

Journal of Health Care Law and Policy

Volume 19 | Issue 2

Article 2

Virtual Clinical Trials: One Step Forward, Two Steps Back

Lori Andrews

Kayla Kostelecky

Stephanie Spritz

Alexandra Franco

Follow this and additional works at: <http://digitalcommons.law.umaryland.edu/jhclp>

Recommended Citation

Lori Andrews, Kayla Kostelecky, Stephanie Spritz, & Alexandra Franco, *Virtual Clinical Trials: One Step Forward, Two Steps Back*, 19 J. Health Care L. & Pol'y 189 (2017).

Available at: <http://digitalcommons.law.umaryland.edu/jhclp/vol19/iss2/2>

This Article is brought to you for free and open access by the Academic Journals at DigitalCommons@UM Carey Law. It has been accepted for inclusion in Journal of Health Care Law and Policy by an authorized editor of DigitalCommons@UM Carey Law. For more information, please contact smccarty@law.umaryland.edu.

VIRTUAL CLINICAL TRIALS: ONE STEP FORWARD, TWO STEPS BACK

LORI ANDREWS, KAYLA KOSTELECKY, STEPHANIE SPRITZ
AND ALEXANDRA FRANCO*

Virtual clinical trials have entered the medical research landscape. Today's clinical trials recruit subjects online, obtain informed consent online, send treatments such as medications or devices to the subjects' homes, and require subjects to record their responses online. Virtual clinical trials could be a way to democratize clinical research and circumvent geographical limitations by allowing access to clinical research for people who live far from traditional medical research centers. But virtual clinical trials also depart dramatically from traditional medical research studies in ways that can harm individuals and the public at large. This article addresses the issues presented by virtual clinical trials with regard to: (1) recruitment methods; (2) informed consent; (3) confidentiality; (4) potential risks to the subjects; and (5) the safety and efficacy of treatments that are approved.

I. OVERVIEW

Medical research on human beings has consisted of triumphs¹ and tragedies.² Like other human endeavors, medical research has been characterized by researchers' capacity for brilliance and compassion at times, but also their baser

© 2018 Lori Andrews, Kayla Kostelecky, Stephanie Spritz & Alexandra Franco.

* Lori Andrews, J.D., is the Director of the Institute for Science, Law and Technology and Distinguished Professor of Law at IIT Chicago-Kent College of Law. Kayla Kostelecky, J.D., is a Ph.D. candidate in Health Care Ethics at Saint Louis University. Stephanie Spritz, J.D., is a Florida lawyer practicing litigation at Fowler, White, Burnett. Alexandra Franco is a law clerk for Judge Franklin Valderrama in the Circuit Court of Cook County and an Affiliated Scholar at the Institute for Science, Law and Technology. We wish to thank Michael Goodyear for his aid in the preparation of this Article.

1. See David Rose, *A History of the March of Dimes*, MARCH OF DIMES (Aug. 26, 2010), <http://www.marchofdimes.org/mission/a-history-of-the-march-of-dimes.aspx> (explaining that through the March of Dimes' support, Salk's research led to the breakthrough of a polio vaccine).

2. See *The Tuskegee Timeline*, CTRS. FOR DISEASE CONTROL AND PREVENTION, <http://www.cdc.gov/tuskegee/timeline.htm> (last visited Oct. 18, 2016) (chronicling the Tuskegee experiments where black men with syphilis were not given treatment so that researchers could observe the natural course of the disease); see also, David S. Jones et al., *Ethics and Clinical Research—The 50th Anniversary of Beecher's Bombshell*, 374 NEW ENG. J. MED. 2393, 2393–98 (2016) (arguing that “many interests—medical, personal, political, military and commercial—have led researchers to conduct studies they knew to be transgressive. It would be hubris to think that such lapses could not happen again”).

emotions of racism,³ sexism,⁴ and avarice.⁵ Legal rules—in particular the U.S. federal research regulations⁶—have been put into place to protect research participants and to ensure that the treatments that are approved are safe and effective.

But now ingenuity in another field—digital technology—is testing the ability of the research regulations to achieve their goals.⁷ Medical researchers have started to recruit research subjects based on their online searches,⁸ social media activities,⁹ and use of health apps.¹⁰ Rather than using an ad for a clinical trial in

3. See generally HARRIET WASHINGTON, *MEDICAL APARTHEID: THE DARK HISTORY OF MEDICAL EXPERIMENTATION ON BLACK AMERICANS FROM COLONIAL TIMES TO THE PRESENT* 157 (2006) (tracing systematic black oppression in medical science throughout American history and documenting abuse and lack of proper notification or consent in experimentation decades before Tuskegee).

4. Rebecca Dresser, *Wanted: Single, White Male for Medical Research*, 22 HASTINGS CTR. REP. 24, 25 (1992) (explaining that women have been excluded from participation in biomedical studies due to perceived weakness, denying them the benefit of such research).

5. See Kurt Eichenwald & Gina Kolata, *Drug Trials Hide Conflicts for Doctors*, N.Y. TIMES (May 16, 1999), http://www.nytimes.com/1999/05/16/business/drug-trials-hide-conflicts-for-doctors.html?pagewanted=all&_r=0 (explaining that financial rewards caused doctors to place patients in research studies that were not appropriate for them).

6. See 45 C.F.R. § 46 (2015); see also 21 C.F.R. § 50 (2016).

7. Zachary Brennan, *Industry Calls for More Guidance From FDA on New Clinical Trials Technology*, RAPS (May, 11 2016), <http://www.raps.org/Regulatory-Focus/News/2016/05/11/24930/Industry-Calls-for-More-Guidance-From-FDA-on-New-Clinical-Trials-Technology/>.

8. *E-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment*, INVENTIV HEALTH, 10 (Oct. 14, 2013), http://www.inventivhealth.com/docs/e-Recruiting_Using_Digital_Platforms_Social_Media_and_Mobile_Technologies_to_Improve_Clinical_Trial_Enrollment.pdf.

9. *Id.*; Maloyre Allison, *Can Web 2.0 Reboot Clinical Trials?*, 27 NATURE BIOTECH. 895, 897 (2009) (detailing companies utilizing social media for clinical trial recruitment).

10. Roughly one-fifth of smartphone owners (nineteen percent) have health apps. Susannah Fox & Maeve Duggan, *Tracking for Health*, PEW RES. CTR.—PEW INTERNET & AMERICAN LIFE PROJECT, http://questromworld.bu.edu/grandchallenge/files/2013/03/PIP_TrackingforHealth_PDF, 11 (Jan. 28, 2013) <http://www.digitaltrends.com/mobile/google-play-store-2014-most-downloaded-apps/> [hereinafter *Tracking for Health*]. Industry estimates suggest that 50% of over 3.4 billion mobile device users will have downloaded a health app by 2018. FOOD AND DRUG ADMINISTRATION, *MOBILE MEDICAL APPLICATIONS*, <http://www.fda.gov/medicaldevices/digitalhealth/mobilemedicalapplications/default.htm> (last updated Sept. 22, 2015). Even game apps can collect information that is revealing about someone's health. In some instances, the app or game or website is sponsored by a pharmaceutical company or biotechnology company seeking information for research. Wayne Usher & James Skinner, *Health Websites and Reliability Components*, 55 ACHPER HEALTHY LIFESTYLES J. 29 (2008) (highlighting that websites can collect health information when the page is sponsored by a pharmaceutical company or biotechnology company seeking data for research); Micol Spinazzi, *Human Behavior and the Health Information Search*, MAKOVSKY HEALTH, (Apr. 24, 2014), <http://www.makovsky.com/insights/blogs/m-k-health/44-insights/blogs/m-k-health/614-human-behavior-and-the-health-information-search> (stating that for health information searches, mobile use is up thirteen percent, while PC use is down fourteen percent over the last year); Nicole May, *Mobile Health Is App-le of Pharma's Eye*, PHARMAPHORUM.COM, (August 9, 2013), <http://pharmaphorum.com/views-and-analysis/mobile-health-is-app-le-of-pharma-s-eye/> (explaining gamification of health apps could be focused on specific drugs or therapies); cf. Manhattan Research, *Few Pharma Websites Optimized for Mobile, According to Manhattan Research's New ePharma Com-*

a local newspaper or paying a physician up to \$5,000 to convince her patients to participate in a clinical trial,¹¹ the sponsor of a clinical trial can directly contact potential research participants based on their digital data, such as someone who did a Google search for “joint pain” or who “liked” the American Diabetes Association on Facebook.¹²

This digital transformation has not only changed the practices of researchers, it has changed the mindset of potential subjects. Clinical trial inquiries are one of the top online searches for health information.¹³ Online services such as TrialX—a free service that matches participants to relevant clinical trials based on their health information¹⁴—use Twitter¹⁵ to match potential research subjects to clinical trials that suit their needs: “all you need is to QuTweet (query tweets pronounced cue-tweets) us at TrialX (@trialx), put in the keyword ‘CT’ (for Clinical Trials) followed by your health profile.”¹⁶

Clinical trial recruiters first used the web to recruit subjects into traditional research settings, asking the potential subject to travel to a university or research center to participate.¹⁷ But, in 2011, a fundamental change occurred. The phar-

petitive Analysis Series, (Dec. 5, 2013), <http://www.prnewswire.com/news-releases/few-pharma-websites-optimized-for-mobile-according-to-manhattan-researchers-new-epharmaceutical-competitive-analysis-series-234601981.html> (foreshadowing a push by pharmaceutical companies into the health app space). For a listing of social media websites [and mobile apps] sponsored by pharmaceutical companies, see *Mobile App Wiki*, DOSE OF DIGITAL, <http://www.doseofdigital.com/healthcare-pharma-mobile-app-wiki/> (last visited Sept. 28, 2016) (listing of mobile health applications sponsored by pharmaceutical companies); *Social Media Wiki*, DOSE OF DIGITAL, <http://www.doseofdigital.com/healthcare-pharma-social-media-wiki/> (last visited Sept. 28, 2016) (listing social media websites sponsored by pharmaceutical companies).

11. See Eichenwald & Kolata, *supra* note 5 (describing a recruitment effort in which Merck & Company offered a bonus to doctors who enrolled a quota of fourteen patients).

12. See generally Allison, *supra* note 9, at 900; cf. FRANK PASQUALE, *THE BLACK BOX SOCIETY: THE SECRET ALGORITHMS THAT CONTROL MONEY AND INFORMATION* 28 (2015) (describing how an individual who conducts an online search for information on a disease, then later completes a seemingly unrelated form, can land themselves on a targeted marketing list).

13. Allison, *supra* note 9, at 900.

14. *Id.*; see also *Connecting Patients to Your Trials*, TRIALX, <http://trialx.com/iconnect/> (last visited Sept. 13, 2016) (explaining that patients can search TrialX for clinical trials related to a specific condition and contact the trial coordinator if they are interested in participating).

