL FOR HUMAN RESEARCH SUBJECTS, *supra* note 41, at 29, 32 (recalling that the subject's major problem was that "the study was so relaxed that I often didn't know whom I'd be seeing and they often didn't know if I was even scheduled for an interview").

62. Bell & Salmon, *supra* note 24, at 88.

63. ABADIE, *supra* note 55, at 48 (quoting repeat volunteer Richard Helms).

64. Lisa McElroy, *The Anxious and the Damned*, in GUINEA PIG ZERO: AN ANTHOLOGY OF THE JOURNAL FOR HUMAN RESEARCH SUBJECTS, *supra* note 41, at 18, 19–20.

65. *Id.* at 19.

66. *Id.* at 19–20.

67. *Id.* at 20.

68. *Id.* at 21.

### 3. *How Volunteers Decide*

When deciding whether to enroll in studies, healthy volunteers weigh the potential benefits and harms of participation. Empirical data indicate that risk is the main reason volunteers turn down studies.<sup>69</sup> Yet it is not clear that all volunteers appreciate the risks they are facing. One participant in a cytomegalovirus vaccine study spoke of her own failure to take study risks seriously.<sup>70</sup> After receiving the vaccine, she became quite ill for a few days.<sup>71</sup> Although she had read the consent form and knew the vaccine could cause flu-like symptoms, she had dismissed the possibility: “I was arrogant enough to think it wasn’t going to happen to me.”<sup>72</sup>

Other volunteers engage in similar risk dismissals. One man commenting on his fellow repeat volunteers noted their reluctance to discuss risk exposure: “They want to make their money, they don’t want to think about the humiliations and the risks they had been through, and maybe they end up being a little dishonest about the risk with themselves.”<sup>73</sup> A journalist reported that the group of student volunteers she interviewed did not worry about adverse events: “They’re young, healthy, and suffering from a shared condition: They believe they’re invulnerable.”<sup>74</sup> Nearly all study volunteers who were interviewed after a healthy subject died unexpectedly were unconcerned about their own safety. Without any supporting evidence, they assumed that the subject had failed to ask enough questions or to follow study requirements.<sup>75</sup>

In interviews, some volunteers do express concern about short-term risks. Few mention any long-term risks of their trial exposures, however.<sup>76</sup> As one volunteer put it, “You are not thinking that these things are going to give you cancer five years from now, or that you might have a high level of radiation in your body.”<sup>77</sup> Some volunteers also admit that the prospect of compensation trumps their reservations about study risks. One volunteer explained, “You become addicted to the easy money, you don’t want

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69. See, e.g., Hermann et al., *supra* note 24, at 207; Stunkel & Grady, *supra* note 24, at 347, 351.

70. Research Subjects Who Also Work in the Field of Subject Protections, *supra* note 49.

71. *Id.*

72. *Id.*

73. ABADIE, *supra* note 55, at 65.

74. Rebecca Meiser, *Guinea Pig Gang*, SCENE (Mar. 22, 2006), <http://www.clevescene.com/gyrobase/guinea-pig-gang/Content?oid=1494231> (reporting on medical and podiatry students volunteering for trials).

75. Caitlin E. Kennedy et al., *When a Serious Adverse Event in Research Occurs, How Do Other Volunteers React?*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, June 2011, at 47, 52–53.

76. See ABADIE, *supra* note 55, at 66.

77. *Id.* at 74.

to do anything else.”<sup>78</sup> Another volunteer said, “If there were a study where they cut off your leg and sewed it back on and you got twenty thousand dollars, people would be fighting to get into that study . . . .”<sup>79</sup>

According to ethical guidelines, payment to volunteers should reflect the time and inconvenience, rather than the level of risk, a study presents.<sup>80</sup> But many subjects think higher risk justifies higher payment.<sup>81</sup> For example, a team interviewing women participating in an imaging study found broad agreement that study time and inconvenience should determine payment amounts.<sup>82</sup> But most of the women thought that payment should reflect the unknown risks of research interventions, too.<sup>83</sup> One of the women said, “If the product is experimental, the reimbursement should be more . . . . Because you’re basically a guinea pig, so you’re putting yourself at risk for something . . . .”<sup>84</sup> When another team asked experienced research participants about their views on study payment, sixty-five percent responded that the level of risk should have a role in setting payment amounts.<sup>85</sup>

The material described above reveals that actual volunteers do not always see research the same way that researchers and other nonparticipants do. Traditional ethical analysis portrays research participation as an essentially altruistic activity, but most healthy volunteers believe they are entitled to compensation. Indeed, most are unwilling to participate without compensation. Like the patients in *What Patients Teach*, research volunteers pay close attention to both kindnesses and slights that occur in routine interactions with professionals conducting studies. The volunteers describe study burdens that researchers and other outsiders do not

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78. *Id.* at 36.

79. Elliott, *supra* note 27, at 40. When one group asked pharmacy students whether they would enroll in hypothetical studies presenting different risk levels, students said that high payment would increase their willingness to enroll in a high-risk study. J. P. Bentley & P. G. Thacker, *The Influence of Risk and Monetary Payment on the Research Participation Decision Making Process*, 30 J. MED. ETHICS 293, 297 (2004).

80. See, e.g., Council for Int’l Orgs. of Med. Scis., *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, Guideline No. 7 (2002), available at [http://www.cioms.ch/publications/layout\\_guide2002.pdf](http://www.cioms.ch/publications/layout_guide2002.pdf); U.S. Dep’t of Health & Human Servs., *When Does Compensating Subjects Undermine Informed Consent or Parental Permission?*, HHS.GOV, <http://www.hhs.gov/ohrp/policy/faq/informed-consent/when-does-compensating-subjects-undermine-informed-consent.html> (last updated Jan. 20, 2011).

81. See Cynthia E. Cryder et al., *Informative Inducement: Study Payment as a Signal of Risk*, 70 SOC. SCI. & MED. 455, 460 (2010).

82. Breitkopf et al., *supra* note 24, at 33–34.

83. *Id.* at 33.

84. *Id.* at 34.

85. M. J. Czarny et al., *Payment to Healthy Volunteers in Clinical Research: The Research Subject’s Perspective*, 87 CLINICAL PHARMACOLOGY & THERAPEUTICS 286, 289 (2010).

always recognize. Some admit that their desire for payment leads them to disregard study risks. On these and other matters, volunteers have distinct perspectives on the ethics of human research.

## B. Patient-Subjects

### 1. Benefits

Potential health benefits are the major reason patients participate in research. Forty-two percent of cancer-trial participants responding to a questionnaire said that receipt of potential medical benefit was the single most important reason for enrolling, with no other reason coming close to this percentage.<sup>86</sup> Similarly, a survey of, and interviews with, cancer-trial participants found that two-thirds of them were motivated by hope for direct medical benefits.<sup>87</sup> Another researcher reported that more than half of the cancer-trial participants she interviewed

described the offer of the trial as being “the light at the end of the tunnel,” because of the hope it offered. This included hoping that the trial treatment would be a miracle cure, that it would be better than current treatment, that they might achieve relief of symptoms, and that they would live longer . . . .<sup>88</sup>

Interviews with patients suffering from pulmonary hypertension produced similar findings. More than half of the patients hoped trial enrollment would result in personal health benefits.<sup>89</sup> In another set of interviews, patients who had participated in a variety of studies cited hope for personal benefits, such as “access to what would become the new gold standard or the miracle drug,” as their reason for enrolling.<sup>90</sup>

Patients joining studies seek other personal benefits as well. Some are attracted by the prospect of “increased physician

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86. Tony H. Truong et al., *Altruism Among Participants in Cancer Clinical Trials*, 8 CLINICAL TRIALS 616, 619, 621 fig.2(a) (2011).

87. Rebecca D. Pentz et al., *Therapeutic Misconception, Misestimation, and Optimism in Participants Enrolled in Phase 1 Trials*, 118 CANCER 4571, 4574 (2012). In reality, participants in early-stage cancer trials rarely receive a direct medical benefit. *Id.* at 4575.

88. Cox, *supra* note 15, at 316.

89. Carroll et al., *supra* note 17, at 351.

90. Ann Freeman Cook & Helena Hoas, *Trading Places: What the Research Participant Can Tell the Investigator About Informed Consent*, 2 J. CLINICAL RES. & BIOETHICS 1, 4 (2011). Another interview study found that most people enrolled to gain access to medications, health care, and health monitoring tools. Anne Townsend & Susan M. Cox, *Accessing Health Services Through the Back Door: A Qualitative Interview Study Investigating Reasons Why People Participate in Health Research in Canada*, BMC MED. ETHICS, Oct. 2013, at 1, 3.

surveillance, including additional clinic visits” that go along with trial participation; they believe this surveillance can supply potentially useful information about their health.<sup>91</sup> Studies sometimes offer patient-subjects financial compensation, and some patients say they are more likely to enroll in such studies.<sup>92</sup> Empirical data show that almost all patient-subjects see the opportunity to learn about study results as an important benefit of participation.<sup>93</sup>

Patients also participate in research for altruistic reasons. For many, participation is a way to help others coping with disease. But altruism is not the main reason most patients enroll in trials. An assessment of cancer trial participants found that “although approximately half of respondents identified altruism as a very important motivation, less than 1 in 7 reported that altruism was their primary reason for joining the trial.”<sup>94</sup> Strikingly, participants in trials with the lowest chance of personal benefit were the least likely to report altruism as motivation to enroll.<sup>95</sup>

Patients have additional motivations for enrolling in studies. Some report that the opportunity to enroll “made them feel special, privileged, pleased, lucky[,] and honoured, because, as they described it, ‘not everyone gets the chance to take part in something like this.’”<sup>96</sup> Participants in HIV trials saw “trials as an opportunity

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91. Carroll et al., *supra* note 17, at 351. One subject portrayed study tests as “free care.” *Id.*

92. *Id.* at 353.

