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Medical Research without Consent?
It’s Like Deja Vu All Over Again*

LOIS SHEPHERD & DONNA CHEN

When patients seek medical care, they trust their physician to offer treatments that are in their best medical interests and to engage them in a shared decision-making process to determine the best way forward. But today, in hospitals and doctors’ offices around the country, physicians also place patients in research studies that randomly assign them to a standard of care treatment, sometimes without the patients’ knowledge or consent. In such studies, patients may receive a treatment that results in worse outcomes for them, some of which can be serious and permanent. What’s more, there are reasons to be concerned that the burdens of this practice may fall more heavily on people of color and those who have less financial means, are less educated, or experience language barriers. Their social disadvantage or vulnerability may be further deepened by their illness.

As these studies are taking place, physician-researchers and ethics scholars have been increasingly advancing arguments in the ethics literature for bypassing consent practices that have been in place for over half a century. Though these arguments are weak and some illogical, government agencies have been funding research without consent and government oversight bodies have stood by doing little.

Advocates for bypassing consent have met some opposition, but thus far debate on this issue has taken place almost exclusively within the research and research-ethics community and has focused almost entirely on ethical and regulatory requirements. The common law has been forgotten.

Yet physicians and other clinicians violate patients’ legal rights to bodily integrity and autonomy—in addition to breaching fiduciary duties of loyalty, discretion, and care—when they place their patients in these types of studies without their knowledge or consent. This Article examines common law duties to inform patients and obtain their consent prior to placing them in research studies that randomize them to medical treatments, even ones that are accepted as standard of care. Courts have yet to specifically address the scope of duties owed, although lawsuits stemming from involvement in such studies have recently been initiated and more should be anticipated in the future. Past cases reveal that patients randomized to medical treatments without their knowledge or consent could successfully sue for battery.

* Scott Stump, ‘It’s deja vu all over again’: 27 of Yogi Berra’s most memorable ‘Yogiisms,’ Today (Sept. 23, 2015). The authors gratefully acknowledge the dedicated research assistance provided by Benjamin Hawkins, Katie Kramer, and Aamina Mariam (while law students at the University of Virginia), as well as Jordan Taylor (as an intern at the Center for Health Humanities and Ethics at the University of Virginia’s School of Medicine). We are also indebted to Jon Merz, Nancy King, Brad Worrall, and Paul Shepherd for helping us think through the issues addressed in this Article and/or for reviewing prior manuscript drafts. This work has been supported in part by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR003015. This content is solely the responsibility of the authors and does not necessarily represent the official views of NIH.
lack of informed consent, and breach of fiduciary duty, among other claims. Understanding the common law duties associated with such claims does more than illuminate potential legal exposure for physicians and others conducting such research. Appreciating the ethical grounding of those legal duties also points the ethical way forward—for researchers to design consent processes that respect patients’ rights to know when decisions about their care will be affected by their placement in a research study and for oversight bodies to interpret existing research regulations as they traditionally have done—to honor a patient’s right to consent and its corollary—the right to refuse.
I. INTRODUCTION

Major research scandals might seem to be a thing of the past. The United States Public Health Service (USPHS) Syphilis Experiment at Tuskegee1 and the Human

1. The “Tuskegee Study of Untreated Syphilis in the Negro Male,” conducted by the United States Public Health Service from 1932–1972, was a study of the natural progression
Radiation Experiments, two of the most egregious large-scale medical research abuses in the United States, ended over fifty years ago. Occasionally the public learns about high-profile bad actors or that research results have been tainted by financial conflicts of interest.

But there is a troubling and growing research practice taking place in hospitals and doctors’ offices around the country that has largely escaped the attention of the public and legal community: physicians placing their patients in research studies without their knowledge or consent, and doing so with the blessing of the ethics committees (known as Institutional Review Boards (IRBs) in the United States) charged under federal research regulations with looking out for the rights and welfare of human research subjects.

These kinds of studies fall within “comparative effectiveness research” (CER). Comparative effectiveness studies (“CER studies”) compare two or more “accepted...
medical practices,” “usual care interventions,” or “standard of care treatments” (terms used somewhat interchangeably) to help determine if one is substantially better, or worse, than the other.

In the comparative effectiveness studies this Article is concerned with, the patients—and there can be thousands of them—are provided a standard of care treatment chosen by a random process in a research study they have been placed in without their knowledge or consent. When this happens, patients’ normal expectations about how their medical care is determined continues undisturbed; that is, they think that the treatment they are receiving or being offered is the treatment their physician thinks is best for them based on their professional judgment in light of known evidence.

Conducting comparative effectiveness studies in this manner violates longstanding ethical and legal requirements to obtain informed consent both for clinical care and for research. Informed consent for clinical care generally requires physicians to inform a patient—or, in the event of the patient’s incapacity, their health care agent—about the nature and purpose of recommended interventions, including information about the risks and potential benefits of all reasonable alternatives, including forgoing treatment. Consent for research requires these disclosures and more—including a clear statement that the patient is being asked to consider participating in research, that research participation is voluntary, and that the patient has a right to withdraw without penalty at any time.

Many in the research community argue that achieving the aims of comparative effectiveness research requires reducing the burdens of research informed consent and that conducting CER studies without informed consent does not compromise patients’ care or their rights. An essential part of their argument is that when a research study is comparing the risks and benefits of two or more commonly accepted medical interventions, the only activities that should qualify as “research” are the randomization process and collection of data. Doctors, in the normal course

different interventions to determine best clinical practice, since unfortunately this information is frequently not available, and this type of research is often “conducted in settings that are similar to those in which the intervention will be used in practice.” Id. at 37–39. But there are a number of terms and slightly different definitions that are used in this sphere and change over time. Throughout this article, all of the following terms are used to refer to a randomized trial of standard of care treatments or interventions: CER studies; CER trials; comparative effectiveness research, standard of care trials, and pragmatic clinical trials.

7.  See infra text accompanying notes 207–17.
8.  45 C.F.R. § 46.116(b) (2023).
9.  For further discussion of this viewpoint, see infra Section II.B.
10.  See generally Scott Y.H. Kim, Comparative Effectiveness Research, Learning Health Systems, and Pragmatic Randomized Controlled Trials: The Need for Both Clinical and Research Ethics, in THE OXFORD HANDBOOK OF RESEARCH ETHICS 5 (Ana S. Iltis & Douglas MacKay eds., 2020) (identifying proponents of this argument, with an in-depth analysis of two sets of authors: Monique L. Anderson et al., The Food and Drug Administration and Pragmatic Clinical Trials of Marketed Medical Products, 12 CLINICAL TRIALS 511 (2015), and John D. Lantos et al., Considerations in the Evaluation and Determination of Minimal Risk in Pragmatic Clinical Trials, 12 CLINICAL TRIALS 485 (2015)). For an example of a study relying on this approach, see Anup Katheria et al., Association of Umbilical Cord Milking vs Delayed Umbilical Cord Clamping with Death or Severe Intraventricular Hemorrhage
of medical care, could provide either of the treatments the patients will be assigned to receive in the research study and no one would ever cry foul. Because patients receive a treatment that is within the standard of care, the argument goes, the fact that their treatment was chosen by a random process imposes no additional risks than are present in clinical care. As long as patients have provided the necessary (if often general) clinical consent for treatment, physicians have violated no ethical or professional duties to them. In addition—proponents of this view claim—such studies often meet qualifications for a waiver of consent under either set of federal regulations governing medical research that are likely to apply—the “Common Rule,” which applies to studies funded or otherwise sponsored by federal agencies, or the FDA regulations that apply to investigations of drugs or devices to be marketed in the United States regardless of funding sources. Both the Common Rule and the FDA regulations contain an explicit provision allowing a waiver of the requirement of consent for certain “minimal risk” studies. What is wrong with the argument that consent should not be required for studies that simply randomize patients to accepted medical practices? First, the claim that randomizing patients between two standard of care treatments for research purposes does not entail research risks is not true. When a patient is randomized to a medical treatment that differs from the treatment they would have received as part of regular care, the risks the patient is exposed to have changed. For example, when a study randomly assigns patients to one of two treatments in clinical practice are provided to patients at roughly equal rates, the process of 1:1 randomization results in approximately half of the patients receiving the same treatment they would have received as part of their regular clinical care and the other half a treatment different from what they would have received. This is what the law of statistics predicts and what is anticipated when the randomization process works as it should. When it turns out that one treatment is substantially worse than the other—less effective, more harmful, or has more side effects—approximately half of the patients assigned to this treatment (25% of the study participants) have been exposed to more potential harms than they would have been otherwise. Of course, some patients (again, 25%) stand to benefit if they are randomly assigned to the better treatment when their physician normally would have provided the other. The remaining half of patients (50%) are no better or worse off since they received the same course of treatment they would have in clinical care. While across the group of study participants there may be no overall increase in risks of harm, any particular individual may face an increased risk of harm. This problem is exacerbated when the potential harms at stake are

Among Preterm Infants, 322 JAMA 1877 (2019) (describing a neonatal study in which consent was waived at some sites for randomization to standard of care treatments; post-intervention consent was sought for collection of data).

11. See generally Kim, supra note 10.

12. For the general informed consent waiver provision for federally sponsored research, see 45 C.F.R. § 46.116(f) (2023). For further discussion of regulatory waiver of informed consent, see infra text accompanying notes 74–79.

13. For research that is subject to the FDA regulations, see Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations 88 Fed. Reg. 88228 (Dec. 21, 2023) (codified at 21 C.F.R. pts. 50, 312, 812) [hereinafter FDA Consent Waiver Rule].
serious and it turns out that one study arm experiences much greater harms than the other.

A second problem with standard of care trials undertaken without patient consent is that physicians participating in them breach the trust patients have placed in them. In normal clinical care, physicians do not choose their patients’ treatments by flipping a coin or another intentionally random process. Nor would a reasonable patient expect their physician to do so, at least not without discussing it with them and gaining their approval to do so (which would be highly unusual). In normal clinical care, physicians also do not make treatment decisions for their patients with a primary intent to benefit others, like the patients in the future who may benefit from the knowledge to be gained from clinical research. Instead, patients trust physicians—and physicians are ethically and legally obligated—to use their professional judgement to determine treatment options that are in their best medical interests and to be honest and open about the options available and the uncertainties involved in determining a way forward. Patients expect physicians to include them in a shared decision-making process in which they can ask questions and consent to or decline an intervention for reasons that may be idiosyncratic but important to them. This trust is encouraged by the medical profession and supported by the law.\(^\text{14}\)

Finally, in the United States, people have long been held to have a right to determine what is done with their bodies.\(^\text{15}\) They are not required to put their bodies in service to research, no matter how important the research may be.\(^\text{16}\) Under the common law, the right to bodily integrity is “sacred”—in fact, “[n]o right is held more sacred,” according to the Supreme Court.\(^\text{17}\) Any assumption that patients would

14. See infra notes 278–315 and accompanying text.

15. See, e.g., Mohr v. Williams, 104 N.W. 12, 16 (Minn. 1905) (describing plaintiff’s unconsented surgery as a “violent assault,” and stating that “every person has a right to complete immunity of his person from physical interference of others.”). The most famous expression of this right is found in Schloendorff v. Society of New York Hospital. 105 N.E. 92, 93 (N.Y. 1914) (“Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault, for which he is liable in damages.”). But see Paul A. Lombardo, Phantom Tumors and Hysterical Women: Revising Our View of the Schloendorff Case, 33 J.L. MED. & ETHICS 791 (2005) (criticizing legal scholars’ reliance on the case as foundational for informed consent; though it did reflect the law of medical battery at the time, plaintiff’s claim against the hospital was rejected under charitable immunity).

16. See, e.g., In re Cincinnati Radiation Litig., 874 F. Supp. 796, 815 (S.D. Ohio 1995) (denying defendants’ motion to dismiss violations of constitutional rights alleged by plaintiffs who were unknowing subjects of government-sponsored human radiation experiments between 1960 and 1972; “[r]espect for an individual's right to bodily integrity is central to American constitutional history and tradition.”). But see Dobbs v. Jackson Women’s Health Org., 597 U.S. 215, 294–98 (2022) (citing Planned Parenthood of Southeastern Pennsylvania v. Casey, 505 U.S. 833, 852 (1992)) (asserting that the right to an abortion is not “deeply rooted in [the United States'] history and tradition,” though also noting that the decision to overturn Roe v. Wade does not relate to a “broader right to autonomy.”).

17. Union Pac. Ry. Co. v. Botsford, 141 U.S. 250, 251 (1891) (“No right is held more sacred, or is more carefully guarded, by the common law, than the right of every individual to the possession and control of his own person, free from all restraint or interference of others, unless by clear and unquestionable authority of law.”); see also Cruzan
not or should not care whether their medical treatments were secretly determined by a random process is antithetical to the right to bodily integrity, which has common law roots going back as far as 350 years.18

What do CER studies without consent look like? In one such IRB-approved study for which consent was waived, 146 patients with moderate to severe agitation determined by paramedics to require sedation for safe transportation by ambulance were given one of two sedating drugs (ketamine or haloperidol) depending not on what paramedics thought was most appropriate, but on the month they were transported to the hospital.19 In order to ensure the study medication was given, county ambulances were stocked only with the drugs to be administered according to the study at that particular point in time.20 The known risks of the two drugs being compared differed from one another and included risks for arrhythmia and respiratory distress severe enough to require intubation. Patients administered one of the studied drugs experienced much higher rates of complications than patients receiving the other drug. Some of these complications were severe enough to require intubation (39% of patients in one group vs. 4% in the other).21 When a similar, ongoing study of sedation for prehospital agitation came to light (this one comparing ketamine to midazolam, another sedative), it was halted amid community outrage; two elected officials called the study “unconscionable and unethical,” and pointed out that the urban safety-net hospital conducting the study “treats a large number of people of color and low-income Minnesotans.”22

ex rel. Cruzan v. Dir., Mo. Dep’t of Health, 497 U.S. 261, 269, 279 (1990) (quoting Botsford with approval and holding that prior cases supported a constitutionally protected liberty interest in refusing medical treatment under the Due Process Clause).

18. See Lombardo, supra note 15, at 799 (explaining that “surgery without consent is actionable” was a “maxim” that at the time of the famous Schloendorff decision in 1914 “could . . . be traced back through two hundred and fifty years in American law”).

19. See Jon B. Cole et al., A Prospective Study of Ketamine Versus Haloperidol for Severe Prehospital Agitation, 54 Clinical Toxicology 556, 557 (2016) (describing study design and results). Notably, in this publication, the study is described as a “prospective observational study” without use of randomization. While we agree that the study did not include randomization of individuals, it was clearly interventional rather than observational since the decision to provide which of the two study interventions according to the month the patient was transported was made for purposes of collecting research data. The study is more appropriately described as a cluster randomized trial. See text accompanying notes 104-106 for further explanation of such trials.

20. Id. For “patient and caregiver safety,” ketamine was included in all ambulances at all times for use in the most profoundly agitated patients, who were excluded from the study. Id.

21. Id. at 556.

In another CER study conducted under an IRB-approved waiver of consent, investigators randomized 540 premature infants to determine how umbilical cord milking compared to delayed cord clamping as a method of transferring a baby’s blood from the placenta during the first few minutes after birth, a process known as “placental transfusion.” (Almost 50% of a premature infant’s blood is circulating in the placenta at birth). The study was abruptly halted before completion due to safety concerns for the youngest of the babies in the cord milking arm of the study. These infants were experiencing a much higher rate of severe intraventricular hemorrhage, bleeding in the ventricles of the brain that can lead to brain injury (22% in one group vs. 6% in the other).

In both the prehospital agitation and placental transfusion studies, researchers and IRBs justified not informing patients before placing them in the study with the same arguments previewed above. That is, the requirement for consent could be waived under the applicable federal regulations because the treatments being studied were within the “standard of care” (meaning that the research should be considered to involve no more than minimal risk), and specific consent for these decisions is not normally obtained in clinical scenarios (meaning no patient rights are violated). In the placental transfusion study, after the results showed a clear difference in harmful outcomes, the investigators acknowledged that parental permission should be obtained in future studies. But they, and many arguing that consent should not be required for these types of studies, continue to misunderstand that the research risks existed before they studied them and that consent is required when the potential for a difference in serious outcomes between two arms of a study is “reasonably foreseeable”—which it is when the study is designed to identify and quantify these differences (as it was in both of these studies).

23. Katheria et al., supra note 10. The investigators had planned to enroll 1500 infants. Id. at 1879. IRBs approved a waiver of consent at six of the nine participating sites on the basis that the study involved only minimal risk. At these sites, “[w]hen prenatal consent could not be obtained (i.e., imminent delivery), the parents were approached after delivery for consent.” Id. at 1882. The “consent” sought after the intervention could not, of course, have been for the intervention itself. The post-intervention consent referred to here was for the continued collection and use of data relating to the intervention. Some refer to pre-intervention consent as “prospective consent” and post-intervention consent for collection and/or use of data as “retrospective” or “deferred consent.” It is important to underscore that when “retrospective” or “deferred” consent is sought, the intervention has already taken place without consent.

24. Id. at 1880.

25. See id. at 1881–82, 1885; Cole et al., supra note 19, at 557.

26. Katheria et al., supra note 10, at 1888. (“Given the statistically significant risk identified in infants born at 23 to 27 weeks’ gestation in this study, the use of deferred consent for future studies would no longer be appropriate.”).

27. For the standard for disclosure of risks in the federal research regulations, see 45 C.F.R. § 116(b) (2023), and for clinical informed consent under the common law, see Holt v. Nelson, 523 P.2d 211, 216 (Wash. Ct. App. 1974) (explaining that in a case of physician negligence for lack of informed consent, the patient must show that the “defendant-doctor failed to inform the plaintiff-patient of . . . the reasonably foreseeable material risks of each alternative”).
We should be careful not to assume any bad faith on the part of researchers who have operated under waivers of consent for studies like these or the IRBs who approved them. Their actions may reflect genuine concerns that the research regulatory environment imposes burdens on researchers that do little to protect research subjects and thwart important research to improve medical practice. We think they also may be acting under the misunderstanding described above about how to identify and describe research risks in CER studies. Moreover, these studies often take place at multiple locations where patient-subjects receive their medical care. The investigators who design the CER protocols and oversee the research may not ever interact with the patient-subjects; instead, the research interventions, including the chosen treatment protocols, are frequently carried out by a variety of other clinicians. Similarly, the data are gathered from the information clinicians enter into patients’ medical records rather than from investigators’ direct interactions with patients. In dispersed research environments like this, where many of those involved travel in discrete professional lanes, it can be difficult to see the whole landscape and to appreciate what is happening from the perspective of a patient.28

The question of whether consent should be required for studies of this kind is not a new one. But the recent proliferation of randomized comparative effectiveness studies has brought renewed attention to the issue. Intense debate about consent requirements is taking place within bioethics, medical, and research communities, but it is focused almost exclusively on ethical and regulatory requirements. What has been missing in this conversation is consideration of the legal duties owed to patients which have been developed through the common law.

This Article provides the first comprehensive common law analysis of the conduct of comparative effectiveness trials without consent. It asks: What common law duties do physician-researchers have to obtain informed consent from patients before randomly assigning them to one of two or more commonly accepted treatments as part of a research study? And what liability might they face when they breach those duties?

The legal academy has likely overlooked this question simply because they are unaware of the recent and growing number of studies without consent of this kind.29 The research community has overlooked the common law for different reasons: many may mistakenly believe the federal research regulations provide the whole of legal guidance on these questions, unaware that the regulations do not preempt the common law30 or that following the regulations does not shield those involved in

30. See, e.g., Grimes v. Kennedy Krieger Inst., 782 A.2d 807, 820 (Md. App. Ct. 2001) (considering claims of research injury and lack of research informed consent in which the court noted that no federal law imposed any limitation on the court’s power to determine the duties that may be owed to research participants). The court further explained that “[w]hen
research from liability. In addition, the caselaw on the duties of researchers to research participants is quite limited. To date, little direct legal precedent delineates the elements of a claim for lack of informed consent in research participation, perhaps making it difficult to incorporate a healthy respect for common law principles when considering modern research designs and associated consent processes.

The limited collection of cases regarding research injury or wrongdoing does not mean, however, that there is uncertainty about the legal duties that physicians owe to patients when they provide clinical care—those duties are well established. These duties include applying their professional expertise to advance patients’ best medical interests and obtaining informed consent for the care provided. In comparative

contested cases arise, the assessment of the legal effect of research on human subjects must always be subject to judicial evaluation. One method of making such evaluations is the initiation of appropriate actions bringing such matters to the attention of the courts, as has been done in the cases at bar.” Id. at 817. See also Kennedy Krieger Inst. v. Partlow, 191 A.3d 425, 449–50, 458 (Md. App. Ct. 2018) (finding that defendant medical research institute owed a duty of care in a lead-abatement study to the sibling of a research participant housed in the same apartment by “follow[ing] traditional tort law principles” and applying “seven classic factors utilized by courts for determining whether a duty of care exists”). The Common Rule itself provides that it “does not affect any state or local laws or regulations . . . that may otherwise be applicable and that provide additional protections for human subjects,” 45 C.F.R. § 46.101(f) (2023), and, in particular, states that “[t]he informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws…that require additional information to be disclosed in order for informed consent to be legally effective.” 45 C.F.R. § 46.116(i) (2023). The FDA regulations for the protection of human subjects include a similar provision. See 21 C.F.R. § 50.25(d) (2023); see also Mack v. Ventracor, Ltd., No. 10-CV-02142, 2011 WL 890795, at *13 (E.D. Pa. Mar. 9, 2011) (finding no preemption by either the Common Rule or FDA regulations because neither provide for a federal civil cause of action and both also clearly state that remedies for lack of informed consent have not been preempted); Kus v. Sherman Hosp., 644 N.E.2d 1214 (Ill. App. Ct. 1995) (allowing medical battery claim against hospital when treatment with intraocular lenses was substantially at variance from treatment to which patient consented; preemption of Medical Device Amendments to the Food, Drug and Cosmetic Act of 1938 did not apply to informed consent requirements).


32. See infra text accompanying notes 199–206.

33. See, e.g., Emmett v. E. Dispensary & Cas. Hosp., 396 F.2d 931, 935 (D.C. Cir. 1967) (“We find in the fiducial qualities of that relationship the physician’s duty to reveal to the patient that which in his best interests it is important that he should know.”); Ison v. McFall, 400 S.W.2d 243, 258 (Tenn. Ct. App. 1964) (holding that any physician, as a fiduciary, who knows that a treatment will not benefit his patient must advise his patient of that fact). For further discussion of physicians’ duty to pursue the best medical interests of their patients, see infra Section VI.C.

34. See, e.g., Canterbury v. Spence, 464 F.2d 772, 782 (D.C. Cir. 1972) (“The patient’s reliance upon the physician is a trust of the kind which traditionally has exacted obligations
effectiveness studies without consent, such personalized medical care is exactly what patients reasonably, but mistakenly, believe they are receiving. It is true that patients and physicians can sometimes modify the legal duties inherent in a physician-patient relationship, such as when patients voluntarily enroll in clinical trials, but they must do so through mutual agreement. In the studies we are addressing, there has been no mutual agreement to modify the physician-patient relationship into one of researcher-subject.

The paper proceeds as follows: In Part II, we review the existing ethical and regulatory debate over consent requirements in comparative effectiveness trials and consider the types and numbers of such studies conducted without consent.

In Part III, we introduce a hypothetical comparative effectiveness study undertaken with a waiver of research consent in order to analyze the primary legal claims that a potential plaintiff might pursue against their physician upon learning of their participation in the trial—battery (Part IV), lack of informed consent (Part V), and breach of fiduciary duty (Part VI). We also focus on the physician-researcher, although our analysis likely extends to other clinicians and health care entities, as some of the cases we discuss will illustrate. The fiduciary relationship between physician and patient is the most well established, as is the duty of physicians to obtain informed consent.

Based on our analysis, the courts’ conclusions with respect to all three potential causes of action are clear: consent for research is required. The fact that a physician-researcher in this category of clinical trials provides a treatment within the “standard of care” (and thus one that would not subject the physician to liability for similar conduct in a pure clinical care context) provides no protection from liability in a research context. For both the battery and lack of informed consent claims, we discuss a legal case that involved a research study so similar to our hypothetical beyond those associated with armslength transactions. His dependence upon the physician for information affecting his well-being, in terms of contemplated treatment, is well-nigh abject.”. For further discussion of informed consent law, see infra Section V.A.

35. We appreciate that a plaintiff might also assert claims based on violations of federal or state constitutional law (in the event of state action) or under state statutes requiring informed consent for medical treatment or research. Specific analysis of these other potential claims is beyond the scope of this Article, although the contours of such claims, and the ethical values underpinning them, would resemble those discussed herein.


37. See, e.g., Espalin v. Child.’s Med. Ctr., 27 S.W.3d 675, 686 (Tex. Ct. App. 2000) (dismissing a claim against a hospital for failure to secure informed consent because “the duty to obtain informed consent is a nondelegable duty imposed solely upon the treating doctor”). Though the language “nondelegable” may be used in cases like Espalin, the court decisions generally mean that “the physician has the ultimate responsibility for obtaining the patient’s informed consent and . . . remains ultimately responsible for defects in the informed consent process if obtained by someone else.” Samuel D. Hodge, Jr. & Maria Zambrano Steinhaus, The Ever-Changing Landscape of Informed Consent and Whether the Obligation to Explain a Procedure to the Patient May Be Delegated, 71 ARK. L. REV. 727, 749 (2019).
research study that the opinions are almost prescriptive. The closest case involving breach of fiduciary duty involved a different type of research study (not a randomized clinical trial), but the court there also clearly concluded that a physician is required to disclose medical research activities that may affect patient care.