15. TrialX (@TrialX), TWITTER, <https://twitter.com/trialx>, (last accessed Sept. 7, 2016) (“Connecting patients to clinical research via trial finders, mobile research apps and more.”).

16. *Trialx*, CROSSOVER HEALTHCARE (Apr. 9, 2009), <https://crossoverhealth.wordpress.com/com/#comment-894>.

17. See, e.g., *E-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment*, *supra* note 8 (outlining practices for efficiently using social media to identify potential research participants, tailor clinical trial messages by using “patient speak,” and target potential participants); FRED HUTCHINSON CANCER RESEARCH CENTER, ACM NEWS, *CLINICAL TRIALS NOW USING SOCIAL MEDIA TO ATTRACT TRIAL PARTICIPANTS*, (Mar. 24, 2010), <http://cacm.acm.org/news/80616-clinical-trials-now-using-social-media-to-attract-trial-participants/fulltext> (describing the use of online advertisements to recruit participants for an HIV vaccine trial); ABOUT MYCLINICALTRIALLOCATOR.COM, MCTL, <http://www.myclinicaltriallocator.com/about/> (last

maceutical company Pfizer received clearance from the Food and Drug Administration (FDA) to conduct a clinical trial entirely online.¹⁸ The Pfizer trial relied on a process for conducting clinical trials over the internet patented by Boston University¹⁹ and exclusively licensed to Mytrus, a clinical trials software company.²⁰ Mytrus has since developed multiple technologies to support direct-to-patient clinical trials, including an electronic informed consent system and remote data collection mechanisms.²¹

Online clinical trials were born of good intentions—to expand the opportunities for both researchers and participants.²² Virtual clinical trials have already been conducted in which treatments have been tested, including for overactive bladder and osteoarthritis.²³ The treatments include medications,²⁴ devices,²⁵ and nutritional supplements.²⁶

visited Jan. 16, 2017) (explaining that the purpose of the website is to search for clinical trials in a specific geographic location).

18. Jennifer Corbett Dooren, *A Clinical Drug Trial Via Phone, Computer*, WALL ST. J. (June 7, 2011), <http://www.wsj.com/articles/SB10001424052702304432304576369840721708396>.

19. U.S. Patent No. 7,251,609 (filed Apr. 28, 2000).

20. See *Mytrus Secures Exclusive Rights to Clinical-Trials Patent from Boston University*, MYTRUS (June 11, 2011), <https://www.mytrus.com/en/news/detail/patent-rights>; see also *Mytrus Launches Pfizer Trial*, MYTRUS (June 8, 2011), <https://www.mytrus.com/en/news/detail/wsj-pfizer> (explaining that Mytrus is supporting Pfizer's study and holds the exclusive patent to conduct virtual clinical trials in the US).

21. MYTRUS, <https://www.mytrus.com/en/products-services/direct-to-patient> (last visited Jan. 15, 2017).

22. See Deborah Covington & Kristin Veley, *The Remote Patient-Centered Approach in Clinical Research*, 24 APPLIED CLINICAL TRIALS 30, Feb./Mar. 2015 (explaining that online clinical trial can overcome geographic obstacles and increase research efficiencies).

23. See *Web-Based Methodology Trial to Evaluate the Efficacy and Safety of Tolterodine ER in Subjects with Overactive Bladder (REMOTE)*, CLINICALTRIALS.GOV, <https://clinicaltrials.gov/ct2/show/NCT01302938> (last visited Jan. 22, 2017) (conducting a remotely controlled exploratory clinical trial with internet based tools to study the effect of tolterodine on subjects with overactive bladder); see also *Amp Orthopedics Initiates Clinical Trial in Knee Osteoarthritis Pain*, MYTRUS (Dec. 7, 2011), <https://www.mytrus.com/en/news/detail/amportho-oa> [hereinafter *Amp Orthopedics*] (conducting remote clinical study completely over a web-based medium to study the amelioration of knee pain in patients with mild to moderate Osteoarthritis using non-thermal Pulsed Radio Frequency treatment); see also Amp Orthopedics, Inc., *Effectiveness Study of the Ivivi SofPulse for Pain Amelioration in Adults with Mild Knee Osteoarthritis*, CLINICALTRIALS.GOV, <https://clinicaltrials.gov/ct2/show/study/NCT01457742?term=Ivivi&rank=1> (last visited Jan. 22, 2017).

24. *Web-Based Methodology Trial to Evaluate the Efficacy and Safety of Tolterodine ER in Subjects with Overactive Bladder (REMOTE)*, *supra* note 23.

25. See *Mytrus Ivivi Osteoarthritis Study*, YOUTUBE.COM, (Aug. 7, 2013), https://www.youtube.com/watch?v=42-_lDa9RLE (advertising the Mytrus Ivivi Osteoarthritis study to potential participants).

26. U.S. Patent No. 7,251,609 (filed Apr. 28, 2000). Timothy McAlindon et al., *Effectiveness of Glucosamine for Symptoms of Knee Osteoarthritis: Results from an Internet-Based Randomized Double-Blind Controlled Trial*, 117 AM. J. MED. 643 (2004).

The characteristics of “virtual clinical trials”²⁷ are that they: (1) identify potential participants by gathering data based on people’s online searches and activities; (2) determine if people qualify for a trial (sometimes based on a medical record or X-ray, but sometimes based merely on the person’s self-report); (3) obtain the individual’s consent over the internet; (4) send the participant the treatment (drug or device) in the mail; (5) get the participant to report if the treatment is working; (6) pay the participant at various points for participating; and (7) base the FDA approval and marketing decisions on those self-reports, or, in some cases, laboratory measures of progress.²⁸

This article examines virtual clinical trials in light of long-standing legal and ethical obligations of researchers.²⁹ Federal regulations require researchers at institutions that receive federal funds to submit proposals for studies of human subjects to Institutional Review Boards (IRBs) that evaluate such proposals

27. Throughout this paper, we will refer to “virtual clinical trial(s)” or “online medical research” interchangeably when we are talking about the entirely remote clinical trials in which subjects are undergoing a clinical experiment at their home and over the internet. We will also use the terms “medical research trial” and “clinical trial” interchangeably.

28. See Covington & Veley., *supra* note 22, at 31 (explaining that many aspects of clinical trials can be completed remotely, including recruitment, informed consent, reporting results, and payment); *see also* Amp Orthopedics, *supra* note 23 (requiring potential participants to submit an x-ray that indicates knee osteoarthritis to participate in the study); *see also* MYTRUS, Overactive Bladder Homepage, Sept. 24, 2011, <https://web.archive.org/web/20110924121322/https://oab.mytrus.com/home> (last visited Jan. 16, 2017 by searching for “oab.mytrus.com/home” in the Internet Archive’s Wayback Machine Index) (asking potential participants whether they experienced urine leakage); *see also* Miguel Orri et al., *Web-based Trial to Evaluate the Efficacy and Safety of Tolterodine ER 4 mg in Participants with Overactive Bladder: REMOTE Trial*, 38 CONTEMPORARY CLINICAL TRIALS 193 (2014) (explaining that Pfizer obtained a waiver from the FDA to ship the study drug to participants via overnight delivery); *see also* *Frequently Asked Questions about the FDA Drug Approval Process*, FDA (Jan. 7, 2015), <http://www.fda.gov/Drugs/ResourcesForYou/SpecialFeatures/ucm279676.htm> (last visited Sept. 14, 2016) (explaining that clinical trials allow the FDA to decide whether a drug should be approved for marketing).

29. These duties include compliance with the Nuremberg Code, Federal Research Regulations, state research laws, and medical ethics codes. NUERNBERG MILITARY TRIBUNALS VOL. II, TRIALS OF WAR CRIMINALS BEFORE THE NUREMBERG MILITARY TRIBUNAL UNDER CONTROL COUNCIL LAW NO. 10 181–82 (U.S. Gov. Printing Office, Oct. 1946–Apr. 1949) (stating that basic principles must be met when experimenting with human participants to satisfy moral, ethical and legal concepts); *see also* DHHS Protection of Human Subjects, 45 C.F.R. § 46 (2015); *see also* CAL. HEALTH & SAFETY CODE § 24170 (West 1978); *see also*, e.g., *AMA Code of Medical Ethics*, AM. MED. ASS., <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics.page> (last visited Jan. 16, 2017) (stating that physicians must gain voluntary consent from the participant, disclose risks of the study, minimize any risks to the participant, and maintain confidentiality).

based on their adherence to federal regulations for the protection of human subjects.³⁰ The regulations provide that the risks to subjects be justified by the benefits that may result from the research,³¹ that voluntary informed consent be garnered,³² that confidentiality be maintained,³³ and that vulnerable populations receive additional special protections.³⁴ Furthermore, any research to be used in support of an application for drug approval to the FDA must comply with regulations protecting human subjects in federally-funded trials, even if the research institutions do not receive federal grants.³⁵ This expands the reach of the federal regulations to pharmaceutical and biotechnology companies planning to market new drugs and devices.³⁶ The regulations are designed to protect research participants from risks and to ensure that, when a treatment is marketed, it is safe and effective.³⁷

Virtual clinical trials could be a way to democratize clinical research and provide access to clinical research for people who live far from traditional medical research centers by breaking down geographical barriers that hinder their participation.³⁸ Such trials could also be more cost-effective than traditional research which takes place at a hospital, university, or other medical institution.³⁹ But virtual clinical trials also depart dramatically from traditional medical research studies. This Article addresses several potential risks to the participants and to society: (1) inappropriate recruitment methods; (2) informed consent concerns; (3) confidentiality issues; (4) potential risk to the subject; and (5) concerns about the safety and efficacy of treatments that are approved. The article also suggests ways in which these risks might be addressed through law.

Consider the following scenario: a teenager is solicited over the internet, based on his social media comments or online searches, for a clinical trial of a treatment of depression. He poses as an adult, submits the informed consent form and is sent a six-week supply of pills. The sponsor adds money to his debit card each time he fills in a form about how he is feeling each day. Nothing could stop him from flushing the drugs down the toilet, saying the drugs are working, and collecting his money. In addition, since many companies collect data about people's activities on the web, the fact that he is in a depression research study could

30. 45 C.F.R. §§ 46.101(a), 46.102(h), 46.102(j), 46.103(b) (2015).

31. 45 C.F.R. § 46.111(a)(2) (2015).

32. *Id.* § 46.111(a)(4).

33. *Id.* at (a)(7).

34. 45 C.F.R. § 46.111(b) (2015).

35. *See* 21 C.F.R. § 50.1(a) (2016).

36. *See id.*

37. *See* 21 C.F.R. §§ 50.1(a) and 21 CFR § 99.201(a)(2) (2016).