93. Conrad Vincent Fernandez et al., *Providing Research Results to Participants: Attitudes and Needs of Adolescents and Parents of Children with Cancer*, 27 J. CLINICAL ONCOLOGY 878, 882 (2009) (discovering that parents and children participating in cancer trials believed they had a “strong right” to see the research results); Rhonda G. Kost et al., *Assessing Participant-Centered Outcomes to Improve Clinical Research*, 369 NEW ENG. J. MED. 2179, 2180 (2013) (finding most participants wanted to receive information about study results).

94. Truong et al., *supra* note 86, at 622; *see also* Carroll et al., *supra* note 17, at 355 (noting that patients cited personal benefits more often than other reasons for joining trials). A recent survey of people who had participated in research at academic research institutions produced somewhat different findings. In the survey, the largest number of patient-subjects chose helping others as the most important factor motivating their participation, with “concern about the topic,” “find[ing] out more about my disease,” and “gain[ing] access to new treatment” as the next most important factors. Kost et al., *supra* note 25, at 433. It is possible that certain features of the study, such as a low survey return rate (twenty-nine percent of survey recipients) and the fact that survey respondents had participated in studies at leading medical centers, rather than in other study settings, contributed to the “altruism-first” findings. *See id.* at 430–31, 433.

95. Truong et al., *supra* note 86, at 622; *see also* Carroll et al., *supra* note 17, at 355.

96. Cox, *supra* note 15, at 316; *see also* Jane Poulson, *Bitter Pills to Swallow*, 338 NEW ENG. J. MED. 1844, 1846 (1998) (criticizing use of the term

to empower themselves in their fight against the disease, a way to take control of their bodies and their lives.”<sup>97</sup> Some patients also enroll in studies out of a desire to help doctors who have cared for them.<sup>98</sup>

## 2. Harms

Patients do not see participation as a purely positive option. Those hoping for medical benefits are deterred from enrolling by research requirements that seem to lessen this possibility.<sup>99</sup> Randomization as a method of determining treatment can be especially disturbing to patients. Randomization is generally seen as ethically defensible as long as all of the interventions in a study are in clinical equipoise.<sup>100</sup> Clinical equipoise exists when experts are uncertain about which intervention has the most favorable balance of benefits and harms.<sup>101</sup> When clinical equipoise exists, patients randomly assigned to any study group have an equal chance of receiving the intervention that will be best for them.<sup>102</sup>

Many patients find it difficult to accept the medical uncertainty underlying clinical equipoise. They are troubled to learn that doctors do not know which drug or other treatment would be best for them.<sup>103</sup> Such patients often develop a belief that one of the study interventions is better than the others.<sup>104</sup> Usually, patients prefer the new intervention, assuming that it must be superior to currently available treatments.<sup>105</sup>

Empirical findings reveal how patients think about randomization. A team conducting interviews with men who were asked to participate in a trial evaluating different treatments for benign prostatic disease found that most had a hard time accepting

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“eligible” in connection with clinical trials because it suggests to patients that experimental treatment is special and desirable).

97. ABADIE, *supra* note 55, at 119.

98. See Roberto Abadie et al., *Consent for Nondiagnostic Research Biopsies: A Pilot Study of Participant Recall and Therapeutic Orientation*, IRB: ETHICS & HUM. RES., May–June 2014, at 9, 13 (finding that some patients in a cancer study regarded participation as a way to care for the investigators, and one patient described participation as, “It’s almost me saying, ‘What can I do to help you?’”).

99. See Cox, *supra* note 15, at 316–17.

100. See Benjamin Freedman, *Equipoise and the Ethics of Clinical Research*, 317 NEW ENG. J. MED. 141, 141 (1987).

101. *Id.*

102. *See id.*

103. See Madsen et al., *supra* note 21, at 54–55.

104. *Id.* at 55 (noting that almost all cancer patients considering trial participation doubted that treatments were in genuine equipoise, resulting in a preference for one treatment).

105. *Id.* at 56 (noting that a cancer patient who did not get assigned to experimental intervention felt she had “lost the drawing of lots”).



randomization.<sup>106</sup> For these men, an understanding of trial design features, including randomization, “did not . . . mean that such concepts made sense or were believable.”<sup>107</sup> Men used different strategies to make sense of the trial. “Some became distrustful because of assumptions about the existence of rationing, others put their trust in their clinician and their beliefs about fate and destiny, while others just keep struggling with the perceived inconsistencies.”<sup>108</sup> One man “wanted the doctors to tell him what treatment would be most suitable for him, and perceived the trial to be a ‘trick.’”<sup>109</sup> Several of the men who refused to participate did so because they wanted to receive a specific form of treatment.<sup>110</sup>

Interviews with potential cancer trial participants generated similar findings. For almost all of these patients, the prospect of being randomized to a treatment was unsettling; some thought it was unethical.<sup>111</sup> One patient explained her discomfort with randomization this way:

When do we draw lots? We do that when we have a lottery or we gamble, I mean—when we take a risk, and that’s not compatible with what doctors should stand for. They should stand for trustworthiness, safety, and “we take over” and “we are able” . . . . [T]he trusting relationship between doctor and patient suffers . . . .<sup>112</sup>

Another patient said, “[I]t’s all wrong to start with a drawing of lots, because you really want to be in safe surroundings and be told that the treatment you’re going to have will help you. And you don’t feel that with a drawing of lots . . . .”<sup>113</sup>

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106. Katie Featherstone & Jenny L. Donovan, “Why Don’t They Just Tell Me Straight, Why Allocate It?” *The Struggle to Make Sense of Participating in a Randomised Controlled Trial*, 55 SOC. SCI. & MED. 709, 717 (2002).

107. *Id.*

108. *Id.*

109. *Id.* at 715.

110. *Id.* at 713; see also Julie Brintnall-Karabelas et al., *Improving Recruitment in Clinical Trials: Why Eligible Participants Decline*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Mar. 2011, at 69, 71 (finding that individuals eligible for studies declined because they preferred to receive standard medical care).

111. Madsen et al., *supra* note 21, at 56.

112. *Id.*

113. *Id.* at 55. Much of the general public appears to share this discomfort with randomization. For example, in a questionnaire and interview study, about half of adults in college classes were “loathe to accept that a doctor might genuinely not know what treatment is best.” Elizabeth J. Robinson et al., *Lay Conceptions of the Ethical and Scientific Justifications for Random Allocation in Clinical Trials*, 58 SOC. SCI. & MED. 811, 821 (2004). About half also said it is unacceptable for a doctor to propose using randomization as a way to decide among treatments. *Id.* at 815. Instead, they “assumed that just as much knowledge would be gained about which treatment is better if patients and doctors chose their treatment, rather than if treatments were allocated at random.” *Id.* at 822.

Studies that include a placebo control group are the hardest for patients to accept. Placebo control groups are seen as ethically acceptable in tests of new interventions under certain circumstances, such as when there is no proven treatment for the subjects' condition.<sup>114</sup> But patients often refuse to participate in placebo-controlled trials.<sup>115</sup> Those who agree to participate are often disappointed if they are assigned to a placebo group, and some who discover this during the trial drop out before the study ends.<sup>116</sup> These patients find it difficult to accept that assignment to a placebo group could turn out to be best for them.<sup>117</sup>

An interview study involving patients with Parkinson's disease documents this reservation. Surgical interventions aimed at improving this disease are typically tested against a placebo—in this case, a “sham” surgical procedure.<sup>118</sup> Some of the patients who were interviewed questioned the necessity of including a placebo group, asking whether there were alternative ways to evaluate the study intervention.<sup>119</sup> For example, one said, “If it was a good operation and the results gave big improvements[,] then I don't see why you'd need a placebo group in that case.”<sup>120</sup> Another who accepted the scientific need for the placebo felt its use was dehumanizing: “[Y]ou take on the semblance of something in a petri dish, rather than a person.”<sup>121</sup> Many saw the use of a placebo as unfair because it would expose subjects to a surgical procedure with no possibility of direct benefit.<sup>122</sup>

Besides distress and even anger at research requirements for randomization and placebo controls, patients worry about the risks

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114. See, e.g., Christopher K. Daugherty et al., *Ethical, Scientific, and Regulatory Perspectives Regarding the Use of Placebos in Cancer Clinical Trials*, 26 J. CLINICAL ONCOLOGY 1371 (2008) (arguing the medical necessity or desirability of placebo-controlled oncology trials).

115. See Brintnall-Karabelas et al., *supra* note 110, at 70 (finding instances where patients declined participation in placebo-controlled studies).

116. See Rebecca Dresser, *Subversive Subjects: Rule-Breaking and Deception in Clinical Trials*, 41 J.L. MED. & ETHICS 829, 831 (2013).

117. Teresa L. Swift, *Sham Surgery Trial Controls: Perspectives of Patients and Their Relatives*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, July 2012, at 15, 21 (noting that patients said they would be disappointed and upset if assigned to placebo, and they did not “acknowledge or value any possible placebo effect or the chance to avoid the potential risks of the real operation”); Dan McDonald & Mary Jo Lamberti, *The Psychology of Clinical Trials: Understanding Physician Motivation and Patient Perception*, CENTERWATCH, [http://www.centerwatch.com/pdfs/tew\\_the\\_psychology\\_of\\_clinical\\_trials.pdf](http://www.centerwatch.com/pdfs/tew_the_psychology_of_clinical_trials.pdf) (last updated July 14, 2006) (finding that twenty-nine percent of the patient-subjects surveyed said their top worry was receiving the placebo).

118. Swift, *supra* note 117, at 15.

119. *Id.* at 23.

120. *Id.* at 22.