In Part VII, we consider what our analysis of common law duties reveals about an ethical path forward as researchers propose and implement research designs that avoid obtaining prospective informed consent. At the end of the day, regulations can be revised or statutes adopted to preempt the common law. What does the reasoning of these cases tell us about the importance of the rights at stake? The legal duties our analysis reveals are consistent with the long-standing ethical duties to obtain informed consent for both clinical care and for medical research and with generally accepted physician duties of loyalty, discretion, and care. These common law duties rest upon fundamental ethical values of respect for bodily integrity, autonomy, trust, and transparency.

Appreciation of these values has been largely overshadowed in the debate about whether comparative effectiveness research can be conducted without informed consent, a conversation, as we’ll see, with a decidedly utilitarian focus on the benefits of advancing evidence-based medical practice at little (so it is argued) cost to patient welfare. The legal recognition of these other values provides further ethical support for researchers to design consent processes that respect those values and for federal agencies and IRBs to continue to interpret existing research regulations to require consent. So, too, does concern for patient welfare, as patients cannot protect their own welfare interests when they do not know they are at risk. It is in this Part that we also point to broader social justice concerns that comparative effectiveness studies without consent will fall disproportionately on already disadvantaged populations. Finally, we lay out the contours of a legally and ethically sound way forward.

The debate about consent for comparative effectiveness trials takes place within a larger conversation about the need for more precise and informative evidence to guide clinical care and whether certain traditional precepts of research ethics can be relaxed to gain that evidence, such as the requirement that research participation be voluntary or that clinical care and research be understood as fundamentally distinct. It is important to appreciate that we are at an inflection point in our approach to medical research, where fundamental, long-held ethical principles are challenged as no longer necessary or desirable. Our legal analysis urges a recommitment to these ethical understandings in the modern research enterprise.


II. REGULATORY REQUIREMENTS FOR CONSENT AND WAIVERS

In this Part, we review the ongoing debate within the research and research ethics communities over consent requirements for “standard of care” studies under the federal research regulations, where the focus has been to date, and review the type and number of comparative effectiveness studies without consent currently taking place.

A. Conflict Within the Research Ethics Community: The SUPPORT Study

The current intense debate about what is required by way of consent in so-called standard of care studies came into full view in the summer of 2013 amid controversy over the SUPPORT (Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial) study.40 In SUPPORT, over 1300 fragile, extremely premature newborns in the Neonatal Intensive Care Units of twenty-two U.S. hospitals were randomized to different levels of oxygen support to determine if lower supplemental oxygen could reduce the incidence of eye disease without increasing the risk of death or neurological injury.41 The study results showed an alarming difference in the treatment arms of the study. While the researchers had anticipated that babies would, on the whole, benefit from lower levels of oxygen support, it turned out that more babies died when they were assigned a low oxygen saturation target than a high oxygen saturation target; for every two cases of severe eye disease prevented, there was one additional death.

Following publication of the SUPPORT Study results, the Office for Human Research Protections (OHRP), the federal agency that oversees the protection of human subjects in much federally sponsored research, sent the University of Alabama, the study’s lead institution, a determination letter faulting it for inadequately disclosing the risks of the study to parents.43 In contrast to the studies that are the focus of this Article, SUPPORT investigators did seek consent from the parents for their infants’ participation in the study, but the consent forms did not include disclosures about risks of death or neurological injury, and many described the interventions relating to oxygen supplementation “as standard of care, usual care, or as a desired approach in some units,” for which there was “no predictable increase

41. Carlo et al., Target Ranges, supra note 40; see also Letter from Lisa R. Buchanan, Compliance Oversight Coordinator, OHRP Div. of Compliance Oversight, to Richard B. Marchase, Vice President for Rsch. & Econ. Dev., Univ. of Ala., Birmingham (Mar. 7, 2013) [hereinafter OHRP SUPPORT Determination Letter], https://www.hhs.gov/ohrp/sites/default/files/ohrp/detrm_lets/YR13/mar13a.pdf [https://perma.cc/GJ2Q-BM66] (indicating the study took place at approximately twenty-two sites and was approved by twenty-three IRBs).
42. See Carlo et al., Target Ranges, supra note 40, at 1967.
43. OHRP SUPPORT Determination Letter, supra note 41.
in risk” to their child. In short, many of the consent forms described participating in the research study as involving little to no risk to the children, the greatest identified risks being a potential loss of medical privacy or minor skin breakdown at the site of a study device (a modified oximeter) placed on the infant’s finger to monitor oxygen levels.

When reports criticizing the study appeared in the media, powerful members of the research community launched a fierce defense of the investigators’ actions. The editors of the New England Journal of Medicine (NEJM) (one of the leading journals in medicine) accused OHRP of “casting a pall over the conduct of clinical research to answer important questions in daily practice” and called SUPPORT “a model of how to make medical progress.” Francis Collins, then the director of the National Institutes of Health, which had funded the study, co-authored an impassioned defense of the investigators in NEJM. In the same issue, a group of forty-six prominent members of the research ethics community published a joint letter to the editor in NEJM to decry OHRP’s claimed overreach. The consent forms, they said, “could have been improved,” but did not fail to disclose any risks required to be disclosed.

44. Irene Cortés-Puch, Robert A. Wesley, Michael A. Carome, Robert L. Danner, Sidney M. Wolfe, & Charles Natanson, Usual Care and Informed Consent in Clinical Trials of Oxygen Management in Extremely Premature Infants, PLOS ONE, (May 18, 2016), https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0155005#references [https://perma.cc/BDZ5-NEMC]. For example, the consent form from the University of California at San Diego, which served as a template for other research sites’ forms, says: “Because all of the treatments proposed in this study are standard of care, there is no predictable increase in risk for your baby.” Michael O’Shea, The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (The SUPPORT Trial), PUB. CITIZEN: SUPPORT Study Consent Form 4 (Dec. 13, 2005), http://www.citizen.org/documents/support-study-consent-form.pdf [https://perma.cc/A7B2-7YAE].


46. See, e.g., Editorial Board, Editorial, An Ethical Breakdown, N.Y. TIMES (April 15, 2013), https://www.nytimes.com/2013/04/16/opinion/an-ethical-breakdown-in-medical-research.html [https://perma.cc/Q2QR-UA4M] (“[SUPPORT is a] research project that failed to meet the most basic standard: providing an informed consent document to parents that accurately described the risks and benefits of the research to be conducted on extremely premature babies.”).


51. Id. (“Although we acknowledge that the permission forms could have been improved, we disagree that the random assignment of infants to a high oxygen-saturation level or a low oxygen-saturation level imposed additional risks that the investigators failed to disclose.”).
There were also many who agreed at the time with OHRP that the consent forms were inadequate. NEJM published (though only online) a counter-letter of a similar number of academics and ethicists expressing this view.\(^52\) Opposing public letters of this kind had never been seen before in bioethics.

Under intense pressure from officials at the National Institutes of Health and other powerful members of the research community,\(^53\) OHRP retracted its determination letter, explaining that there was “widespread misunderstanding” about requirements to disclose risks in trials studying standard of care treatments.\(^54\) The agency called a rare public meeting later that summer where the debate continued.\(^55\) An issue of the *American Journal of Bioethics*, the highest impact journal in the bioethics field, was devoted to articles debating whether the consent forms adequately informed parents about the experimental nature and risks of SUPPORT.\(^56\) The debate continues to this day, and at its heart is essentially the same question this Article addresses: What must patients be told before their medical treatment is randomly assigned as part of a research study?

To be clear, the question debated in the SUPPORT controversy was whether the disclosures to parents were adequate, and thus whether their consent was informed, not whether consent for research randomization had to be obtained at all. But the essential arguments made in defense of the SUPPORT investigators are also made when arguing that no consent is required at all for certain comparative effectiveness studies. Advocates for waiving the requirement for consent argued then and continue to assert now that patients in these types of studies are exposed to no or minimal research risks by virtue of having their care determined by randomization.\(^57\) Any

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risks they face from usual care interventions are clinical risks and should therefore be subject only to the disclosure and consent requirements associated with clinical care. According to this argument, when the clinical care intervention does not require specific consent—such as the level of oxygen saturation levels hospitals target for premature infants in their intensive care units—then neither clinical nor research consent is required.

This is a radical suggestion, essentially an argument that the randomized trial comparing oxygen targets in the SUPPORT study was “minimal risk” and thus could have even qualified for a waiver of the consent requirement under the federal regulations if other research elements had not been involved, such as the use of experimental oximeters. The types or magnitudes of the potential harms being compared—death, eye disease, lung disease, and neurological injury—did not matter.

Though OHRP retracted its original determination letter criticizing the SUPPORT consent forms, it nevertheless thoroughly refuted this argument in that retraction.

Further, in 2014, the agency published for comment draft guidance on the issue, reinforcing the agency’s position that the foreseeable comparative risk and potential for differential benefit between two randomized standard treatments should be considered “risks of research” and should be disclosed to potential participants as such. Nevertheless, ten years later, that draft guidance has not been formally adopted.

since it refers to the true claim that the randomization itself introduced no further risk than the standard of care.”); see also Kim, supra note 10, at § 2 (identifying others making this argument, which he calls “a novel method for categorizing [Pragmatic Clinical Trials’] research risks”).


60. DEP’T HEALTH & HUM. SERVS., OFFICE HUM. RSch. PROTS., DRAFT GUIDANCE ON DISCLOSING REASONABLY FORESEEABLE RISKS IN RESEARCH EVALUATING STANDARDS OF CARE (2014) [hereinafter OHRP Draft Guidance].

61. Several years after the SUPPORT controversy, summary judgment was granted for defendants in a case brought by patients claiming injury from participation in the study. Looney v. Moore, 886 F.3d 1058, 1064 (11th Cir. 2018). The principal investigator and IRB members were sued under negligence, negligence per se (for failing to follow the Common Rule), breach of fiduciary duty, and lack of informed consent. Id. at 1060. The court granted summary judgment on both the informed consent and fiduciary duty claims (without differentiating between the two) because plaintiffs failed to establish causation and injury. Id. at 1064. Alabama does not recognize “loss of chance” doctrine. For an explanation of “loss of chance,” see infra note 210. Because the “plaintiffs had failed to prove that their injuries were caused by participation in the SUPPORT study, as opposed to being a consequence of their premature births,” the Eleventh Circuit determined summary judgment was appropriate. Looney, 886 F.3d at 1062. No determination was made regarding the adequacy of the informed consent disclosures, despite the assertion by some SUPPORT defenders that the judgment “vindicated” the study. See, e.g., John D. Lantos, Vindication for SUPPORT, 373 NEW ENG.
In the meantime, and in contravention of the Draft Guidance, some IRBs have gone further and granted requests for a waiver of research consent altogether for some randomized comparative effectiveness studies, determining that they meet the regulatory criteria for “minimal risk” studies because the compared interventions are within the standard of care. Some of these studies have looked at comparative risks for mortality and other serious outcomes. Similarly, funding agencies and medical journals—two important ethics and regulatory “gatekeepers”—have lent support to such research without consent by funding or publishing the results of such studies.

In section C of this Part, we will discuss what is known about the numbers and types of these studies. We turn now to analyze more fully this argument.

B. The Argument that Randomized Standard of Care Studies Do Not Require Consent Because They Involve Only “Minimal Risk”

The view that patients do not need to be told when placed in a clinical trial of usual care interventions is not actually new. From 1947, when the first modern randomized controlled trial took place, until at least the late 1960s, it was not uncommon for patients to be randomized to standard treatments without disclosure or consent in order to evaluate their comparative risks and benefits. In 1974, Charles Fried wrote an extended critique of this practice, explaining that distinguished researchers of that era believed that when the evidence about alternative treatments was balanced—a situation known as “clinical equipoise”—“tell[ing] the patient that he is being randomized . . . would add nothing of relevance regarding the expected outcome of his treatment, and thus nothing of relevance to his choice whether or not to consent to the treatment.”

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63. See infra text accompanying notes 100–01.
64. See, e.g., supra text accompanying notes 18–26 (regarding the prehospital agitation and placental transfusion trials).
65. “The randomised control trial (RCT) is a trial in which subjects are randomly assigned to one of two groups: one (the experimental group) receiving the intervention that is being tested, and the other (the comparison group or control) receiving an alternative (conventional) treatment . . . . RCTs are the most stringent way of determining whether a cause-effect relation exists between the intervention and the outcome.” J.M. Kendall, Designing a Research Project: Randomised Controlled Trials and Their Principles, 20 EMERGENCY MED. J. 164, 164 (2003) (citations omitted); see also Arun Bhatt, Evolution of Clinical Research: A History Before and Beyond James Lind, 1 PERSPS. CLINICAL RSCH. 6, 8 (2010) (discussing the first RCT, which began in 1947 in the United Kingdom).
67. CHARLES FRIED, MEDICAL EXPERIMENTATION: PERSONAL INTEGRITY & SOCIAL POLICY 32 (Franklin Miller & Alan Wertheimer eds., 1974). This is essentially the same argument being made today to justify conducting modern comparative effectiveness studies without consent. Miller & Kim, supra note 66, at 421; Jerry Menikoff, Commentary, The Unbelievable Rightness of Being in Clinical Trials, HASTINGS CTR. REP. (SPECIAL REPORT)
This view did not survive the civil rights era of the sixties and seventies and state courts’ recognition around the country of the right to informed consent for medical care. Nor did it survive the federal government’s increasing regulation of research. Following public revelation of the USPHS Syphilis Study at Tuskegee in 1972, the federal government established the National Commission for the Protection of Human Subjects of Medical and Behavioral Research to identify the basic ethical principles that should govern research done on humans. In 1979, the Commission issued the famous Belmont Report, which laid down the ethical framework for federal human subject research regulations, adopted soon thereafter. Altogether, these developments seemed to have put the matter to rest.

Today, federally sponsored research must be conducted within the standards set by the Department of Health and Human Services’ “Common Rule,” so called because it is followed by multiple (currently 39) federal agencies in regulating the research those agencies sponsor. The Common Rule requires research institutions to establish IRBs to review federally sponsored research studies to ensure that risks to subjects are minimized and reasonable, selection of subjects is equitable, informed consent is sought from prospective subjects, studies are monitored for safety, and the privacy and confidentiality of subjects are protected. For clinical trials involving drugs or devices that will be marketed in the United States, regardless of their source of funding, the Food and Drug Administration has its own set of regulations for the protection of human subjects.

Both sets of regulations have extensive rules requiring informed consent for research, with only narrow exceptions. The Common Rule contains a long-standing explicit allowance for waivers or modifications of informed consent in studies involving only “minimal risk.” In December 2023, the FDA adopted a rule that...

S30, S30 (2013).


69. Id. at 601–02.


74. See Austin Connor Kassels & Jon F. Merz, The History and Policy Evolution of Waivers of Informed Consent in Research, 41 J. LEGAL MED. 1 (2021). In addition to the general exception for research activities that involve only minimal risk, there is a narrow exception for “emergency research.” See infra note 196.

allows for a similar exception for informed consent for minimal risk research. The current debate about consent requirements for comparative effectiveness studies has centered on the language contained in the Common Rule’s minimal risk exception, for which the following requirements must be met:

1. The research activity involves no more than minimal risk,
2. A waiver or alteration of consent would not adversely affect the rights and welfare of the subjects,
3. The research cannot practically be carried out without a waiver, and
4. When appropriate, research subjects are provided with pertinent information following participation.

In the years following adoption of this rule, it was generally understood to allow researchers to request a waiver of informed consent only for narrowly circumscribed non-interventional research, such as studies that involved research on medical records or biospecimens. As we noted before, the idea that researchers would request a waiver of consent for a randomized clinical trial under this regulatory provision is fairly radical.

A paper published in 1999 by Robert Truog, a prominent physician-bioethicist, and co-authors re-opened the question about the necessity for consent in randomized clinical trials comparing standard of care treatments—though with few apparent takers at the time. The paper argued that such studies should not require specific research consent because a patient’s general consent for medical treatment—the consent given “as part of the process of establishing a fiduciary relationship with a physician”—could be understood as authorizing the patient’s participation in such trials as long as there was genuine uncertainty about the comparative effectiveness and risks of the treatments being studied and those treatments did not involve high risk-to-benefit ratios or implicate the values and preferences of the patient. Specifically, Truog et al. argued the requirement for specific research informed consent could be ethically waived when all the following criteria are met:

76. Prior to adoption of this rule, the FDA regulations did not include a provision allowing a waiver of consent for “minimal risk” studies; its rule tracks the pre-2018 Common Rule revision. See FDA Consent Waiver Rule, supra note 13; see also Kassels & Merz, supra note 74, at 21–22 (discussing rule in proposed form).
77. “Minimal risk” is defined in the regulations to mean “that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.” 45 C.F.R. § 46.102(j) (2023).
78. 45 C.F.R. § 116(f)(3) (2023). When the Common Rule was revised in 2018, this provision added specific considerations for identifiable private information and identifiable biospecimens, which have been omitted here.
79. Kassels & Merz, supra note 74, at 16. Even these applications of the waiver rule appear not to have been originally intended. Id.
81. Id. at 804.
1) the treatment interventions could be offered outside of the trial without the specific informed consent of the patient (i.e., the intervention would be covered by the general medical consent);
2) the treatments “should not involve more than minimal additional risk in comparison with any of the alternatives”;\textsuperscript{82}
3) clinical equipoise exists between the treatments (meaning there is “honest uncertainty about which treatment is superior”\textsuperscript{83});
4) “no reasonable person should have a preference for one treatment over any other, regardless of the differences between the treatments being compared”;\textsuperscript{84}
5) “patients should be informed that the institution or clinical setting in which they are being treated” is randomizing patients to treatments in this manner without specific consent, thus allowing them the opportunity to seek care elsewhere.\textsuperscript{85}

There is little in the paper explaining how to understand the second criterion—that the treatments “should not involve more than minimal additional risk in comparison with any of the alternatives.” Does this refer just to the other treatments to which patients are randomized or also to other available treatments that are not part of the study? Does it mean that other than the treatment risks and benefits being compared in the study, one treatment should not involve known additional risks as compared with the other? Or does it mean that that the comparative risks and benefits between the two treatments that the research is designed to discover are unlikely to be of consequence to patients?\textsuperscript{86} Moreover, the authors also specify that the risks associated with each of the treatment options should not be “qualitatively dissimilar,” such as you would see in a study that compares drugs with “substantially different side effects” or “therapies that involve a trade-off between efficacy and safety.”\textsuperscript{87} In

\textsuperscript{82} \textit{Id.} at 805.
\textsuperscript{83} \textit{Id.} (citing Benjamin Freedman, \textit{Equipoise and the Ethics of Clinical Research}, 317 N. ENG. J. MED. 141, 141 (1987)).
\textsuperscript{84} \textit{Id.} A number of contemporary responses to Truog et al.’s paper countered that whether or not patients would prefer one medical treatment over the other, reasonable people would want to know their care was being determined by a research study. \textit{See, e.g.}, Michael A. Carome et al., Commentary, \textit{Is Informed Consent Always Necessary for Randomized, Controlled Trials?}, 341 NEW ENG. J. MED. 448 (1999) (correspondence from Michael A. Carome, Rebeca Dresser, and Nancy M.P. King, among others). Nancy King writes: “An important purpose of informed consent, which the authors ignore, is to let subjects know they are subjects. In the proposed scenario, everyone knows but the subjects. How can this be justifiable?” \textit{Id.} at 449.
\textsuperscript{85} Truog et al., \textit{supra} note 80, at 805.
\textsuperscript{86} We note that Robert Truog signed onto the group New England Journal of Medicine letter defending the SUPPORT investigators, in which the random assignment of infants to a high oxygen-saturation level or a low oxygen-saturation level was described as imposing no additional risks of death, neurological injury, eye disease, or chronic lung disease (the comparative risks of harm being studied in the trial but not disclosed to parents). See Wilfond et al., \textit{supra} note 50. Whether Truog’s endorsement of this claim sheds any light on how one should understand the 1999 paper’s discussion of minimal risk is unclear.
\textsuperscript{87} Truog et al., \textit{supra} note 80, at 805.
such cases, patients would need to provide specific informed consent for both the research study and clinical treatment.\textsuperscript{88}

Since then, some commentators have been more explicit about when and why they believe a study that randomizes patients to standard of care treatments involves no or minimal research risks, and thus why in many such studies, research consent is not required, either as a matter of ethics or the federal regulations. They posit that before a study determines which of two commonly accepted medical interventions is superior in terms of efficacy and side effects, the risk associated with being randomized in a study comparing them is \textit{per se} “minimal risk.”\textsuperscript{89} Under this approach, all studies that randomize to usual care interventions would be considered minimal risk, as long as there were not extra tests or procedures, or patient questionnaires, etc., that introduce risk, and there were no differences in the way the intervention was performed in the study vs. usual care—for example, by standardizing the intervention beyond that which was typical in usual care.\textsuperscript{90} (Often interventions are strictly standardized in research protocols in order to achieve clearer comparative results between the arms of a study.)

In our view, these arguments are unacceptably utilitarian or have logical problems, as we have previewed in the introduction.\textsuperscript{91} In comparative effectiveness studies, any particular patient-subject might be subjected to greater risks by being in the study if they are randomized to receive treatment that is different from that which they would otherwise have received from their physician. One treatment might have a greater probability of a harm occurring or greater magnitude of harm. Lower effectiveness is also a potential harm.\textsuperscript{92} By receiving the treatment that is less effective, patients face risks of harms from their medical condition that may have

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\begin{enumerate}

\item \textsuperscript{88} \textit{Id.}


\item \textsuperscript{90} When comparative effectiveness studies are performed in this way—following “real world practices”—they are sometimes called “pragmatic clinical trials.”

\item \textsuperscript{91} \textit{See Kim, supra note 10; Shepherd, supra note 45; Annas & Annas, supra note 29; see also} Scott Y.H. Kim & Franklin G. Miller, \textit{Varieties of Standard-Of-Care Treatment Randomized Trials: Ethical Implications}, 313 \textit{JAMA} 895 (2015).

\item \textsuperscript{92} \textit{See Ruth Macklin & Lois Shepherd, Informed Consent and Standard of Care: What Must Be Disclosed}, 13 \textit{AM. J. BIOETHICS} 9, 11 (2013) (pointing out that if there is a benefit to being in one treatment arm of a study, there is a corresponding risk to being in the other).
\end{enumerate}
\end{footnotesize}
been reduced if they had received the other treatment. It is also true that randomization could work to a particular patient’s benefit if they ended up in the treatment arm that turns out to be better and their physician would typically have provided the other treatment.

For example, in a study that randomly assigns patients to one of two treatments that in clinical practice are provided at roughly equal rates, randomization results in approximately 50% of the patients receiving the same treatment and 50% a different treatment than they would have received as part of their regular clinical care. When one treatment turns out to be substantially worse than the other, approximately half of the patients assigned to this (inferior) treatment face greater risks for harms than they would have otherwise. Overall, then, approximately one in four patients placed in the study (25%) receive a treatment that exposes them to more risk of harms than they would have faced outside the study. (Similarly, approximately 25% of the patients stand to benefit from being in the “superior” arm of the study when their physicians would have provided the other treatment.) The argument that these studies are “minimal risk” prioritizes a group perspective over an individual perspective, in contrast with the ethics and regulation of human subject protections, which places importance on protecting individual persons.

And from a logical perspective, just because differential risk between treatments is unknown prior to the study’s completion and a study generally satisfies the ethical requirement of clinical equipoise, that does not mean those risks do not exist, as some authors have argued.\(^\text{93}\) If a differential risk only exists when it is known, then we would have to characterize many studies that satisfy the generally accepted ethical requirement of clinical equipoise as involving minimal or no risk (unless there were extra research procedures like imaging studies and blood draws, etc.). No one appears to be arguing, however, that studies comparing an unproven or experimental intervention against placebo or standard of care is minimal or no risk for reasons that are obvious, even though the differential risks between arms is unknown and such studies also are generally expected to meet the ethical requirement of clinical equipoise.\(^\text{94}\)

The fact that some participants will face a higher risk of decreased benefit or increased harm than they would have otherwise due to randomization is also reasonably foreseeable. “Reasonably foreseeable risks” must be disclosed to prospective research subjects according to the research regulations.\(^\text{95}\) Those risks, of course, have not been quantified before the study’s completion (that is one of the points of the study), but if the study is designed as a randomized clinical trial to identify and measure these “comparative” risks, then the expectation that some individuals face a higher risk in the study than they would have in regular clinical care is arguably not only foreseeable, but foreseen by the investigators. Other, completely unexpected risks of harm may also be discovered by conducting the study. These risks cannot be disclosed to research subjects, although they should be

\(^{93}\) See supra note 89.

\(^{94}\) See Shepherd, supra note 45, at 360.

\(^{95}\) 45 C.F.R. § 46.116(b)(2)(2023). The Draft Guidance points out that the risks in standard of care clinical trials are “reasonably foreseeable” (and thus, under the regulations should be disclosed to patient-subjects) if the study is aimed at measuring and comparing them. OHRP DRAFT GUIDANCE, supra note 60.
made aware of the possibility that they might be exposed to unknown risks from being randomized to a treatment they might otherwise not have received in clinical care—something they cannot be aware of if they do not know they are participating in a study that will randomly assign treatments to patients.

It is true that some CER studies may be comparing differences in treatments that, even if they materialized, would likely not matter much to patients and could even be considered minimal risk. But that is far different from assuming that all such studies are minimal risk simply by virtue of the fact that they compare widely accepted treatments. As the OHRP Draft Guidance points out, the comparative risk/benefit profile between the two arms of the study is unlikely to be of little significance to patients’ health—in order to justify doing the study in the first place, important discoveries should be anticipated.