38. *See* Covington & Veley, *supra* note 22, at 24.

39. *See id.* at 31. *See* Michael J. McFarland, *Ethical Implications of Data Aggregation*, SANTA CLARA U.: MARKKULA CTR. FOR APPLIED ETHICS (June, 1, 2012), <https://www.scu.edu/ethics/focus-areas/internet-ethics/resources/ethical-implications-of-data-aggregation/>.

be sold by data aggregators to third party institutions, such as employers and life insurers, and used to discriminate against him. In the meantime, the potentially dangerous drug could be approved based on “faked” data and a patient who takes the drug could be harmed.

II. HOW DO VIRTUAL CLINICAL TRIALS WORK?

For a medical research trial to succeed, researchers must recruit and maintain an adequate number of participants for the duration of the study.⁴⁰ An astounding 19.8 million participants were needed globally for clinical trials in 2005; this figure has undoubtedly increased.⁴¹ As many as two-thirds of investigative sites are unable to recruit a sufficient number of participants.⁴² In fact, one-third of investigative sites are unable to recruit even one participant.⁴³ Even the National Cancer Institute has trouble enrolling patients for clinical trials; more than one in five trials it sponsored failed to enroll even one participant.⁴⁴ Fewer than 20% of trials meet their deadline; half of the delays are due to difficulty recruiting participants.⁴⁵

This great demand for research participants reflects the increase in clinical research over the last twenty years, fueled in part by an increasing commercial interest in developing pharmaceutical products.⁴⁶ At the same time, other forces

40. Trudo Lemmens & Paul B. Miller, *The Human Subjects Trade: Ethical and Legal Issues Surrounding Recruitment Incentives*, 31 J.L. MED. & ETHICS 398, 400 (2003).

41. See VICKI ORANSKY WITTENSTEIN, *FOR THE GOOD OF MANKIND?: THE SHAMEFUL HISTORY OF HUMAN MEDICAL EXPERIMENTATION* 60 (Twenty-First Century Books, 2014) (stating that the number of participants needed for clinical trials rose from 2.8 million to 19.8 million between 1999 and 2005); cf. *Trends, Charts, and Maps*, CLINICALTRIALS.GOV, <https://clinicaltrials.gov/ct2/resources/trends#RegisteredStudiesOverTime> (last visited Jan. 16, 2017) (showing that the number of registered clinical trials rose from 24,921 to 207,083 between 2005 and 2015).

42. Press Release, Tufts Center for the Study of Drug Development, *Drug Developers Actively Improving Efficiency of Clinical Trials* (Apr. 26, 2011), http://csdd.tufts.edu/news/complete_story/rd_pr_apr_2011.

43. Allison, *supra* note 9, at 895.

44. *Id.* at 896.

45. *Id.* at 895.

46. Trudo, *supra* note 40. The top 15 pharmaceutical companies with the highest market earnings combined made approximately \$526 billion in profits in 2014. See Tracy Staton, *The Top 15 Pharma Companies by 2014 Revenue* [hereinafter *The Top 15*], FIERCE PHARMA (Mar. 18, 2015), <http://www.fiercepharma.com/special-report/top-15-pharma-companies-by-2014-revenue>; see also *Who Has the Biggest One? Sales of the Top Pharma Products by Revenue*, PHARMACOMPASS (Apr. 23, 2015), <http://www.pharmacompass.com/radio-compass-blog/who-has-the-biggest-one-sales-of-the-top-pharma-products-by-revenue> (explaining that *THE TOP 15* calculated revenue based on every division within the companies analyzed, listing the following companies and their revenue in millions of dollars: Johnson & Johnson — 74,331; Novartis — 57,996; Roche — 47,462; Pfizer — 49,605; Sanofi — 43,070; Merck — 42,237; GlaxoSmithKline — 39,960; AstraZeneca — 26,095; Bayer — 25,47; Gilead Science — 24,474; Teva — 20,270; Amgen — 20,063; AbbVie — 19,960; Eli Lilly — 19,615; Bristol Myers Squibb — 15,879); see also Richard Anderson, *Pharmaceutical Industry Gets High on Fat Profits*, BBC NEWS (Nov. 6, 2014) (listing similar revenue numbers and estimating that the top companies have profit margins ranging from ten to forty-three percent).

deter people from participating in research. The costs of participation, lack of insurance coverage for experimental treatments in clinical trials, and distrust arising as a result of past abuses of research subjects can deter enrollment in clinical trials.⁴⁷

This shortfall in participation is occurring at a time when people are increasingly turning to online search engines to find health information. The 2015 Rock Health Digital Health Consumer Survey found that 71 percent of adults in the United States have searched online for health information.⁴⁸ The survey also found that 17 percent of the adult population is currently tracking a key health factor in a mobile application.⁴⁹

Drawing on the fact that people reveal their medical conditions on the web, researchers began to use that information to recruit research subjects. In June 2011, the pharmaceutical company Pfizer began the first virtual clinical trial in the U.S. under an investigational new drug application, with nearly every step of the trial—from candidate screening to data reporting—completed remotely.⁵⁰ The trial, Research on Electronic Monitoring of OAB [Overactive Bladder] Treatment Experience, or REMOTE, involved a drug that had already been approved by the Food and Drug Administration for that condition.⁵¹

The goal was to recruit 600 participants for the REMOTE trial through targeted advertisements that appeared when internet users entered certain words into search engines or social network sites and through banner advertisements on

47. See *Paying for Clinical Trials*, NIH, <https://www.cancer.gov/about-cancer/treatment/clinical-trials/paying> (last updated June 22, 2016) (describing the costs involved with participating in a cancer clinical trial); see also Janet Leah Richards, *Geography is Destiny: Disparate Insurance Coverage for Cancer Clinical Trials Demands a Federal Mandate*, 76 U. MO-K.C. L. REV. 141, 143, 144 (2007) (finding that insurance carriers use policy exclusions deny claims for experimental treatment); see also Osagie K. Obasogie, *Prisoners as Human Subjects: A Closer Look at the Institute of Medicine's Recommendations to Loosen Current Restrictions of Using Prisoners in Scientific Research*, 6 STAN. J. C.R. & C.L. 41, 72–73 (2010) (noting the changing landscape in clinical trials along with isolated incidents has drastically decreased public trust in clinical trials).

48. Malay Gandhi & Teresa Wang, *Digital Health Consumer Adoption: 2015*, ROCK HEALTH (2015), <http://rockhealth.com/reports/digital-health-consumer-adoption-2015/#survey-overview>.

49. *Id.*

50. See *Web-based Methodology Trial to Evaluate the Efficacy and Safety of Tolterodine ER in Subjects with Overactive Bladder (REMOTE)*, *supra* note 23; see also Press Release, PFIZER, Pfizer Conducts First “Virtual” Clinical Trial Allowing Patients to Participate Regardless of Geography (June 7, 2011), <http://press.pfizer.com/press-release/pfizer-conducts-first-virtual-clinical-trial-allowing-patients-participate-regardless>.

51. See Hannah Waters, *FDA Approval Signals More ‘Homework’ on the Horizon in Trials*, 17 NATURE MED. 754 (2011); see also Jennifer Ringler, *Pfizer Asks Patients to Test Themselves*, PHARMABLOG (June 14, 2011), <http://iqpc-pharma.blogspot.com/2011/06/pfizer-asks-patients-to-test-themselves.html> (describing that REMOTE would use cell phone and internet access to recruit and track trial participants). Rachel E. Sherman, associate director for medical policy at the Center for Drug Evaluation and Research stated that the main reason for the study was to test the methodology of virtual clinical trials. See Mike Mitka, *Strategies Sought for Reducing Cost, Improving Efficiency of Clinical Research*, 306 J. AM. MED. ASS’N, 364, 365 (2011) (providing a high level overview of the participant recruitment process mapped for the REMOTE trial by startup company Mytrus).

health websites.⁵² Those advertisements directed interested individuals to the trial's website,⁵³ which promised eligible participants \$25 payments for each online assessment or lab visit, with the possibility of earning a maximum of \$175.⁵⁴

The website, which was operated by the clinical trial software company Mytrus, screened potential participants through a two-part online questionnaire with basic questions such as, "Will you have access to the Internet for the next 16 weeks (the study period)?" and "During the last 3 months: Have you leaked urine (even a small amount)?"⁵⁵ After this initial questionnaire, researchers attempted to verify a participant's identity by asking questions that "only [the potential participant] can answer" such as, "Select a street address you had in 1985," "Select a hospital in which you were born," and "Select a model of car you owned in 1997,"⁵⁶ and comparing the answers with public records databases.⁵⁷

Upon completion of the initial part of the questionnaire, the website prompted the participant to review and sign an electronic informed consent document with information about "the benefits and risks of the trial."⁵⁸ The informed consent document also included what Mytrus calls a "friendly" questionnaire, but the inability to answer questions correctly would not necessarily preclude the person from participating in the study.⁵⁹

Next, Mytrus would contact the individual and send a package that included a debit card which would be filled with money after a participant completed "each study milestone" and lab supplies for a blood draw that could be conducted

52. CLINPAGE, *Pfizer's Web Experiment: No Site? No PI? No Problem*, (Apr. 5, 2011), http://www.clinpage.com/article/no_site_no_pi_no_problem/C24.

53. *Id.*; see also MYTRUS, <https://www.mytrus.com/> (last visited Jan. 22, 2017) (private company conducting recruitment).

54. Peter Mansell, *Pfizer Announces 'Virtual Clinical Trial Pilot in US*, PHARMATIMES (June 9, 2011), http://www.pharmatimes.com/news/pfizer_announces_virtual_clinical_trial_pilot_in_us_980906.

55. See Orri et al., *supra* note 28. (explaining how the web-based screening process worked during the trial); see also Association ELA, *Mytrus 16-wk Paid Overactive Bladder Clinical Trial for Women*, YOUTUBE at 1:07 (Apr. 2011), <https://www.youtube.com/watch?v=Aya-BYQyMQz8&list=PL1gonBvfnk1lEtILWBxAI0m9B7qTnyuNo&index=9> (describing the screening process with example screening questions in a video designed to attract potential participants).

56. See Orri et al., *supra* note 28 (explaining that screening included precautionary procedures to confirm participant identities); Association ELA, *supra* note 55, at 1:15 (giving examples of questions that may be asked to confirm the participant's identity).

57. *Pfizer's Web Experiment: No Site? No PI? No Problem*, *supra* note 52.

58. See Association ELA, *supra* note 55, at 1:24–1:30 (explaining that the informed consent contained information about the risks and benefits of the REMOTE trial); see also Orri et al., *supra* note 28, at 193 (describing the informed consent process for the REMOTE trial).