121. *Id.*

122. *Id.* at 23.

involved in exposure to a relatively untested intervention.<sup>123</sup> Some decline participation because they are “scared of the unknown.”<sup>124</sup> This fear can be especially strong among patients with serious illnesses. Such feelings were evident in one group’s interviews with cancer patients: “The graver the patients evaluated their situation[,] the more they wanted to choose the right thing and consequently also the more negatively they assessed any factor imposing risk or uncertainty.”<sup>125</sup>

At times, patients coping with a serious diagnosis find that enrolling in a trial “is just too much to think about.”<sup>126</sup> People with generally positive attitudes toward research can become more cautious and skeptical when facing a personal research decision. One patient who declined participation said, “It was a shocking experience to realise that now it was personal and I couldn’t participate. I was shocked that I couldn’t contribute in helping others . . . . I would very much have liked to do that, but I wasn’t capable of it . . . .”<sup>127</sup>

Some patients are also repelled by what they perceive as the research team’s impersonal manner. One health professional with serious cancer had this reaction. She initially thought she would enroll in a trial, but after being screened for eligibility, she changed her mind.<sup>128</sup> In contrast to her own doctor’s “compassion and empathy,” the “competent and professional” study investigators seemed “oddly disconnected from the fact that she was a woman told she might be facing a death sentence.”<sup>129</sup> Because she “felt experimented on,” rather than “cared for,” she decided against trial participation.<sup>130</sup>

The practical aspects of trial participation can present problems for patients, too. Like healthy volunteers, patient-subjects are expected to arrange their lives around study requirements. But patients can be ill-equipped to deal with study demands. As one

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123. Carroll et al., *supra* note 17, at 352.

124. Madsen et al., *supra* note 21, at 55.

125. *Id.* at 57.

126. Gina Kolata, *Lack of Study Volunteers Is Said to Hobble Fight Against Cancer*, N.Y. TIMES, Aug. 3, 2009, at A1 (“It is one of the worst times imaginable—a cancer diagnosis, all the terror that goes with it, and then, sitting in a doctor’s office and being asked to make difficult decisions about treatment. Then add questions about joining a trial.”); *see also* Abadie et al., *supra* note 98, at 14 (finding that breast cancer trial participants “were preoccupied with their diagnosis and treatment during the consent process for the parent study”); Behrendt et al., *supra* note 20, at 78 (finding that cancer patients were “tired, impatient[,] and distracted” when trial information was being discussed).

127. Madsen et al., *supra* note 21, at 53; *see also* Dresser, *supra* note 14, at 72–73 (describing a similar experience).

128. Korn, *supra* note 17.

129. *Id.*

130. *Id.*

writer put it, “Often, clinical trials are aptly named: they are trials—difficult and exhausting, at a time when a patient’s physical and emotional capacities are already stretched thin.”<sup>131</sup> In interviews, sixty-five percent of patients with pulmonary hypertension said that time demands, travel requirements, and other inconveniences could deter them from participating in studies.<sup>132</sup> People with mental health disorders cited travel distance, time away from work, and lack of flexible schedules as reasons for declining participation.<sup>133</sup> Because research participation can generate extra costs for patients, some also fail to enroll because they cannot afford the added expense.<sup>134</sup>

Some patients who enroll in trials have second thoughts once they are dealing with travel, visits, tests, hospital stays, and other study demands.<sup>135</sup> A qualitative study of cancer trial participants found that all had “an increasing sense of being burdened” as the trial proceeded.<sup>136</sup> Patients often wondered “why they were putting themselves through the trial in the first place, and whether it was all worthwhile.”<sup>137</sup> Many became disillusioned and antagonistic, saying things like, “I shouldn’t feel like this because the results have been so good for me—you know the [tumour] shrinkage has been great. I should be feeling more encouraged than I am. I don’t know. It’s got to be a real drag coming here.”<sup>138</sup> One complained, “We can’t plan anything. I just feel as though I’m not in control of my life at all. All I see is hospitals, white coats[,] and nurses.”<sup>139</sup> Most of the

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131. Margaret Anderson, Letter to the Editor, *Why Patients Turn Down Clinical Trials*, N.Y. TIMES, Aug. 7, 2009, at A18.

132. Carroll et al., *supra* note 17, at 353.

133. Brintnall-Karabelas et al., *supra* note 110, at 70; *see also* McDonald & Lamberti, *supra* note 117 (finding that thirty-one percent of the patient-subjects were concerned about accessibility to public transportation and that twenty-one percent were concerned about keeping the number of visits to a minimum).

134. *See* O’MEARA, *supra* note 52, at 11–12 (describing a patient’s inability to pay for drugs in a trial involving a novel procedure); Ana S. Iltis, *Costs to Subjects for Research Participation and the Informed Consent Process: Regulatory and Ethical Considerations*, IRB: ETHICS & HUM. RES., Nov.–Dec. 2004, at 9, 10.

135. *See, e.g.*, Iris F. Groeneveld et al., *Factors Associated with Non-Participation and Drop-Out in a Lifestyle Intervention for Workers with an Elevated Risk of Cardiovascular Disease*, 6 INT’L J. BEHAV. NUTRITION & PHYSICAL ACTIVITY 80, 81, 84 (2009) (finding that some common reasons for dropouts were time constraints and problems with organization, such as scheduling appointments). Another team interviewing subjects observed that the “cumulative effects of relatively trivial burdens led to dissatisfaction and even alienation, particularly for debilitated individuals.” McDonald et al., *supra* note 42, at 118.

136. Cox, *supra* note 15, at 317.

137. *Id.*

138. *Id.*

139. *Id.* at 318; *see also* Cook & Hoas, *supra* note 90, at 5 (finding that the former participants who said they would not enroll again “reported negative

patients decided to stay in the trial despite their negative feelings, but researchers eventually removed seventy percent of them because they suffered serious side effects or their cancer progressed.<sup>140</sup> When this happened, patients were upset and disappointed.<sup>141</sup>

There is also evidence that patient-subjects care about matters that are given relatively little attention in research oversight. Patients care about the value of the studies they are asked to join. Interviews with experienced subjects found many concerned about the commercial aspects of research.<sup>142</sup> These participants expressed antipathy toward trials done primarily for business purposes, such as trials of “me-too” drugs or trials aimed at extending a drug’s patent protection.<sup>143</sup> One subject put it this way: “I assume it is on the up and up and not so that [the pharmaceutical company] can make a million dollars marketing the drug . . . . [I]f I am in the guinea pig group, I want to make sure . . . I am not sacrificing my body for someone’s bottom line.”<sup>144</sup>

The experienced subjects in this interview study also wanted to know more about the compensation investigators received for conducting research. A mere statement that researchers are compensated was not enough for at least some subjects—they wanted to know how much the researchers would earn.<sup>145</sup> One subject said, “[W]hen there is something like that statement in the consent form—‘the researcher is getting compensated’—I would think it was like \$10—not anything big. It wouldn’t occur to me. The way it is written, it is like they want you to gloss over it.”<sup>146</sup> Researchers ought to disclose these details, another subject said, as “a matter of respect” for the individuals taking part in a study.<sup>147</sup>

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experiences with their research participation,” and that one participant stated, “I would have liked to have [had] a better understanding of how I was going to feel.”).

140. Cox, *supra* note 15, at 318.

141. *Id.*; see also C. Daniel Mullins et al., *Patient-Centeredness in the Design of Clinical Trials*, 17 VALUE HEALTH 471, 471 (2014) (finding that patients in cancer trials “are disappointed not to learn more about their disease through their involvement in research[,] and they find that trial participation takes more time and effort than they thought it would”).

142. Ann Freeman Cook et al., *The Protectors and the Protected: What Regulators and Researchers Can Learn from IRB Members and Subjects*, 3 NARRATIVE INQUIRY BIOETHICS 51, 60–63 (2013).

143. *Id.* at 61–62.

144. *Id.* at 62; see also S. M. Madsen et al., *Attitudes Towards Clinical Research Among Cancer Trial Participants and Non-Participants: An Interview Study Using a Grounded Theory Approach*, 33 J. MED. ETHICS 234, 236–37 (2007) (“Most patients in all groups expressed doubts about industrial financing of trials owing to worries about industry placing commercial motives before the interests of patients.”).

145. Cook et al., *supra* note 142, at 61.

146. *Id.*

147. Cook & Hoas, *supra* note 90, at 5.

These experienced subjects also criticized researchers who failed to inform them of study results. As the interview team reported, many “were disappointed that they had not been re-contacted and informed about study results as was promised or anticipated when enrolling.”<sup>148</sup> This research omission reduced their interest in participating in future studies.<sup>149</sup>

### 3. *How Patients Decide*

Like healthy volunteers, patients making research decisions evaluate the potential benefits and harms of participation. But the psychology of patient decision making differs from that of healthy individuals considering study enrollment. As one interview team reported, “The data suggest that participants’ beliefs and expectations about healthcare may make it difficult for them to absorb key information when trying to make informed decisions about participating in research.”<sup>150</sup>

Many patients exhibit what ethicists call the “therapeutic misconception” about research. This state of mind exists in patients who fail to understand the ways in which research participation differs from ordinary medical care.<sup>151</sup> Some patients believe that research is governed by concern for their individual best interests, when in fact it is governed by the need to gather accurate and useful data to guide the care of future patients.<sup>152</sup> In research, decisions about their treatment will be based on scientific needs rather than on what physicians think would be best for them as individuals. Patients’ failure to understand the nature and goals of research can lead them to overestimate the chance that they will obtain personal medical benefits from trial participation.<sup>153</sup>

Besides a general misunderstanding of research requirements, patients may misunderstand how research rules and goals will apply to them as individuals. Some patient-subjects appear to understand the study population’s overall chance of receiving

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148. *Id.*

149. *Id.*; see also Kost et al., *supra* note 93 (reporting that seventy-two percent of prior trial participants surveyed said information on research results was a “very important” consideration for future trial participation).