C. Studies Conducted Without Knowledge or Consent

It is not known how many CER trials have taken place or are taking place for which consent is not obtained because an IRB has waived the regulatory requirement for consent under this minimal risk theory, although some commentators note that they appear to be on the increase. Randomized comparative effectiveness studies undertaken without consent are not prevalent but neither are they rare. Some of the trials conducted without consent have involved thousands of participants and compared treatments that proved to have differential risks of serious harms, such as respiratory distress, brain injury, and death; the prehospital agitation trial and placental transfusion trial highlighted in the introduction are examples, but there are others.

96. Kim, supra note 10, at 10.
97. Id.
98. OHRP DRAFT GUIDANCE, supra note 60 (“The merits of devoting the resources needed to carry out such studies, and the ethical justification for asking prospective subjects to agree to participate in them, depend on there being real uncertainty about the outcomes of the studies in terms of meaningful differences in harms or benefits that may result from receiving one standard of care versus another.”)
100. See, e.g., Craig S. Anderson et al., Cluster-Randomized, Crossover Trial of Head Positioning in Acute Stroke, 376 NEW ENG. J. MED. 2437 (2017) (international study involving over 11,000 patients who were instructed to either sit up or lie flat for twenty-four hours after ischemic stroke; participating hospitals were randomized to one or the other intervention; patients were less likely to follow the instructions to lie flat, suggesting that patients have preferences regarding position); R. G., Brower et al., Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome, 342 NEW ENG. J. MED. 1301 (2000) (randomizing patients with acute respiratory distress syndrome to larger or smaller machine-delivered breaths to compare rates of survival and improved ability to breathe without ventilator assistance; requirement for consent was waived at one of ten hospitals participating in the study). The latter study was controversial for not including a true “usual care” arm in which physicians would adjust the breathing support according to the patient’s condition. The treatment in the “traditional” arm of the study was also no longer widely used. Ruth Macklin & Charles Natanson,
One recent review of the top 100 most highly cited randomized controlled trials for each of the five years from 2014 to 2018 found that 9% (44 of 500 studies) reported not obtaining fully informed consent from at least some of the enrolled subjects. While most of these involved emergency treatments under circumstances in which informed consent could not be obtained (for which a different, narrow regulatory exception to informed consent exists), one-third (15 studies) did not, “meaning that subjects from whom consent was waived had capacity and would be capable of providing consent, if informed and asked.” In eleven of the trials, no notice was ever provided to subjects about the study at all, but, more typically, and particularly for those involving emergency care and incapacitated individuals, follow-up notice and requests for continued participation occurred (often, to use study-related patient health information). Most of the trials in which research subjects were given neither pre- nor post-participation notice of the research interventions “were cluster randomized, where institutional structures such as hospitals, intensive care units (ICU), clinical practices or healthcare providers, or time periods are the units of randomization [rather than the individual].” In cluster randomized trials, patients receive the treatment assigned by the trial protocol to the cluster in which they appear for medical care. (The prehospital agitation study described in the introduction used a cluster randomized design.)

Misrepresenting “Usual Care” in Research: An Ethical and Scientific Error. A signed written consent form was not required to count as fully informed consent by the study authors. Id. at 1343; see also Lisa Y. Lin, Nicole Jochym & Jon F. Merz, Refusal Rates and Waivers of Informed Consent in Pragmatic and Comparative Effectiveness RCTs: A Systematic Review, 104 CONTEMP. CLINICAL TRIALS 253 (2020).
D. Challenges to Obtaining Informed Consent in Research

Thus far, we have explained how proponents of comparative effectiveness research without consent argue that it is unnecessary. But why do they advance this argument? What is the motivation? Is it that hard to just go ahead and get meaningful consent?

It turns out that it actually can be, and we acknowledge that. Though the ideal of informed consent for research is rarely questioned by medical researchers, they often voice frustration with current informed consent processes. Consent processes are expensive. Recruiting adequate numbers of study participants is difficult, and many studies are begun but never completed due to insufficient enrollment. There is widespread agreement that consent forms are too long, difficult to understand, and include information that is not helpful to potential participants in deciding whether to participate or not. Researchers’ frustrations with obtaining informed consent can be further exacerbated when CER studies aim to generate data from settings as close as possible to those in which regular medical care is provided—the additional trappings of a setting designed for research, including lengthy and formal consent processes, arguably detract from the study’s purpose to provide information relevant to improving the “real world.”

Reforms to the Common Rule in 2018 aimed, among other things, to simplify the written consent forms and processes that are required, but did not change the essential elements to be included in them. Nor, with few exceptions, did it expand

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108. See, e.g., Wade D. Rich, Kathy J. Auten, Marie G. Gantz, Ellen C. Hale, Angelita M. Hensman, Nancy S. Newman & Neil N. Finer, Antenatal Consent in the SUPPORT Trial: Challenges, Costs, and Representative Enrollment, 126 PEDIATRICS, July 2010, at 4 (estimating that the personnel costs devoted to screening and obtaining consent for the SUPPORT study was between $161,311 and $266,920).

109. One study calculated that 12% of clinical trials registered on ClinicalTrials.gov from February 2000 to 2013 were ended prematurely, and the lead reason for termination was insufficient accrual of subjects. Rebecca J. Williams, Tony Tse, Katelyn DiPiazza & Deborah A. Zarin, Terminated Trials in the ClinicalTrials.gov Results Database: Evaluation of Availability of Primary Outcome Data and Reasons for Termination, PLoS ONE, May 26, 2015, at 1, 5; see also David B. Fogel, Factors Associated with Clinical Trials that Fail and Opportunities for Improving the Likelihood of Success: A Review, 11 CONTEMP. CLINICAL TRIALS COMM'NS 156 (2018).


the categories of research for which the requirement for written informed consent could be waived. There is little sign that these reforms have addressed researchers’ concerns about either the administrative burdens of consent processes and forms or their ease of navigation by and usefulness to potential participants. To be fair, the content of consent forms is largely dictated by the IRBs overseeing the study. IRBs generally require more content than the regulations do, and much of what they require sometimes appears designed to limit institutional liability (e.g., listing every conceivable risk no matter how small or remote) and is frequently written in language that reads like “legalese.”

To researchers, however, it likely does not matter whether the particular requirements imposed on them come from legal requirements like the federal regulations or the “quasi-law” established by internal, institutional practices.

There is another concern about informed consent requirements for some studies. Requiring consent may result in skewed or ungeneralizable results if the people from whom consent cannot be obtained—because of refusal or other reasons—differ from those who consent to be enrolled in a study in ways that are important to the question researchers seek to answer. This form of selection bias is called “consent bias.”


114. Id.; see also SACHRP Recommendations, supra note 110.

115. See Carol A. Heimer, Responsibility in Health Care: Spanning the Boundary Between Law and Medicine, 41 WAKE FOREST L. REV. 465, 466 (2006) (explaining that “health law is not just statutes and regulations, but includes guidelines and other kinds of ‘rules’ that form the penumbra of law”) (emphasis in original).

116. INST. MED., BEYOND THE HIPAA PRIVACY RULE: ENHANCING PRIVACY, IMPROVING HEALTH THROUGH RESEARCH 268 (Sharyl J. Nass, Laura A. Levit & Lawrence O. Gostin eds., 2009) (recommending, in part because of consent bias, that the requirement for consent be eliminated for research on health records and biospecimens because the risks to subjects were low and did not merit the same protection of subjects’ welfare as “interventional” research).

117. See, e.g., Mark A. Rothstein & Abigail B. Shoben, Does Consent Bias Research?, 13 AM. J. BIOETHICS 27, 27–37 (2013) (examining the problem of consent bias). Other articles in the same issue of the journal also discuss the same problem. See also Cornelia Junghans & Melvyn Jones, Consent Bias in Research: How to Avoid It, 93 HEART 1024 (2007) (noting requirement of written consent may bias heart disease research because enrollees are more likely to have healthy lifestyles, have benefited from prior medical treatment, and have well-managed heart disease).
Researchers sometimes argue that consent bias can be so strong that requiring consent for their studies would make doing them “impracticable.”  

(Recall that impracticability is another criterion, along with minimal risk, necessary to qualify for a waiver or modification of regulatory consent.) In studies whose primary purpose is to learn from and inform what goes on in regular medical settings, the “impracticability” of obtaining research informed consent arguably stems directly from this research aim. But questions about these challenges to obtaining informed consent in this context are far from settled; some commentators question researchers’ perceptions of the difficulties in obtaining consent from some subjects as well as the extent to which the requirement to obtain consent actually does negatively affect research results.

Following our analysis of the common law duties to obtain consent for these studies, we discuss how those duties might be satisfied by consent processes that are not as burdensome as those required by the federal regulations or IRBs. In this way, turning to the common law may reveal productive ways forward that can simultaneously protect patients’ rights to know and control what happens to their bodies and relieve some of the regulatory consent burden on researchers and the research enterprise.

118. See, e.g., Junghans & Jones, supra note 117; Nils T. Songstad, Calum T. Roberts, Brett J. Manley, Louise S. Owen & Peter G. Davis, Retrospective Consent in a Neonatal Randomized Controlled Trial, 141 PEDIATRICS 1 (2018) (noting important differential patient characteristics in two phases of a study, one conducted with prospective consent, the other with retrospective consent). See generally Shona Kalkman, Ghislaine J.M.W. van Thiel, Mira G.P. Zuidgeest, Iris Goetz, Boris M. Pfeiffer, Diederick E. Grobbee & Johannes J.M. van Delden, Pragmatic Trials and Real World Evidence: Paper 4. Informed Consent, 89 J. CLINICAL EPIDEMIOLOGY 181, 183 (2017) (reviewing arguments that traditional consent requirements for pragmatic clinical trials might “deter specific groups of patients from participating,” and thus result in the “underrepresentation of particular groups of patients,” making the “trial results . . . less applicable to the more heterogeneous real-world population”). Kalkman et al. note that “[i]mpracticability in terms of pragmatic trials tends to refer to a compromise on real-world features that makes it (almost) impossible to answer the research question. This can be because of limited generalizability, low recruitment rates, and/or selection bias.” Id. at 183. For further discussion of consent bias concerns in CER studies, see infra text accompanying notes 397–407.

119. “Impracticability” can be understood in two primary ways, as meaning either that consent is so difficult to secure in the subject population that research cannot practically be done or that securing consent would introduce enough concern that consent bias would skew the results sufficiently to make them unable to answer the research question. IRBs have sometimes accepted the argument that consent bias would mean conducting the research was impracticable and waived the requirement for consent for some clinical trial subjects or for entire trials. See Dhamanaskar & Merz, supra note 101, at 1341.

120. Kalkman et al. supra note 118 at 181.

121. See id. at 183.

122. See infra Section VII(B).
III. A HYPOTHETICAL RESEARCH STUDY AND RESULTING LAWSUIT

The debate about consent requirements for comparative effectiveness studies shows no signs of resolution. Neither those who advocate for waived consent requirements nor those who oppose them appear to be moved by the arguments of the other side. OHRP, as noted earlier, has not formally adopted its Draft Guidance confirming that consent is required. The FDA has also not issued guidance on consent for standard of care studies even though it has recently adopted a rule to waive or modify informed consent for minimal risk studies that is nearly identical to the Common Rule’s waiver provision.\(^{123}\)

Can the common law move this debate forward? As the most recent draft of the Restatement Third of Torts recognizes, “informed consent is an area where law notably has led, rather than followed, professional practice” and had a “pronounced influence . . . on foundational aspects of medical practice.”\(^ {124}\) As noted above, the common law relating to informed consent is not pre-empted by the federal research regulations even when they apply.\(^ {125}\)

In this Part, we describe a hypothetical research study in order to test the reach and strength of the common law’s potential to provide redress for a patient placed in a CER study without consent. In the following three Parts we examine potential legal claims of battery, lack of informed consent, and breach of fiduciary duty.

Imagine the following: The parents of a premature infant who died soon after birth have filed a lawsuit against the physicians who cared for their child immediately after birth and the hospital in which the care was delivered. In learning more about the circumstances surrounding their baby’s death, the parents have discovered that, while in the hospital, their child was placed in a research study. The study randomly assigned premature infants to one of two interventions, A or B, both of which were in widespread use, to see if there were differences in terms of patient deaths prevented as well as the prevention of other serious outcomes associated with premature birth, like brain injury. They also learned that everyone involved in the care of their baby knew about the research study except them, the parents.

Before the study, published data supported the potential benefits of each intervention over its burdens and risks of harm, thus supporting either intervention A or B over doing nothing. But because the interventions had never been compared against one another in a rigorous way, it was uncertain whether one intervention was superior to the other in general or for particular subsets of patients (i.e., “clinical equipoise” existed). While physicians could competently provide either intervention, they generally did not provide both; some of the study physicians routinely provided one, some the other. In clinical practice, the two interventions are provided in a standardized manner so no individualization would be potentially lost by research participation. Only physicians who accepted that they did not know which intervention was superior (or who have “personal equipoise”) participated in the

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\(^{123}\) See FDA Consent Waiver Rule, supra note 13.


\(^{125}\) See supra notes 29–30 and accompanying text.
Finally, this is an intervention about which physicians do not normally talk to patients, even to acknowledge the existing uncertainties about which treatment is better, or to get their consent. The intervention the infant will receive is considered—rightly or wrongly—part of the bundle of care provided in the delivery of a premature infant covered by a general consent.

(To make the hypothetical study even more realistic, we might assume, although not relevant for the common law analysis, that the research study was federally funded and thus subject to the Common Rule, and that an IRB approved (in our view, mistakenly) a waiver of consent under the “minimal risk” exemption. For simplicity’s sake, however, we are assuming an intervention that does not place the study under the purview of the FDA, although, as previously noted, the FDA now has a similar waiver rule.)

In the study, significantly more infants who received Intervention A died than those who received Intervention B. The child on whose behalf this lawsuit is brought received Intervention A, and his parents have learned that the physicians usually provided Intervention B. The lawsuit does not claim that Intervention A was negligently provided. Instead, it claims that the physicians’ decision to place their baby in a study in which he was randomized to receive Intervention A was made without obtaining the required voluntary informed consent from them. The parents claim that if they had been asked to enroll their child in the study, they would have declined and their child would have received Intervention B, and that receiving Intervention A rather than Intervention B caused the child to experience a greater risk of death.

In constructing this hypothetical research study, we have tried to avoid creating a “straw man,” such as a study involving an intervention for which specific clinical consent is clearly required or in which a patient would have a reasonable basis for preferring one intervention over the other. We intentionally have presented a research study similar to those proposed in Truog et al.’s highly influential paper setting out the argument that consent could be ethically waived for standard of care studies and in line with others described in the published medical literature.

126. See Priscilla Alderson, Equipoise as a Means of Managing Uncertainty: Personal, Communal and Proxy, 22 J. MED. ETHICS 135, 135 (1996) (describing equipoise as “a state of uncertainty . . . characterized by the belief that, in a trial, no arm is known to offer greater harm or benefit than any other arm”). After interviewing forty healthcare workers providing care to breast cancer patients, Alderson and her team concluded that only a quarter felt that physicians could achieve personal equipoise. Id. at 136.

127. Arguably, if there is sufficient uncertainty about how the interventions compare with one another to justify doing a head-to-head comparison (e.g., which provides more benefit, which has greater risks for harm, etc.), then patients in the clinical context should be informed about this as well as the potential trade-offs being made by physicians in choosing one over the other, and be given an opportunity to make an informed choice for themselves about which intervention should be performed. We are grateful to Nancy King, in comments supplied on an earlier draft, for encouraging us to think more deeply about this issue. We agree that this is an important point deserving of more attention, and one that CER studies and learning health systems (discussed later in the Article) in some ways aim to tackle. Further elaboration on the complexities of the role of uncertainty in informed consent for medical care generally, however, is beyond the scope of this paper.

128. See Truog et al., supra note 80, and text accompanying notes 80–88. There are two deviations from the criteria set out in their paper. We added that study physicians had no
We must emphasize, however, that it would be difficult to find a research study that would satisfy all these criteria at once. It seems unlikely, for example, that two interventions would be so highly standardized in clinical care that there would be no individualization that would potentially be lost by protocol-driven standardization for research, or that physicians, who routinely provide one of two interventions, would be equally skilled in providing both. There are also questions about the circumstances under which “community equipoise” can be claimed (e.g., whether reliance is placed on a minority of experts rather than a majority of practicing physicians) and how often physicians can be said to experience personal equipoise. As former OHRP Director Jerry Menikoff has written, “It is likely a relatively rare study where there are genuinely no good reasons for a patient or doctor to prefer one treatment over the other.”

Although we have tried to create a hypothetical research study that would present favorable facts to the theoretical argument in favor of waived consent, we have also tried to create one that could reasonably become the subject of a lawsuit. This led us to present a study in which the potential consequences of receiving one intervention rather than the other could be a matter of life and death or serious physical harm, like brain injury. It is more likely that a lawsuit would be brought on behalf of research participants if they believed they suffered serious injury or death because a decision was made to place them in a study employing randomization without their consent. Our plaintiff has suffered the harm for which they were placed at increased risk through randomization. We could instead have imagined a plaintiff who received the same intervention they would have received outside the study or was in the arm of the study that experienced lower mortality risk. Physicians may also have breached a legal duty to these patients by placing them in a study that randomized them to a personal preference between the two interventions, as some ethicists argue that personal equipoise is necessary for physicians to satisfy their duty of care to patients (even in studies with consent). See Alderson, supra note 126. Second, we did not include that the study takes place within an institution or clinical setting that gives patients broad notice that studies of this kind may take place without specific consent so that they may have an opportunity to find care elsewhere. For more discussion on this point, see infra text accompanying notes 370–78.

129. See Menikoff, supra note 67.
130. Often, protocols for comparative effective trials will set out standards for performing the treatments to be compared. For example, in the placental transfusion study referenced in the introduction, the protocol set forth standards for the way the two methods being compared would be performed (i.e., the number of seconds before cord clamping and the number of times cord blood was “milked”). Katheria et al., supra note 10, at 1879–80.
131. See Alderson supra note 126, at 136 (questioning, in addition, whether other clinical staff members participating in the intervention also need to have personal equipoise for them to ethically participate in a clinical trial). As Merz and Yerramilli note, the target saturation levels used in the SUPPORT Study may not have truly reflected existing practices, as a “detailed survey study of NICU nurses conducted at the time SUPPORT began described policies and practices that range far outside that adopted for the SUPPORT trial.” Jon F. Merz & Divya Yerramilli, SUPPORT Asked the Wrong Question, 13 Am. J. Bioethics 25, 25–26 (2013) (citing Nghiem et al., Nurse Opinions and Pulse Oximeter Saturation Target Limits for Preterm Infants, 121 Pediatrics 1039 (2008)).
treatment for research purposes. However, lacking physical injury or a change in
treatment due to research, it is unlikely they would bring suit.133

Imagining a plaintiff who experienced an increased risk of harm from being in
the study also highlights the fact that the argument for waiving consent is being made
for studies in which patients face high-stakes outcomes. Advocates for waiver do not
argue that the risk of being in a randomized comparative effectiveness study is
minimal because no serious outcomes are at stake. They argue that the risk is minimal
because patients could face these same risks and benefits in regular clinical care
through “random physician preference”134 and the differences in risks and benefits
between the studied interventions are unknown.

Given the set of facts presented in the hypothetical case, the most promising
avenues for relief are battery, lack of informed consent, and breach of fiduciary
duty.135 As will be evident in the discussion that follows, the elements of, and
justifications for, each of these causes of action tend to overlap, especially in the
medical research context, though there are important differences in terms of whether
physical injury must be proved and the legal remedies available to patients. For the
sake of simplicity, we focus in the following analysis on the physicians, though other
clinicians as well as health systems and hospitals could also face potential direct or
vicarious liability.

IV. BATTERY

A. Essential Elements of Battery

Battery is a claim of unauthorized touching or intrusion upon the body of a
person.136 As an intentional tort, it does not require one to prove actual injury.137

133. In addition, the situations of these other potential plaintiffs would add further
complexity with little gain to this analysis. The overall question here is whether the study
can be done without consent for any patients. In a typical randomized trial, no one knows a priori
which treatment they will receive nor what their outcome will be.
134. See Magnus & Caplan, supra note 57, at 1865.
135. Other potential claims include medical malpractice, breach of contract, negligence
per se (for failing to follow the research regulations, where applicable), and perhaps even fraud
or others. With respect to fraud see, e.g., Keithley v. St. Joseph’s Hosp., 698 P.2d 435, 439
(“[W]here a fiduciary duty or confidential relationship exists, as between a physician and a
patient, a duty arises to disclose all material information concerning patient's treatment . . . .
A failure to do so may constitute fraudulent concealment.”).
that sometimes privilege will provide “an affirmative defense to a prima facie tort such as
battery, assault, or trespass. If a defendant can show that either she had the plaintiff’s consent
or she was acting in furtherance of a goal of sufficient social importance, then privilege will
insulate her from liability for the plaintiff’s damages (assuming she was otherwise observing
the appropriate standard of care).” Baker & Merz, supra note 29, at 580 (emphasis in original).
137. Mink, 460 F. Supp. at 716 (holding that an action in battery may lie “notwithstanding
the lack of an allegation of personal physical injury”).
Punitive damages may be awarded to punish and deter the intentional offensive conduct. ¹³⁸

Claims for lack of informed consent for medical treatment originally sounded in battery, but since the 1960s and 1970s most jurisdictions have located lack of informed consent in negligence. ¹³⁹ Patients today usually complain about inadequate disclosures prior to consent rather than a complete lack of consent, due in part to the general acceptance of the importance of informed consent in today’s practice of medicine. And most failures to disclose information are unintentional and thus more appropriately judged by negligence standards. ¹⁴⁰

Battery claims, however, are still seen in some medical suits, though even here plaintiffs rarely allege completely unauthorized treatment. ¹⁴¹ More frequently, battery is claimed when “a doctor obtains consent of the patient to perform one type of treatment and subsequently performs a substantially different type of treatment for which consent was not obtained.” ¹⁴² Battery can also be pursued when a patient consents to a procedure to be performed by one physician and it is instead performed by another. ¹⁴³ “These latter two scenarios,” writes Morreim, “in which something to which the patient did not consent is substituted for something to which he did consent (different procedure, different doctor), emphasize that battery is a matter of agreements and boundaries.” ¹⁴⁴

¹³⁸. See, e.g., Brandner v. Hudson, 171 P.3d 83, 89 (Alaska 2007) (“Punitive damages serve to punish the wrongdoer and to deter the wrongdoer and others like him from repeating the offensive act.”) (quoting Chizmar v. Mackie, 896 P.2d 196, 209 (Alaska 1995)).


¹⁴⁰. See Joan H. Krause, Recategorizing Informed Consent in an Era of Health Care Cost Containment, 85 IOWA L. REV. 261, 309 (1999) (explaining the substantial differences in battery and negligence from the viewpoint of the parties: “[I]n an action for battery, a plaintiff need only prove that the required disclosure did not occur, and thus no consent was given. In a battery action, there is no need to prove that knowledge of the undisclosed information would have changed the patient’s treatment decision, to demonstrate that the patient suffered any remediable harm as a result of the nondisclosure, or to introduce extensive expert testimony. . . . For these reasons, battery generally is viewed as more favorable to patients, and the move from battery to negligence has been characterized as an attempt to protect physicians from liability for minor disclosure failures.”).

¹⁴¹. Morreim, supra note 139, at 478.

¹⁴². Daley v. Regents of Univ. of Cal., 252 Cal. Rptr. 3d 273, 278 (Ct. App. 2019) (permitting battery claim where plaintiff alleged that as part of a research study she consented to a percutaneous surgery but defendants instead performed an open laparotomy and hysterotomy).

¹⁴³. See, e.g., Allen v. Richardson, 2020 Guam 13 ¶ 2 (plaintiff alleged he had specifically instructed the emergency department attending physician not to treat him because of concern physician may “exact revenge” because of plaintiff’s prior lawsuit against him); Perna v. Pirozzi, 457 A.2d 431 (N.J. 1983) (patient consented to operation by one physician but was operated on by two others). Morreim also notes that “[i]n some instances courts have been willing to see a physician’s misrepresentation of his credentials or experiences as an instance of battery.” Morreim, supra note 139, at 478 n.93 (citing Hales v. Pittman, 576 P.2d 493 (Ariz. 1978) and others).

¹⁴⁴. Morreim, supra note 139, at 478.
Morreim points out that when clinical research takes place without notice or consent,

“a very distinctive kind of substitution takes place, arguably even more offensive than medical battery. It is a substitution of goals. . . . [W]hen patients are subjected to research without their knowledge or consent, the investigator has covertly made a profound change of goals.”

Morreim is referring to the long-recognized difference between the goal of medical care—which is to advance the best interests of the patient—and the goal of research—which is to advance science for the benefit of future patients. When these goals are substituted—when research aims rather than the patient’s best medical interests are driving treatment recommendations or decisions—and the patient is unaware of that substitution, an action for battery can be appropriate.

Whether liability can be established in a particular case of “medical research battery” often depends on the scope of the medical treatment consent the patient has given and the information known to the patient at the time of consent, facts generally to be determined by the jury. For example, in Kus v. Sherman Hospital, a patient alleged he did not know he was receiving experimental intraocular lenses because the consent form he signed was altered by the surgeon to delete any reference to clinical investigation. Although the trial court initially dismissed the battery claim brought against the hospital, the Illinois Court of Appeals reversed: “Clearly, the medical battery claim is warranted under existing law.” The jury was tasked with determining whether the treatment the plaintiff received was “substantially at variance” with what he had consented to or whether he knew of the experimental nature of the treatment.