59. See, Mytrus, Inc., *Mytrus Enroll Introduction*, YOUTUBE (May 8, 2014), <https://www.youtube.com/watch?v=1AqJWkYoOVs> (advertising the Mytrus Enroll electronic informed consent product); see also Orri et al., *supra* note 28, at 191, 192 (explaining the informed consent process as it was conducted in the REMOTE trial).

either “during a home visit or at a nearby designated lab.”⁶⁰ Mytrus would send the participants a digital diary device to “record urination volume and frequency of urinations throughout the study.”⁶¹ At the conclusion of the trial, participants received individual trial results for export into personal medical records.⁶²

Remarkably, during this process, participants receive a package containing enough of the drug to last 14 weeks without having to set foot inside a research facility.⁶³ Because this methodology was unprecedented, Pfizer had to obtain a waiver from the FDA in order to send the drugs to the participants at their homes.⁶⁴

Other virtual clinical trials have been conducted using a similar methodology. One such trial tested the effectiveness of glucosamine and chondroitin sulfate in treating osteoarthritis.⁶⁵ Researchers recruited participants through the internet using links on health-related internet sites, such as the Arthritis Foundation’s webpage, and through advertisements in online publications unrelated to health.⁶⁶ Similar to the REMOTE trial, a potential participant who viewed the study website and indicated interest in participation would be screened over the internet by self-administered questionnaires.⁶⁷ The screening questions included: “Do you get pain in one or both knees after walking 2-3 city blocks (~1/4 mile)?” and “Have you ever been diagnosed by a physician as having arthritis in your knees?”⁶⁸ The glucosamine and chondroitin sulfate would then be sent directly to the participants’ homes and participants would record their reaction on an online form.⁶⁹

60. See Association ELA, *supra* note 55, at 2:02–2:27 (describing the virtual overactive bladder clinical trial to potential participants).

61. *Id.* at 2:55–3:05.

62. See Pfizer Press Release, *supra* note 51; see also Association ELA, *supra* note 55, at 2:40, 3:00–3:05.

63. See Association ELA, *supra* note 55, at 2:36–2:46.

64. See Ringer, *supra* note 51 (reporting on Pfizer’s announcement of its new REMOTE clinical trial). One year after starting the REMOTE trial, Pfizer stopped enrolling subjects. See *Pfizer Ends Social Media Bid for Trial Recruitment*, BIOSPACE (June 2012), <http://www.biospace.com/News/pfizer-inc-ends-social-media-bid-for-trial/264338>. Pfizer was ultimately not able to recruit enough people to participate in the study. See Nick Taylor, *Pfizer Director Defends Virtual Trial After Recruitment Struggle*, OUTSOURCING-PHARMA.COM (Mar. 6, 2012), <http://www.outsourcing-pharma.com/Clinical-Development/Pfizer-director-defends-virtual-trial-after-recruitment-struggle>.

65. Tim McAlindon et al., *Conducting Clinical Trials Over the Internet: Feasibility Study*, 372 *BMJ* 484, 484 (2003).

66. U.S. Patent No. 7,251,609 col. 18, l. 58–67 (filed Apr. 28, 2000); see also McAlindon et al., *supra* note 26, at 644.

67. U.S. Patent No. 7,251,609 col. 3, l. 3–15 (filed Apr. 28, 2000); see also McAlindon et al., *supra* note 65, at 485.

68. U.S. Patent No. 7,251,609 col. 19, l. 23–28 (filed Apr. 28, 2000); see also McAlindon et al., *supra* note 65, at 485.

69. U.S. Patent No. 7,251,609 col. 5, l. 47–60 (filed Apr. 28, 2000) (participants could also obtain the supplements at a pharmacy or clinic); see also McAlindon et al., *supra* note 65, at 485.

Devices, as well as drugs, have been mailed to research participants. Mytrus enrolled patients for a virtual clinical trial, sponsored by Ivivi Health Sciences, using an electromagnetic field therapy (EMF) device for the treatment of osteoarthritis.⁷⁰ The device emitted a pulsed magnetic field to reduce inflammation caused by osteoarthritis.⁷¹ The criteria for qualification in this study included submission of an X-ray of each knee taken at least twelve months preceding the study, self-reported constant knee pain in the two months preceding the study in at least one knee, the ability to read and complete survey questionnaires in English, and access to the internet on a daily basis.⁷² Mytrus' website encouraged participation by exclaiming: "You'll be glad to know we value your time. Patients who choose to participate in the study will sent a special debit card, that can be used anywhere that accepts normal debit cards. You may earn up to \$200, and payments will be automatically added to your card as you complete portions of the study."⁷³

Mytrus collected information daily about how the participant was feeling using standard pain scales and questionnaires.⁷⁴ Mytrus would ask participants questions such as: "How much knee pain are you experiencing today?" "Did you sleep well last night?" and "How difficult is it to walk up a flight of stairs?"⁷⁵ Mytrus finished the trial and anticipates that the results "could become the basis for market clearance" of the device.⁷⁶

Mytrus has expressed interest in conducting virtual clinical trials for binge eating, chronic obstructive pulmonary disease, diabetes, sleeping disorders and other maladies.⁷⁷ In March 2016, Mytrus also announced that it would be providing the virtual trial infrastructure for the ADAPTABLE (Aspirin Dosing: A Pa-

70. See Amp Orthopedics, *supra* note 23 (announcing a direct-to-patient clinic trial in knee osteoarthritis pain that allows patients to participate in the study from their own homes); see also *id.* (explaining that the purpose of the study is to evaluate the effectiveness of non-thermal pulsed radio frequency treatment for alleviating knee pain in patients with mild to moderate osteoarthritis); *Mytrus Ivivi Osteoarthritis Study*, YOUTUBE (Aug. 7, 2013), https://www.youtube.com/watch?v=42-_Ida9RLE (explaining the study to potential trial participants).

71. See Amp Orthopedics, *supra* note 23 (testing non-thermal pulsed radio frequency will be used for pain amelioration in adults with knee osteoarthritis); see also *id.* (announcing a clinic trial that uses non-thermal pulsed radio frequency technology to alleviate pain from knee osteoarthritis.); *Mytrus Ivivi Osteoarthritis Study*, *supra* note 70, at 1:22. (explaining to potential participants that the study treatment is given through knee wrap devices).

72. Amp Orthopedics, *supra* note 23.

73. *Mytrus Ivivi Osteoarthritis Study*, *supra* note 70.

74. *Id.*

75. *Id.* at 4:00.

76. Amp Orthopedics, *supra* note 23.

77. Wouter Stomp, *Pfizer Integrating Telemedicine into Clinical Trials*, MEDGADGET (June 15, 2011), <http://www.medgadget.com/2011/06/pfizer-integrating-telemedicine-into-clinical-trials.html> (noting that Mytrus has trials slated for "osteoarthritis, binge eating, COPD, diabetes, sleep disorders and informed consent validation.").

tient-Centric Trial Assessing Benefits and Long-Term Effectiveness) trial conducted by the Duke Clinical Research Institute.⁷⁸ The study plans to compare the dosing effects of aspirin in 20,000 subjects diagnosed with atherosclerotic cardiovascular disease.⁷⁹

The virtual clinical trials model is being embraced by pharmaceutical companies, device companies, and even traditional research settings such as universities.⁸⁰ But do the federal research regulations, drafted before the widespread use of the internet, adequately protect either subjects or the public when a virtual clinical trial is undertaken?

III. CONCERNS ABOUT ONLINE RECRUITMENT OF POTENTIAL RESEARCH SUBJECTS

The federal research regulations provide little guidance about the recruitment of research subjects, whether in traditional or virtual trials.⁸¹ When the regulations were enacted, it was expected that medical research subjects would be recruited by their physicians, who owed independent ethical and legal obligations to their patients.⁸² In that scenario, physician intermediaries had the duty of

78. PCORI, COMPARING TWO ASPIRIN DOSES TO PREVENT HEART ATTACK AND STROKES IN PEOPLE LIVING WITH HEART DISEASE: THE ADAPTABLE STUDY, <https://www.pcori.org/research-results/2015/comparing-two-aspirin-doses-prevent-heart-attacks-and-strokes-people-living> (last visited Feb. 16, 2017) (Trial website stating that as of January 2017, the trial's status is "In Progress-Not yet recruiting"); *see also*, NIH, ASPIRIN DOSING: A PATIENT-CENTRIC TRIAL ASSESSING BENEFITS AND LONG-TERM EFFECTIVENESS (ADAPTABLE), https://wwwcf.nlm.nih.gov/hsr_project/view_hsrproj_record.cfm?NLMUNIQUE_ID=20153384 (National Institutes of Health website listing the ADAPTABLE trial's status as "Ongoing").

79. *Mytrus Technology Chosen for Precedent-Setting ADAPTABLE Aspirin Trial*, MYTRUS (Mar. 7, 2016), <https://www.mytrus.com/en/news/detail/20160307-dcri>.

80. *See Virtual Reality: Where Does the Clinical Trial Industry Go from Here?*, CLINICAL TRIALS ARENA (Aug. 12, 2015), <http://www.clinicaltrialsarena.com/news/operations/virtual-reality-where-does-the-clinical-trial-industry-go-from-here-4644601> (noting that the pharmaceutical companies Pfizer, Sanofi, and Shire have each conducted at least one virtual clinical trial); *see also Amp Orthopedics Initiates Clinical Trial in Knee Osteoarthritis Pain*, MYTRUS (Dec. 7, 2011), <https://www.mytrus.com/en/news/detail/amportho-oa> (explaining that medical device manufacturer Amp Orthopedics has conducted a virtual clinical trial for one of its products); *see also Mytrus Technology Chosen for Precedent-Setting ADAPTABLE Aspirin Trial*, *supra* note 79 (noting that Duke Clinical Research Institute, an academic institution, is partaking in a virtual clinical trial).

81. Covington & Veley., *supra* note 22, at 24 ("There is little regulatory guidance on designing and conducting remote patient centered studies.").

82. *Clinical Trials and Human Subject Protection*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm>, (last visited Feb. 20, 2018), (noting that regulations protecting human subjects in clinical trials have been in existence since the 1970s); *see also* AM. MED. ASS'N. CODE MED. ETHICS § 7 (2016) (noting ethical and legal obligations of physicians recruiting patients for clinical trials, and for the general presumption that it is physicians who recruit patients for clinical trials); *Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479, 483 (Cal. 1990) (finding a legal cause of action when a physician who performed medical research on his patient without informed consent breached his fiduciary duty to the patient).

ensuring that participation in the trial was in the patient's best interest⁸³ and that the patient had the capacity to give informed consent.⁸⁴ Even when a physician-patient relationship did not exist between the potential subject and the recruiter, the clinical backgrounds of subject recruiters (such as nurses and doctors) ensured an awareness of the responsibility as medical professionals to protect individual welfare.⁸⁵ Although health care professionals (especially those paid to recruit patients into studies) did not always act in the patients' best interests,⁸⁶ patients did have recourse to lawsuits based on malpractice,⁸⁷ lack of informed consent⁸⁸ or breach of fiduciary duty⁸⁹ if the health care professional entered them into inappropriate and risky research.