150. Cook et al., *supra* note 142, at 55.

151. See Gail E. Henderson et al., *Clinical Trials and Medical Care: Defining the Therapeutic Misconception*, 4 PLOS MED. e324, e324 (2007).

152. See, e.g., Steven Joffe et al., *Quality of Informed Consent in Cancer Clinical Trials: A Cross-Sectional Survey*, 358 LANCET 1772, 1774 (2001) (finding that cancer trial participants failed to recognize that the purpose of the trial was to benefit future patients and that the study intervention had not been proven to be the best treatment for their cancer).

153. See *id.* at 1776. In an interesting twist, experienced subjects in one interview study understood that research offered uncertain medical benefits but said that benefits from medical care were similarly uncertain. See Townsend & Cox, *supra* note 90, at 8.

medical benefits but mistakenly believe that certain factors give them a higher-than-average chance of receiving personal medical benefits.<sup>154</sup> Ethicists refer to this bias as “unrealistic optimism.”<sup>155</sup>

An example of unrealistic optimism surfaced in interviews with parents considering whether to enroll their children in a phase I cancer trial. One mother thought that her child had a better-than-average chance of benefit because he had previously benefited from a drug similar to the one being evaluated in the trial.<sup>156</sup> But the mother failed to recognize that other children in the trial might also have benefited from drugs resembling the study drug.<sup>157</sup> Thus, her reason for believing her son was exceptional lacked a firm basis in reality.<sup>158</sup>

Such misconceptions do not account for all of patients’ optimism about study results. Even patients with a realistic view of their trial prospects may maintain high hopes for personal medical benefit. In one interview study, cancer trial participants who overestimated their chance of personal benefit said they were not making a factual statement but were “expressing their hope or a positive attitude.”<sup>159</sup> Another group of cancer trial participants gave several reasons for their rosy expectations, such as their belief that optimism can have positive health effects, their desire to keep fighting their disease, and their faith in religion, science, or doctors.<sup>160</sup> Some participants in this group also explained that they were trying to behave in ways that would please “the medical community, their families, and even their faith networks.”<sup>161</sup>

Patient-subjects may underestimate the risks associated with participation, too. Such underestimations are often tied to unrealistic optimism: subjects believe that their personal risk is

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154. See Lynn A. Jansen et al., *Unrealistic Optimism in Early-Phase Oncology Trials*, IRB: ETHICS & HUM. RES., Jan.–Feb. 2011, at 1, 4 (finding that cancer trial participants who responded to surveys generally believed that they had a better-than-average chance of experiencing health benefits from the investigational drugs they were taking, despite understanding that the purpose of the trials was to help future patients, not trial participants).

155. See *id.* at 2; Don Swekoski & Deborah Barnbaum, *The Gambler’s Fallacy, the Therapeutic Misconception, and Unrealistic Optimism*, IRB: ETHICS & HUM. RES., Mar.–Apr. 2013, at 1, 1.

156. Joshua Crites & Eric Kodish, *Unrealistic Optimism and the Ethics of Phase I Cancer Research*, 39 J. MED. ETHICS 403, 404 (2013).

157. *Id.* at 405.

158. *Id.*

159. Pentz et al., *supra* note 87, at 4576; see also Scott Y. H. Kim et al., *Research Participants’ “Irrational” Expectations: Common or Commonly Mismeasured?*, IRB: ETHICS & HUM. RES., Jan.–Feb. 2013, at 1, 1 (discussing other factors that led research participants to express optimism about personal benefit).

160. Daniel P. Sulmasy et al., *The Culture of Faith and Hope: Patients’ Justifications for Their High Estimations of Expected Therapeutic Benefit When Enrolling in Early Phase Oncology Trials*, 116 CANCER 3702, 3705 (2010).

161. *Id.* at 3707.

lower than the risk faced by others in a trial.<sup>162</sup> Underestimations of risk may also reflect a participant's failure to understand or attend to trial information. In interviews, for example, some experienced subjects characterized participation as a way to "give back with no real risk at all."<sup>163</sup> Some did not take risk information seriously; instead, they thought risk disclosure was "a formality—like what you sign before surgery, the form saying you might die. It was just like the legal language thing on the consent forms . . ."<sup>164</sup> Some also said that the government would not permit, and doctors would not recommend, any study that presented serious risks to participants.<sup>165</sup>

Trust in clinicians and the medical system plays a big role in patients' willingness to participate in research. In interviews, experienced subjects said they assumed that doctors would not suggest or recommend trial participation if it were not the best option for them.<sup>166</sup> Some assumed that trials conducted in hospitals or other medical facilities must be beneficial for patients.<sup>167</sup> Some also said it would be difficult to say no if a doctor they trusted asked them to consider study participation.<sup>168</sup>

In light of these high trust levels, it is not surprising that many patients want doctors to tell them what to choose. For example, nearly eighty percent of the cancer trial participants in one qualitative study said they wanted a doctor's recommendation on whether to enroll.<sup>169</sup> In interviews, many women considering cancer trial participation said that because their knowledge was inadequate, they "would have preferred the doctor to make that choice for them."<sup>170</sup> One woman said, "I was really surprised that they put me in that situation with such a serious disease, [wanting] me to make choices about my own disease. It had an incredible

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162. Pentz et al., *supra* note 87, at 4576. This study of cancer trial participants also found a subgroup of what the authors called therapeutic "pessimists." *Id.* These participants believed they had a lower chance of benefit or higher chance of harm than did others enrolled in the trials. *Id.*

163. Cook et al., *supra* note 142, at 56; *see also* Behrendt et al., *supra* note 20, at 77 (finding that the cancer trial participants thought trial presented no risk); Pentz et al., *supra* note 87, at 4576 (finding that only three trial subjects recognized distinct burdens in research, such as extra biopsies and other procedures, which "supports the concern that participants either do not understand or do not focus on the key differences between individualized care and research").

164. Cook et al., *supra* note 142, at 57.

165. *Id.*

166. *See id.* at 55.

167. *See id.* at 55–56.

168. *See* Cook & Hoas, *supra* note 90, at 3; *see also* Abadie et al., *supra* note 98 (finding that the choice to participate in a trial was based on trust in the institution and investigators).

169. *See* Cox, *supra* note 15, at 316.

170. Madsen et al., *supra* note 21, at 54.



effect on me, I felt bad about it, and I couldn't get the doctor to just give me . . . advice . . . ."<sup>171</sup>

For many patients, clinical trial participation is a confusing and unnerving variation on the medical care they are accustomed to receiving. The shift from ordinary clinical care to the different and usually foreign territory of research takes patients by surprise. Making research decisions in the context of serious illness is also an emotionally demanding task. The pressures and distractions of serious illness make it difficult for patients to learn what they need to know. It can be hard for patients to understand the differences between research and medical care, and patients who do understand the differences search for reasons why their prospects could be better than those of other patients in a trial. Patients also expose research burdens that are easy for outsiders to overlook. Patients involved in research reveal the human dimensions of becoming a human subject.

### C. *Deciding for Others*

Not all people make their own research choices. Parents must decide whether their children participate in studies.<sup>172</sup> Surrogate decision makers, typically family members, decide for adults with dementia and other conditions that impair decision-making capacity.<sup>173</sup> Besides facing many of the same problems as adults navigating the world of research, parents and surrogates confront distinct challenges. Parents and surrogates operate with a heavy sense of responsibility for the welfare of their loved ones. They blame themselves for any adverse consequences that flow from their choices. If children or adults with impaired capacity have opinions on research participation, parents and surrogates must decide how much influence those opinions should have on the final decision.

#### 1. *Children*

Ethical guidelines and legal rules authorize parents to make research decisions for their children.<sup>174</sup> This is a daunting task for many parents, especially those whose children are seriously ill. Parents considering research aspire to make the best possible

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171. *Id.* at 55; *see also* Carroll et al., *supra* note 17, at 348 (finding that one-third of the patients interviewed preferred that their doctors decide about trial enrollment).

172. *See* David Wendler et al., *The Ethics of Paying for Children's Participation in Research*, 141 J. PEDIATRICS 166, 166 (2002).

173. *See* Paul S. Mueller et al., *Ethical Issues in Geriatrics: A Guide for Clinicians*, 79 MAYO CLINIC PROC. 554, 556 (2004).

174. *See, e.g.*, 21 C.F.R. § 50.55 (2014) (outlining the Food and Drug Administration's additional safeguards for the protection of children in clinical investigations); 45 C.F.R. §§ 46.402, 46.408 (2014) (describing the Department of Health and Human Service's protections for children involved in research).

choices for their children but fear they will not succeed in doing so. For example, in interviews, mothers of children enrolled in a study involving bone marrow transplantation said they “dreaded the possibility that they might have to live with the knowledge that they had made the ‘wrong’ decision[,] and this was intensified when things did not go well for the child.”<sup>175</sup> Another group of parents said that it would be much harder to make research decisions for their children than to make research decisions for themselves.<sup>176</sup>

Parents can also be extremely cautious about exposing their children to research risks. For example, one-third of parents responding to a survey said they would be more reluctant to accept certain research risks for their newborns than to accept those risks for themselves.<sup>177</sup> Parents also assess risks differently than health professionals do. As two scholars observed, “To the clinician research can be considered low risk when it involves no greater risk than conventional treatment. To the parent everything is high risk because they have a sick child.”<sup>178</sup>

Potential medical benefit is the overwhelming reason parents agree to their child’s research participation.<sup>179</sup> One mother of a child with a congenital heart defect frankly acknowledged this focus. In deciding whether to enroll her son in a trial, the mother said, “If we could prolong the time to needing another open-heart surgery, then we were all for that.”<sup>180</sup> Many parents list altruism as one of their motivations for agreeing to trials but often do so only after being prompted to consider whether altruism played a role.<sup>181</sup>

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175. Valerie Shilling & Bridget Young, *How Do Parents Experience Being Asked to Enter a Child in a Randomised Controlled Trial?*, BMC MED. ETHICS, Feb. 2009, at 1, 2, available at <http://www.biomedcentral.com/content/pdf/1472-6939-10-1.pdf>.