B. Mink v. University of Chicago

The 1978 case of Mink v. University of Chicago is the most informative case on battery in connection with our hypothetical research study and resulting injury. Three women alleged that in the early 1950s, without their knowledge or consent, they had been given diethylstilbestrol (DES), a synthetic estrogen, as part of a hospital-based research study, and that their children, as a result of in utero exposure

145. Id. Morreim calls for courts to explicitly recognize claims for “medical research battery” with potential punitive damages when “research is substituted for or added to treatment and the investigator has not clearly informed the patient.” Id. at 478–79.

146. Id. at 475. The substitution Morreim refers to also involves a substitution of relationships. Whereas the physician ordinarily is in a fiduciary relationship with the patient, the introduction of research into medical treatment shifts the “fiduciary physician-patient relationship to a nonfiduciary investigator-subject connection.” Id. at 478. For the implications of this shift in terms of fiduciary law, see infra Section VI(D).

147. Id. at 478.

148. Id. (apparently coining the term).


150. Id. at 1220.

151. Id.

to DES from the study, experienced an increased risk of certain forms of cancer. According to the district court’s opinion in the case, DES was given to a thousand patients at the University of Chicago’s Lying-In Hospital as part of “a double blind study to determine the value of DES in preventing miscarriages.” At the time, DES was an approved drug for miscarriage prevention.

The University moved to dismiss the plaintiffs’ battery claim, arguing that it was more properly understood as a claim for lack of informed consent, which, sounding in negligence, requires proof of actual personal injury. Because the plaintiffs alleged that their children, rather than they themselves, had been physically injured by exposure to DES, an informed consent claim could not be made.

The court refused to dismiss the plaintiffs’ battery claim, explaining that the negligence theory of informed consent was appropriate for cases in which a physician failed to disclose information to the patient; battery was appropriate when no consent was given at all. The court wrote:

“The question thus becomes whether the instant case is more akin to the performance of an unauthorized operation than to the failure to disclose the potential ramifications of an agreed to treatment. We think the situation is closer to the former. The plaintiffs did not consent to DES treatment; they were not even aware that the drug was being administered to them.”

As a matter of law, the University owed patients a duty to obtain consent for what the court described as an “experiment whereby non-emergency treatment was performed upon them.”

Liability would depend upon whether the consent the patients had given upon admission to the hospital covered the treatment they received in the study, as the

153. Id. at 715.
154. See infra text accompanying notes 167–74.
156. Id. at 716–17 (citing Cobbs v. Grant, 502 P.2d 1, 18 (Cal. 1972)).
157. Id. at 717. The drug was administered through pills ingested by patients without knowledge they were being given DES. The court explained that “[w]e find the administration of a drug without the patient's knowledge comports with the meaning of offensive contact. Had the drug been administered by means of a hypodermic needle, the element of physical contact would clearly be sufficient. We believe that causing the patient to physically ingest a pill is indistinguishable in principle.” Id. at 718.
158. Id. at 717. See also Happel v. Wal-Mart Stores, Inc., 319 F. Supp. 2d 883, 886 (N.D. Ill. 2004) (citing Mink with approval: “[t]he fact that [the plaintiffs in Mink] consented to treatment for prenatal care did not give defendants the right to treat them in any manner. Instead, that consent was limited to acts that were substantially similar to those to which there was actual consent.”) (citations omitted).
University alleged. This would be a question for the jury. The court’s opinion does not describe the document the patients signed upon admission or any conversations that might have constituted consent. The court did, however, explain that “[i]f the defendants went beyond the consent given, to perform substantially different acts, they may be liable.” Because the action would lie in battery rather than negligence, the plaintiffs did not have to prove that had they been asked to consent to DES, they would have refused.

The case ultimately settled before trial, with the three plaintiffs receiving a total of $225,000 from the University for the battery claim. The University also agreed to provide free treatment for vaginal or cervical cancer for the daughters of any women who received DES as part of the study and regular medical exams to all offspring who may have been exposed prenatally to DES from the study.

Today, the harms of DES prenatal exposure are well-established. Women exposed in utero (referred to as “DES daughters”) have higher rates of certain forms of cancer and problems with fertility and pregnancy; “DES sons” have an increased risk of testicular abnormalities. Some studies show other serious health risks for these offspring, and even some of their children—“DES granddaughters” and “DES grandsons”—because DES may cause changes to DNA that are passed on to subsequent generations.

C. Standard of Care Treatments

The research study in Mink parallels our hypothetical research study in important ways. Research interventions in both took place without prior disclosure to patients that their medical treatments were selected by a research study protocol. In both, a general consent to hospital treatment was obtained that could be argued covered the specific treatment the patients received in the study. What makes Mink so prescriptive, though, is that it also involved a research study comparing “standard of care” interventions.

DES was not an experimental drug at the time the research study in Mink took place. The FDA had approved the drug for marketing as a miscarriage preventative

159. Mink, 460 F. Supp. at 718; see also Kus v. Sherman Hosp., 644 N.E.2d 1214, 1221 (Ill. App. Ct. 1995) (explaining that for research battery claim, it would be up to the jury to determine whether the consent the patient had given was “‘substantially at variance’ with the treatment he actually received—that of an experimental nature—or whether [the patient] did or did not know of the experimental nature of the treatment.”) (citation omitted).

160. Id. at 718.

161. *Id.*

162. See Krause, supra note 140, at 309 (explaining this proof is not required).


164. Id.


166. Id.
in 1947,\textsuperscript{167} and it was widely prescribed for this purpose from the 1940s through the 1970s.\textsuperscript{168} As many as four million women in the United States alone took the drug “for the purpose of improving pregnancy outcomes.”\textsuperscript{169} Its routine use continued until the FDA issued a warning in 1971 about an increased risk of vaginal and cervical cancer in girls and young women exposed prenatally to the drug.\textsuperscript{170} As Troisi and colleagues explain, “By the time DES was formally evaluated, it was standard of care in high-risk obstetrics practices.”\textsuperscript{171} Its use even extended beyond high-risk pregnancies; at the time of the study in \textit{Mink}, manufacturers advertised DES to the medical community for “routine prophylaxis in ALL pregnancies” (emphasis in original advertisement).\textsuperscript{172} The drug was even included in some prenatal vitamins.\textsuperscript{173}

The \textit{Mink} court did not directly address whether it makes any difference to the University’s duty to obtain consent for the “medical experiment” that the patients were receiving a treatment that was within the standard of care. But the court was aware that DES had been widely prescribed to patients in the normal course of treatment in the 1950s.\textsuperscript{174} By letting the battery claim proceed and indicating the jury would decide the scope of the patients’ consent, the court necessarily rejected the idea that research consent is not required when the treatments to which patients will be randomized are within the standard of care.

\textbf{D. The Scope of Consent—A Question for the Jury}

On a battery claim relating to our hypothetical research study, the question, as in \textit{Mink}, would come down to whether random assignment to one treatment rather than

\begin{itemize}
  \item \textsuperscript{167} Hymowitz v. Eli Lilly & Co., 539 N.E.2d 1069, 1072 (N.Y. 1989). The drug was initially approved for other purposes in 1941. \textit{Id.}
  \item \textsuperscript{169} Sarina Schrager & Beth E. Potter, \textit{Diethylstilbestrol Exposure}, 69 AM. FAM. PHYSICIAN 2395, 2395 (2004).
  \item \textsuperscript{170} Rebecca Troisi, Elizabeth E. Hatch & Linda Titus, \textit{The Diethylstilbestrol Legacy: A Powerful Case Against Intervention in Uncomplicated Pregnancy}, 138 PEDIATRICS S42 (2016).
  \item \textsuperscript{171} \textit{Id.} at S43.
  \item \textsuperscript{172} \textit{Id.} at S42–S43; \textit{Healthy Baby Ad}, DES ACTION, https://desaction.org/healthy-baby-ad [https://perma.cc/3T3Z-JKEX].
  \item \textsuperscript{173} See Anita Bernstein, \textit{Hymowitz v. Eli Lilly and Co.: Markets of Mothers, in TORTS STORIES} 151, 154 (Robert L. Rabin & Stephen D. Sugarman eds., 2003).
another for research purposes was a “substantially different act” from that to which
the parents had consented.\footnote{Mink, 450 F. Supp. at 718.}

As the court in Mink noted, a general consent may cover many smaller decisions
that a health care provider makes.\footnote{Mink, 460 F. Supp. at 717–18. The court quoted
Prosser on Torts for the proposition that, in medical treatment, “[i]t is . . . possible that the consent given will be sufficiently
general in its terms to cover the particular operation (or treatment), or that the surgeon may be
authorized with complete freedom to do whatever he thinks best to remedy whatever he finds,
particularly where the patient has signed one of the written forms in common use in hospitals.”}

\textit{Id.} at 718 (quoting \textsc{William L. Prosser, Handbook of the Law of Torts} § 9, at 104 (4th
ed. 1971)).

At some unit level of decision-making, patients must defer to providers for practical reasons—the physician’s superior knowledge of
which scalpel to use, for example, or when unanticipated events require that
decisions be made while the patient is under anesthesia.\footnote{See Steven Joffe & Robert D. Truog, Consent to Medical Care: The Importance of
Fiduciary Context, in \textsc{The Ethics of Consent: Theory and Practice} 347, 355 (Franklin Miller & Alan Wertheimer eds., 2009).}

We have assumed in our hypothetical study that physicians do not usually give
parents the option of choosing between the two interventions being performed in the
study. Assuming this is reasonable, it may be true that in the \textit{medical treatment}
context, the parents’ general consent for treatment of their newborn upon delivery
would cover either Intervention A or Intervention B, as chosen by the physician.
However, that is very different from concluding that the parents’ general consent
covered the placement of their newborn into a research study that would randomize
him to either A or B.\footnote{See infra notes 189–194 and accompany text for studies showing refusal rates for
CER studies.}

\textit{Patients} entrust physicians to make decisions of this kind
because they are obligated to exercise their professional judgment to make those
decisions in the best medical interests of the patient, not for purposes of research,
which, by definition, is designed to produce knowledge for the benefit of future
patients.\footnote{See Joffe & Truog, supra note 177, at 352 (discussing “[t]rust in physicians as professionals” and “a corresponding duty of loyalty that binds physicians to their patients” in the context of fiduciary relationships). See \textit{infra} Part VI for further discussion of fiduciary duties.}

A court could potentially determine that no reasonable jury could find that a
general consent to treatment, with no mention of research, includes consent to be part
of a “medical experiment” in which patients will be randomized to standard of care
treatments. In other words, a court could determine as a matter of law that the act of
randomizing patients to treatments for research is not “substantially similar” to the
course of medical treatment that patients consent to in pursuit of their own best
medical interests. The Mink court did not discuss this possibility in its opinion. But
other courts have determined that physicians’ reliance on general or blanket hospital
forms is misplaced and that such forms are sometimes nearly “worthless.”\footnote{See, e.g., Rogers v. Lumbermens Mut. Cas. Co., 119 So. 2d 649, 652 (La. Ct. App. 1960) (holding that plaintiff’s signed general consent form did not cover removal of her reproductive organs when she specifically consented to an appendectomy and determining the

\footnote{175. Mink, 450 F. Supp. at 718.}

\footnote{176. Mink, 460 F. Supp. at 717–18. The court quoted Prosser on Torts for the proposition that, in medical treatment, “[i]t is . . . possible that the consent given will be sufficiently general in its terms to cover the particular operation (or treatment), or that the surgeon may be authorized with complete freedom to do whatever he thinks best to remedy whatever he finds, particularly where the patient has signed one of the written forms in common use in hospitals.”}

\footnote{Id. at 718 (quoting \textsc{William L. Prosser, Handbook of the Law of Torts} § 9, at 104 (4th ed. 1971)).}

\footnote{177. See Steven Joffe & Robert D. Truog, Consent to Medical Care: The Importance of Fiduciary Context, in \textsc{The Ethics of Consent: Theory and Practice} 347, 355 (Franklin Miller & Alan Wertheimer eds., 2009).}

\footnote{178. See \textit{infra} notes 189–194 and accompany text for studies showing refusal rates for CER studies.}

\footnote{179. See Joffe & Truog, supra note 177, at 352 (discussing “[t]rust in physicians as professionals” and “a corresponding duty of loyalty that binds physicians to their patients” in the context of fiduciary relationships). See \textit{infra} Part VI for further discussion of fiduciary duties.}

\footnote{180. See, e.g., Rogers v. Lumbermens Mut. Cas. Co., 119 So. 2d 649, 652 (La. Ct. App. 1960) (holding that plaintiff’s signed general consent form did not cover removal of her reproductive organs when she specifically consented to an appendectomy and determining the
particular, hospital admission forms signed by patients that waive any claims of negligence have been determined to be unenforceable as a matter of law.\footnote{See Tunkl v. Regents of Univ. of Cal., 383 P.2d 441, 447 (Cal. 1963) (finding admission form’s waiver contrary to public policy and noting that “The admission room of a hospital contains no bargaining table where, as in a private business transaction, the parties can debate the terms of their contract.”).}

Alternatively, the question of the scope of the consent would be a question of fact that would go to the jury, as it would have in \textit{Mink} had the case not settled.

In that event, the parents in our case would seek to persuade the jury that placing the infant into a research study that would determine the infant’s treatment was a “substantially different act” from that to which the parents consented. To demonstrate this difference, they could seek to introduce evidence of the traditional distinction between research and clinical care and of the long-standing ethical norm of informed consent for research, embodied in the Nuremberg Code (the highly influential set of ethical principles for human experimentation adopted to judge the Nazi doctors at trial),\footnote{The set of ten research ethics principles known as the Nuremberg Code were enumerated in United States v. Brandt, Case No. 1, Judgment, Vol. 2, 181–82 (Nuremberg Military Tribunals 1949) (The Medical Case)[hereinafter Nuremberg Code].} the Declaration of Helsinki (the international code of ethics adopted by the World Medical Association),\footnote{WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects, \textsc{World Med. Ass’n} (Sept. 5, 2022), https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ [https://perma.cc/45M5-EPQS] (“In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study.”).} the Belmont Report,\footnote{BELMONT REPORT, supra note 70 (“Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them.”).} the Common Rule,\footnote{45 C.F.R. § 46.116 (2023) (general requirements for informed consent).} and other sources of authority.\footnote{See generally Ezekiel J. Emanuel, David Wendler & Christine Grady, \textit{What Makes Clinical Research Ethical}, 283 JAMA 2701, 2701–02 (2000) (outlining seven requirements necessary and sufficient to make research ethical as found in numerous ethics codes).} Courts have allowed, and to some extent relied upon, evidence of this kind in other research injury lawsuits.\footnote{See, e.g., Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 850–51 (Md. 2001) (relying on the Declaration of Helsinki, the Nuremberg Code, and scholarly sources to establish a duty to protect research subjects from unreasonable harm and to inform participants of potential hazards); Wright v. Fred Hutchinson Cancer Rsch. Ctr., 269 F. Supp. 2d 1286 (W.D. Wash. 2002) (considering Nuremberg Code and Declaration of Helsinki in determining whether informed consent was sufficient); Whitlock v. Duke Univ., 637 F. Supp. 1463, 1470–71 (M.D.N.C. 1986) (considering Nuremberg Code, Declaration of Helsinki, and Common}
would also likely call an expert on research ethics to testify about past research scandals to explain the historical development and understanding of the ethical and regulatory norm of informed consent. A court might even allow a research ethics expert to describe the DES study as a comparable study in which two accepted treatment approaches were used in order to illustrate how such a study can have risks of harm and requires consent.

Evidence about research participation refusal rates would also be probative. When asked to participate in research, significant numbers decline—roughly thirty percent—and this appears to hold true whether the study compares standard of care treatments or is another type of study. If patients refuse at such high rates upon being asked to participate in research using standard of care treatments, it is difficult to presume that their general consent to treatment, which includes no mention of research or randomization between treatments, should be read to include it.

Survey data suggest a jury representative of the American public would have a negative view of comparative effectiveness studies without specific research consent. Five studies of nationally representative populations have recently examined public attitudes on waivers and alterations of consent for comparative effectiveness research that is deliberately integrated into the delivery of medical care. Employing hypothetical research scenarios, researchers conducting these

Rule to determine the disclosures owed by a researcher in a research study not involving medical treatment); In re Cincinnati Radiation Litig., 874 F. Supp. 796, 821 (S.D. Ohio 1995) (writing that “[t]he Nuremberg Code is part of the law of humanity. It may be applied in both civil and criminal cases by the federal courts in the United States”). But see Ancheff v. Hartford Hosp., 799 A.2d 1067, 1079 (Conn. 2002) (affirming trial court’s decision to exclude from evidence Belmont Report—which plaintiff sought to introduce for definition of research—because doing so would be unfairly prejudicial).

188. See, e.g., Grimes, 782 A.2d at 807 (allowing such expert testimony).

189. See Lin et al., supra note 101, at 4 (“[T]he rate of refusal in P&CE [Pragmatic and Comparative Effectiveness] RCTs is roughly the same as for other types of research . . . . [T]he average refusal rate found here should raise a flag about the appropriateness of use of waivers in P&CE trials, because participation is presumptively unacceptable to an average of one-third of potential participants . . . .”), Baker & Merz, supra note 29, at 582 (also finding approximately one-third of people do not take part in research when asked). For example, the Acute Respiratory Distress Syndrome Network (ARDS-Net) ARMA trial, a comparative effectiveness study randomizing patients requiring mechanical ventilation to one of two tidal volumes, had a refusal rate of 28.0%. The ARMA trial operated under a waiver of consent at one of ten sites. Id.; see also Katheria et al., supra note 10, at 1879 (in the placental transfusion study, which operated under a waiver of consent if consent could not be obtained because delivery was imminent, 347 of 932 (37%) of pregnant women meeting eligibility criteria for the study refused to consent; twenty-four even refused to provide “deferred consent” post-intervention).

190. Baker & Merz, supra note 29, at 583 (arguing that the unwillingness of a plurality of people to participate in research suggests that any presumption of consent would be mistaken).

191. Stephanie R. Morain & Emily A. Largent, Public Attitudes Toward Consent When Research Is Integrated into Care—Any “Ought” from All the “Is?” 51 HASTINGS CTR. REP. 22, 23 (2021) (referring to the types of studies that these surveys were concerned with as “pragmatic research,” which they used as “an umbrella term . . . to cover PCTs, comparative effectiveness research (CER), research on medical practices (ROMP), and other approaches that deliberately integrate research into the...
studies asked participants about the acceptability of four different approaches to consent—traditional written consent, streamlined consent (e.g., verbal consent or a brief written consent), general notification to patients of a health system, and post-enrollment notification. Morain and Largent write that “A consistent finding across these surveys is that most respondents prefer prospective, study-specific consent to other approaches.” Importantly, bypassing consent and providing only notification of the study to those participating, either before or after enrollment, was unacceptable to a “supermajority.”

The fact that in our hypothetical study, versus the study in Mink, the care is time-sensitive may be raised by the defendant physician, but this is unlikely to be persuasive on the question of whether the parents’ general consent covered research employing treatment randomization. The treatment in our hypothetical study may have been time-sensitive after the baby was born, but there was time to obtain consent before delivery. Physicians routinely seek consent to use forceps or to perform cesarean sections in the midst of active labor, even for premature births; they also routinely seek consent for neonatal research interventions.

An emergency context might yield different results. There are specific regulatory guidelines for waiving consent for research in emergency contexts; waiver can only be granted in situations that are life-threatening, where no proven therapy exists, and when it is impossible to obtain consent in the therapeutic window. Consultation
with and public disclosure to the communities from which research subjects will be
drawn is also required.\footnote{197} Courts applying the common law might be similarly open
to permitting a waiver of consent in similar emergency contexts because of the
potential for benefit to the patient beyond what is otherwise available outside of the
study. But that is not the case here.

In sum, the plaintiff in our case could bring a persuasive case for battery. \textit{Mink}
provides strong support for the proposition that a general consent to treatment does
not equate to consent to be randomized to a treatment for research purposes, even
when the treatment is considered to be within the acceptable standard of care.

V. LACK OF INFORMED CONSENT—A CLAIM IN NEGLIGENCE

\textbf{A. Negligence in Obtaining Informed Consent for Research and for Medical Care}

While carefully specified in the federal regulations governing human subjects
research,\footnote{198} the requirement to obtain informed consent from human subjects for
research in general is underdeveloped in the common law, and as Francis Baker and
Jon Merz have pointed out, analysis is “long overdue” concerning when research
may be conducted without consent.\footnote{199} Nevertheless, Jon Merz reported in 2018 that
a review of the caselaw found nineteen published opinions “that recognize the duty
of researchers to secure an informed consent from research participants.”\footnote{200} “Without
exception,” he wrote, “every court in which the issue has been presented on the
merits has found that research participants have the right to consent.”\footnote{201} Our own
more recent review confirmed a similar number of research informed consent cases,
and the equally unqualified consensus among them that research participants have a
right to consent.

To date, however, there is no clearly established and precise statement of the
elements of a negligence claim for lack of informed consent in research. There are
likely several reasons for this. First, though research-injury cases are on the rise, they
are still rather uncommon.\footnote{202} Claims based in negligence generally require proof that
plaintiffs suffered physical harms from the negligent acts of others and, in many

\begin{footnotes}
\item[198] See supra text accompanying note 8.
\item[199] Baker & Merz, supra note 29, at 579.
\item[200] Jon F. Merz, The Nuremberg Code and Informed Consent for Research, 319 JAMA
85, 85 (2018).
\item[201] Id. (“The only courts that have not so concluded are those that found plaintiffs’ claims barred by statutes of limitation or other policies limiting the civil liability of the federal government.”).
\end{footnotes}
instances, research participants will have trouble proving their injury came from research interventions rather than their underlying and preexisting medical condition. In cases of injury to “healthy volunteers” or participants with mild conditions, injury related to research should be easier to prove, but quick settlements are common in such suits, allowing research institutions to reduce negative publicity and also to keep court-imposed rules for the conduct of research at bay. Second, the cases that result in published opinions involve a wide variety of research studies: some interventional and others noninterventional, some medical and others nonmedical. One court has noted—in a case involving research on biospecimens—that “the law regarding a duty of informed consent for research subjects is unsettled and fact-specific.” Finally, for studies that involve randomizing among medical treatments or other interventions, the requirement of research consent is usually assumed by the court and all parties; defendant researchers, who have generally obtained some measure of consent, base their defense instead on the quality of the disclosures they have made to subjects.

Thus, while researchers clearly owe legal duties to obtain consent from research subjects when they intervene in their lives, and a separate “research informed consent” claim can be brought, the plaintiffs in our hypothetical lawsuit have a more readily available claim for lack of informed consent as a subset of medical negligence, or medical malpractice law. The requirement of physicians to obtain informed consent for medical treatment is very well established, and the elements of a cause of action for failure to obtain informed consent are clear. When a physician provides medical treatment, whether as part of purely clinical care or when clinical care and research are combined, informed consent for that treatment must be obtained.

203. See id. at 79 (explaining that in Heinrich v. Sweet, 308 F.3d 48 (1st Cir. 2002) “the First Circuit ultimately determined that people with terminal brain cancer had no cause of action for wrongful death when they were allegedly subjected to experimental radiation treatments, because there was no evidence that the experiment hastened these patients’ already-imminent deaths.”).


205. Greenberg v. Miami Child.’s Hosp. Rsch. Inst., Inc., 264 F. Supp. 2d 1064, 106970 (S.D. Fla. 2003) (distinguishing between “medical research” like the defendants’ research on biospecimens and “human experimentation” and holding that “in certain circumstances a medical researcher [who is not in a therapeutic relationship with a subject] does have a duty of informed consent,” but that duty did not extend to a researcher’s economic interests). But see Moore v. Regents, 793 P.2d 479 (Cal. 1990) (holding that a physician must disclose research and economic interests that may affect their medical judgment in providing patient care).

206. See, e.g., Univ. Med. Ctr., Inc. v. Shwab, 628 S.W.3d 112, 120 (Ky. 2021) (defendants asserted that the consent form sufficiently informed plaintiff “of all known or reasonably anticipated risks associated with participation in the clinical trial”); see also Greenberg; 264 F. Supp. (defendant researchers did not question that the duty to obtain informed consent is owed to patients receiving medical treatments).

207. See Shwab, 628 S.W.3d at 130–31 (rejecting defendants’ argument that Kentucky’s
component of the treatment are required; combining medical treatment and research generally only adds more requirements for disclosure and consent; it certainly does not reduce them. To successfully bring a claim for lack of informed consent for medical treatment, a plaintiff must generally prove the following elements:

(a) the physician failed to disclose information about a risk of treatment that the physician had a duty, under the governing standard, to disclose;
(b) a reasonable patient would have decided not to undergo the procedure as proposed (causation); and
(c) the patient suffered a physical harm stemming from the undisclosed risk (injury/damages).