Online recruitment for clinical trials provides no such backstop to curtail inappropriate enrollment. When trial recruitment occurs outside of the fiduciary relationship between physician and patient, the ethical imperative of acting consistently with the patient's best interest is removed.⁹⁰ In place of a medical professional with a well-established ethical duty to patient wellbeing, a questionnaire is responsible for safeguarding individual interests.⁹¹ Even the most beneficent questionnaire design will be crude in its assessment of patient best interests, as patient interests cannot be inferred from information about a patient's online profile alone. A patient who is harmed by enrollment in a study, or who has not provided informed consent, may have limited legal recourse when a trial is conducted virtually without the direct involvement of medical professionals.⁹² Legal causes of action that have traditionally protected trial partici-

83. AM. MED. ASS'N. CODE MED. ETHICS § 7 (2016) (noting the ethical obligation to protect the participants' interests).

84. *See id.* (requiring informed consent as an ethical obligation); *see also* A. D. Nieuw, *Informed Consent*, 12 MED. L. 125, 125–26 (1993) (noting that there is a legal duty to provide informed consent).

85. *See* Kurt Eichenwald & Gina Kolata, *supra* note 5 (emphasizing the responsibility that private-practice doctors conducting research feel toward trial participants).

86. *See id.* (describing instances in which doctors with financial stakes in recruiting participants recommended patients for trials that were inappropriate for them, such as a patient who was referred despite a known heart condition that made him ineligible).

87. *Karp v. Cooley*, 493 F.2d 408, 423–24 (5th Cir. 1974) (noting in *dicta* the existence of a medical malpractice cause of action for experimentation).

88. *Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479, 483 (Cal. 1990) (finding a cause of action for performance of medical procedures without informed consent)

89. *Id.*

90. *Id.* (stating that when there is a physician-patient relationship, the physician is ethically bound to disclose "personal interests unrelated to the patient's health" because of the fiduciary relationship).

91. *Id.* at 483 (declaring that medical professionals are bound by ethical duties, when a physician-patient relationship exists); *see also* Covington & Veley, *supra* note 22 (describing how potential virtual clinical trial participants self-enroll online and submit trial data online, rather than through a doctor intermediary).

92. *Id.* (requiring a physician-patient relationship before finding medical malpractice liability in the context of a clinical trial); *see also* Anthony Francis, *Is This a Real Doctor-Patient Relationship?*,

pants, such as breach of fiduciary duty or malpractice, are grounded in the particularities of the clinical relationship and professional norms.⁹³ As the virtual trial is driven largely by private companies with no direct relationship to the patient, a harmed subject may be limited to causes of action such as breach of contract.⁹⁴ Unlike causes of action that emerged in response to power imbalances between patients and the medical establishment, contract law is likely to regard the patient as an autonomous party, ignoring the vulnerabilities of individuals who are ill, dependent on the expertise of others, and may be desperate for therapeutic benefit.⁹⁵

There is little regulation of online recruitment and that which does exist is not focused on virtual clinical trials.⁹⁶ The FDA has issued a guidance document about the recruitment of clinical trial subjects through an advertisement which “includes, but is not necessarily limited to: newspaper, radio, TV bulletin boards, posters, and flyers that are intended for prospective subjects.”⁹⁷ According to the FDA guidance, advertising for clinical trial recruitment constitutes “the start of the informed consent and subject selection process.”⁹⁸ The FDA requires that Institutional Review Boards review ads to ensure that they are not “unduly coercive and [do] not promise a certainty of cure beyond what is outlined in the consent and the protocol.”⁹⁹ The FDA states that this requirement is particularly important when research “may involve subjects who are likely to be vulnerable

MEDSCAPE (Mar. 1, 2012), <http://www.medscape.com/viewarticle/759163> (explaining that while it is possible to form a physician-patient relationship online, it requires the physician to take an affirmative action to be involved in the patient’s medical care).

93. See *Moore*, 793 P.2d at 484 (finding a legal cause of action for a person who had been subjected to research without consent only because the participant had a physician-patient relationship with the researcher).

94. See *Mytrus And Pfizer Win Best Practices Award For Pioneering Work In Electronic Consent And Virtual Trials*, MYTRUS (Feb. 10, 2014), <https://www.mytrus.com/en/news/detail/20140211-scope-award> (awarding Mytrus and Pfizer, two private companies, for pioneering the clinical trial process); see also Covington & Veley, *supra* note 22 (describing virtual clinical trials with technology platforms that offer patient recruitment, consent, and data management, meaning the entire trial can be completed remotely via the internet); see also Covington & Veley, *supra* note 22 (describing virtual clinical trials with technology platforms that offer patient recruitment, consent, and data management, meaning the entire trial can be completed remotely via the internet); see also *Grimes v. Kennedy Krieger Inst., Inc.*, 366 Md. 29 (2001) (finding that informed consent agreements in nontherapeutic research projects can constitute contracts and create a special duty between participant and investigator).

95. Russell A. Hakes, *Focusing On The Realities Of The Contracting Process—An Essential Step To Achieve Justice In Contract Enforcement*, 12 DEL. L. REV. 95, 100–01 (2011) (explaining that contract theory assumes the freedom and autonomy of the actors when enforcing contracts, resulting in injustice when reality does not match this assumption).

96. See *Recruiting Study Subjects—Information Sheet: Guidance for Institutional Review Boards and Clinical Investigators*, FDA, <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm> (last updated Jan. 25, 2016) (stating that advertising for clinical trials online requires “no additional safeguard” but fails to mention the regulation of a virtual trial).

97. *Id.*

98. *Id.*

99. *Id.*

to undue influence.”¹⁰⁰ The guidance applies to online recruitment; however, it also states that IRB review of advertisements over the internet is not necessary if the advertisement displays limited information about the trial “such as the title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s) and how to contact the site for further information.”¹⁰¹

The problem with the FDA’s approach is that it focuses on what is presented to the potential participant.¹⁰² As such, it pays no attention to how the potential participant came to be targeted to begin with.¹⁰³ In traditional medical research, potential subjects were referred by their own physicians based on their actual medical conditions.¹⁰⁴ In virtual clinical trials, people who may be on the internet for wholly unrelated purposes are subjected to posts, banner ads, personal emails, and other tactics asking them to participate in research.¹⁰⁵ This new approach—targeting based on what a person does on the internet—raises several problems.¹⁰⁶ These include violation of privacy, exploitation of individuals who are vulnerable (or more likely to be “good” trial participants in terms of adherence, not reporting adverse events, etc.) and coercion.¹⁰⁷

The web is a target-rich area for finding research subjects because people use the web in all aspects of their lives.¹⁰⁸ They communicate with family members and friends, seek information, schedule appointments and trips, and reveal personal, lifestyle, and medical information.¹⁰⁹ Through their searches, purchases, and posts, people reveal information about their medical conditions.¹¹⁰ Health-related data can be analyzed from people’s general internet activities—such as when they Google a particular ailment or medication, “like” a patients’ group such as a cancer society, or post unusual symptoms and request help from friends to identify the cause of the disease or condition.¹¹¹ Health-related data

100. *Id.*

101. *Id.*

102. *Id.* (directing the IRB to review materials).

103. *Id.*

104. Joseph Walker, *Data Mining to Recruit Sick People*, WALL ST. J. (Dec. 17, 2013), <http://www.wsj.com/articles/SB10001424052702303722104579240140554518458>.

105. *Id.*

106. *Id.*; see also Brenda L. Curtis, *Social Networking and Online Recruiting for HIV Research: Ethical Challenges*, 9 J. EMPIRICAL RES. HUM. RES. ETHICS 58, 58, 66 (Feb. 20, 2014), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4316828/pdf/nihms576496.pdf>.

107. See *infra* note 218–219.

108. Alicia Shelton, *A Reasonable Expectation of Privacy Online: “Do Not Track” Legislation*, 45 U. BALT. L.F. 35, 35, 38 (2014).

109. *Id.* LORI ANDREWS, I KNOW WHO YOU ARE AND I SAW WHAT YOU DID 2–3 (2012).

110. Shelton, *supra* note 108.

111. See Walker, *supra* note 104 (describing how health care companies are examining aggregated data for clues about an individual’s health); see also Deborah Kogen, *How Facebook Saved My Son’s Life*, SLATE (Jul. 13, 2011), www.slate.com/id/2297933 (describing a mother whose son was diagnosed with a rare disease with the help of her friends after she posted her son’s symptoms on Facebook).

can also be gathered through medical and fitness apps (such as Fitbit)¹¹² and through digital games designed to help patients deal with certain diseases (such as children with diabetes).¹¹³

When a person posts something related to health on a social networking site, undertakes a web search for information about a particular disorder, or emails a health professional through Gmail, data aggregators and medical researchers make assumptions about that person's health and well-being.¹¹⁴ Medical researchers sometimes use data about people's web searches, "likes," and health disclosures in private emails (such as over Gmail) to target potential research subjects.¹¹⁵

Online recruitment relies heavily on the collection and analysis of sensitive health information and other personal information that people may not even realize they have revealed online. Clinical trial recruiters are using patient community sites, social networks, behavior-specific and disease-oriented sites, and search engine queries about health behavior and medical conditions to identify potential research subjects.¹¹⁶ But researchers are also using online data unrelated to health to make inferences about people's health status and then recruit them into studies. If a person subscribes to premium cable TV and eats in fast-food restaurants, he or she may be targeted for an obesity drug trial.¹¹⁷ According to Roger Smith, Senior Vice President at the data aggregation company Acurian, "We are now at a point where, based on your credit-card history, and whether

112. See FITBIT, FITBIT: CHARGEHR, <http://www.fitbit.com/chargehr> (the FitbitHR model of the fitness tracker tracks heart rate in addition to other health metrics); see also Stephen Armstrong, *What Happens to Data Gathered by Health and Wellness Apps?*, BMJ (2016), <http://www.bmj.com/content/353/bmj.i3406> (reporting that much of the data tracked by health and fitness apps like Fitbit are sold to third party companies).

113. See *id.* (reporting that much of the data tracked by health and fitness apps like Fitbit are sold to third party companies); see also Sarah R. Blenner et al., *Privacy Policies of Android Diabetes Apps and Sharing of Health Information*, 315 JAMA 1051 (2016) (reporting the results of a study that found that diabetes apps often collected and shared sensitive health information with third parties).