176. Patrina H. Y. Caldwell et al., *Parents’ Attitudes to Children’s Participation in Randomized Controlled Trials*, 142 J. PEDIATRICS 554, 557 (2003).

177. Shilling & Young, *supra* note 175.

178. *Id.* at 5.

179. See Jérémy Vanhelst et al., *Effect of Child Health Status on Parents’ Allowing Children to Participate in Pediatric Research*, BMC MED. ETHICS, Feb. 2013, at 1, 4–5, available at <http://www.biomedcentral.com/content/pdf/1472-6939-14-7.pdf> (finding that one hundred percent of parents of sick children said that direct benefits to the child would be the main motivation for the child’s trial enrollment). See generally Shilling & Young, *supra* note 175 (reviewing research evidence on parents’ views of their children’s participation in trials).

180. Audio tape: Annual HRRP Conference: Human Research Protection Programs in an Evolving Landscape, held by Public Responsibility in Medicine and Research, *In Our Own Voices: Pediatric and Adolescent Research Subjects Share Their Stories* (Dec. 2, 2007), available at <http://www.meetingproceedings.us/2007/primr/contents/audio/web/81973/player.html>.

181. Shilling & Young, *supra* note 175, at 7 (noting that some parents might cite altruism to justify their decision to enroll their children or to portray that decision in socially positive terms).

Like adults deciding about research, parents are often troubled by randomization. Parents seeking the best treatment for their children can be alarmed to learn that in a clinical trial, the child's treatment is determined by chance. Many parents do not understand randomization; in one study, fifty percent of parents deciding about cancer trials failed to understand the concept.<sup>182</sup> Other parents understand that randomization is an allocation method but fail to understand or accept its scientific rationale. For example, in interviews involving parents of children enrolled in a trial, some parents said that randomization was a way to allow parents and doctors to avoid the burden of choosing among treatments.<sup>183</sup> Some said it was a way to ration interventions that could not be provided to all children.<sup>184</sup> Some parents concluded that randomization allowed their child to receive the best intervention.<sup>185</sup>

Many parents are anxious and distracted when making research decisions. The mother of a child with a brain tumor described how she and her husband felt during a study discussion: "We were an emotional wreck . . . . Both of us were . . . nodding our heads and didn't hear a damn word [the doctors] said."<sup>186</sup> It was almost impossible to concentrate on the information, she said, because she and her husband were grieving the loss of their healthy son as they made those decisions.<sup>187</sup> Other parents considering study participation for seriously ill children report similar distress, distress that can keep them from actively participating in study discussions.<sup>188</sup>

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182. Eric Kodish et al., *Communication of Randomization in Childhood Leukemia Trials*, 291 JAMA 470, 471–73 (2004); see also Rebecca Schaffer et al., *Parents' Online Portrayals of Pediatric Treatment and Research Options*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Sept. 2009, at 73, 81 ("Parents are vulnerable both to misunderstanding the distinction between research and treatment and to misunderstanding and overestimating the potential of medical research to benefit their children.").

183. Snowdon et al., *supra* note 21, at 1345.

184. *Id.*

185. *Id.*

186. Video: Living Room Conversation: A Discussion with Research Subjects and Their Advocates (Public Responsibility in Medicine and Research 2009), available at <http://www.meetingproceedings.us/2009/aerc/contents/audio/web/LRCSunday/player.html>.

187. *Id.*

188. Shilling & Young, *supra* note 175, at 4; see also Kerry Woolfall et al., *Parents' Agendas in Paediatric Clinical Trial Recruitment Are Different from Researchers' and Often Remain Unvoiced: A Qualitative Study*, PLOS ONE, July 2013, at 1, 5, available at <http://www.plosone.org/article/fetchObject.action?uri=info:doi/10.1371/journal.pone.0067352&representation=PDF> (finding that parents, who were interviewed after a study was presented to them, asked many questions and raised many concerns they had not voiced in the actual study discussion with the physician-researchers).

Parents also struggle to reconcile their protective responsibilities with their dependence on clinicians. One mother of a child with hemophilia described her reaction after being approached about enrolling her son in a trial: “You’ve become really reliant on these people, . . . and they are asking you to participate in this study . . . . The last thing you want to do is tick these people off.”<sup>189</sup> She worried that declining trial participation would damage her relationships with the clinicians caring for her child.

Many parents seek clinicians’ advice on enrollment, yet few want to transfer their decision-making power to clinicians. For example, one group of parents who agreed to their children’s trial participation said that even though the choice was difficult, “they felt it was theirs to make.”<sup>190</sup> In several surveys, almost all parents said they did not want clinicians to take responsibility for this choice.<sup>191</sup>

Guidelines and regulations promote children’s involvement in research decision making and give children the power to veto participation in certain circumstances.<sup>192</sup> Studies show that children themselves want to be involved in the process,<sup>193</sup> and many parents agree that their children should be included. For example, a mother considering research for her six-year-old said that even children this young should have an opportunity to ask questions about research options: “They might not have any,” she said, “but they’re so happy to be asked.”<sup>194</sup>

At the same time, children and parents may have different views on when participation is appropriate. For example, when a group of parents and children were asked about hypothetical research participation, over twice as many children as parents

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189. *In Our Own Voices: Pediatric and Adolescent Research Subjects Share Their Stories*, *supra* note 180.

190. Shilling & Young, *supra* note 175, at 3.

191. *Id.*

192. *See, e.g.*, 21 C.F.R. § 50.55 (2014) (outlining the Food and Drug Administration’s requirements for children’s assent to research); 45 C.F.R. §§ 46.402, 46.408 (2014) (defining assent as a child’s agreement to participate in research and outlining when it is appropriate to require a child’s assent before conducting research funded by the Department of Health and Human Services); Comm. on Bioethics, *Informed Consent, Parental Permission, and Assent in Pediatric Practice*, 95 PEDIATRICS 314, 315 (1995) (stressing the importance of including children in the decision-making process).

193. *See* Ulrica Swartling et al., “My Parents Decide if I Can. I Decide if I Want to.” *Children’s Views on Participation in Medical Research*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Dec. 2011, at 68, 71–72; Yoram Unguru et al., *The Experiences of Children Enrolled in Pediatric Oncology Research: Implications for Assent*, 125 PEDIATRICS e876, e880 (2010).

194. *In Our Own Voices: Pediatric and Adolescent Research Subjects Share Their Stories*, *supra* note 180.

expressed a willingness to enroll in higher-risk trials.<sup>195</sup> When there is disagreement about participation, parents may urge their children to reconsider or may overrule their children altogether.

Parents are most likely to question or dismiss a child's position when they believe a trial offers the child a potential medical benefit. For example, the mother of a fourteen-year-old with a heart defect reported that she and her husband did not consult her son when enrolling him in a study of a new stent.<sup>196</sup> Parents of children with chronic medical conditions like diabetes said they would not hesitate to persuade their children to join studies that offered a potential medical benefit.<sup>197</sup> In interviews, nearly half of a group of children enrolled in cancer trials said they had no part or very little part in the enrollment decision.<sup>198</sup> Thirty-eight percent of these children said they did not feel free to object to participation, usually because they felt pressure from their parents, doctor, or both.<sup>199</sup>

## 2. *Cognitively Impaired Adults*

Research decision making for adults with cognitive impairments presents its own distinct challenges. Surrogates deciding for cognitively impaired adults occupy a less established legal and social role than that of parents deciding for their children. Surrogate decision making is also more complex, for in most cases the potential research subject was once a fully functioning individual with particular values and preferences. It is not always clear how those values and preferences should influence research choices. Laws and ethical guidelines typically instruct surrogates to give first priority to the incapable adult's former views,<sup>200</sup> but empirical evidence indicates that most surrogates take a different approach.

Most studies of surrogate decision making in research examine the experiences of surrogates choosing for adults with Alzheimer's disease ("AD") or other forms of dementia. As in other research contexts, the most common reason for enrolling people with

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195. David Wendler & Tammara Jenkins, *Children's and Their Parents' Views on Facing Research Risks for the Benefit of Others*, 162 ARCHIVES PEDIATRIC & ADOLESCENT MED. 9, 11 (2008).

196. *In Our Own Voices: Pediatric and Adolescent Research Subjects Share Their Stories*, *supra* note 180.

197. Shilling & Young, *supra* note 175, at 8.

198. Unguru et al., *supra* note 193.

199. *Id.*

200. See, e.g., 38 C.F.R. § 17.32(e) (2014) (stating that surrogates must premise their decisions on "knowledge of what the patient would have wanted"); *AMA Code of Medical Ethics, Opinion 8.081—Surrogate Decision Making*, AM. MED. ASS'N (Dec. 2004), <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion8081.page>; *White Paper on Surrogate Decision-Making and Advance Care Planning in Long-Term Care*, AMDA, <http://www.amda.com/governance/whitepapers/surrogate/> (last visited Mar. 5, 2015).

dementia in studies is to help the patient.<sup>201</sup> Surrogates also report having the same sense of heightened responsibility that parents have. In interviews, for example, some surrogates said they were reluctant to consent to research because they “would not want to feel regret if they did make the choice and a bad outcome occurred to the patient.”<sup>202</sup> Another surrogate observed, “It’s very different when you’re thinking about it for somebody else than for yourself.”<sup>203</sup>

Contrary to legal and ethical directives to make the choice an incapable person would make if he or she were capable of choosing (an approach known as “substituted judgment”), actual surrogates are equally or more focused on protecting the patient’s current well-being (an approach known as “best interest”). For example, one team asked surrogates for AD patients how they would decide whether to enroll the patients in clinical trials.<sup>204</sup> The majority of surrogates said their decisions would reflect both what the patient would choose if capable and what would be in the patient’s best interests.<sup>205</sup> A majority said their primary consideration would be the patient’s best interests.<sup>206</sup>

In interviews, some surrogates also distinguished the patient’s former self from the present patient, voicing greatest allegiance to the present patient. For example, one said:

The situation is that there was a person there that kind of went away and can’t judge for themselves anymore[,] so you could either judge from their past self, before they had

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201. See, e.g., Betty S. Black et al., *Decision Making for Participation in Dementia Research*, 21 AM. J. GERIATRIC PSYCHIATRY 355, 359 (2013) (reporting that eighty percent of surrogates interviewed cited this reason and fifty-three percent cited altruistic reasons).