Informed consent law did not apply to a Phase I clinical trial because no physician-patient relationship existed: “[W]e conclude that a physician-patient relationship clearly does exist, . . . and our . . . informed consent law, tied to standards of accepted medical practice and an objective assessment of the information provided to the patient, adequately protects the interests of both patients and medical care professionals participating in a clinical trial.” Heinrich v. Sweet, 308 F.3d 48, 69 (1st Cir. 2002) (explaining that “a doctor who proposes an experimental course of treatment must not only tell the patient about the treatment and its consequences, but must also inform the patient that he is conducting an experimental treatment and that the patient is part of a study. The doctor must not only tell the patient the known risks of the treatment, as he would in a conventional setting, but must also inform the patient that there may be unknown risks.”) (emphasis added). 208. Shwab, 628 S.W.3d at 130–31 (noting that defendant researchers were required to meet both the informed consent requirements for medical treatment and the additional research informed consent requirements under FDA regulations). The Belmont Report notes that “the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care.” Belmont Report, supra note 70. 209. See, e.g., Spar v. Cha, 907 N.E.2d 974, 979–80 (Ind. 2009) (“To succeed on a lack of informed consent action, the plaintiff must prove ‘(1) nondisclosure of required information; (2) actual damage . . . (3) resulting from the risks of which the patient was not informed; (4) . . . the plaintiff would have rejected the medical treatment if she had known the risk; and (5) that reasonable persons, if properly informed, would have rejected the proposed treatment.’” (quoting Dan B. Hobbs, The Law of Torts § 250 (2001))). 210. See, e.g., Cobb v. Grant, 502 P.2d 1, 10 (Cal. 1972) (en banc) (holding that an “integral part” of the physician’s obligation to the patient “is a duty of reasonable disclosure of the available choices with respect to the proposed therapy and the dangers inherently and potentially involved in each”); Harbeson v. Parke Davis, Inc., 746 F.2d 517, 525 (9th Cir. 1984) (holding that “a risk must be disclosed even if it is but a potential risk rather than a conclusively determined risk”). 211. Krause, supra note 140, at 317, 321 (explaining most jurisdictions have adopted this “objective” test of causation, often maligning by scholars for its failure to respect patient autonomy; a patient may prefer, for example, a less disfiguring lumpectomy to a radical mastectomy, but, when that alternative is not offered and the patient is cured by the radical mastectomy, “arguably the only injury sustained is to the patient’s dignity,” and “negligence doctrine . . . has not been sympathetic to intangible harms.”). 212. Because the children in our hypothetical study were already at risk of death and other
The standard by which to determine what information should be disclosed differs according to whether a state follows the “reasonable patient” standard\textsuperscript{213} or the “reasonable physician” standard.\textsuperscript{214} U.S. jurisdictions are about evenly split on which of these two general disclosure standards they follow.\textsuperscript{215} In states employing the reasonable patient standard, a jury generally determines what a reasonable patient would find material in making a treatment decision.\textsuperscript{216} In a jurisdiction that follows the reasonable physician standard of disclosure, an expert witness would need to testify as to what a reasonably prudent physician would disclose.\textsuperscript{217}

harms from their underlying prematurity, it may be challenging to prove the choice of intervention more likely than not caused a particular child’s death (the traditional causation standard). The plaintiff parents may instead only be able to show that their child faced an increased risk of death by being randomized to Intervention A (and the study’s own statistical conclusions are evidence to which they can point). Yet this may be sufficient in jurisdictions—now the majority—that recognize the “loss of chance” doctrine in medical malpractice suits. See Matsuyama v. Birnbaum, 890 N.E.2d 819, 828 n.23 (Mass. 2008) (collecting cases). “Loss of chance” in medical malpractice suits allows recovery when a provider’s negligence reduces a patient’s chance for survival or recovery. For example, a physician’s failure to order certain diagnostic tests might mean that a patient’s chance for her cancer to be detected and cured was reduced; under the “loss of chance” doctrine, damages could be allowed even if early diagnosis would not always or even usually result in cure. See David A. Fischer, Tort Recovery for Loss of Chance, 36 WAKE FOREST L. REV. 605, 612 (2001). The doctrine of loss of chance can be understood as either a relaxation of the traditional more-likely-than-not standard, or as a separate injury in and of itself. See Stephen Paul, Note, Proving Causation in Clinical Research, 108 VA. L. REV. 535, 558–560 (2022). Damages under the loss of chance doctrine are generally lower than if the plaintiff can prove injury by traditional causation standards. Many courts hold the provider responsible only for that percentage of the patient’s injury represented by the reduced chance of survival or recovery. See Fischer, supra, at 611 (explaining that where a physician’s failure of diagnosis “deprive[s] the patient of a 40 percent chance of survival . . . [u]nder the loss of a chance theory, some courts hold the physician liable for 40 percent of the damages caused by the patient’s death, and other courts hold the physician liable for all the damages.”). Though the trend is toward greater acceptance of the loss of chance doctrine, some jurisdictions do not recognize it, and this can doom a lawsuit before a court even considers what duties a physician-researcher may owe to patients. See supra note 61 (discussing award of summary judgment for SUPPORT investigators because Alabama does not recognize loss of chance doctrine).

\textsuperscript{213} Also called the “material risk” standard. Morse & Wilson, supra note 29, at 405.

\textsuperscript{214} Also called the “professional standard.” Id.


\textsuperscript{216} See, e.g., Canterbury v. Spence, 464 F.2d 772, 787 (D.C. Cir. 1972) (stating that a risk is material “when a reasonable person, in what the physician knows or should know to be the patient’s position, would be likely to attach significance to the risk or cluster of risks in deciding whether or not to forego the proposed therapy.” (omitting citation)).

\textsuperscript{217} See, e.g., Di Filippo v. Preston, 173 A.2d 333, 339 (Del. 1961) (“Whether or not a physician or surgeon is under a duty to warn a patient of the possibility of a specific adverse result of a proposed treatment . . . must be established by expert medical testimony.”). Note that the Common Rule revision in 2018 incorporated a “reasonable person” standard for disclosures in consent forms and processes. 45 C.F.R. § 46.116(a) (2023). See Revised Common Rule Q&As, supra note 111 (“One change is introducing the requirement that
B. Lack of Informed Consent Claim for Comparative Effectiveness Research

Most lack of informed consent claims are about undisclosed risks. Our case is a bit different in that the very fact of research activity has remained hidden, along with the attendant risks of being randomized to a treatment arm that could prove to be substantially inferior. Given that the practice of randomizing patients to medical treatments according to a research protocol differs so substantially—differs in kind—from the usual practice of medical treatment, it is possible a court could determine that as a matter of law the physician has a duty to disclose the existence and purpose of the study as well as the comparative risks being studied. (We have argued above that such disclosures are already required as a matter of regulatory law for research governed by the federal regulations, making negligence per se a possibility.)

Determining that these disclosures are required as a matter of law would mean the jury would be left only with determining whether any such disclosures were made and whether they were adequate to cause the parents’ general consent to treatment to be informed, as in Mink. (This, in fact, appears to be what happened in Burton v. Brooklyn Doctors Hospital, discussed in Section C, which, like Mink, also involved an early trial comparing standard treatments without obtaining patient consent).

If, instead, the plaintiff had to prove that disclosures about the research activity were required under either the “reasonable patient” standard or “reasonable physician” standard, this should not be difficult to do.

informed consent must give prospective subjects the information that a reasonable person would want to have in order to make an informed decision about whether to participate.”)

218. Most jurisdictions have held that an unexcused violation of federal or state law constitutes negligence per se. See Roger L. Jansson, Researcher Negligence in Human Subject Research: Informed Consent and Researcher Malpractice Actions, 78 WASH. L. REV. 229, 245 (2003). Patient-subject plaintiffs have thus argued that failure to obtain informed consent consistent with the requirements in 45 C.F.R. § 46.116 (2023) (the “Common Rule”) constitutes negligence per se. See, e.g., Complaint with Jury Demand at 20–21, Buckley v. Hennepin County, No. 0:18-cv-03124 (D. Minn. Nov. 7, 2018). Although the authors are unaware of a case in which a defendant has been found negligent per se for violating the Common Rule, courts have looked to the stringent disclosure requirements of 45 C.F.R. § 46.116 when determining the type of disclosures required under state law in lack of research informed consent cases. See, e.g., Whitlock v. Duke Univ., 637 F. Supp. 1463, 1471 (M.D.N.C. 1986) (analyzing informed consent requirements under North Carolina law to include disclosure of “any reasonably foreseeable risks” to subjects in a nontherapeutic experiment consistent with the Common Rule). In Daum v. SpineCare Med. Grp., Inc., the court held plaintiff-subjects were entitled to an instruction on negligence per se relating to defendant physician’s failure to obtain informed consent as required by FDA regulations to which he had agreed to comply. 61 Cal. Rptr. 2d 260, 273–277 (Ct. App. 1997). In addition, the jury should have been allowed to consider the informed consent requirements in the FDA regulations in determining what plaintiff-subject should have been told and how, rather than being instructed to rely solely on expert medical testimony. Id. at 271.

219. 452 N.Y.S.2d 875 (App. Div. 1982). See also infra Section VI.E for a discussion of Moore v. Regents of Univ. of Cal., 793 P.2d 479 (Cal. 1990) (holding that under informed consent law, disclosure of physician’s research interests is required because it would be material to a reasonable patient’s decision to consent to a proposed course of treatment).
Most parents, the plaintiffs would argue, would want to know if their child’s medical treatment were going to be determined by a research study employing randomization, rather than chosen by the child’s treating physician in the exercise of their professional judgment to advance the best interests of the child, even in the face of uncertainty. This is especially so when, as in our case, the treatments received in the study may have serious health consequences and entail such a degree of comparative uncertainty. Although the physician was unable to quantify the differential risks and benefits of the two treatments (because the study had not been done yet), the physician should have told parents the purpose of the study, including the reason for randomization, and what was known at the time about the potential risks and benefits of the interventions being compared, along with the fact that both were known to be better than doing nothing. 220 Although a reasonable parent may expect their general consent to a course of treatment to include myriad technical, means-oriented decisions that a physician typically makes, they would not expect to be kept in the dark when a decision is made to place their child in a research study where decisions of that nature will be made through a randomization process. Given the public’s negative views about comparative effectiveness studies without specific, prospective consent, 221 it seems likely that a jury would agree that such disclosures would be material to a reasonable parent’s consent to treatment for their child.

If the case were heard in a jurisdiction that followed the “reasonable physician” standard, plaintiffs should not find it difficult to obtain an expert to testify that a reasonable physician randomizing their patients to different treatments for research purposes would typically disclose that fact, as they are required to do by longstanding ethical norms and research regulations. 222 Reasonable physicians, the expert

220. The argument that the comparative risks between study arms were not known (and therefore could not be disclosed) was made by the SUPPORT investigators and some of those who defended the consent forms in that study. The research regulations require that reasonably foreseeable risks be disclosed, 45 C.F.R. § 46.116, and if the purpose of a study is “to determine the existence, likelihood, or magnitude” of certain harms, then they are reasonably foreseeable even when the actual comparative risks are unknown. Shepherd, supra note 45, at 358. See also OHRP Draft Guidance, supra note 60. If, counter to our hypothetical, there were any aspect of the interventions that had been standardized for purposes of the study—e.g., the physician will wait x many seconds before doing y; or in the event of w complication, will administer z—then those changes to usual care should have been disclosed as well, along with any reasonably foreseeable risks associated therewith.

221. See supra text accompanying notes 186–191; see also E. Burgess N. Singhal, H. Amin, D. D. McMillan & H. Devrome, Consent for Clinical Research in the Neonatal Intensive Care Unit: A Retrospective Survey and a Prospective Study, 88 Archives Disease Childhood Fetal & Neonatal Ed. F280, F281 (2003) (In a Canadian study of parental attitudes about consent for clinical trials in the NICU, “[m]ost parents (93%) disagreed with the idea of the doctor making the decision to enroll the newborn into a research study and then informing the parents.”). 222. Indeed, the Common Rule requires that prospective research subjects “be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.” 45 C.F.R. § 46.116(a)(4). See also OHRP Draft Guidance, supra note 60; Morse & Wilson, supra note 29. Morse and Wilson point out that even if the physician custom were to not disclose in these research circumstances, “courts sometime refuse to be guided by physician practice.” Id.
could further testify, also explain what is known or being studied about the comparative risks and benefits that may be associated with the two interventions. The expert could also testify that formal regulatory waivers of research-informed consent were not intended to be applied to studies in which patients were randomized to different medical interventions. These types of disclosures should be and typically are made by investigators in comparative effectiveness trials, the vast majority of whom do still seek and obtain consent prior to enrolling patients in a research study.

In sum, in a negligence action, whether it is the court or a jury that will determine the kind of disclosures required, it would be surprising if a physician had no duty to disclose and obtain consent before placing their patient into the types of research studies discussed here, even if relieved of the requirement for regulatory research informed consent by an IRB approving a waiver of this process (which, as we have explained earlier, we think would be inconsistent with the federal regulations).

We turn now to proof of causation, which can be a vexing hurdle in any medical informed consent case. As Morse and Wilson have pointed out, even if a patient can prove required disclosures were not given, it is difficult to win a medical informed consent claim: “If a prudent person in the patient's position would have undergone the procedure, plaintiffs cannot make out the third prong [causation] for recovery.” “Objective causation,” these authors point out, “reduces informed consent to 'an almost useless claim' when a statistical majority of patients would choose to proceed with treatment regardless of the risks.”

The physician actually has a good argument that a reasonable parent would not—in fact, should not—prefer one intervention over the other. The medical community as a whole has not agreed that one is better than the other, and the physician in the study also does not have a belief that one is preferable. If parents were expected to prefer one intervention to the other for their child, then the duty to obtain informed consent for medical treatment (i.e., when no research is taking place) would require they be given that choice and the disclosures to go along with it. Instead, the custom and practice (which we’ve assumed in the hypothetical to be acceptable) has been to allow a general consent to treatment to cover the physician’s choice between interventions, rather than to ask the patient to specifically consent to one or the other.

But research is different. Franklin Miller and Scott Kim point out that, although patients may not have a preference between the treatments to which they may be randomized in a clinical trial, they have a legitimate expectation and authority to decide whether to enter a clinical trial or not. Participation in research in the United States is voluntary. We do not judge a person’s decision to participate or not as automatically flawed.

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223. See Kassels & Merz, supra note 74.
224. See Lin et al., supra note 101, at 4 (finding that only a small number of comparative effectiveness trials not involving behavioral interventions waived consent).
225. See supra Section II.B.
226. Morse & Wilson, supra note 29, at 406.
227. Id.
228. See Miller & Kim, supra note 66.
decline to participate in research by a standard of “reasonableness”; no one is required to justify their decisions about research participation, which can be made for highly subjective reasons. The objective causation standard typically followed in medical informed consent cases does not fit a cause of action for clinical research without consent and it is uncertain whether a court would impose it in a case like ours.

But if a court did, a jury could easily determine that a reasonable person would decline to participate in a standard of care trial of this sort. We know from high refusal rates that many do decline research participation when asked, for comparative effectiveness trials and even for non-interventional studies. Some may be uncomfortable that research goals would drive medical treatment in a particular instance. Others may distrust the research enterprise generally. In addition, in a case such as ours, a reasonable person could well prefer a physician who did profess a belief that one intervention was better for the patient and switch to a physician who exhibited more certainty and confidence in a particular treatment. They could also prefer a physician to provide the intervention that they usually provided rather than the alternative, believing (rightly or wrongly) that the physician would be more skilled at providing that intervention. Above all, they could prefer a physician who was honest and upfront with them.

C. Burton v. Brooklyn Doctors Hospital

In the 1982 case of Burton v. Brooklyn Doctors Hospital, a patient successfully sued for lack of informed consent relating to alterations to his medical care from placement in a CER study. This case involved a study similar to the SUPPORT Study that took place in the early 1950s. Daniel Burton claimed he had been

229. See supra text accompanying notes 186–91.
230. See, e.g., Raegan W. Durant, Anna T. Legedza, Edward R. Marcantonio, Marcie B. Freeman & Bruce E. Landon, Different Types of Distrust in Clinical Research Among Whites and African Americans, 103 J. NAT’L MED. ASS’N 123, 123 (2011) (noting that “distrust is the most frequently cited disincentive for research participation among minority populations”); Geri L. Schmotzer, Barriers and Facilitators to Participation of Minorities in Clinical Trials, 22 ETHNICITY & DISEASE 226, 227 (2012) (reporting that “patients were fearful of the concept of experimentation, did not want to be experimented on or feel like a ‘guinea pig’”).
231. In Cobbs v. Grant, a California Supreme Court case cited in the Burton opinion (discussed infra Section V.C.), the court explained that once the doctor, “being the expert,” has explained the risks of a procedure and the probability of success, “that aspect of the doctor’s expert function has been performed. The weighing of these risks against the individual subjective fears and hopes of the patient is not an expert skill. Such evaluation and decision is a nonmedical judgment reserved to the patient alone.” 502 P.2d 1, 10 (Cal. 1972). Annas and Annas, similarly write: “It is the patient’s life and future that is at stake, and the patient has a legal right to rely on the physician to disclose information that affects their decision to put their life and future in the physician’s hands.” Annas & Annas, supra note 29, at 21.
233. See Annas & Annas, supra note 29. To our knowledge, George Annas was the first to bring this case to the attention of the research ethics community in the context of the controversy surrounding the SUPPORT study. See also U.S. Dep’t of Health & Human Servs.,
treated as a premature infant in a clinical study of supplemental oxygen without his parents’ knowledge or consent and experienced blindness as a result. His action was based on medical malpractice and lack of informed consent, rather than battery.

At the time of plaintiff’s birth in 1953, the court explained, although “liberal exposure to oxygen continued to be routine treatment for premature babies . . . the view that increased oxygen was a necessary life saver had . . . become suspect.”

Prolonged liberal use of oxygen was suspected to be a primary contributor to retrolental fibroplasis (RLF), a progressive disease that can result in blindness.

Burton arrived at New York Hospital, one of the defendants in the case, as the hospital was participating in a national study to compare levels of oxygen supplementation that placed one out of every three premature infants under a certain weight in an increased oxygen environment, while the other two-thirds would receive reduced oxygen.

Burton was transferred to New York Hospital a day after birth, having received supplemental oxygen from the time of birth to the time of transfer. A pediatric resident, Dr. Ross, examined him upon arrival and concluded he was “a vigorous premature infant” who could tolerate a reduction in supplemental oxygen.

Concerned that increased oxygen contributed to RLF, the resident placed an order that, he later testified, was “good medical practice and in accordance with [my] judgment.”

This order was initially followed, and the infant did well with concentrations of oxygen between 30% and 35%. On the plaintiff’s third day in the hospital, however, a physician on the hospital’s staff, Dr. Engle, countermanded Dr. Ross’s order and placed the plaintiff in the national oxygen study. Thereafter, Burton was placed in an environment of prolonged oxygen at a concentration greater than 50% and at one point up to 82%. Dr. Engle did not examine the plaintiff or speak to his parents. She had no responsibility to care for or treat premature infants in the hospital or to supervise the residents, serving instead as the point person for coordinating the hospital’s participation in the study.

At trial, the jury found Dr. Engle and New York Hospital liable under theories of medical malpractice and lack of informed consent; Dr. Ross was found liable for failing to obtain informed consent. On appeal, the New York appellate court affirmed the verdicts against Dr. Engle and the hospital but reversed the verdict against Dr. Ross because he did not order the increase in oxygen and his own order to reduce it had been countermanded.


235. Now called Retinopathy of Prematurity (ROP), the same condition studied in SUPPORT. See Annas & Annas, supra note 29, at 22.

236. The court noted that “[t]his method of distribution was designed to subject the least number of babies to the risk of blindness that statistics would permit.” Burton, 452 N.Y.S.2d at 878.

237. Id. at 877–78.

238. Id. at 878 (alteration in original).

239. Id. at 879.
One of the primary arguments Dr. Engle and the hospital advanced on the medical malpractice claim was that the liberal administration of oxygen delivered through the research study was the standard of care at the time and that “the medical community was unsure whether premature babies were better or worse off in routine (increased) oxygen.”240 This defense fell flat: “Adher[ing] to acceptable practice” does not “automatically” free a physician from liability; instead, a physician must “employ his expertise or best judgment.”241 Dr. Engle, in particular, could not have been acting according to “acceptable medical practice” because she was making “an administrative judgment, based upon a random allocation of babies,” rather than exercising medical judgment.242

The court concluded that Burton should never have been placed into the study without his parents’ informed consent.243 Burton commenced his suit in 1975, having filed the complaint once he was an adult.244 The defendants argued that the study took place before the legal doctrine of informed consent was formally recognized by a court in New York—or in any state.245 They argued that no legal duty to inform the parents of the study or the increased oxygen environment existed at the time of the study. The court disagreed. It found that the practice at the time of plaintiff’s treatment was sufficient to establish the duty to obtain informed consent. Dr. Engle’s own testimony was “that it was the hospital’s practice, quite apart from any written consent, to have the house officer or resident, in this case Dr. Ross, inform a patient’s parents of all the risks involved and the options available before any patient was put into an experimental study.”

The plaintiff also brought in an expert witness, a medical doctor, who “although not a physician in 1953, stated that the practice for ‘centuries’ had been to inform patients of the type and risks of treatment, and to obtain their consent.”246

240. Id. at 878.
241. Id. at 880. For this proposition, the court quotes an earlier New York case which explains that while conformity to community standards of practice “usually insulates [a physician] from tort liability . . . [t]here is, however, a second principle involved in medical malpractice cases[,] . . . that a physician should use his best judgment and whatever superior knowledge, skill and intelligence he has. . . . The necessary implication of this latter principle is that evidence that the defendant followed customary practice is not the sole test of professional malpractice. If a physician fails to employ his expertise or best judgment, and that omission causes injury, he should not automatically be freed from liability because in fact he adhered to acceptable practice.” Toth v. Cmty. Hosp. at Glen Cove, 239 N.E.2d 368, 372–73 (N.Y. 1968) (citations omitted).
243. The court did not condemn the research study as a whole, as courts have sometimes done. See, e.g., Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 815–16 (Md. 2001) (In a case involving a study that assessed the impact of residential lead paint on children’s blood lead content, the Court compared it to the USPHS Syphilis Study and stated: “The research relationship proffered to the parents of the children the researchers wanted to use as measuring tools, should never have been presented in a nontherapeutic context in the first instance.”).
244. Burton, 452 N.Y.S.2d at 879.
245. Id. at 881.
246. Id.
247. Id.
The question for members of the jury was whether the defendants had met the duty to obtain consent that the court determined existed as a matter of law. Burton's parents had signed a consent form upon his hospital admission, which the court described as "general in nature and authorized 'the doctors of the New York Hospital to give such treatment and medication to my son which in their judgment becomes necessary while he is a patient in the New York Hospital.'" The general consent even "waived all claim to prior notification of any treatment." The jury found this written general consent to be insufficient to show that the duty of informed consent had been satisfied. The consent form did not relieve the hospital or Dr. Engle of their obligation to obtain permission from the plaintiff's parents to enroll him in a research study that would determine his course of treatment. The New York appellate court affirmed this judgment, determining that the consent form was inadequate to meet the duty of informed consent that existed even by the standards of physicians at that time, in 1953.

The jury awarded Burton $2,887,000; the appeals court determined this amount was excessive and reduced the award to $1,500,000.

D. Informed Consent and Protocolized vs. Personal Care

It is important to emphasize that Burton's claim was specifically about unconsented-to protocolized care received through a research study, rather than a complaint about hospital protocolized care in general. Appreciating this distinction is critical because proponents of conducting comparative effectiveness research without consent often liken it to the curtailment of physician discretion and lack of patient choice that happens when hospitals adopt protocols that dictate patient care.

Physicians and other health care providers sometimes follow hospital-wide protocols developed for treating large groups of similarly situated patients. NICUs, for example, generally target a certain oxygen level for premature infants based on professional or clinical practice guidelines, although variation for individual patient care and the application of professional judgment is still expected. Assuming that adoption of a treatment protocol is ethically and legally acceptable, does it matter if a hospital adopts a protocol to improve patient care versus adopts it for the purpose

248. Id. at 880.
249. Id.
250. Id. at 878, 881.
251. Id. at 882. As compared to the SUPPORT plaintiffs, Burton was able to overcome the hurdle of proving actual injury from his treatment in the national oxygen study. The Court's opinion discusses how he was a "vigorous" infant, doing well on reduced oxygen before being placed in the high oxygen research environment. His progressive eye disease was observed by physicians over many days, yet they did not remove him from the study. Id. at 877–79.
253. See Lantos & Feudtner, supra note 252.
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of research, i.e., to systematically compare how patients fare under that protocol to another course of medical treatment?

Ancheff v. Hartford Hospital\textsuperscript{254} says it does and provides further support for the need to obtain informed consent before enrolling patients in studies randomizing patients to accepted medical treatments. In that case, the plaintiff claimed he was the subject of medical research when treated in the hospital with a protocolized daily dosage of the antibiotic Gentamicin for a deep wound infection that developed following back surgery. Although Ancheff’s physician initially ordered a lower dose of Gentamicin, the hospital pharmacy automatically increased that dosage pursuant to an inpatient dosing program adopted by the hospital.\textsuperscript{255} The physician thereafter examined the patient and “determined that the increased dosage was appropriate.”\textsuperscript{256} The higher dosage allegedly caused the plaintiff to suffer side effects from the drug, including permanent hearing loss.\textsuperscript{257}

The critical issue of the case was whether the Gentamicin dosing protocol constituted medical research or clinical care.\textsuperscript{258} If research, the requirement of informed consent was taken as a given. On appeal, the court noted that “[t]he hospital did not challenge the proposition that, if the Gentamicin program had constituted medical research,” a consent form for research “would have been required.”\textsuperscript{259} According to the court, “the critical issue was whether the hospital was required to secure written consent from the plaintiff because, as he claimed, the Gentamicin program of medication constituted medical research.”\textsuperscript{260}

Five expert witnesses testified on the research/clinical care distinction, one for the plaintiff and four for the defendant.\textsuperscript{261} The jury ultimately determined that although the protocolized dosage was higher than commonly used, the dosing program had not been adopted for research purposes. Patients were not randomized and there were no comparison groups. The jury accepted the hospital’s defense that it had adopted the dosing protocol for the purpose of improving patient care and safety, not research. The higher dosage was ultimately adopted by most hospitals.\textsuperscript{262}

\begin{thebibliography}{99}
\bibitem{254} 799 A.2d 1067 (Conn. 2002).
\bibitem{255}  Id. at 1069–70.
\bibitem{256}  Id. at 1069.
\bibitem{257}  Id. at 1070.
\bibitem{258}  See id. at 1081. On appeal, the Connecticut Supreme Court considered narrow issues of whether the trial court had properly excluded the Belmont Report, offered in its entirety, and whether it had issued appropriate jury instructions. See id. at 1082.
\bibitem{259}  Id. at 1070 (emphasis in original).
\bibitem{260}  Id. at 1081 (emphasis in original). The requirement for written consent comes from federal research regulations. See id. at 1070.
\bibitem{261}  Id. at 1072. Among other things, the plaintiff’s expert witness pointed out that the program involved “the systematic collection of data” which was “not in the [patient’s medical] chart, but in a research office,” and that “the purpose of the program ‘was to be able to publish [its results] in the medical literature and in newsletters for the hospital staff.’” Id. at 1071 n.10 (alterations in original). Defense experts, in opining that the program was not medical research, focused on the fact that there was no control or comparison group and that there was substantial prior research supporting the program. See id. at 1072. Our hypothetical case clearly involves research.
\bibitem{262}  See id. at 1069.
\end{thebibliography}
In our hypothetical case, there is no question that patients' care is being randomized for research purposes. Both Burton and Ancheff provide persuasive precedent for the proposition that before patients are placed in a research study that randomizes them to standard of care treatments, they must be asked for specific research consent. This duty is owed by physicians and sometimes, as evidenced in these cases, by hospitals as well.