114. See Lauren Solberg, *Regulating Human Subjects Research in the Information Age: Data Mining on Social Networking Sites*, 39 N. KY. L. REV. 327, 342–346 (2012) (stating that academic researchers are data mining social networking sites for biomedical, social, and behavioral research); see also Julia Angwin, *The Web's New Gold Mine: Your Secrets*, WALL ST. J. (Jul. 30, 2010) <http://online.wsj.com/article/SB10001424052748703940904575395073512989404.html> (noting that website cookies and web beacons – tiny snippets of tracking code – allow companies to scan an individual's browsing patterns and make assumptions about that individual's income, shopping habits, and medical conditions); *Google Privacy and Terms*, GOOGLE, <https://www.google.com/policies/terms/> (last visited Jan. 22, 2017) (stating that Google scans the content of emails to provide tailored advertising and other relevant product features).

115. See Walker, *supra* note 104; see also *E-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment*, *supra* note 8, at 10 (outlining how recruitment companies can monitor social media sites and discussion boards to improve recruitment methods and target potential participants); see also ANDREWS, *supra* note 109, at 45.

116. See *E-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment*, *supra* note 8, at 10 (Oct. 14, 2003) (explaining that targeted advertisements on digital platforms are a growing and effective way to recruit clinical trial participants).

117. Walker, *supra* note 104.

you drive an American automobile and several other lifestyle factors, we can get a very, very close bead on whether or not you have the disease state we're looking at."¹¹⁸ Ken Shore, the Executive Vice President of Blue Chip (another data aggregation company like Acurian) explains that "[t]he types of magazines you buy, how often you buy running shorts, all of those things tell a story."¹¹⁹

When data aggregators obtain health data through online tracking mechanisms, individual privacy protections are limited to the dictates of company policies, which generally strip information divulged online of any privacy protections.¹²⁰ While some data aggregators claim to protect sensitive personal information, they adopt a definition of "sensitive" that fails to correspond to social expectations of privacy.¹²¹ Healthline Networks, Inc. places health-related advertisements on sites such as Dr. Oz, AARP,¹²² Ask.com,¹²³ and U.S. News¹²³ based on the content of the page that the person is reading.¹²⁴ Healthline claims that it does not allow advertisers to track sensitive health information such as HIV/AIDS, impotence, or eating disorders.¹²⁵ However, it does permit tracking of other potentially stigmatizing conditions such as anxiety and bipolar disorder.¹²⁶

When data aggregators surreptitiously collect personal information about online activity, they invade privacy and disregard the integral role that online health resources play in today's health care experience. Online health resources may represent the only form of health care available to those who cannot afford a doctor or otherwise lack access to professional medical help, are too embar-

118. *Id.*

119. *Id.*

120. See Sarah R. Blenner et al., *supra* note 113. (reporting the results of a study that found that diabetes apps often collected and shared sensitive health information with third parties).

121. See *id.* at 1053 (explaining that even apps with privacy policies commonly collect and share sensitive information with third parties).

122. Wade Roush, *Healthline Battles WebMD with Personalized Medical Search Tools, Body Maps*, XCONOMY (Nov. 30, 2011), <http://www.xconomy.com/san-francisco/2011/11/30/healthline-battles-webmd-with-personalized-medical-search-tools-and-3d-body-maps/#>.

123. *Healthline Networks Takes in \$21M Series B*, VENTUREWIRE (July 17, 2007), [http://healthtools.aarp.org/corporate/news/Venture_Wire_HL_Networks_Takes_In_\\$21m.pdf](http://healthtools.aarp.org/corporate/news/Venture_Wire_HL_Networks_Takes_In_$21m.pdf) (noting that Healthline secured distribution agreements to improve web site content for Aetna, AOL, Ask.com and U.S. News and World Report).

124. See Angwin, *supra* note 114 (explaining that targeted advertising is growing to meet demand for data on individual behavior and interests).

125. *Id.*

126. *Id.*

rassed to seek in-person treatment, struggle daily with chronic illness, or are dissatisfied with past treatment results.¹²⁷ Thus, many people view divulgence of personal health information online as crucial to their personal welfare.¹²⁸

The chronically ill are more likely than those who are healthy to search online to learn more about medical conditions, such as depression or anxiety, as well as drugs, insurance, and investigational treatments.¹²⁹ Therefore, these people may have more data available for collection and are more likely to be solicited for clinical trials. According to a study by the Pew Research Center, the chronically ill are more likely than other people to seek information online about medical conditions, drugs and treatments, read drug and treatment reviews on the internet and gather information on the internet about another person's health situation.¹³⁰ Sixty-two percent of internet users with two or more chronic illnesses have looked online for information about a specific illness or problem.¹³¹ The chronically ill, especially the homebound, tend to be more reliant on the internet not only for health care information but also for social support.¹³²

Some research and clinical trial recruitment services create websites that provide medical information but may additionally or primarily exist to recruit research participants. The clinical trial recruitment service MediGuard¹³³ operates a website that offers to alert users about drug safety warnings and drug-drug interactions and provides users with information about side effects, safety alerts,

127. See Daniel J. Amante, *Access to Care and Use of the Internet to Search for Health Information: Results From the US National Health Interview Survey*, 17 J. MED. INTERNET RES. (2015), https://www.jmir.org/article/viewFile/jmir_v17i4e106/2 (reporting that people who lack access to care for various reasons are more likely to use the internet to search for health information); see also Magdalena Berger et al., *Internet Use and Stigmatized Illness*, 61 SOC. SCI. & MED. 1821, 1826 (2005) (describing a study that found that people with stigmatized illnesses are more likely to use the internet for health information than those with non-stigmatized illnesses); Susannah Fox & Kristen Purcell, *Chronic Disease and the Internet*, PEW RES. CTR., 2 (Mar. 24, 2010), http://www.pewinternet.org/files/old-media/Files/Reports/2010/PIP_Chronic_Disease_with_topleftine.pdf (noting that "internet users living with chronic disease are slightly more likely than other internet users to access health information online."); Miriam McMullan, *Patients Using the Internet to Obtain Health Information*, 63 PATIENT EDUC. & COUNSELING 24, 26 (2006) (describing a survey of cancer patients indicating that people who are dissatisfied with information provided to them by health professionals often turn to the internet for information).

128. Amante, *supra* note 127. (finding that more than 40% of adults use the internet to search for health information).

129. Fox & Purcell, *supra* note 127, at 2 and 17.

130. Susannah Fox & Maeve Duggan, *Part One: Who Lives with Chronic Conditions, The Diagnosis Difference*, PEW RES. CTR., at 2 (Nov. 26, 2013), <http://www.pewinternet.org/2013/11/26/part-one-who-lives-with-chronic-conditions/>.

131. Susannah Fox & Maeve Duggan, *Part Two: Sources of Health Information*, PEW RES. CTR., at 14 (Nov. 26, 2013), <http://www.pewinternet.org/2013/11/26/part-two-sources-of-health-information/>.

132. Claire Cain Miller, *Social Networks a Lifeline for the Chronically Ill*, N.Y. TIMES, Mar. 25, 2010, at B3.

133. *Patient Recruitment*, QUINTILES, <http://www.quintiles.com/services/patient-recruitment> (last accessed Nov. 2, 2016) (advertising patient recruitment services on digital patient communities such as Mediguard.org).

recalls and a pill reminder app for smartphones¹³⁴—but only after individuals provide information about their medical problems, drug allergies, medications, age, sex, race, and email address.¹³⁵ While the site appears to offer a public service,¹³⁶ MediGuard’s creator and CEO, Hugo Stephenson, says, “Our business is identifying patients for clinical research projects.”¹³⁷ As of May 2016, MediGuard had over 2.6 million members.¹³⁸

Researchers also advertise on more traditional social networks such as Facebook because it is easy for the researcher to target subjects and for Facebook users to share advertisements.¹³⁹ Advertisements displayed on Facebook are placed according to users’ membership in condition-related groups, forums, or “likes,” and can be targeted according to gender, birthdate, and geographic location (as precise as a specific city radius or ZIP code).¹⁴⁰ The Acurian Facebook page, for example, shows an advertisement that reads: “Is asthma holding your child back? Enroll now in research studies offering up to \$1500.”¹⁴¹ The advertisement also gives Facebook users the option to “like” the ad, expanding its audience by sending the information to others in their friend networks.¹⁴² As Acurian notes, “because of the ‘viral’ character of social networks and activity, message reach can expand exponentially—without exponential investment.”¹⁴³ Social networks also allow recruiters to exploit social pressures to increase participation. Acurian encourages the use of social network site advertising because “social networks provide the potential for—and advantage of—peer-to-peer influence and referral.”¹⁴⁴ Targeted advertising on Facebook has already been used

134. MEDIGUARD, <https://www.MediGuard.org> (last visited Nov. 2, 2016); Press Release, QuintilesIMS, Patients Get Safety Information, Pill Reminders with New Mobile App from Quintiles, (Jan. 8, 2014), <http://www.quintiles.com/news/2014/01/patients-get-safety-information-pill-reminders-with-new-mobile-app-from-quintiles> (announcing MediGuard’s new app that functions as a pill reminder).

135. *Privacy Notice for Website*, MEDIGUARD, <https://www.mediguard.org/help/what-is-iguard/privacy> (last updated Dec. 2013) (explaining that users must provide “sensitive” information such as “race and ethnicity, medicines, or health conditions of interest” to the site).

136. Allison, *supra* note 9, at 899; *About Us*, MEDIGUARD, https://www.mediguard.org/help/about_us (last updated Nov. 1, 2013) (noting MediGuard is also known as iGuard).

137. Allison, *supra* note 9, at 899.

138. MEDIGUARD, <https://www.mediguard.org/> (last visited Feb. 16, 2017).

139. Michael Kosinski et al., *Facebook as a Research Tool for the Social Sciences*, 70 AM. PSYCHOLOGIST 543 (2015).

140. *How to Target Facebook Ads*, FACEBOOK BUS., <https://www.facebook.com/business/a/online-sales/ad-targeting-details> (last visited Jan. 22, 2017).

141. AcurianHealth, FACEBOOK (Nov. 17, 2015), <https://www.facebook.com/AcurianHealth/?fref=ts>.

142. *Id.*

143. Scott Connor, *Leveraging On-Line Social Networks for Clinical Trial Patient Recruitment*, ACURIAN WHITEPAPER SERIES, at 2 (2010), <http://www.clinicalleader.com/doc/social-media-for-patient-recruitment-0001>.