202. Jason Karlawish et al., *The Views of Alzheimer Disease Patients and Their Study Partners on Proxy Consent for Clinical Trial Enrollment*, 16 AM. J. GERIATRIC PSYCHIATRY 240, 244 (2008).

203. Laura B. Dunn et al., *“Thinking About It for Somebody Else”: Alzheimer’s Disease Research and Proxy Decision Makers’ Translation of Ethical Principles into Practice*, 21 AM. J. GERIATRIC PSYCHIATRY 337, 343 (2013).

204. *Id.* at 338–39.

205. *Id.* at 340–41.

206. *Id.* at 341. A different research team found similar results. This team examined decision making by the “study partners” (the surrogates) of research participants with mild to moderate AD. Karlawish et al., *supra* note 202, at 240. Fifty-nine percent of the study partners said that research decisions should maximize the patient’s well-being. *Id.* at 245. Just twenty-four percent said that decisions should be based on what the patient would want if he or she were competent. *Id.* The remaining seventeen percent saw no difference in the two approaches because they assumed that AD patients would want what was best for them now. *Id.* In a third inquiry, researchers found that forty-two percent of surrogates favored the best-interests standard and twenty percent favored a combination of the best-interests and substituted-judgment standards. Black et al., *supra* note 201, at 360. Just nine percent favored the substituted-judgment standard. *Id.*

Alzheimer's, or you could judge from their present selves, or you could judge from their future selves. And, mostly I kind of center around their present self. And so I think that whatever is making that person happy right now is what I should be centering my decisions on . . . .<sup>207</sup>

Another surrogate said of her mother with AD: "If she wasn't already compromised[,] she might think like, 'Oh, this is, you know, I would like to help.' But she just doesn't have that tolerance anymore."<sup>208</sup> Even the surrogates who assigned priority to a patient's past preferences said their research decisions would also take into account any risks, discomfort, or distress that would affect the patient in his or her current state.<sup>209</sup>

Many surrogates say that they rely heavily on the incapable individual's current preferences, as opposed to past preferences, to guide research decision making. One team reported, "Unexpectedly, we found that honoring their relatives' *current* wishes was explicitly emphasized by many of the [surrogates] interviewed, who often distinguished these from premorbid preferences."<sup>210</sup> Moreover, a collaborative process of choosing often occurs even when the patient's abilities are impaired. For example, a group of investigators examining research decision making for people with AD found that incapable patients were just as likely to be involved in research decisions as were patients who retained decision-making capacity.<sup>211</sup>

Like parents making research decisions concerning their children, surrogates labor under a heavy burden of responsibility. They appear most concerned about the patient's current well-being and look to the patients themselves to determine how to proceed. Perhaps because surrogates and prospective subjects were once equals, they seem to have an easier time collaborating than do parents and children facing research decisions.

This look at the experiences of healthy volunteers, patient-subjects, and decision makers for children and incapable adults reveals a side of research that rarely appears in standard research ethics and oversight analyses. And the material I present merely skims the surface. Research ethicists and policy makers have much more to learn about research subjects' perspectives. In Part II, I

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207. Dunn et al., *supra* note 203, at 342.

208. *Id.*

209. Some surrogates "explicitly described the need to weigh numerous factors concurrently—including their relative's preferences and personality before becoming ill, possible benefits to society, possible discomfort to their loved one, and current quality of life, particularly given the patient's age or stage of illness." *Id.* at 343.

210. *Id.*

211. Karlawish et al., *supra* note 202, at 245.

describe how ethicists and oversight officials can begin this education.

## II. INCLUDING SUBJECTS IN RESEARCH ETHICS AND OVERSIGHT

To maintain an ethical and effective subject-protection system, we must hear from the people we are trying to protect. Ethical and policy deliberations should include people who know what it is like to participate in research. Input from subjects and their surrogate decision makers could help ethicists and officials devise more defensible and effective human research protections. Individuals who have actually participated in research should be regarded as experts whose knowledge and opinions are as valuable as those of professionals and scholars involved in ethics and oversight work.

People with experience making research-participation decisions should serve as members of Institutional Review Boards (“IRBs”) that evaluate proposed human studies. Experienced subjects should be recruited to advise IRBs on specific research questions, too. Community-engagement and participatory-research approaches should enlist experienced subjects in study planning and execution as well. Experienced subjects should also be included in deliberations about specific research matters, such as the proper approach to securing informed consent to participate in research.

### A. *Inclusion in IRBs and Other Oversight Activities*

To promote “complete and adequate review of research activities,” federal regulations require IRBs to include not only researchers and clinicians, but also “outsiders”—nonscientists and people with no employment or other affiliation with the research institution.<sup>212</sup> The regulations fail to assign to particular IRB members a responsibility to represent subjects, but many nonscientist and unaffiliated members see this as one of their primary responsibilities.<sup>213</sup> For example, most of the unaffiliated members interviewed for one study said that “their responsibility was to take the perspective of potential research participants when reading protocols and consent forms.”<sup>214</sup> Another team that

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212. 45 C.F.R. § 46.107(a), (c)–(d) (2014).

213. See, e.g., Joan P. Porter, *How Unaffiliated/Nonscientist Members of Institutional Review Boards See Their Roles*, IRB: REV. HUM. SUBJECTS RES., Nov.–Dec. 1987, at 1, 4 (reporting that ninety-six percent of nonscientist and unaffiliated members surveyed indicated that their role is to advocate for human subjects); Marcia Jacobson Slaven, *First Impressions: The Experiences of a Community Member on a Research Ethics Committee*, IRB: ETHICS & HUM. RES., May–June 2007, at 17, 18 (explaining that, as an unaffiliated member, she does “try to represent, advocate for, and guard the rights of the potential study participant”).

214. Charles W. Lidz et al., *The Participation of Community Members on Medical Institutional Review Boards*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Feb. 2012, at 1, 6.



interviewed unaffiliated members found that most saw their role as “represent[ing] or giv[ing] a voice to the ‘community’ of human subjects.”<sup>215</sup>

The ethical and regulatory presumption is that all IRB members will consider how subjects could experience study participation,<sup>216</sup> and empirical evidence suggests that members do attempt to put themselves in the subjects’ position. But for the most part, their judgments rest on speculation. For example, most of the forty IRB members interviewed in one project said that they “had little knowledge of the values, expectations, . . . and needs of those whom they are charged to protect.”<sup>217</sup> Few of the nonscientist and unaffiliated IRB members interviewed for another project said they had experience as either a research subject or a patient with a serious illness.<sup>218</sup>

Sociologist Laura Stark learned firsthand about the approach IRB members take in attempting to include subjects’ perspectives. Stark observed multiple meetings of three different IRBs and found that all of the members—scientists and nonscientists alike—relied on “their own life experiences” to form judgments about how study procedures would affect potential study participants.<sup>219</sup> Members developed their views on subjects’ perspectives by envisioning how people like their students, parents, friends, and neighbors would respond to various research issues.<sup>220</sup> Instead of eliciting the views of experienced subjects, IRB members “imagined the people who featured in their own lives as stand-ins for research participants.”<sup>221</sup>

Some advisory groups have recognized the shortcomings of relying on conjecture. In 2001, an Institute of Medicine committee evaluating the U.S. human-subject protection system urged institutions to include more research participants in their review

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215. Sohini Sengupta & Bernard Lo, *The Roles and Experiences of Nonaffiliated and Non-Scientist Members of Institutional Review Boards*, 78 ACAD. MED. 212, 215 (2003).

216. See LAURA STARK, BEHIND CLOSED DOORS: IRBS AND THE MAKING OF ETHICAL RESEARCH 13 (2012) (noting that regulations “require [experts] to imagine the perspectives of people whom the law is controlling or safeguarding”).

217. Cook et al., *supra* note 142, at 60.

218. Emily E. Anderson, *A Qualitative Study of Non-Affiliated, Non-Scientist Institutional Review Board Members*, 13 ACCOUNTABILITY RES. 135, 151 (2006). There are exceptions, however. One unaffiliated member wrote that for a few unaffiliated members like herself, “the motivation to serve is more personal. We or our loved ones have been research subjects, so we bear an especially poignant responsibility. The memory of the peculiarly uneven power relationship between investigator and subject is one that still burns bright.” Patricia E. Bauer, *A Few Simple Truths About Your Community IRB Members*, IRB: ETHICS & HUM. RES., Jan.–Feb. 2001, at 7, 7.

219. STARK, *supra* note 216, at 15.

220. *Id.* at 14.