VI. BREACH OF FIDUCIARY DUTY

Battery and informed consent claims redress primarily infringement of patients' bodily integrity and autonomy. But placing patients into research that randomizes them to medical treatments without telling them also raises issues of trust, promise-keeping, and truth-telling. This makes fiduciary law particularly apt for applying to comparative effectiveness studies without consent. Physicians are widely recognized to be in a fiduciary relationship with their patients, requiring them to exercise their professional judgment to pursue their patients' best medical interests above all other interests.

Like a claim in battery, the plaintiff in a breach of fiduciary duty claim does not have to prove actual injury or that a reasonable patient would have refused to undergo the treatment plan had required disclosures been made. A court enforcing a fiduciary claim also has the power to award punitive damages and enjoin future misconduct by the fiduciary.

A. General Principles of Fiduciary Law

Scholars have long criticized fiduciary law as being imprecise, inchoate, and lacking overarching governing principles, especially concerning when a fiduciary relationship exists. Courts have been clearer about the broad duties that inhere in

263. See Matthew, supra note 36, at 732–33 (“Procedurally, fiduciary law places a reduced burden of proof upon plaintiffs making out a prima facie case. Plaintiffs can access equitable remedies by merely showing that a fiduciary obligation existed and was breached. Many jurisdictions allow a fiduciary cause of action with or without proof of actual injury. Courts enforcing fiduciary rights have the power to award restitutionary damages and punitive damages and to enjoin future misconduct.”); see, e.g., Moore v. Regents of Univ. of Cal., 793 P.2d 479, 500 (Cal. 1990) (en banc) (Broussard, J., concurring in part) (“[U]nlike in the traditional ‘informed consent’ context . . . a plaintiff should not be required to establish that he would not have proceeded with the medical treatment in question if his physician had made full disclosure, but only that the doctor’s wrongful failure to disclose information proximately caused the plaintiff some type of compensable damage. . . . [I]t is worth noting that, in appropriate circumstances, punitive as well as compensatory damages would clearly be recoverable in such an action.”). But see Looney v. Moore, 886 F.3d 1058, 1063 (11th Cir. 2018) (in case brought by SUPPORT patients, summary judgment was affirmed in the defendants’ favor for all claims, including breach of fiduciary duty, due to the plaintiffs’ failure to provide proof of injury).

264. See Matthew, supra note 36, at 733.

265. See Carl H. Coleman, Duties to Subjects in Clinical Research, 58 Vand. L. Rev. 387, 424–25 (2005) (Fiduciary principles are “widely regarded as among the most indefinite, imprecise, and elusive legal abstractions.”) (quoting Alan M. Weinberger, Expanding the...
a fiduciary relationship—duties of loyalty, discretion, and care—but because there are many different types of fiduciary relationships, the contours of those duties vary and can be challenging to pin down with precision.266

As Paul Miller and Charles Weijer explain, in a fiduciary relationship, “[o]ne party entrusts another with discretionary power over the legal, economic or other practical interests of a beneficiary, and the other party undertakes, expressly or impliedly, to exercise that power.”267 In these relationships, the beneficiary is dependent on the fiduciary not to abuse the power given to them, a dependency that is particularly acute when the fiduciary is an expert and the beneficiary does not have the knowledge to monitor the fiduciary’s actions.268 Law professor Dayna Matthew explains that in these situations, the law requires the expert to “exercise prudent judgment and selfless discretion to protect the weaker party.”269

The paradigmatic fiduciary relationship is between trustee and beneficiary, which is characterized by the strictest obligations because trustees have complete control over the beneficiaries’ properties placed in their trust.270 Other well-established fiduciary relationships include, among others, guardian and ward, principal and agent, lawyer and client, corporate directors/officers and shareholders, and partners (to one another).271 The duties of fiduciaries to beneficiaries, or “entrustors,” are dependent on the category of fiduciary that their relationship might fall in and the

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Fiduciary Relationship Bestiary: Does Concurrent Ownership Satisfy the Family Resemblance Test?, 24 SETON HALL L. REV. 1767, 1779 (1994); Paul B. Miller & Charles Weijer, Fiduciary Obligation in Clinical Research, J.L. MED. & ETHICS 424, 425–26 (2006) (writing that because “the categories of relationship recognized as fiduciary have evolved through a process of analogical reasoning” (i.e., this relationship is similar to those recognized as fiduciary in the past), the courts have not clearly and consistently identified the governing principles that make a relationship fiduciary); E. Haavi Morreim, The Clinical Investigator as Fiduciary: Discarding a Misguided Idea, J.L. MED. & ETHICS 586, 588 (2005) (“Admittedly, ‘[f]iduciary obligation is one of the most elusive concepts in Anglo-American law.’”).

266. See Miller & Weijer, supra note 265, at 431–32.
267. Id. at 427–28.
268. Matthew, supra note 36, at 722.
269. Id. It is common for courts and scholars, in describing the fiduciary relationship between physician and patient, to emphasize the superior knowledge of the physician and the vulnerability of the patient—a vulnerability often heightened by illness. See, e.g., Coleman, supra note 265, at 435 (characterizing serious illness as the “quintessential state of extreme vulnerability”); Maxwell J. Mehlman, Why Physicians are Fiduciaries for Their Patients, 12 IND. HEALTH L. REV. 1, 3–4 (2015) (explaining that physicians are in a position to take advantage of patients because of their knowledge, and because they have control over patients, who are ill and otherwise vulnerable). Although this contextual feature is meaningful, the vulnerability in fiduciary relationships is structural, rather than circumstantial. Even when patients are medically well and have a great deal of medical knowledge, they are vulnerable when they depend on someone else to make important decisions affecting their interests.
270. See Morreim, supra note 265, at 588 (noting that fiduciary principles initially arose in the law of trust); see generally Robert H. Sitkoff, Fiduciary Principles in Trust Law, in THE OXFORD HANDBOOK OF FIDUCIARY LAW 41 (Evan J. Criddle, Paul B. Miller, & Robert H Sitkoff eds., 2019).
271. See Coleman, supra note 265, at 425 (listing examples of traditional fiduciary relationships).
particular facts of the relationship.\textsuperscript{272} Sometimes these duties can be modified by consent.\textsuperscript{273}

Fiduciary relationships differ from “special relationships” in law. In a special relationship, such as between an innkeeper and guest, one party may owe special duties to protect another party or their interests, as an innkeeper may owe special duties to protect its guests that it would not owe to strangers.\textsuperscript{274} But they do not owe a duty of loyalty that would require them to protect or advance the interests of the one with whom they are in a special relationship over their own interests or the interests of others. In \textit{Grimes v. Kennedy Krieger}, an important case involving a claim of research injury that did not involve medical treatment, the highest court in Maryland held in 2001 that a “special relationship” will normally exist between researchers and subjects, requiring researchers to protect subjects from unreasonable harm and to affirmatively inform them of potential hazards.\textsuperscript{275} It stopped short of holding that researchers owe fiduciary duties to subjects.\textsuperscript{276} Other courts have also determined that researchers who are not otherwise in a recognized fiduciary relationship (as physicians are with patients, discussed below) do not become fiduciaries by virtue of the research relationship.\textsuperscript{277}

\textbf{B. Physicians as Fiduciaries}

With few exceptions, U.S. courts and legal scholars have concluded that physicians are fiduciaries for their patients, or, if that legal term is not used, are in a relationship of “trust and confidence” that imposes similar duties.\textsuperscript{278} For example,

\begin{itemize}
\item \textsuperscript{272} \textit{See id.} at 426 (“While all fiduciaries are obligated to promote the beneficiary’s best interests, the nature and scope of that obligation depends on the type of relationship.”).
\item \textsuperscript{273} \textit{See id.} at 429–31 (describing how the function of consent differs under the various legal standards for fiduciary relationships); \textit{see also} Miller & Weijer, \textit{supra} note 265, 435–36 (“With . . . consent of the beneficiary, the fiduciary is usually allowed to exercise her powers despite [a] conflict, subject to important conditions . . . .”).
\item \textsuperscript{274} \textit{See} Coleman, \textit{supra} note 265, at 432 (citing \textit{Restatement (Second) of Torts} § 314A (\textit{Am. L. Inst.} (1977))).
\item \textsuperscript{275} \textit{See} Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 834–35, 851 (Md. 2001); \textit{see also} Kennedy Krieger Inst., Inc. v. Partlow, 191 A.3d 425, 458 (Md. 2018) (determining allegations supported recognizing a special relationship, in addition to a traditional tort law duty of care, in a case involving the sibling of a study participant).
\item \textsuperscript{276} \textit{See also} Suthers v. Aagen Inc., 441 F. Supp. 2d 478, 488 (S.D.N.Y. 2006) (declining to impose fiduciary obligations on pharmaceutical sponsor of drug trial).
\item \textsuperscript{277} \textit{See}, \textit{e.g.}, Moore v. Regents of Univ. of Cal., 793 P.2d 479, 486 (Cal. 1990) (holding that defendant non-physician researchers could only be considered fiduciaries because of their physician colleague’s acts “and on the basis of a recognized theory of secondary liability, such as respondeat superior”) (emphasis added).
\item \textsuperscript{278} \textit{See} Mehlman, \textit{supra} note 269, at 3–6 n.5 (collecting cases). Mehlman critiques some scholars’ characterization of the physician-patient relationship as confidential rather than fiduciary. Under the former formulation, the patient bears the burden of proving an abuse of power, weakening legal protections for patients. \textit{Id.} at 17–18. \textit{See also} Matthew, \textit{supra} note 36, at 722 (“[C]ourts have developed a nearly unanimous consensus on applying the fiduciary doctrine to protect at least some interests of individual patients in their relationships with physicians and other health care providers.”). Alabama is the exception. \textit{See Gunter v. Huddle,}
the Supreme Court of Arkansas wrote in 1921 that “[t]he relation of a physician to his patient and the immediate family is one of the highest trust. On account of his scientific knowledge and his peculiar relation, an attending physician is, in a certain sense, in custody of a patient afflicted with infectious or contagious disease.”

Physicians are fiduciaries because as a profession they invite and accept the trust of patients to exercise their best medical judgment to protect and advance the patient’s health. Whether a doctor-patient relationship exists in a given situation depends upon the interactions between an individual doctor and patient, but when it does exist, it is by its very nature fiduciary.

Physician-ethicists Steve Joffe and Robert Truog point out that physicians sometimes act as fiduciary advisors and sometimes as fiduciary agents. Physicians act as advisors in recommending a course of medical treatment. In this role, they have a “robust” responsibility to obtain informed consent for treatment and to “help the patient make choices that cohere with and advance his individual life plan.”

724 So. 2d 544, 546 (Ala. Civ. App. 1998) (in case alleging improper sexual relationship between physician and patient, court affirmed summary judgment for defendant physician on medical malpractice claim because “Alabama caselaw holds that a physician-patient relationship is not a fiduciary relationship as a matter of law.”) (emphasis in original) (citing Mitchell v. Harris, 246 So. 2d 648, 651–52 (Ala. 1971)). In 1993, legal scholar Marc Rodwin published an influential book that argued “fiduciary law for doctors is now all but nonexistent,” and the fiduciary role of physicians is “very limited.” M. RODWIN, MEDICINE, MONEY, & MORALS: PHYSICIANS’ CONFLICTS OF INTEREST 184, 210 (1993). Rodwin questioned the application of fiduciary principles to physician financial conflicts of interest but acknowledged that courts did apply fiduciary law to physicians in the duty not to abandon patients, and the duty to keep patient information confidential and to obtain informed consent. Id. at 244–47. See generally Mehlman, supra note 269, at 18–21 (countering Rodwin’s conclusions of the limited applicability of fiduciary law to physicians).

280. See Mehlman, supra note 269, at 2–3; see also id. at 8–10 n.8 (collecting ethical statements by major physician groups as to the fiduciary nature of the physician-patient relationship).

281. See Steven E. Pegalis, Physician-Patient Relationship, in AM. L. MED. MALPRACTICE § 2:3 (3d ed. 2021) (creation of the relationship is essentially a question of whether “the patient entrusted himself to the care of the physician and whether the physician accepted . . . .”).

282. See Robert Sokolowski, The Fiduciary Relationship and the Nature of Professions, in ETHICS, TRUST AND THE PROFESSIONS: PHILOSOPHICAL AND CULTURAL ASPECTS 23, 31 (Edmund D. Pellegrino, Robert M. Veatch, & John P. Langan eds., 1991) (“There is an elegant anonymity to professional trustworthiness; if I get sick away from home and must go to the emergency room of a hospital, I can in principle trust doctors and nurses I have never met before. I enter into a fiduciary relationship with them because they are presented as members of the medical profession . . . .”) (emphasis in original).

283. See Joffe & Truog, supra note 177, at 353–55 (writing that when a physician acts as advisor opposed to agent depends on the decision that must be made and how much it involves ends (which requires greater patient involvement because of the values implicated) vs. means (about which the patient is less likely to have a preference). The authority to act as agent for the patient with respect to certain decisions comes from the patient’s “higher-order consent, up to and including the patient’s general agreement to enter into the relationship with the physician in the first place.” Id. at 355.

284. Id.
Physicians act as agents—making decisions for or on behalf of patients—when they make certain technical, means-oriented decisions about which patients are unlikely to have a preference. When acting as an agent, physicians are entrusted to use their judgment to select a course of action to promote the patient’s welfare.

C. Fiduciary Duties of Physicians

Once a fiduciary relationship is established, the precise duties fiduciaries owe to beneficiaries are often less clear than ideal and vary, both in intensity and specification, by the relationship. For example, trustees have greater obligations to avoid self-dealing than do partners, who are considered better able to protect their individual interests vis-à-vis one another. Nevertheless, there are three general duties that the law recognizes of fiduciaries: the duty of loyalty, the duty of discretion, and the duty of care.

1. The Duty of Loyalty

The duty of loyalty is the one most often associated with fiduciary relationships. The fiduciary must avoid conflicts between the interests of the fiduciary and the beneficiary. In addition, the fiduciary must avoid and/or manage conflicts between the interests of the beneficiary and others. In the context of physicians or other health care providers, the fiduciary duty is often described as the duty to put the patients’ best medical interests first.

285. Id. at 353. An example of a physician’s means-oriented decision is determining which tools to use in a procedure or similar decisions regarding technique, particularly when patients are under general anesthesia and physicians “must make decisions without the possibility of securing input from the patient.” Id. at 355. The authors draw on a similar distinction in the lawyer-client context between ends (e.g., whether to settle) and means (whether to call a particular witness) known as the “subject-matter/procedure rule.” Id. at 357. Some legal cases have held that “alternative ways of performing the recommended treatment” need not be disclosed. RESTATEMENT (THIRD) OF TORTS: MEDICAL MALPRACTICE § 12, cmt. 1 (Tentative Draft No. 1, May 2023) (citing, among other cases, Valles v. Albert Einstein Med. Ctr., 569 Pa. 542, 555 (2002) (“[T]he manner or method in which the surgeon performs the proposed procedure is not encompassed within the purview of the informed consent doctrine.”).

286. See Joffe & Truog, supra note 177, at 349.

287. See Coleman, supra note 265, at 435.

288. See Miller & Weijer, supra note 265, at Part III. Together, the three duties mean that “the fiduciary is obliged to exercise judgment in the best interests of the beneficiary, and to demonstrate reasonable care, diligence, and skill in doing so.” Id. at 434. Other scholars have identified other duties that are generally subsumed under these three. For example, law professor Sam Halabi lists instead the three primary fiduciary duties as the duty of loyalty, the duty of care, and the duty “of utmost candor and disclosure.” Sam F. Halabi, Against Fiduciary Utopianism: The Regulation of Physician Conflicts of Interest and Standards of Care, 11 U.C. IRVINE L. REV. 433, 440 (2020)

289. See Halabi, supra note 288, at 439 (“The duty of loyalty is the ‘core’ fiduciary duty . . .”).


291. See, e.g., Ison v. McFall, 400 S.W.2d 243, 258 (Tenn. Ct. App. 1964) (holding that
the duty of physicians to advance patients’ medical interests above other interests as a given, without explicitly referring to it as “fiduciary.”

The duty of loyalty does not require physicians to avoid all conflicts of interest in treating patients. In fact, they always will have conflicts of interest when they are charging for the medical services they provide. According to the type of health insurance coverage of the patient, they may face financial incentives to provide more rather than fewer medical services or vice versa. As law professor Max Mehlman has pointed out, “if the stronger party in a service relationship did not have conflicts of interest with the weaker party, there would be no reason for the law to make the stronger party a fiduciary to begin with.”

Rather than avoiding all conflicts of interest, the key instead is that physicians should, except in rare and justified circumstances, put the interests of the patient above their own interests and the interests of others. And they are often required to disclose to patients when other potential interests are present, as discussed further below.

As fiduciary, defendant-chiropractor was obligated to cease treatment of patient and advise patient to seek relief from another practitioner when he knew or should have known his treatment was unproductive. Patients’ interests in privacy and confidentiality are also entrusted to physicians as fiduciaries. See, e.g., Sorensen v. Barbuto, 177 P.3d 614, 619–20 (Utah 2008) (holding that fiduciary duty of confidentiality prohibited communications between a tort plaintiff’s treating physician and defense counsel). See generally Matthew, supra note 36, at 726–27.

293. See Mehlman, supra note 269, at 39–40 (observing that, although a strict interpretation of duty of loyalty suggests fiduciaries breach their duty any time they act in their own self-interest, this is not true; they are entitled to reasonable compensation, for the entrustor would not be better off in the absence of such relationships). Similarly, the AMA Code of Ethics only prohibits fees that are “illegal or excessive.” Am. Med. Ass’n, AMA Code of Ethics, Ethics Opinion E-605, Fees for Medical Services (1994 update).
294. Under a fee-for-service model of payment, physicians face financial incentives to provide greater rather than fewer medical services while under the capitated payment model of the HMO era, physicians may face financial incentives to provide less of certain services, such as referrals to specialists and hospitalization. See Leonard S. Kurfurst, The Duty to Disclose HMO Physician Incentives, A.B.A. HEALTH L. 18, 18 (2001); see also Frances H. Miller, Secondary Income from Recommended Treatment: Should Fiduciary Principles Constrain Physician Behavior?, in THE NEW HEALTH CARE FOR PROFIT: DOCTORS AND HOSPITALS IN A COMPETITIVE ENVIRONMENT 153, 154–55 (Bradford H. Gray ed., 1983).
296. Id. at 38. There are three commonly recognized situations in which physicians may put others’ interests before their patients’ without breaching legal duties: (1) in the midst of triage, (2) when they must breach confidentiality to protect another from imminent danger, and (3) when meeting obligations to report to public health authorities that their patients have contracted certain infectious diseases. Id.
297. See infra text accompanying notes 333–34.
2. The Duty of Discretion

The duty of discretion tends to be discussed less frequently than the duty of loyalty, but is nevertheless important. The duty of discretion “requires the fiduciary to exercise the discretion with which she has been entrusted.”

According to Miller and Weijer, the fiduciary cannot delegate its discretion to others, cannot act under the direction of another in the exercise of its discretionary powers, and cannot prospectively limit its own discretion.

The duty of discretion played a large role in the Burton case, discussed above, although the court did not use the language of fiduciary law. The court affirmed the jury’s finding that Dr. Engle, the physician coordinating the research study at the hospital, was liable for Burton’s injury because, although high oxygen environments may have commonly been in use (i.e., been within the “standard of care”), Dr. Engle had not exercised her medical judgment in placing Burton in that environment, but had instead made an “administrative judgment.”

The duty of discretion has been referred to by one court as the “second principle” of medical malpractice.

Those who support comparative effectiveness studies without consent often point to the number of external factors that already constrain the discretion of physicians and that may influence or even determine the care that patients receive in the modern delivery of health care, such as the formularies hospitals follow in prescribing medications or those used by insurance companies for reimbursement.

Insurance often limits the tests or treatments available to patients, and, as seen in the Ancheff case, hospitals often standardize care by adopting clinical protocols.

Some scholars claim that the constraints imposed by research protocols are not fundamentally different from accepted constraints on physician discretion in clinical care.

These other constraints may or may not be legally and ethically acceptable, as many are untested, and whether they are would likely depend on a number of factors: disclosure to patients, or their reasonable expectations in the absence of disclosure;

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298. Miller & Weijer, supra note 265, at 433.
299. Id. at 436.
302. Id.
303. See, e.g., Kass et al., supra note 39, at S7 (discussing external constraints on patient care from pharmaceutical formularies, reimbursement policies that limit diagnostic tests, and hospitals’ adoption of standardized care protocols).
304. See Ancheff v. Hartford Hosp., 799 A.2d 1067 (Conn. 2002); see also supra text accompanying notes 249–57.
305. See Kass et al., supra note 39, at S11 (“Our claim is that the control over therapeutic options in research and clinical care contexts is often not so widely different as some have portrayed it and that ‘personalization’ of therapy is neither a given in clinical care (even though there is often an illusion of such) nor unobtainable in clinical trials.”).
306. See Neade v. Portes, 739 N.E.2d 496, 505–06 (Ill. 2000) (declining to recognize a duty on behalf of physicians to disclose HMO incentives, but stating patients should know of
patients’ realistic opportunity to seek care elsewhere; whether the protocols were adopted with due care and in the best interests of patients; and finally, the preservation of clinicians’ opportunity to exercise the discretion entrusted in them and to deviate from the protocol if required to put the best medical interests of patients first.

3. The Duty of Care

Finally, the duty of care “requires that the fiduciary demonstrate reasonable care, diligence and skill” in the exercise of the discretionary powers granted to fiduciaries. Whether a fiduciary has met their duty of care will be judged by whether they have acted with the same amount of care and skill that a reasonably prudent fiduciary would in a like position under similar circumstances. For physicians, it is not clear how the duty of care they owe by virtue of being a fiduciary differs, if at all, from the duty of care owed under general negligence or medical malpractice standards.

incentives and noting Illinois law placed disclosure burden on HMOs themselves).

307. See, e.g., Ancheff, 799 A.2d at 1071 (explaining that defendant hospital introduced evidence to show that before enacting the Gentamicin program, “the physicians in the hospital’s department of infectious diseases, pharmacy and therapeutics committee, antibiotic [sic] subcommittee, and medical executive committee approved it” after “determin[ing] that the program embodied sound policy for the well-being of patients.”). But see Kate Greenwood, Physician Conflicts of Interest in Court: Beyond the “Independent Physician” Litigation Heuristic, 30 GA. STATE UNIV. L. REV. 759, 771 (2014) (citing studies showing a correlation between physicians’ receipt of monies from drug companies in the form of speaking fees or research support and physicians’ requests to add drugs to hospitals’ formularies).

308. See Ancheff, 799 A.2d at 1069–70 (explaining that plaintiff’s physician reviewed the change in drug dosage made by the pharmacy and affirmed its appropriateness); see also Garcia v. Coffman, 946 P.2d 216, 218 (N.M. Ct. App. 1997) (where owner of a chiropractic practice was determined to have breached his fiduciary duty when patient received unnecessary testing and treatment from clinicians who were strictly following a clinical care protocol established to increase revenues).

309. Miller & Weijer, supra note 265, at 433.

310. See MODEL BUS. CORP. ACT § 8.30 (AM. BAR ASS’N 2023); see also Michael P. Dooley, Rules, Standards, and the Model Business Corporation Act, 74 L. & CONTEMP. PROBS. 45, 48 n.18 (noting that forty-one states have adopted similar statutory provisions); RESTATEMENT (THIRD) OF AGENCY § 8.08 (AM. L. INST. 2006) (“[A]n agent has a duty to the principal to act with the care, competence, and diligence normally exercised by agents in similar circumstances. . . . If an agent claims to possess special skills or knowledge, the agent has a duty to the principal to act with the care, competence, and diligence normally exercised by agents with such skills or knowledge.”).

311. Some scholars have challenged the distinctiveness of the fiduciary duty of care in light of the recognition of duties of care in other areas of the law. See, e.g., Julian Velasco, A Defense of the Corporate Law Duty of Care, 40 J. CORP. L. 647, 677 (2015). Paul Miller and Charles Weijer argue for a distinctive duty of care for fiduciaries: “The care requirement is familiar from the law of negligence, but is heightened in fiduciary law, differing also to the extent that it specifies a positive obligation (i.e., to exercise discretion in the best interests of the beneficiary) rather than a negative one (i.e., to avoid causing another reasonably
In many situations, the fiduciary duty claim and the medical malpractice claim will be dependent on the same set of facts—for example, when a plaintiff claims that their physician’s treatment deviated from the standard of care because of the external interests of the physician. In these circumstances, the fact that the physician has violated fiduciary duties may not add any information that would change the potential for plaintiff’s recovery. A court may—and often will—dismiss the fiduciary claim as duplicative of the plaintiff’s claim of medical negligence or dismiss it as an inappropriate recasting of a medical negligence claim, which plaintiffs may sometimes attempt in order to avoid a procedural bar such as the statute of limitations.