144. *Id.*

to reach young women for a sexual desire study¹⁴⁵ and to recruit teenagers for a smoking cessation study.¹⁴⁶

Federal regulators have not amended research guidelines to address internet recruitment, even though internet recruitment creates unique risks.¹⁴⁷ A person may be harmed psychologically when a research recruiter calls or emails and says, “Your Facebook profile indicates that you are at a high risk for an early heart attack. Would you like to participate in a clinical trial to test a drug to avert heart disease?” He may be harmed if he is aggressively targeted for participation with promises of possible improvement and then denied admission to the trial because of eligibility criteria without explanation or an offer of other support services. He may be physically harmed by the experimental drug sent to his home if the social media information or the Google searches do not actually reflect his health status. In addition, if a drug is approved for widespread use because of a faulty diagnosis, it may be ineffective or even harmful to people who actually have the condition.

People have complained about unsolicited research recruitment, but such complaints have not resulted in changes to the federal research regulations.¹⁴⁸ A website called Complaints Board features some people’s experiences with receiving unsolicited mail from Acurian.¹⁴⁹ One person commented: “I agree with complaint posted by person who received unsolicited mail from Acurian. I also

145. Deborah Borfritz, *A Social Approach to Patient Recruitment*, BIO-IT WORLD (May 18, 2010), http://www.bio-itworld.com/BioIT_Article.aspx?id=98953.

146. Michelle A. Rait, et al., *Recruitment of Adolescents for a Smoking Study: Use of Traditional Strategies and Social Media*, 5 *TRANSL. BEHAV. MED.* 254 (2015) (recruited teenage substance abusers via social media).

147. See Covington & Veley, *supra* note 22 (commenting that there is little regulatory guidance for conducting a virtual clinical trial); see also U.S. DEPT. HEALTH & HUMAN SERV., SEC’Y’S ADVISORY COMM. ON HUMAN RESEARCH PROT., ATTACHMENT B: CONSIDERATIONS AND RECOMMENDATIONS CONCERNING INTERNET RESEARCH AND HUMAN SUBJECTS RESEARCH REGULATIONS (2013) (discussing how current human research regulations are outdated and do not address unique issues of internet research). FDA guidance for recruiting study subjects only references the internet to note that IRB review and approval of listing of clinical trials on the internet is not required in most instances. See *Recruiting Study Subjects—Information Sheet Guidance for Institutional Review Boards and Clinical Investigators*, *supra* note 97. The U.S. Department of Health and Human Services, and fifteen other federal departments announced proposed revisions to modernize the federal policy for protection of human subjects in September 2015. Federal Policy for the Protection of Human Subjects, 80 FR 53931 (proposed September 8, 2015). While the proposed rule addresses certain technological advances in human subject research, it does not address online recruitment of human subjects. *Id.* at 53936–37.

148. See *Recruiting Study Subjects—Information Sheet Guidance for Institutional Review Boards and Clinical Investigators*, *supra* note 96 (explaining current regulations governing recruitment, which do not specifically address online recruitment); see also *E-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment*, *supra* note 8, at 10 (stating that there are no regulations that govern what media may be used to recruit human subjects).

149. Comments Forum to Acurian, Inc.: *Unsolicited Mail*, COMPLAINTS BOARD, <http://www.complaintsboard.com/complaints/acurian-inc-pennsylvania-c574582.html> (last updated Aug. 23, 2016).

received a letter. Don't have a clue as to where Acurian got my name and address. This can't be legal. . . ."¹⁵⁰ Another entry on the website reads: "My child just received a letter asking her to participate in a clinical study, she's a minor! The only people who know of her disorder is her pediatrician and Walgreens pharmacy!!! This can't be legal!"¹⁵¹ Yet another comment states: "I worked in clinical trials for over 10 years and agree that trials are very important. However, my son (a minor) received the same letter. I have worked very hard safeguarding his medical diagnosis. Outside of his doctor, pharmacy and school his name isn't attached or listed on anything."¹⁵² Others complained about receiving an invitation from Acurian to participate in a clinical trial for a condition that they did not have, but had only researched on the internet.¹⁵³ In fact, Acurian was the cause of over 500 Federal Trade Commission ("FTC") complaints over a two-year period, and has been sued because of its telemarketing practices.¹⁵⁴

Rather than expanding access to desperately needed experimental treatments, as expected by early advocates of online clinical trial listings and online researchers, the internet may actually diminish opportunities for clinical trial participation.¹⁵⁵ Targeted exclusively at individuals fitting a particular profile, clinical trial information will reach some eligible participants but not others.¹⁵⁶ A person's social media profile is likely to contain inaccuracies, or have little bearing on medical eligibility, but it may nevertheless become the sole determinant of whether an individual is selected for clinical trial participation.¹⁵⁷ Able to quickly and cheaply sort through thousands of potential clinical trial participants, the clinical trial industry can now exploit narrow selection criteria.¹⁵⁸ Instead of contributing to the robustness of study design, online participant selection gives

150. L.N. Johnson, Comment to *Acurian, Inc: Unsolicited Mail*, COMPLAINTS BOARD (Jan. 5, 2012), <http://www.complaintsboard.com/complaints/acurian-inc-pennsylvania-c574582.html>.

151. Montezumas Mom, Comment to *Acurian, Inc: Unsolicited Mail*, COMPLAINTS BOARD, (June 14, 2009), <http://www.complaintsboard.com/complaints/acurian-inc-pennsylvania-c574582.html>.

152. Keeping eyes open, Comment to *Acurian, Inc: Unsolicited Mail*, COMPLAINTS BOARD, (June 15, 2013), <http://www.complaintsboard.com/complaints/acurian-inc-pennsylvania-c574582.html>.

153. See, e.g., Walker, *supra* note 104.

154. See *id.* (explaining how the FTC alleges that Acurian violated standard telemarketing laws; however, the commission has not made comments on the current investigation as a matter of policy).

155. See text *infra* at notes 156–159.

156. See, e.g., *E-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to improve Clinical Trial Enrollment*, *supra* note 8 at 3, 8 (describing how e-recruiting on social media can target niche patient groups precisely).

157. Erica Naone, *When Social Media Mining Gets It Wrong*, MIT TECH. REV. (Aug. 9, 2011), <https://www.technologyreview.com/s/424965/when-social-media-mining-gets-it-wrong/> (describing an experiment in which data mining misidentified a person two thirds of the time and concluding that a Facebook profile is not a reliable source of information); see also Chetan Khatri et al., *Social Media and Internet Driven Study Recruitment*, PLOS, at 2 (Mar. 16, 2015) (describing a study that evaluated the effectiveness of recruiting solely through social media and concluded that it was cost effective).

158. See, e.g., Walker, *supra* note 104 (explaining online recruiting companies can sort through thousands of clinical trial participants and enroll larger numbers of patients in fast timeframes).

researchers the opportunity and means to favor the efficient and successful completion of product testing.¹⁵⁹ Will a segment of “optimal” participants—perhaps characterized by a lack of assertiveness as to side effects, the absence of a support system to oversee the process, or the lack of access to affordable alternatives—define the future of clinical trials?

The online process for recruitment of clinical trial subjects not only threatens the privacy of people’s medical information but also lacks the transparency that should be associated with medical or scientific research.¹⁶⁰ Luring people to a website which promises to provide a free service to help manage a person’s condition when it instead exists primarily to collect and disclose people’s sensitive health information is dishonest and unethical.¹⁶¹ When people turn to the online world to share medical information—for example, through social networks or patient support forums—they do so because they are seeking support for a medical condition or concern.¹⁶² An online forum post is the virtual equivalent of a conversation in a physical support group, only more accessible.¹⁶³ A person may believe that a computer screen will protect his or her identity and the privacy of his or her health information.¹⁶⁴ Even if websites decide to engage in greater transparency and tell users up front whether they disclose their personal information to third parties, people should not have to decide between access to information and attempting to safeguard their privacy.¹⁶⁵

159. See Mark Zetin & Cara T. Hoepner, *Relevance of Exclusion Criteria in Antidepressant Clinical Trials*, 27 J. CLINICAL PSYCHOPHARMACOLOGY 295, 300 (2007) (replicating and concurring with a study that found that exclusion criteria in antidepressant trials is being used to find particular participants that would produce ideal results for FDA marketing approval); see also, e.g., *E-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment*, supra note 8, at 3, 8 (advertising e-recruiting services capable of targeting precise groups of prospective subjects).

160. Allison, supra note 9, at 895, 899 (describing privacy concerns related to recruiting online and noting that some companies appear to offer free services to help people manage their medication without explaining that their business model is recruiting patients for clinical trials).

161. See *id.* at 899 (explaining how iGuard identifies patients for clinical research projects by offering free tools to manage medications).

162. See, e.g., Jam Kotenko, *The Doctor Will See You Now: How The Internet and Social Media Are Changing Healthcare*, DIGITAL TRENDS (Apr. 18, 2013), <http://www.digitaltrends.com/social-media/the-internet-and-healthcare> (noting how people use Twitter, Tumblr, and Facebook as virtual support groups); see also Fox & Purcell, supra note 127 at 17, 20 (explaining how twenty-eight percent of internet users living with disease use the internet to research their symptoms or talk to other users to inquire about their experiences with the same disease).

163. Marsha White & Steve M. Dorman, *Receiving Social Support Online: Implications for Health Education*, 16 HEALTH & EDUC. RES. 693, 694 (2001) (explaining how online support groups offer many benefits like 24/7 access without having to leave home and anonymity).

164. See *FTC Recommends Congress Require the Data Broker Industry to be More Transparent and Give Consumers Greater Control over Their Personal Information*, FTC (May 27, 2014), <https://www.ftc.gov/news-events/press-releases/2014/05/ftc-recommends-congress-require-data-broker-industry-be-more> (noting that many consumers are unaware that their data is being collected and sold).

165. See, e.g., INSTITUTE OF MEDICINE, *HEALTH DATA IN THE INFORMATION AGE: USE, DISCLOSURE, AND PRIVACY* 17 (Molla S. Donaldson & Kathleen N. Lohr eds., 1994) (showing how consumers often feel compelled to consent to waivers or they will forego the benefit sought and how those same consumers

The vast amount of information that people knowingly, or sometimes inadvertently, reveal about themselves online creates benefits and risks in the health research context.¹⁶⁶ On the positive side, researchers can contact potential subjects directly, providing interested people with the opportunity to participate in research.¹⁶⁷ On the negative side, the information that study participants provide online can be used by data aggregators in ways that disadvantage them.¹⁶⁸ People may be upset by the invasion of privacy and may suffer psychological harm.¹⁶⁹ Moreover, the quality of the research may suffer due to this form of recruitment if the targeted research subject looks for health information for someone else online or if the researchers' assumptions about the health status of consumers based on their purchases are wrong (such as when someone who purchases premium cable is not obese).¹⁷⁰

Targeted recruitment of clinical trial participants promises to increase awareness of relevant trials while relieving researchers of some of the burden of screening out the large percentage of interested individuals who are ultimately deemed ineligible.¹⁷¹ However, online recruitment based on information acquired through non-transparent practices also threatens individual privacy rights, the well-being of participants, the integrity of the trial process, and ultimately the health of the public.

are not informed of how their records will be used in the future); *see also* *Privacy Notice for Website*, *supra* note 135 (explaining how in order to receive services from MediGuard, customers must sign a waiver that allows MediGuard to collect sensitive information).