221. *Id.*

and oversight activities.<sup>222</sup> The committee recommended that IRBs involve experienced subjects or other individuals “who genuinely understand and represent the perspective of [particular subject] populations.”<sup>223</sup> The organization that accredits subject protection programs includes in its standard on IRB membership the expectation that an IRB will have “one or more members who represent the general perspective of participants.”<sup>224</sup> According to the organization’s president, “current or former research subjects” have the necessary understanding to represent participants’ perspectives.<sup>225</sup>

Institutions could promote more accurate and justifiable subject-protection programs by involving experienced subjects in other ethics oversight activities. For example, groups that monitor the safety of ongoing human studies could include experienced subjects.<sup>226</sup> Research oversight programs could establish advisory groups of individuals with different types of research experience, too. Programs with such groups could then call on advisory group members with relevant experience when specific study issues arise. And educational sessions for IRB members and oversight staff could include presentations by experienced subjects about what it is like to be in different types of studies.<sup>227</sup>

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222. COMM. ON ASSESSING THE SYS. FOR PROTECTING HUMAN RESEARCH SUBJECTS, INST. OF MED., PRESERVING PUBLIC TRUST: ACCREDITATION AND HUMAN RESEARCH PARTICIPANT PROTECTION PROGRAMS 73 & n.3 (2001).

223. *Id.* at 73; see also NAT’L BIOETHICS ADVISORY COMM’N, ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS 63 (2001), available at <https://bioethicsarchive.georgetown.edu/nbac/human/overvol1.pdf> (suggesting that IRBs include members who “reflect the views of the research participants”).

224. *AAHRPP Accreditation Standards*, ASS’N FOR ACCREDITATION HUM. RES. PROTECTION PROGRAMS 5 (Oct. 1, 2009), [https://admin.share.aahrpp.org/Website%20Documents/AAHRPP\\_Accreditation\\_Standards.PDF](https://admin.share.aahrpp.org/Website%20Documents/AAHRPP_Accreditation_Standards.PDF).

225. Marjorie A. Speers & Susan Rose, *Labeling Institutional Review Board Members Does Not Lead to Better Protections for Research Participants*, 87 ACAD. MED. 842, 844 (2012). For similar arguments, see McDonald et al., *supra* note 42, at 116, 117–18; and Govind Persad, *Democratic Deliberation and the Ethical Review of Human Subjects Research*, in HUMAN SUBJECTS RESEARCH REGULATION: PERSPECTIVES ON THE FUTURE, *supra* note 42, at 157, 158–64.

226. COMM. ON ASSESSING THE SYS. FOR PROTECTING HUMAN RESEARCH SUBJECTS, *supra* note 222, at 41–42. Others argue that the human research oversight system should actively track subjects’ experiences in trials rather than continuing to rely on complaints and anecdotes for information about potential problems in ongoing studies. McDonald et al., *supra* note 42, at 119–20.

227. See Rebecca Dresser, *Personal Knowledge and Study Participation*, 40 J. MED. ETHICS 471, 471–73 (2014) (proposing that IRB members and staff participate in studies themselves to obtain valuable insight into their work).

### B. *Inclusion in the Research Process*

IRBs and other oversight groups evaluate completed research proposals. Making the revisions these groups call for can be time consuming and disruptive for researchers. In contrast, if experienced subjects are enlisted to help with proposal development, subjects' perspectives can more easily be taken into account. Through this approach, people with the greatest impact on subjects—the research team—will be directly exposed to subjects' viewpoints. Direct exposure can help researchers see studies from the subjects' point of view, increasing the chance that they will design and conduct studies with subjects' perspectives in mind.

During the 1990s, researchers and officials began to include patients, patient advocates, community members, and other “outsiders” in study planning, implementation, and merit evaluation, as well as research priority-setting and policy activities.<sup>228</sup> This approach has different names and variations, but includes activities known as community engagement, community consultation, participatory research, patient-centered research, and deliberative democratic proceedings on research issues.<sup>229</sup>

The primary motivation for including patients and community members is to improve the quality and value of health research. Researchers and policy officials seek to make research more responsive to patients' actual needs, increase recruitment and retention of study subjects, and produce maximum health benefits from research investments.<sup>230</sup> They portray patients and other potential members of study populations as experts with knowledge that can advance these objectives.<sup>231</sup> They believe that researchers

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228. See REBECCA DRESSER, *WHEN SCIENCE OFFERS SALVATION: PATIENT ADVOCACY AND RESEARCH ETHICS* 23–28 (2001).

229. For description and discussion of these models, see Adam Braddock, *Children as Research Partners in Community Pediatrics*, in *HUMAN SUBJECTS RESEARCH REGULATION: PERSPECTIVES ON THE FUTURE*, *supra* note 42, at 79; DRESSER, *supra* note 228, at 21–43; Raymond De Vries et al., *Assessing the Quality of Democratic Deliberation: A Case Study of Public Deliberation on the Ethics of Surrogate Consent for Research*, 70 *SOC. SCI. & MED.* 1896 (2010); Juan Pablo Domecq et al., *Patient Engagement in Research: A Systematic Review*, *BMC HEALTH SERVICES RES.*, Feb. 2014, at 1; Loretta Jones & Kenneth Wells, *Strategies for Academic and Clinician Engagement in Community-Participatory Partnered Research*, 297 *JAMA* 407 (2007); and Joseph V. Selby & Steven H. Lipstein, *PCORI at 3 Years—Progress, Lessons, and Plans*, 370 *NEW ENG. J. MED.* 592 (2014).

230. Domecq et al., *supra* note 229, at 1 (pointing to the increasing consensus that patient involvement in research activities can improve the value of health research, improve research quality by increasing enrollment and retention, and produce results more applicable to patients).

231. See DRESSER, *supra* note 228, at 28–29, 32–33; see also Lori Frank et al., *The PCORI Perspective on Patient-Centered Outcomes Research*, 312 *JAMA* 1513, 1513 (2014) (“[P]atients have unique perspectives that can change and improve the pursuit of clinical [research] questions.”).

and policy makers can learn from these experts, just as they learn from traditional research experts.

Supporters of patient and community engagement say the practice can advance ethical and regulatory objectives, too. For example, a National Institutes of Health statement describes how engagement can promote ethical research: “Engagement creates opportunities to improve the consent process, identify ethical pitfalls, and create processes for resolving ethical problems when they arise.”<sup>232</sup> Others see an “overarching ethical mandate for patient participation in research as a manifestation of the ‘democratization’ of the research process.”<sup>233</sup>

What is missing from the literature on patient-centered research, community engagement, and similar models is explicit recognition of the singular contributions that experienced research participants can make. Experienced subjects know how the research process works, including problems that can arise in that process. They know about practices that promote subject well-being and practices that make participation harder than it needs to be. And they are well-equipped to make specific suggestions on how to improve studies for participants.

As the material I have presented demonstrates, researchers who talk with subjects about the research experience will learn how to reduce study risks and burdens. Researchers aware of subject perspectives will minimize study visits, tests, procedures, and time demands imposed on participants.<sup>234</sup> They will also consider subjects’ preferences about scheduling and other logistical matters.<sup>235</sup> They will measure outcomes that are important to

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232. NAT’L INSTS. OF HEALTH, PRINCIPLES OF COMMUNITY ENGAGEMENT 9 (2d ed. 2011), available at [http://www.atsdr.cdc.gov/communityengagement/pdf/PCE\\_Report\\_508\\_FINAL.pdf](http://www.atsdr.cdc.gov/communityengagement/pdf/PCE_Report_508_FINAL.pdf); see also Shawn M. Kneipp et al., *Women’s Experiences in a Community-Based Participatory Research Randomized Controlled Trial*, 23 QUALITATIVE HEALTH RES. 847, 856 (2013) (finding that the community-based participatory approach “facilitated the sensitive and respectful treatment and positive experiences women had in the [randomized controlled trial]”).

233. Domecq et al., *supra* note 229, at 89; see also DRESSER, *supra* note 228, at 29–32 (providing multiple examples of the ethical benefits resulting from increased patient engagement in research study planning).

234. See generally Brintnall-Karabelas et al., *supra* note 110 (reporting that potential research subjects would be more willing to participate in clinical trials if researchers adopted practices that saved subjects time and increased convenience); Caldwell et al., *supra* note 176, at 559 (suggesting that adopting practices that minimize the number of required hospital visits and procedures might lead to an increase in participation in pediatric trial participation).

235. See Patricia A. Marshall et al., *Negotiating Decisions During Informed Consent for Pediatric Phase I Oncology Trials*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Apr. 2012, at 51, 53 (describing negotiations on such matters between researchers and parents of children in cancer trials); see also Dunn et al., *supra* note 203, at 344 (“As a society wishing to advance research, we should recognize the immense responsibility that proxy decision makers must shoulder, not only

patients, such as pain and distress, in addition to traditional laboratory and clinical outcomes.<sup>236</sup> They will recruit skilled and attentive staff members who treat subjects with respect.<sup>237</sup> And they will adopt study methods that minimize the number of patient-subjects exposed to risky and ineffective interventions.<sup>238</sup>

Patients and members of the general community lacking actual research experience can provide useful input on research improvements, but their views and attitudes are likely to differ from those of experienced study subjects. Researchers and policy officials involved in the effort to incorporate patient and community perspectives should recognize the special status of people with real research experience and act to ensure that experienced participants are part of the effort.

### C. *Inclusion in Developing Ethical Guidelines and Regulations*

The voices of experienced subjects belong in deliberations over specific research ethics and policy questions, too. For example, experienced subjects should be involved in efforts to promote informed decisions about study participation. Individuals who have actually made study decisions know what was helpful and what was confusing when researchers talked with them about participation. They also know how the process could be improved. People who have faced research choices say they would have appreciated an opportunity to talk with subjects enrolled in the studies they were considering.<sup>239</sup> Children have recommended this, too: three-quarters of a group of children enrolled in cancer trials said they

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ethically but also physically, emotionally, and logistically. Services to help make research participation more convenient and rewarding, for example, respite care, transportation, education, and other services . . . , should be incorporated into research protocols.”)