Some legal scholars lament that while the courts often describe the physician-patient relationship as fiduciary or one of trust, they have not been willing to apply fiduciary principles in many actual doctor-patient disputes. One explanation for this is they have not needed to; the principles of medical malpractice and informed consent incorporate duties that the law also recognizes as fiduciary and in most situations (though not all—for example, when a patient has been wronged but not harmed by a breach of fiduciary duty) provide potential plaintiffs with adequate relief.

foreseeable harm).” Miller & Weijer, supra note 265, at 437.

312. See, e.g., Neade v. Portes, 739 N.E.2d 496 (Ill. 2000) (dismissing plaintiff’s claim that physician breached a fiduciary duty when he failed to approve a recommended angiogram due to HMO financial incentives; fiduciary claim was duplicative of the medical negligence claim).

313. Neade, 739 N.E.2d at 501 (citing cases from Minnesota, Colorado, Arizona, and New Mexico, which hold that a breach of fiduciary duty claim is duplicative of a negligence claim). Relatedly, in Garcia v. Coffman, the court would not allow claims for both fraudulent misrepresentation and breach of fiduciary duty since they relied on the same set of facts and would result in double recovery. 946 P.2d 216, 223 (N.M. Ct. App. 1997).

314. See, e.g., Mehlman, supra note 269, at 23 (noting that “the United States Supreme Court and courts in ten other states, while acknowledging or at least not rejecting the fiduciary nature of the relationship, have held that a patient has no cause of action for breach of a physician’s fiduciary duties that is distinct from an action for medical malpractice”) (referring to Pegram v. Herdrich, 530 U.S. 211 (2000) (involving a claim that a physician had violated fiduciary duties as a health benefit plan trustee under ERISA)).

315. See, e.g., Burton v. Brooklyn Drs. Hosp., 452 N.Y.S.2d 875, 879 (N.Y. App. Div. 1982) (finding that a physician could be found liable under medical malpractice principles for failing to exercise their discretion to pursue the best medical interests of the patient and to obtain informed consent as a reasonably prudent physician would do). Max Mehlman, however, has pointed out that the burdens of proof between the two causes of action differ. “[I]n an action for breach of fiduciary duty, once a plaintiff establishes that a fiduciary had a conflict of interest with the entrustor, the burden shifts to the fiduciary to prove that he or she nevertheless acted loyally; in a malpractice action, on the other hand, the plaintiff bears the burden of proving that the defendant failed to meet the applicable standard of care.” Mehlman, supra note 269, at 28.
D. Fiduciary Duties of Physicians Conducting Research on Their Patients

It is unresolved in ethics and law whether physicians who have obtained consent from patients for medical research continue to owe fiduciary duties to those patients, and if so, what the contours of the duties are. This question was intensely analyzed by legal and ethics scholars about twenty years ago, in a debate sparked in part by a rise in research injury litigation. Ethicists were trying to figure out what standards physician-researchers should be held to when following a research protocol that could entail patients receiving treatments divergent from their best medical interests. Clinical research often involves discomforts and risks occasioned by research activities, like extra imaging studies or blood draws that are not performed for the benefit of the individual patient-subjects, but instead to obtain data for research purposes. A research protocol may provide for standardized rather than individualized dosages of drugs, or adopt double-masking (in which neither the patient nor the provider know which treatment the patient-subject is receiving), constraints that may make it more difficult for a physician-researcher to respond to the medical needs of individual patients in the course of a study. And, of course, compared treatments—whether experimental, placebo, or standard of care—may differ, and a patient is exposed to the risks associated with the possibility of being randomized into the inferior treatment arm of the study.

Some scholars argue that physician-researchers, because they are physicians first, remain in a fiduciary relationship, or a close approximation thereof, with patient-subjects enrolled in their research, although the specification and intensity of those duties change when they are no longer simply in the role of physicians. Others reject the idea that a strict fiduciary relationship can be maintained in the research context, but propose other ways of understanding physician-researchers’ duties to patient-subjects, such as a duty to refrain from exploiting patients or the recognition of “side constraints,” such as accommodating patient preferences when permitted by a protocol or removing a person from a study altogether when it poses significant problems for the person.

Though commentators in this debate disagreed on the contours of the ethical and legal relationship between physician-researcher and patient-subject, they all recognized patient consent was required before any of the physician’s normally recognized fiduciary duties could be considered reduced or suspended. As Haavi

316. See, e.g., Coleman, supra note 265; see also Paul B. Miller & Charles Weijer, Trust Based Obligations of the State and Physician-Researchers to Patient-Subjects, 32 J. MED. ETHICS 542 (2006) (arguing that the relationship of trust between doctor-researcher and patient-subject gives rise to obligations, including duties of loyalty and care).
318. See Coleman, supra note 265, at 398; Morreim, supra note 139, at 16–17.
319. See Coleman, supra note 265; Miller & Weijer, supra note 265.
321. Morreim, supra note 139, at 19.
322. See, e.g., id. at 46; see also Miller & Brody, supra note 320, at 25 ("Research
Morreim has written, physician-investigators have a duty “to make it clear [to subjects] that the relationship is not a traditional physician-patient kind of relationship.”

E. Moore v. Regents

The closest precedent for a claim by our hypothetical plaintiff for breach of fiduciary duty is the famous California case of Moore v. Regents, even though the plaintiff-patient had not been placed in a randomized study. John Moore received care from Dr. David W. Golde at the Medical Center of the University of California at Los Angeles for treatment for hairy-cell leukemia. Moore alleged that when Golde examined him in 1976, Golde discovered that Moore’s blood and other biological specimens might be “of great value in a number of commercial and scientific efforts.” Golde recommended a splenectomy to treat Moore’s leukemia. Although Moore had no complaint about the splenectomy, which was medically indicated and performed well, he alleged that Golde and another researcher had, prior to the operation, “formed the intent and made arrangements to obtain portions of [Moore’s] spleen following its removal’ and to take them to a separate research unit.” These activities, undertaken for research purposes, “were not intended to have . . . any relation to [Moore’s] medical . . . care.” Neither Golde nor the other researcher informed Moore of their plans to conduct research on his spleen or requested his permission to do so.

Over the course of the following seven years, according to the complaint, Moore repeatedly travelled long distances for health monitoring by Golde, based on the doctor’s representations that such visits were necessary for his health, “and based upon the trust inherent in and by virtue of the physician-patient relationship.” At these visits, further biospecimens were recovered. From Moore’s specimens, Golde and others created a valuable cell line. Once Moore learned this, he sued Golde and others involved in the research under several theories. The case is best known for

participants need to know that the overall activity is aimed not at their own ultimate benefit, but at discovering new knowledge to help future patients.”

323. Morreim, supra note 139, at 49.
324. 793 P.2d 479 (Cal. 1990).
325. Id. at 480–81. In Moore’s complaint, he stated that, while the value of the lymphokines was hard to predict, “competing commercial firms in . . . relevant fields . . . predict[] a potential market of approximately $3.01 Billion Dollars by the year 1990.” Id. at 482 (quoting Moore’s complaint). Moore eventually settled his suit for an undisclosed amount, which he characterized as a “token” settlement following the California Supreme Court ruling. Dennis McLellan, John Moore, 56; Sued to Share Profits from His Cells, L.A. TIMES (Oct. 13, 2001, 12:00 AM), https://www.latimes.com/archives/la-xpm-2001-oct-13-me-56770-story.html [https://perma.cc/99ES-JPD6].
326. Moore, 793 P.2d at 481 (quoting Moore’s complaint). Golde did not actually remove the spleen; surgeons at UCLA, who were not named as defendants, performed the splenectomy after Golde recommended it. Id.
327. Id.
328. Id.
329. Id. at 481 n.4 (listing conversion, lack of informed consent, breach of fiduciary duty, fraud and deceit, unjust enrichment, quasi-contract, bad faith breach of the implied covenant
Moore’s unsuccessful claim for conversion—essentially a claim that the defendants had stolen his property interest in his body parts. But he also sued for lack of informed consent and breach of fiduciary duty, and these claims were determined sufficient to state a cause of action by the California Supreme Court. The court generally combined Moore’s breach of fiduciary duty and lack of informed consent claims, holding that under both theories Golde had a duty to disclose any research and economic interests in Moore’s cells prior to providing medical treatment. The court explained that under informed consent law, disclosure is required because “[t]he possibility that an interest extraneous to the patient’s health has affected the physician’s judgment is something that a reasonable patient would want to know in deciding whether to consent to a proposed course of treatment.” Physicians also have a “fiduciary duty to disclose all information material to the patient’s decision,” including “personal interests unrelated to the patient’s health, whether research or economic, that may affect the physician’s professional judgment.” The court acknowledged that physicians are not barred from conducting medical research while caring for their patients, and in fact, medical progress often depends on this practice. At the same time, “a physician who treats a patient in whom he also has a research interest has potentially conflicting loyalties. This is because medical treatment decisions are made on the basis of proportionality—weighing the benefits to the patient against the risks to the
Research, by contrast, may involve procedures and tests that have marginal or no benefit to the patient. Whether Golde had in fact been influenced by a preexisting research interest in his medical treatment recommendations was irrelevant; he could still be liable for failing to disclose that interest to the patient. It also did not matter that the recommended splenectomy was within the standard of care, because the physician “might, consciously or unconsciously, take [preexisting research interests] into consideration in recommending the procedure.”

F. Applying Fiduciary Law to Our Scenario

As with our plaintiff’s claims to battery and lack of informed consent, the fiduciary duty to obtain consent for treatment randomization is clear. Fiduciary law provides additional clarity that what must be disclosed in our scenario is how research aims are influencing the treatment process and what that might mean for the patient.

In Moore, the physician was faulted for failing to disclose his research interests in the patient’s bodily materials prior to the clinically-indicated splenectomy Moore underwent on the physician’s recommendation. In our case, the physicians did more than fail to disclose research interests (such as interests in the patient’s health information or biospecimens); they failed to disclose the fact that the patient’s treatment may be altered solely for research purposes—in fact, that there was a roughly fifty percent chance that it would be altered.

In any claim for breach of fiduciary duty, a plaintiff has the burden of proving that the fiduciary had a conflict of interest relating to the activity in question (here, the assignment to treatment by a research protocol). This should not be difficult to do. The conflict of interest that exists when physicians conduct research on their patients has long been recognized in the legal and ethics literature, and is clearly recognized in the Moore case. It is inherent. It is structural. It is present whether or not the physician has financial or other incentives—like career advancement or

336. Id. (emphasis in original).
337. Id. (“If a physician has no plans to conduct research on a patient’s cells at the time he recommends the medical procedure by which they are taken, then the patient’s medical interests have not been impaired. . . . On the other hand, a physician who does have a preexisting research interest might, consciously or unconsciously, take that into consideration in recommending the procedure. . . . [T]he physician’s extraneous motivation may affect his judgment and is, thus, material to the patient’s consent.”).
338. Id.; see also id. at 486 (correcting superior court’s holding that Moore did not state a cause of action based on the splenectomy because he did not allege it lacked therapeutic purpose).
339. Id. at 483. The post-splenectomy retrieval of biospecimens under the guise of medical monitoring was obviously also a problem, but we focus here on the recommendation for splenectomy because it was within the standard of care.
340. See, e.g., Coleman, supra note 265, at 442.
341. Id. at 396–403.
professional recognition—to participate in research.\textsuperscript{343} It results from combining two roles with different and often competing goals; physicians in medical practice aim to meet the individualized medical needs of a particular patient whereas researchers aim to advance knowledge to help future patients.\textsuperscript{344} The fact that this conflict of interest exists does not mean that a physician-researcher is unethical or will do unethical things. Although physicians often believe conflicts of interest “relat[e] to the individual’s character and ability to resist temptation,” lawyers see them as “objective, structural, and rule-based.”\textsuperscript{345} Many conflicts of interest are ethically and legally acceptable. The conflict of interest inherent in the physician-researcher context is generally one of those—as long as it is disclosed and the patient-subject has consented.

This is where the problem lies with CER studies that do not obtain patients’ consent. To return to the mechanics of pursuing a claim for breach of fiduciary duty, once the conflict of interest is proven, the fiduciary must show that they acted appropriately. This requires the fiduciary to prove that the beneficiary, after receiving all material information, consented to the activity in issue; usually, the fiduciary is also required to show that their action was “fair.”\textsuperscript{346} The beneficiary’s consent to the

\begin{footnotesize}
343. Moore v. Regents of Univ. of Cal., 793 P.2d 479, 483 (Cal. 1990) (holding that research interests alone in a patient’s treatment create a conflict of interest); see also Wilson, supra note 204, at 251 (discussing researcher’s independent “desires to cure and to profit” in an early first-in-human gene therapy experiment that resulted in the death of Gelsinger). See generally Jesse A. Goldner, Regulating Conflicts of Interest in Research: The Paper Tiger Needs Real Teeth, 53 ST. LOUIS UNIV. L.J. 1211, 1212 (2009) (examining various conflicts of interest in modern medical research). But see Ward v. Schaefer, No. CV 16-12543-FDS, 2021 WL 1178291, at *19 (D. Mass. Mar. 29, 2021) (determining that the fact that the patient-subject’s personal physician “intended to” or ‘attempted to’ publish one or more articles about [a consented-to] study in a peer-reviewed publication cannot form the basis of a failure to obtain informed consent claim due to inadequate disclosure”).

344. Chen et al., supra note 317, at 699 (explaining the “guiding ethos” in clinical practice is referred to as “personal care” whereas “clinical research is oriented toward developing knowledge to help future patients”).


346. This would be the case whether physicians are seen in this context as trustees or agents. See Coleman, supra note 265, at 442–43 (arguing that physician-researchers should be considered trustees); Matthew, supra note 36, at 753–54 (arguing that physicians, and other health care providers, are better understood as agents). For trustees, in the absence of consent, there is an irrebuttable presumption of wrongdoing subject to limited exceptions. So strong is the trustee’s fiduciary duty that even with consent, a trustee’s conflicted transaction is often voidable. RESTATEMENT (THIRD) OF TRUSTS § 78 cmt. b (AM. L. INST. 2007).

Is it possible that a court considering the fiduciary duties of a physician in this context might look not to the high fiduciary standards required of agents and trustees requiring clear and informed consent for conflicted activity—but instead look to a lower standard such as that imposed on corporate officers, which may allow conflicted activities if they can be shown to be fair to shareholders? This is highly unlikely as the corporate context involves primarily financial interests, whereas the medical—and medical research—contexts involve highly personal decisions affecting health and bodily integrity. Nevertheless, some may be drawn to the argument that just as corporate officers and directors are allowed to make charitable contributions or otherwise commit the corporation’s resources toward societal good, physicians conducting medical research might be considered similarly—i.e., physicians are
action complained of must be based on knowledge of material facts, including knowledge of the conflict of interest itself.\textsuperscript{347} With respect to our hypothetical research study, the parents could not have consented to the conflicted activity, as they knew nothing about the research at all. Even though the parents gave permission for medical treatment through a general consent, they did not consent to having that treatment determined by a research protocol. They were thus denied the opportunity to determine the course of their child’s medical treatment and to ensure that decisions would only be made in the child’s best interests. They could not say “no” because they were completely unaware of the research study. They had no opportunity to ask their child’s physician about the study and the treatments being compared—for example, about the prevalence of their use, the experience of the physician with respect to each intervention, and the outcomes that potentially were at stake if one intervention proves to be better than the other. These are all questions they may reasonably have had in seeking to protect the health and well-being of their child. Although we have assumed in our hypothetical study that the two interventions were clearly within the standard of care and that they were in approximate equal use, at least one recent review has revealed that what was represented as “usual care” in several large “standard of care” studies was actually “unusual care.”\textsuperscript{348}

VII. ETHICAL ANALYSIS AND A PATH FORWARD

A. Ethical Values Underpinning Common Law Principles

It should not be surprising that the common law generally requires basic informed consent for research from patients before research activities alter their care. Informed consent is often called the “bedrock” of research ethics, “foundational,” or the “first principle.”\textsuperscript{349} The Nuremberg Code begins with the statement, “[t]he voluntary not self-dealing by randomizing their patients to treatments but are instead advancing societal interests in learning what treatments work best. But this argument too is unconvincing. Courts have made clear that when officers and directors make charitable contributions, they do so ultimately for the benefit of the corporation. See David G. Yosifon, The Law of Corporate Purpose, 10 BERKELEY BUS. L.J. 181, 217 (2013) (“[T]he corporate charitable contribution is acceptable because of the long-term benefits it may bring to shareholders.”). Physicians conducting research on their patients do so ultimately for the benefit of future patients—not their current patient.

347. \textsc{The Oxford Handbook of Fiduciary Law} 37 (Evan J. Criddle, Paul B. Miller & Robert H. Sitkoff eds., 2019) (giting \textsc{Restatement (Second) of Torts} § 10A) (\textsc{Am. L. Inst, 1958}).

348. Macklin & Natanson, supra note 100, at 31 (“The reasons why misconceptions of usual care may exist include at least the following: (a) investigators may make errors in collecting or using inaccurate or inappropriate sources of evidence to document usual care practices; (b) study populations often include subgroups requiring different care approaches; (c) a widely used, universally accepted clinical practice may not be easily identified; (d) a usual-care practice may be rapidly evolving and change before approval and implementation of the study; (e) instead of using pertinent, accurate information describing usual care, investigators may rely on the opinion of ‘experts’ in the field, whose information may be out of date or otherwise inaccurate.”).

349. See, e.g., Rothstein & Shoben, supra note 117, at 27, 33 (“Since the 1947 publication
The consent of the human subject is absolutely essential.\textsuperscript{350} The Belmont Report begins its section on informed consent explaining the requirement in fundamental terms: “Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them.”\textsuperscript{351}

Advocates who favor reducing or eliminating consent requirements for comparative effectiveness studies tend to focus almost exclusively on whether patient or subject welfare is compromised by trial participation. Goldstein and colleagues, in a recent literature review about waiver of consent for CER studies, write that “[t]he current ethical discussion is framed by the assumption that the function of research oversight is to protect participants from risk.”\textsuperscript{352} This is indeed an important function. The research regulations direct researchers and IRBs to minimize risks to research subjects and to justify any risks to individuals from research participation with anticipated benefits from the knowledge to be gained from the research.\textsuperscript{353} And with respect to informed consent, the “foreseeable risks” in research are among the most important disclosures that the regulations require be included in consent forms and processes. We have also seen that the common law, in respect to informed consent for both clinical care and research, tends to focus on the risks that must be disclosed.

In Part II above, we have explained in some detail how randomized comparative effectiveness studies usually will involve foreseeable research risks: if important research is being done, a difference in meaningful benefits or harms between the treatments being compared should be anticipated. Even if, in the aggregate, the study population as a whole does not experience higher risks of harm, that does not mean an individual subject does not experience a higher risk of harm. As Jerry Menikoff has written, “The study a patient is enrolled in could be one in which there ends up being major differences in mortality or morbidity between the two arms. This is not the sort of thing that averages out for an individual.”\textsuperscript{354}

All this is to say that even if patient welfare were the only, or even the most important, ethical consideration in medical research, comparative effectiveness studies do affect patient welfare and do involve research risks. Thus, when the requirement for consent is waived, patients miss out on a recognized means of protecting themselves—their own ability to say no or alert the investigators, or their of the Nuremberg Code, informed consent has been the foundational doctrine for the ethical conduct of research with human subjects.”); John P. A. Ioannidis, Informed Consent, Big Data, and the Oxymoron of Research that Is Not Research, 13 AM. J. BIOETHICS 40, 40–42 (2023) (“Informed consent has been the cornerstone of conducting ethical research involving humans”).

\textsuperscript{350} Nuremberg Code, supra note 182, at 181.
\textsuperscript{351} BELMONT REPORT, supra note 70, at (c)1.
\textsuperscript{352} Cory E. Goldstein, Charles Weijer, Jamie C. Brehaut, Dean A. Fergusson, Jeremy M. Grimshaw, Auston R. Horn & Monica Taljaard, Ethical Issues in Pragmatic Randomized Controlled Trials: A Review of the Recent Literature Identifies Gaps in Ethical Argumentation, 19 BMC MED. ETHICS. 1, 1 (2018) (summarizing arguments of those advocating reducing or eliminating consent requirements in pragmatic randomized controlled trials).
\textsuperscript{353} 45 C.F.R. §46.111 (2023).
\textsuperscript{354} Menikoff, supra note 67, at 31.
own doctor (if different from the investigator)—if they are concerned about something they are experiencing.355

In this section, however, we would like to emphasize other ethical commitments beyond protection of the welfare of research subjects. When consent is waived for randomized comparative effectiveness trials, ethical and legal rights to bodily integrity and self-determination are also at stake. So too are values of trust, transparency, and protection of vulnerable persons, which ground the common law’s recognition of physicians’ fiduciary duties.

Those who support continuing the long-standing requirement to obtain consent for these trials have urged greater consideration of the provider-patient relationship and the expectation and authority of patients to make their own choices within and about that relationship. Charles Fried, writing in the 1970s, explained that the issue was not simply about patient welfare but what patients had a right to reasonably expect from their doctors, which he identified as “personal care,” involving transparency, respect for patient autonomy, fidelity (devotion to the patient’s best medical interests), and humanity (attention to the particular patient).356

In an analogy legal readers may find compelling, Fried, himself a lawyer, compared the physician-patient relationship to the lawyer-client relationship. He asked readers to imagine a public defender who, as part of a research project on sentencing, decides to determine by a process of randomization whether to recommend clients enter a guilty plea or go to trial.357 The study he imagines is aimed at learning how these decisions affect the sentence defendants receive. The lawyer’s clients are not told “how the lawyer’s ‘advice’ as to plea is determined.”358 The lawyer’s breach of fiduciary duty is self-evident. He wrote:

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\text{The law of conflict of interests and of fiduciary relations clearly provides that the fiduciary may not pursue activities that either do in fact conflict with the exercise of his judgement as a fiduciary, or might conflict with or influence the exercise of his judgement, or might appear to do so, without the explicit consent of his client.} \]

If consent from the client is obtained but without “the fullest disclosure of all facts not only which the fiduciary deems relevant but which he knows his client might consider relevant,” that consent “is fraudulently obtained.”359

Jerry Menikoff asks what has changed since Fried’s time to warrant taking away patient choice:

355. See Chen et al., supra note 317.
357. Fried, supra note 67, at 33–34.
358. Id. at 34.
359. Id. The analogy is not perfect in relation to our hypothetical research trial because—to make the case more favorable for the defendant physician—we intentionally chose an intervention for which physicians usually do not get specific consent in clinical care and have assumed that practice is appropriate. By contrast, the decision to plead guilty or go to trial is one which attorneys must defer to their clients. MODEL RULES OF PRO. CONDUCT r. 1.2. (AM. BAR ASS’N 2023).
360. Fried, supra note 67, at 34.
For decades now, we have had the system Fried envisioned, protecting the rights of subjects in clinical trials to make their own such choices, even where the two treatments being studied were in equipoise. Now we face an apparent attempt to dramatically move our system back to what was happening in Fried’s time, based on arguments not dissimilar to those he rejected. Have conditions changed so much that what has long been considered unethical now is ethical?\(^{361}\)

Implicit in Menikoff’s question is the conclusion that there have not been any changes that warrant such a fundamental backing away from the requirement to obtain informed consent. The common law supports that conclusion. In fact, legal recognition of rights to bodily integrity and patient self-determination has only strengthened since the 1970s through the evolution of informed consent doctrine, which has trended toward a more patient-centered approach, and includes the right to informed refusal\(^{362}\) and to information about characteristics of providers that may be material to patients.\(^{363}\) The right to be free of forced medical treatment, recognized in both the common law and constitutional law, has also strengthened since Fried’s time.\(^{364}\) And in the United States, people strongly value consent and expect consent to be sought.

Fiduciary law has likewise not declined, generally or as applied to physicians. Some have persuasively argued that in order to protect the rights of patients in the modern health care environment, fiduciary law must be extended beyond individual physicians to institutions and other organizations, including insurers.\(^{365}\) The common law rights of persons affected by research studies outside the clinical context, such as in studies using biospecimens,\(^{366}\) have also recently been affirmed and even

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\(^{361}\) Menikoff, supra note 67, at 31; see also Miller & Kim, supra note 66, at 421 (also drawing attention to this text).

\(^{362}\) See, e.g., Truman v. Thomas, 611 P.2d 902, 908 (Cal. 1980) (holding that trial court erred in refusing to give jury instruction stating jury could find physician owed duty to patient to inform patient of risks of not undergoing certain diagnostic tests).

\(^{363}\) See, e.g., Johnson ex rel. Adler v. Kokemoor, 545 N.W.2d 495, 504–505 (Wis. 1996) (holding that trial court did not abuse its discretion in admitting evidence regarding the defendant physician’s lack of experience in performing a difficult surgical procedure as “[a] reasonable person in the plaintiff’s position would have considered such information material in making an intelligent and informed decision about the surgery”).

\(^{364}\) See, e.g., Cruzan ex rel. Cruzan v. Dir., Mo. Dep’t of Health, 497 U.S. 261, 278 (1990) (“The principle that a competent person has a constitutionally protected liberty interest in refusing unwanted medical treatment may be inferred from our prior decisions.”); Washington v. Harper, 494 U.S. 210, 229 (1990); (“The forcible injection of medication into a nonconsenting person’s body represents a substantial interference with that person’s liberty”).

\(^{365}\) E.g., Matthew, supra note 36, at 743.

\(^{366}\) See, e.g., Kanuszewski v. Shah, 636 F. Supp. 3d 781 (E.D Mich. 2022), vacated in part, 2022 WL 11964348 (holding that state officials’ post-testing research, storage, transfer, sale, discard, and other uses of newborns’ dried blood spots obtained without obtaining parents’ informed consent violated parents’ due process rights). Following the initiation of this case and others, Congress passed a law specifying that research on newborn blood spots was, if federally funded, human subjects research under the Common Rule. See Kassels & Merz, supra note 74.
expanded, for example, in a case extending the duties of researchers to parties affected by research studies who are not actually enrolled study participants.367

B. Differences Between Regulatory and Common Law Consent for Research

The costs and burdens of regulatory informed consent for research are real.368 And we should take seriously the claim of researchers that the informed consent requirements imposed by the regulations, and/or the way they are enforced by IRBs, may sometimes impede valuable research without offering meaningful protection for patient-subjects. Critics of modern informed consent processes argue that the overprotection of patients in research comes at the cost of harm to patients in clinical care when commonly used treatments have not been adequately compared in terms of their safety and effectiveness.369

Although it is clear from the foregoing analysis that the common law imposes a duty on physicians to obtain informed consent before placing patients in a study that randomizes them to medical treatments, even those within the standard of care, we should not assume that the common law requirements for consent are identical to or even closely resemble the informed consent processes required by the federal research regulations. The rights of patients in some interventional research studies may be adequately protected by something less demanding than full regulatory consent.370 Intuitively, the kind of consent process and form needed for someone to be informed enough to participate in a Phase I first-in-human clinical trial of a novel intervention of unproven safety seems different from that needed for a comparative effectiveness trial that actually does only compare two long-approved medications widely used for seasonal allergies.

For years, researchers and scholars have urged change in the regulations to allow for less extensive consent processes and forms, but with little success. Some advocates who argue that studies that simply randomize patients to compare standard of care treatments qualify as “minimal risk” under the federal regulations may actually support continuing to obtain consent from patients in the way that the common law would require, but simply find that the “one-size-fits-all” default written consent form and processes mandated by the regulations constitute too burdensome a standard for the benefit they provide patients. Because modifications to those regulatory requirements for consent cannot generally be made for covered research outside the emergency context unless it presents no more than “minimal risk,”371 arguing that a study is minimal risk is the only avenue, other than revision


368. See supra text accompanying notes 107–114.


371. 45 C.F.R. 46.117(c)(1) (2023).
of the regulations, available to researchers seeking a reduction—not an elimination—in the requirements for consent.

Much of the recent advocacy for consent waivers or modifications comes amid intense interest in and efforts to conduct comparative effectiveness research on clinical interventions in real-world settings through “learning health systems” (also called “learning healthcare systems”). A robust learning health system—to date, an aspirational model—has been described as one “in which knowledge generation is so embedded into the core of the practice of medicine that it is a natural outgrowth and product of the healthcare delivery process and leads to continual improvement of care.”372 Advocates for learning health systems suggest that some randomized CER studies can be embedded into the routine practice of care with either no or reduced requirements for research consent.373 Some have described research informed consent as “a critical barrier for learning health systems.”374

Proponents of modified consent processes have offered many alternative paths forward for comparative effectiveness trials, from “streamlined” consent that may not include a written form, to “integrated consent” that combines consent for both clinical care and research into one process (though clearly delineating the two), to “opt out” mechanisms that may involve individual notification to patients about specific research activities or may involve only a general notice to patients that certain kinds of research activities may take place within the health system from which they seek care.375 (Recall that Truog et al., in laying the foundation for...


373. See, e.g., Ruth R. Faden, Tom L. Beauchamp & Nancy E. Kass, Informed Consent, Comparative Effectiveness, and Learning Health Care, 370 NEW ENG. J. MED. 766 (2014). The main proponents of learning health systems propose that they would satisfy transparency and consent requirements by informing patients “in routine and systematic ways of the policies that are in place to provide ethical oversight of learning activities,” listing ongoing research activities on the internet and reporting on past results of research activities. “In addition,” they write, “a learning health care system would publicize to patients that while they might not be informed routinely about each learning activity – since many have little, if any, effect on patients’ interests or rights – they will be adequately informed, and their consent sought, whenever a learning activity might have a negative impact on quality of care or impose burdens above and beyond what they would otherwise experience.” Faden, et al., supra note 372, at 25. But see Menikoff, supra note 67, at 30 (writing that these authors “are surprisingly sketchy on the details about which clinical trials would still require informed consent. They allow that randomized, controlled trials of an ‘investigational new device,’ and perhaps of ‘first-in-class medications,’ would still require consent. Interestingly, they make no such comment about, for example, trials involving comparisons of marketed medications being used consistent with Food and Drug Administration-approved labeling.”).


375. Flory et al., supra note 369.
waiving consent in standard-of-care studies, included as a condition that institutions inform patients that research is being conducted utilizing waivers of consent, and allow patients to “obtain additional information about the policy or to seek care elsewhere”—a broad institution-wide “opt out” of sorts.)

Some of these proposed modes of consent could well meet the common law requirements for informed consent and satisfy providers’ fiduciary duties, though the details in each instance would be important. We would caution, however, against much, if any, relaxation of research informed consent standards in randomized CER trials with high-stakes outcomes in terms of patients’ health and welfare, such as the hypothetical research study we have described in this Article. For these trials, the research regulations’ required disclosures about the research activity, its purpose, potential risks and benefits, alternatives, and the rights of participants (among others) plus the requirement of consent prior to the research activity taking place, continue to be appropriate and necessary to protect and honor patients’ rights.

Although an in-depth analysis is beyond the scope of this paper, “opt outs” would likely not meet the common law requirements for informed consent for a randomized clinical trial, even if it is a comparative effectiveness study. The content of the disclosures themselves may not be a problem. One could imagine an opt-out notice that contained adequate disclosures about the specific research activity taking place. But careful safeguards would need to be in place to ensure that a patient received that notice and could reasonably be expected to have understood both (1) how the patient’s care would be altered by the research activity and (2) the notice’s instruction that the patient’s failure to object would be taken as authorization to proceed. The voluntariness of the patient’s failure to opt out would also be important—were other means of accessing needed health care available? The efforts that would need to be made for an “opt out” mechanism to satisfy common law duties may end up being just as or more onerous than obtaining individual informed consent. Even after all that, a court would likely look unfavorably on any attempt to read a patient’s silence as authorization to have their care determined not by what is best for them but in order to conduct research to benefit future patients. Presumed consent in the context of both emergency medical treatment and emergency research is justified by the potential for benefit to the patient. See Baker & Merz, supra note 29, at 580. (The exception from informed consent for emergency research “must offer a reasonable prospect of direct therapeutic benefit, so enrollment could potentially help the subjects themselves.”) (emphasis omitted).

In such a world, placing responsibility on patients to learn about the research activities taking place and to opt out of the ones they object to might very well suffice but such a world, if it might legally exist in the future—an open question—does not exist now.

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376. Truog et al., supra note 80, at 805.
377. Presumed consent in the context of both emergency medical treatment and emergency research is justified by the potential for benefit to the patient. See Baker & Merz, supra note 29, at 580. (The exception from informed consent for emergency research “must offer a reasonable prospect of direct therapeutic benefit, so enrollment could potentially help the subjects themselves.”) (emphasis omitted).
378. E.g., Faden et al., supra note 372, at 23–24.
Finally, we offer a variation of Menikoff’s question about changed conditions: have conditions changed so much that we should no longer be concerned that research without consent will fall disproportionately on people who are socially vulnerable or disadvantaged? Even Truog et al.’s influential 1999 paper, which posited that some randomized standard of care trials might be ethically conducted without consent, recognized the legacy of the USPHS Syphilis Study, and noted that potential subjects might wish to avoid research participation not because of the details of a particular study, but because of “important historical and cultural issues of concern.” In such contexts, there “may be grounds for insisting on specific informed consent for participation . . . .” Harriett Washington’s 2006 book, Medical Apartheid, documents the history of the exploitation of African Americans by medical researchers—extending long before the infamous syphilis study and long after as well. Her exhaustive account makes clear that any continuing distrust of the U.S. medical research system on the part of African Americans and other people of color is justified. The indefensible American history of research without consent extends as well to other populations who have been taken advantage of because of their reduced ability to know of or be able to protest their participation, such as people with fewer financial means or less education, prisoners, military personnel, people who are institutionalized, and people with mental impairments. Will things be different with waivers of consent for comparative effectiveness trials?

379. Truog et al., supra note 80, at 805.
380. Id.
382. See infra notes 395–400 and accompanying text.
383. Advisory Committee on Human Radiation Experiments, Final Report of the Advisory Committee on Human Radiation Experiments (1995) (available at https://ehss.energy.gov/ohre/roadmap/achre/chap9_4.html [https://perma.cc/6ZQU-QHBG]) (“It is difficult to overemphasize just how common the practice became in the United States during the postwar years. . . . After the Food and Drug Administration’s restructuring of drug-testing regulations in 1962, prisoners became almost the exclusive subjects in nonfederally funded Phase I pharmaceutical trials designed to test the toxicity of new drugs. By 1972, FDA officials estimated that more than 90 percent of all investigational drugs were first tested on prisoners.”).
384. See, e.g., Susan E. Lederer, The Cold War and Beyond: Covert and Deceptive American Medical Experimentation, in Military Medical Ethics 507, 507–31 (David E. Lounsbury et al. eds., 2003) (describing long history of military experimentation on military personnel and civilians, including children of service members); United States v. Stanley, 483 U.S. 669 (1987) (describing secret administration of LSD to military service personnel who had volunteered to participate in a program to test protective clothing and equipment).
The potential for a disproportionate share of research without consent to be performed on people of color and people of lower socioeconomic means is beginning to receive attention from scholars concerned about the use of consent waivers in comparative effectiveness trials. The data necessary to evaluate this concern are generally lacking. But there is reason to be concerned.

When the rule allowing for an exception from informed consent for emergency research (the EFIC rule) was adopted by the FDA in 1996, commentators at that time asked whether the waiver would disproportionately affect people of color and those with fewer resources because much of this research would take place at research institutions in inner cities and associated public hospitals, as the latter take all comers regardless of financial means. A recent analysis of clinical trials granted an exception from informed consent requirements by the FDA from 1996 to 2017 concluded this fear was well-founded. African Americans, who make up only 12% of the U.S. population, made up 29% of U.S. participants in the EFIC trials. As recently as 2021, Public Citizen, a national consumer advocacy organization, called on OHRP and the FDA to investigate a study that qualified for a consent waiver under the EFIC rule for its disproportionately high enrollment of Black subjects. The study took place at fifty-eight hospital emergency departments across the


388. E-mail from Jon Merz (March 23, 2022) (who with others is presently studying this concern) (on file with author).

389. Paul Root Wolpe & Jon F. Merz, Hospital ERs on Front Line in Informed-Consent Debate, in 12 FORUM FOR APPLIED RESEARCH & PUBLIC POLICY 127, 130 (1997) (raising question whether the then newly adopted EFIC rule would “disproportionately affect minorities” because “many large research hospitals are located in inner-city areas”); Annette Dula, Bearing the Brunt of the New Regulations: Minority Populations, 27 HASTINGS CTR. REP. 11, 11–12 (1997) (predicting that under the FDA EFIC rule, “African Americans, Hispanics, and poor people will be disproportionately the subjects of experimentation without informed consent. Because of the location of trauma centers and because of the disproportionately high rate of certain kinds of trauma, poor people and people of color will probably bear a great deal of the burdens of research.”). But see William B. Feldman, Spencer Phillips Hey & Aaron S. Kesselheim, A Systematic Review of the Food and Drug Administration’s ‘Exception from Informed Consent’ Pathway, 37 HEALTH AFFAIRS 1605, 1611 (2018) (showing that although EFIC trials did disproportionately enroll African American patients, this did not appear “to be a function of the ready application of EFIC to trauma trials”).

390. Feldman et al., supra note 389, at 1611. The authors point out that while African Americans make up 29% of EFIC participants, they represent only 5% of clinical trial participants overall. Id. Furthermore, “[m]ost EFIC trials did not demonstrate a benefit from the experimental intervention or interventions.” Id. at 1609.

391. Id. The authors surmise that a “likely explanation for the racial disparities in EFIC trial enrollment is that trials were conducted in geographic areas with large African American communities.” Id. at 1612.

country, comparing three medications commonly used to treat status epileptus (sustained seizures) that is unresponsive to an initial first-line treatment. Among other concerns, Public Citizen noted that “enrollment of subjects who were Black in [the study] was disproportionately high compared with the proportion of patients hospitalized in the U.S. for status epilepticus who are Black.”

At least two large clinical trials have allowed for a comparison of patient characteristics of study participants when consent is required versus when it is waived. Both trials initially required consent; when it was later waived, higher percentages of people of color and of lower socioeconomic means were enrolled.

One, the National Acute Brain Injury Study: Hypothermia (NABISH), conducted in the 1990s, studied an experimental emergency treatment for severe brain injury. The research trial began with a requirement for prospective consent (from patients’ surrogates), but when enough subjects could not be recruited to complete the study, the Department of Health and Human Services allowed study investigators to enroll patients without consent if consent could not be obtained within the treatment window of the studied intervention. Waiver of consent increased the enrollment of minority patients (defined in the study as being of African, Hispanic, or Asian origin) and unskilled workers. Moreover, minority patients and unskilled workers were more likely to be enrolled without consent than non-minority patients and skilled workers: waiver of consent was used for 53% of minority patients and 33% of nonminority patients; and for 47% of unskilled workers compared to 29% of “clerical, homemaker, professional, and skilled workers.”

The second trial was a non-emergency international (non U.S.) neonatal randomized controlled trial in which consent (i.e., parent permission) was also initially required for patient-subjects but later waived. Authors conducting a retrospective review of patient characteristics between the two groups concluded that there were “important differences in the demographics of mothers and infants.” Enrollment of non-“Caucasian” mothers increased once prospective consent was waived and researchers only sought retrospective consent (i.e., consent to collect and use data post-intervention) for infants to remain in the study after initial treatment through randomization. The percentage of patients eligible for the study but from whom prospective (pre-intervention) consent could not be obtained for “social

394. Letter from Michael A. Carome, supra note 392, at 3. A pre-planned post-enrollment survey of patients and surrogates for the ESETT study to ascertain their perspectives on research using the emergency exception from informed consent also usefully informs this debate, finding that “[b]lack participants were more likely than white, other race, and unknown-race participants to disagree with enrollment without prospective consent (36% versus 23%, 14%, and 14%, respectively).” Victoria M. Scicluna et al., Patient and Surrogate Postenrollment Perspectives on Research Using the Exception From Informed Consent: An Integrated Survey, 76 ANNALS EMERGENCY MED. 343 (2020).
396. Id.
397. Songstad et al., supra note 118, at 4.
398. Id. at 4.
reasons or language” also declined once the requirement for prospective consent was waived. In addition, more infants whose mothers had not received certain prenatal treatments (presumably a sign of reduced health care access) were represented in the group when only retrospective consent was required.

Perhaps counterintuitively, evidence of the disparate impact of waived consent has led some commentators to urge that it be waived more often. In other words, waiver of consent has been explicitly justified by some researchers because of the difficulty in obtaining consent from people who fall into certain racial groups or have lower socioeconomic means and/or lack access to consistent health care. These researchers urge waiver of consent in order to ensure that the results of the research are less affected by consent bias and therefore more applicable to guiding treatment for these groups of people.

This argument was made, in fact, by some of the SUPPORT investigators about SUPPORT. Post-study, researchers reviewed the characteristics of those infants enrolled with required prospective consent and those eligible but not enrolled, either because they were not approached (e.g., if their arrival to the hospital was too close to delivery), refused to consent, or were excluded for other reasons (such as language barriers). (Recall that SUPPORT did not use a waiver of consent, so there would be no comparison of patient-subjects before and after waived consent.) The authors determined that mothers of infants enrolled in SUPPORT were more likely to have private insurance and to have received prenatal care than infants eligible but not enrolled. They concluded that “SUPPORT infants were less disadvantaged than the overall eligible population.” Enrolled infants were also slightly more likely to be White, non-Hispanic. These observations led the authors to conclude there was likely enrollment bias stemming from the requirement to obtain consent, threatening the generalizability of the study’s results. Waiving consent may “increase the inclusion of the sickest and most at-risk populations.” They suggested that the study could have been considered “minimal risk” under the test Truog et al. have proposed and that in the future a waiver of consent for trials of that sort should be considered.

399. Id. at 3.
400. Id. at 5.
401. See, e.g., Rich et al., supra note 108.
402. This argument was also made during the debate about the adoption of the FDA’s rule allowing waiver of consent for emergency research. See Wolpe & Merz, supra note 389, at 128 (“Requiring consent in Emergency Research might, some contend, skew research results by preventing the equitable inclusion of members of some racial and economic groups who are typically less likely to consent to research participation.”); see also Roma Dhamanaskar et al., supra note 387.
403. See Rich et al., supra note 108. Consent was not obtained for 45.3% of eligible women who were approached for consent, presumably because they refused. Id. at 218. 108
404. Id. at 482.
405. Id. at 482 tbl. 1.
406. Id.
407. Id. at 6.
408. Id. at 483.
While difficulties in obtaining generalizable results are at the forefront of this argument, some have gone further and suggested that loosening consent requirements with the goal of increasing underrepresented populations in research would be a step forward in terms of equity. Requiring consent means that some groups of people—those from whom consent is less easily obtained—may not benefit as much from the research results (because the results are not as applicable to them) and therefore may not benefit as much from whatever medical advances may follow. For example, evidence of differences in the patient characteristics of those enrolled in NABISH led some commentators to argue that even if it had been practicable to complete the study with consent, it would not have been ethical to do so because “underrepresentation of minorities and the poor violates the ethical principle of justice as expressed in the Belmont Report.”

All the following may be true: it may be true that better science requires more inclusion, that requiring consent makes that inclusion difficult to achieve, and that when studies are done without broad inclusion the benefits of that research will not be shared equally. But the proposed solution is frankly disturbing.

Even if this strategy is proposed with good intentions—to improve medical care for those groups of people from whom it is more difficult to obtain research informed consent—it fails to respect their fundamental rights as people. It looks like the “benevolent paternalism” characteristic of past practices in medicine and research, rightly rejected decades ago. Using disadvantage as a justification to pile on a further disadvantage in the form of nonvoluntary research inclusion is wrong.

It is also terribly shortsighted. Waiving the requirement for consent in one study or a few studies may lead to more scientifically reliable results for those studies but would further deepen any existing mistrust in the research enterprise and the medical profession and potentially worsen existing barriers to broader research inclusion. Rather than waiving consent requirements so that a more representative population of study participants can be enrolled, we should be asking why it appears more difficult to obtain consent from people of color and of lower socioeconomic means. Past historic research abuses and continuing distrust of the medical profession may explain higher refusal rates among certain populations. Less access to consistent healthcare may mean patients show up with a smaller treatment window and thus less time to participate in an informed consent process. It could also mean fewer relationships in which patients trust the physicians who wish to enroll them in their studies. Rather than enrolling people in research studies without their consent—

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409. Clifton et al., supra note 395, at 1125.
410. Id.
411. Timia Raven-Gregg & Victoria Shepherd, Comment, Exploring the Inclusion of Under-Served Groups in Trials Methodology Research: An Example from Ethnic Minority Populations’ Views on Deferred Consent, 22 TRIALS 589 (2021) (reviewing use of and attitudes towards “deferred consent” (i.e., consent following the research intervention) in emergency research, and concluding that there is “evidence showing that black participants are the largest racial group enrolled into studies using deferred consent, despite studies showing they express greater aversion to its use”). See also K. Aagaard-Tillery et al., Sample Bias Among Women with Retained DNA Samples for Future Genetic Studies, 108 OBSTETRICS & GYNECOLOGY 1115 (2006) (finding that African American and Hispanic women were less likely to agree to future research on maternal and fetal DNA).
especially studies that could change the medical treatment they receive and affect their health—we should instead be working to increase trust in the medical profession and research enterprise by demonstrating trustworthiness and working to decrease barriers to care.

Finally, we should also be concerned that when waivers of consent are allowed, they will be unequally applied. Consent waivers are not necessarily blanket waivers—when granted, IRBs might still require researchers to obtain consent from potential research subjects when possible.\footnote{This means that some people eligible to be included in a study will be given the opportunity to consent or refuse while others will not be approached for consent at all but still receive the research intervention as if they had consented. Making the decision whether a person should be approached for consent or whether, instead, the barriers for obtaining consent from them will be too great, will necessarily include a subjective element and therefore be vulnerable to improper biases. Approving a waiver for all subjects would eliminate or at least reduce this problem but would mean failing to respect a greater number of people’s rights to autonomy, bodily integrity, and fidelity within the physician-patient relationship.}

This means that some people eligible to be included in a study will be given the opportunity to consent or refuse while others will not be approached for consent at all but still receive the research intervention as if they had consented. Making the decision whether a person should be approached for consent or whether, instead, the barriers for obtaining consent from them will be too great, will necessarily include a subjective element and therefore be vulnerable to improper biases. Approving a waiver for all subjects would eliminate or at least reduce this problem but would mean failing to respect a greater number of people’s rights to autonomy, bodily integrity, and fidelity within the physician-patient relationship.

\section*{VIII. CONCLUSION}

Gelinas and colleagues suggest that whether comparative effectiveness studies without consent infringe on patient rights depends upon whether we think patients have a right to receive “personalized care,” or only “good enough” medical care.\footnote{The answer the common law provides is a hybrid of sorts. Applying the medical malpractice standards used to determine negligence in diagnosis and treatment, the physician is only held to the standard of a minimally competent physician, to providing “good enough” care. We can’t expect our doctors to always be the best or to deliver the best care. But the law does require them to provide that “good enough” care with a particular aim—to further the best medical interests of their patient. Otherwise, the care may be “substantially at variance” with what the patient reasonably expects and is covered by that patient’s general consent to medical treatment, resulting in a medical battery. The patient’s consent to the medical treatment may also not be properly informed because the physician has not disclosed one of the most important things—if not the most important thing—the patient needs to know before proceeding. The physician has not disclosed that, contrary to the patient’s natural and reasonable expectations, the physician is prioritizing research aimed to further the interests of future patients rather than the patient’s current medical interests by placing the patient in a research study without informing them or asking for their consent. And finally, when a physician does this, the relationship the patient reasonably believes they have entered with their physician—a doctor-patient relationship—is replaced, or at least is replaced.}

412. This is required under the EFIC exception. 21 C.F.R. § 50.24 (2023). The waivers granted in the pre-hospital agitation and placental transfusion trials discussed in the introduction also appeared to require researchers to obtain consent if possible. See Cole et al., supra note 19, at 558; Katheria et al., supra note 10, at 1878.

running consecutively along with, a different relationship—a researcher-subject relationship. The patient has no inkling that this has occurred. They continue to assume that this doctor-patient relationship is like all previous ones they’ve known, a relationship within which they can trust that their physician is being open and honest with them and that the treatments they have been offered or are receiving have been chosen by their physicians specifically for them using their professional judgment. The advocates of waiving consent for comparative effectiveness studies downplay these physician commitments and patient expectations by saying, essentially, that there is no harm done by waiving the requirement for consent in these studies. It is surprising how many have failed to see through that fallacy. In the SUPPORT study, for which advocates argued that there were no undisclosed risks associated with research participation, investigators read their own data as suggesting “there is one additional death for approximately every two cases of severe retinopathy that are prevented.”\(^{414}\) In the prehospital agitation study, unwitting subjects in mental health crises experienced respiratory distress and other serious harms when treated according to the research protocol.\(^{415}\) The placental transfusion study had to be stopped early because too many of the youngest newborns were suffering brain bleeds in one arm of the study.\(^{416}\) In order to benefit future patients, these types of CER studies place some current patients at increased risks for harm they would not be facing if they had not been placed in the study. In some cases, the potential harms they face in the study are substantial. This possibility is expected at the outset, even when investigators have correctly represented and replicated standard of care treatments.\(^{417}\)

Patients in these trials may also stand to benefit. But whether or not to roll the research dice—or in the language of advocates for no consent, flip a coin—is firmly within the patients’ legal and ethical rights, as the cases we have described in this Article clearly show.

Some of the most prominent advocates for reducing traditional consent requirements argue that they are outdated—they overprotect patients from research yet underprotect them from inappropriate medical management because it is too difficult to conduct research that is actually able to improve clinical care.\(^{418}\) “The current oversight system requiring informed consent for most clinical research,” they write, “grew out of a scandal-ridden period in which people were included in research and exposed to considerable risk without their knowledge or consent. In intervening decades, the clinical-research enterprise has changed.”\(^{419}\) In many ways, the clinical-research enterprise has changed since those days, though improvements in ethical standards and conduct came only after hard-fought battles. Our legal analysis urges a recommitment to ethical understandings that are long held and embedded in the common law. In this way, innovations in research design and

\(^{414}\) Carlo et al., Target Ranges, supra note 40, at 1967.
\(^{415}\) Cole et al., supra note 19, at 559 (“Complications occurred in 49% (27/55) of patients receiving ketamine vs. 5% (4/82) in the haloperidol group.”).
\(^{416}\) See supra text accompanying notes 19–20.
\(^{417}\) See Macklin & Natanson, supra note 100 (raising concerns that in some CER studies, all treatment arms have not represented usual care).
\(^{418}\) Faden et al., supra note 373, at 766.
\(^{419}\) Id.
oversight for CER studies can strive to honor these ethical commitments, rather than seek ways to skirt them.