236. See Mullins et al., *supra* note 141, at 472 (arguing that the use of outcome measures that are more relevant to participants versus measuring only laboratory values or clinical indicators increases the likelihood that the study results will be useful to the affected population); see also Korn, *supra* note 17 (describing a researcher’s decision to monitor pain in a cancer trial as a result of seeking input from prospective trial participants).

237. See Korn, *supra* note 17 (describing a clinical trial participant’s decision to withdraw from the trial because the staff failed to treat her with compassion).

238. See Mullins et al., *supra* note 141, at 472–73 (describing such methods).

239. Eder et al., *supra* note 15, at e855 (finding that parents of children in cancer trials sought support by speaking with parents of children who had experienced the decision-making process); Sandra Crouse Quinn et al., *Improving Informed Consent with Minority Participants: Results from Researcher and Community Surveys*, J. EMPIRICAL RES. ON HUM. RES. ETHICS, Dec. 2012, at 44, 49 (finding in a community survey that “talking to a study participant” was one of the top four preferred ways to learn about studies).

would have liked to speak to other child-subjects “to help them understand what it means to be part of a study.”<sup>240</sup>

Experienced subjects reveal a neglected aspect of research decision making, too. Empirical data show that many patients making decisions about research need emotional support, as well as clear and accessible information, during this time. In interviews, adult patients in trials said that including family members and nurses in study discussions was a “highly important” source of support.<sup>241</sup> Another group found that parental understanding of randomization was strongly associated with the presence of a nurse in the study discussion.<sup>242</sup> This group’s finding points to “the benefits of better emotional support for parents at this difficult time, creating an environment in which parents feel empowered to speak up, ask questions, and seek clarifications.”<sup>243</sup> Experienced study participants could advise researchers on ways to support people confronting research choices in the midst of serious illness.

Some experienced subjects share what they have learned about trials on websites and publications aimed at people considering research participation.<sup>244</sup> These information sources vary in quality but often contain useful information left out of conventional consent discussions. Bringing experienced subjects into the research mainstream would allow researchers, ethicists, and officials to discover what subjects themselves think people should know before enrolling in research.

Research ethicists and policy makers should also solicit experienced subjects’ views on broader issues addressing research consent. We ought to know what experienced subjects think about questions like the following: Are existing research practices defensible in light of the substantial empirical evidence that many people join studies without a good understanding of important study facts? If not, what should be done to address the situation? Should researchers be required to assess and verify prospective subjects’

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240. Unguru et al., *supra* note 193.

241. Behrendt et al., *supra* note 20, at 78.

242. Kodish et al., *supra* note 182, at 473.

243. *Id.* at 474.

244. See, e.g., *Get Paid to Volunteer for Medical, Clinical, Drug Trials and Various Other Research Studies, Throughout the UK, US, Canada and Europe*, GPGP.NET, <http://www.gpgp.net> (last visited Mar. 10, 2015) (encouraging website visitors to help themselves “financially by volunteering to be a subject in medical trials, paid clinical trials[,] and various other research studies!”); *Statement of Purpose*, GUINEA PIG ZERO, <http://www.guineapigzero.com> (last updated Aug. 22, 2014) (describing itself as “an occupational jobzine for people who are used as medical or pharmaceutical research subjects”); *Welcome!*, JUST ANOTHER LAB RAT!, <http://www.jalr.org> (last visited Mar. 10, 2015) (advertising itself as “your one stop guide for learning how to volunteer for a clinical research study and the best resource for veteran volunteers”); see also Schaffer et al., *supra* note 182 (discussing websites created by parents whose children have undergone pediatric treatments).

understanding before enrollment?<sup>245</sup> Should researchers be required to exclude prospective subjects who cannot demonstrate an adequate understanding of the facts, even though doing so would make it harder to fill enrollment quotas?

Consent in comparative-effectiveness research is another policy question in need of subject input. Comparative-effectiveness research evaluates approved therapies to determine whether one therapy is superior to the others.<sup>246</sup> Some ethicists and researchers argue that the usual informed consent requirements should not apply to this form of research because all of the tested interventions are used in clinical practice. Since patients could receive any of the interventions in ordinary medical care, they say, the regulatory requirements for informed consent in research should be weakened or waived for comparative-effectiveness research.<sup>247</sup> Some also argue that patients have a duty to participate in research that could improve health care; thus, the usual consent requirements should be relaxed.<sup>248</sup> Other ethicists and researchers contend that randomization and other aspects of comparative-effectiveness research justify applying the usual consent requirements to such trials.<sup>249</sup>

Largely missing from this debate are the perspectives of study subjects.<sup>250</sup> We ought to find out what patients think people should know before they are enrolled in comparative-effectiveness research. We ought to find out whether people who have participated in this form of research think it would be acceptable to bypass or abbreviate the usual consent requirements. Scholars and officials cannot defensibly resolve these questions without considering the views of

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245. For proposals to this effect, see Rebecca Dresser, *Aligning Regulations and Ethics in Human Research*, 337 *SCIENCE* 527, 527 (2012); and David Wendler, *Can We Ensure that All Research Subjects Give Valid Consent?*, 164 *ARCHIVES INTERNAL MED.* 2201, 2201 (2004). In interviews, parents of children in cancer trials wanted the decision-making process to include more breaks to check on parents' understanding and allow them to ask questions. Eder et al., *supra* note 15, at e858.

246. *Comparative Effectiveness Research*, NAT'L PHARMACEUTICAL COUNCIL, <http://www.npcnow.org/issues/comparative-effectiveness-research> (last visited Mar. 10, 2015).

247. See, e.g., Ruth R. Faden et al., *Informed Consent, Comparative Effectiveness, and Learning Health Care*, 370 *NEW ENG. J. MED.* 766, 768 (2014).

248. See, e.g., *id.* at 766.

249. See, e.g., Jerry Menikoff, *The Unbelievable Rightness of Being in Clinical Trials*, *HASTINGS CENTER REP.*, Jan.–Feb. 2013, at S30, S30–31.

250. See Jeremy Sugarman & Robert M. Califf, *Ethics and Regulatory Complexities for Pragmatic Clinical Trials*, 311 *JAMA* 2381, 2381 (2014) (finding that “there is little information regarding patients’ attitudes” toward proposals to replace traditional consent with “largely untried approaches,” such as opt-out or notification procedures).

the people who would be most affected by a change in consent requirements.<sup>251</sup>

Experienced subjects should be asked to weigh in on the issue of consent in comparative-effectiveness research and other contested research issues. Deliberations on topics like subject compensation, researcher compensation, return of research results, and appropriate standards for surrogate decision making should include the voices of people who have participated in research. Discussions of subjects' responsibilities in research and acceptable limits on research risks should incorporate subjects' views as well.<sup>252</sup> Without subjects' input, ethical guidelines and regulatory requirements addressing these and other research matters will lack normative legitimacy.

### CONCLUSION

Conventional approaches to medical ethics and research ethics have similar deficits. Research policies and ethics principles are removed from the realities of research participation. Professional narcissism and myopia have led traditional experts, including ethicists, to focus on abstract concepts, overlooking the day-to-day interactions of subjects and researchers. Neither subjects' knowledge nor their ethical judgments have a place in this approach.

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251. See Emily E. Anderson & Stephanie Solomon, *Community Engagement: Critical to Continued Public Trust in Research*, AM. J. BIOETHICS, Dec. 2013, at 44, 45 (arguing that the consent process should be developed through a community-engagement process to determine what the reasonable participant would want to know about the study); Rebecca Dresser, Correspondence, *Is Informed Consent Always Necessary for Randomized, Controlled Trials?*, 341 NEW ENG. J. MED. 448, 449 (1999) (arguing that the determination of when full consent is required should be made by a group representing prospective subjects, not by an institutional review board composed primarily of professionals).

252. See Sarah J. L. Edwards, *Assessing the Remedy: The Case for Contracts in Clinical Trials*, AM. J. BIOETHICS, Apr. 2011, at 3, 6–8 (proposing that agreements to serve as subjects in research trials be governed by the law of contracts, thus providing research subjects the contract law protections available for “misrepresentation, duress, undue influence, minority, mental noncapacity, and known intoxication or insanity,” and suggesting that the consideration requirement of contract law would in some ways “set a higher standard than noncontractual consent” for ensuring that subjects receive something of value by participating in a study); David B. Resnik & Elizabeth Ness, *Participants' Responsibilities in Clinical Research*, 38 J. MED. ETHICS 746, 749 (2012) (discussing patients' responsibilities during clinical research and suggesting increased research into patients' reasons for noncompliance so that investigators can better understand and address noncompliance issues). *But see* F. G. Miller & S. Joffe, *Limits to Research Risks*, 35 J. MED. ETHICS 445, 448–49 (2009) (proposing policies on subject responsibilities and risk limits without considering subjects' perspectives on these matters).



Research experts like to speak of research subjects as partners in an enterprise that will enable people to live longer and improve lives in the future. But talk of this partnership is more promotional than descriptive. Subjects have relatively little power in the research world.<sup>253</sup> And so far, experts have shown little interest in developing a true partnership with subjects.

Engaging communities and developing patient-centered models of human research are moves in the right direction. But research ethicists and policy officials should adopt a more inclusive approach, too. It is time for everyone to learn what subjects can teach about the ethics of human research.

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253. Research ethics and regulation expert Alexander Capron writes, “I regard it as wishful thinking to suppose that most of the people on whom research is conducted today in the United States are on a par with—that is, are co-equal participants with—the research team and sponsors.” Alexander Morgan Capron, *Subjects, Participants, and Partners: What Are the Implications for Research as the Role of Informed Consent Evolves?*, in HUMAN SUBJECTS RESEARCH REGULATION: PERSPECTIVES ON THE FUTURE, *supra* note 42, at 143, 150.