166. *See* Walker, *supra* note 104 (explaining how health researchers can now find individuals who would not show up through traditional profiling methods by using data information that they inadvertently disclose, like online purchasing habits, or knowingly disclose, like their demographics).

167. Connor, *supra* note 143, at 1 (explaining how social media sites like Facebook and Snapchat allow companies to place ads and trial information directly in front of potential subjects).

168. *See, e.g.*, Walker, *supra* note 104 (explaining concerns that data may be used to deny employment or reveal illnesses that people would like to keep private); *see also* Angwin, *supra* note 114 (noting that there are no legal limits on how consumer data can be used).

169. *See* Michael McFarland, *Why We Care about Privacy*, MARKKULA CTR. FOR APPLIED ETHICS, <https://www.scu.edu/ethics/focus-areas/internet-ethics/resources/why-we-care-about-privacy/> (last accessed Jan. 22, 2017) (explaining how people can be harmed or disadvantaged if their personal information becomes public).

170. *See* Walker, *supra* note 104 (explaining that Blue Chip Marketing found patients for an obesity drug by targeting people who subscribe to premium cable and frequent fast food dining, characteristics that suggest a sedentary lifestyle).

171. *See* Chetan Khatri et al., *supra* note 157, at 2 (noting that targeting on social media could reach new pools of interests subjects and lead to more efficient recruitment); *see also* *e-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment*, *supra* note 8, at 2, 12 (describing targeted e-recruitment efforts which increased traffic to a trial website by about 6,500% and another that tripled the number of patient's recruited while reducing recruitment costs).

IV. EQUITABLE SELECTION IN RECRUITMENT

Although the federal research regulations do not comprehensively address recruitment, they do require that the selection of subjects be “equitable.”¹⁷² This means that even if the requirement of informed, voluntary participation in research is satisfied, doing research on a specific group of people if the research is intended to benefit another group would violate the federal regulations.¹⁷³ For example, it would be inequitable to do research primarily on babies of color if a particular condition affects babies of all races, especially if the parents of white babies are more likely to afford treatments produced from such research. Equally problematic is choosing a powerful group in society, such as men, and using them as subjects in research for a condition that affects both men and women, if the type of treatment developed will mainly benefit men.¹⁷⁴ The federal research regulations state that in order to ensure equitable selection, Institutional Review Boards are required to consider the goals of the particular study, the setting in which it will be conducted, and the special concerns raised by vulnerable research subjects such as children, prisoners and the disabled.¹⁷⁵

In the process of drafting the federal research regulations, a government commission analyzed the ethical concerns raised by research on humans in the Belmont Report.¹⁷⁶ The Report states that justice requires “researchers to exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only ‘undesirable’ persons for risky research.”¹⁷⁷ The Belmont Report also states that injustice in the recruitment of

172. 45 C.F.R. § 46.111(a)(3) (2015); 21 C.F.R. § 56.111 (a)(3) (2016).

173. See *Equitable Selection of Participants*, U. UTAH INSTITUTIONAL REV. BD., at 1, http://irb.utah.edu/_pdf/BMGS-EquitableSelectionofParticipants.pdf (last visited Jan. 22, 2017) (requiring that benefits and burdens from research be distributed fairly); see also Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 44 Fed. Reg. 23,192–93 (Apr. 18, 1979) [hereinafter Belmont Report] (explaining how the distribution of benefits and burdens should be guided by the concept of justice).

174. See, e.g., Rebecca Dresser, *Wanted Single, White Male for Medical Research*, 22 HASTINGS CTR. REP. 24, at 24, 27 (Feb. 1992) (noting how male-only studies of heart disease and cholesterol led the American Heart Association to recommend a diet that could exacerbate the risk of heart disease among women); Karen H. Rothenberg, *Gender Matters: Implications for Clinical Research and Women’s Health Care*, 32 HOUS. L. REV. 1201, 1208 (1996) (describing how women were frequently left out of clinical trials for AIDS therapies); R. Alta Charo, *Protecting Us to Death: Women, Pregnancy, and Clinical Trials*, 38 ST. LOUIS U. L.J. 135, 156 (1993) (stating that the exclusion of fertile women from research trials for the sake of protecting the women and their future offspring ultimately leads the FDA to authorize marketing of untested drugs to such women).

175. See 45 C.F.R. § 46.111(a)(3) (2015); see also 21 C.F.R. § 56.111(a)(3) (2016).

176. See THE NAT’L COMM’N FOR THE PROT. OF HUM. SUBJECTS OF BIOMED. & BEHAV. RES., THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (1979); see also Belmont Report, *supra* note 173, at 192–93 (Apr. 18, 1979) (providing a summary of the 1979 Belmont Report and noting the abuses of human subjects in biomedical experiments during World War II, which led to the Nuremberg code).

177. THE NAT’L COMM’N FOR THE PROT. OF HUM. SUBJECTS OF BIOMED. & BEHAV. RES., *supra* note 176, at 6-1, 6-2; Belmont Report, *supra* note 173, at 196.

subjects may arise as a result of “social, racial, sexual and cultural biases institutionalized in society,” which may skew the distribution of risks and benefits of research.¹⁷⁸ Although the report clarifies that it is not the researchers’ duty to correct institutionalized social injustices, it emphasizes that researchers can help by “consider[ing] distributive justice in selecting research subjects,” thus minimizing the effect of social inequality.¹⁷⁹

Another concern raised by inequitable selection is sampling bias.¹⁸⁰ Sampling bias is an error introduced into the methodology of a particular research initiative by recruiting subjects who are not truly representative of the population that the sample is meant to study.¹⁸¹ As an example, a study to test the average bone density of women between the ages of 35 to 40 that recruits only women from a high-income urban neighborhood has a biased sample.¹⁸² Because women living in a wealthy, city neighborhood are likely to have both better access to quality nutrition and more time to exercise than women of the same age living in a low-income neighborhood or in a rural area, the sample of recruited subjects is likely to skew the results of the study.¹⁸³

Equitable selection of subjects is not adequately protected in virtual clinical trials.¹⁸⁴ At a basic level, the online platform is biased against people who are poorer, older, and live in rural areas.¹⁸⁵ Virtual clinical trials exclude those who do not use the internet or those who do not own a computer or smartphone.¹⁸⁶ If

178. Belmont Report, *supra* note 173, at 196.

179. *See id.* at 23,196–97; THE NAT’L COMM’N FOR THE PROT. OF HUM. SUBJECTS OF BIOMED. & BEHAV. RES., *supra* note 176, at 6-1, 6-2.

180. *See* Dresser, *supra* note 174, at 26–27 (stating that injustice in the selection of human subjects has contributed to imbalance in study populations).

181. *See* Elden Henson, *A Pocket Guide to cGMP Sampling*, INST. OF VALIDATION TECH., at 7–8 (2006), <http://www.ivtnetwork.com/sites/default/files/A%20Pocket%20Guide%20to%20cGMP%20Sampling.pdf> (providing the definition of sampling bias).

182. *See* Susan E. Parks et al., *Differential Correlates of Physical Activity in Urban and Rural Adults of Various Socioeconomic Backgrounds in the United States*, 57 J. EPIDEMIOLOGY & CMTY. HEALTH 29, 34 (2003) (describing how lower income, rural residents were less likely than higher income, suburban residents to meet physical activity recommendations).

183. *See id.*; *see also* *Access to Healthy Foods in Low-Income Neighborhoods*, RUDD CTR. FOR FOOD POL’Y & OBESITY, 6 (2008), http://www.ct.gov/dph/lib/dph/hems/nutrition/pdf/yale_rudd_center_access_to_healthy_foods_report_2008.pdf (explaining that there are fewer supermarkets in low-income and rural areas, which makes access to healthy and affordable foods more difficult than individuals who are oppositely situated); Gina Shaw, *Osteoporosis Tips: Build Stronger Bones*, WEBMD (Jan. 14, 2011), <http://www.webmd.com/osteoporosis/features/build-stronger-bones?page=3> (explaining how nutrition and exercise positively associate with greater bone density).

184. *See* Kathryn Zickuhr & Aaron Smith, *Home Broadband 2013*, PEW RES. CTR., 1, 3 (2013), http://www.pewinternet.org/files/old-media/Files/Reports/2013/PIP_Broadband%202013_082613.pdf (noting that only sixty-two percent of Americans living in rural areas, forty-three percent of those over the age of sixty-five, thirty-seven percent of people who did not graduate from high school, and fifty-four percent of those earning less than \$30,000 per year have access to a fast internet connection).

185. *Id.*

186. *See* Kai Langel, *Patient-Centric Engagement and the Digital Age*, APPLIED CLINICAL TRIALS (Apr. 1, 2014), <http://www.appliedclinicaltrialsonline.com/patient-centric-engagement-and-digital-age>

the studies require extensive data collection through a computer, this may be more difficult for people with a slow internet connection. Furthermore, if the study is limited to individuals using a more expensive smartphone (such as an iPhone), the research would only involve wealthier individuals.¹⁸⁷ Currently, all three of these problems exist.

A 2014 poll conducted by the Pew Research Center found that 13 percent of adults in America do not use the internet.¹⁸⁸ Another study also conducted by the Pew Research Center found that although the use of the internet and ownership of computers is prevalent in U.S. households, there are still disparities in the way internet connectivity is distributed across different geographic areas.¹⁸⁹ The study found that, for example, in the Boulder metropolitan area approximately eight out of ten homes had access to a fast, broadband internet connection whereas in other metropolitan areas such as Harlingen, Texas, only approximately half of the homes have access to a fast internet connection.¹⁹⁰ In general, approximately 30 percent of the U.S. population does not have access to a fast internet connection at home.¹⁹¹ The most affected groups include those who did not graduate from high school, people over the age of 65, those earning less than \$30,000 per year, and those living in rural communities.¹⁹²

Inequitable internet access means that although computer use and internet access is prevalent in the U.S., some populations may not be easily accessible for recruitment or for participation in online medical research.¹⁹³ If people in specific geographic areas are significantly less likely to turn to the internet for medical information because they have no access to a fast internet connection, researchers recruiting subjects based on their online searches would be less likely

(noting how there is some bias in virtual clinical trials due to individuals who lack Internet access being unable to participate).

187. See Zickuhr & Smith, *supra* note 184, at 2, 6 (finding those with high income and educational attainment are much more likely to own iPhones).

188. See Susannah Fox & Lee Rainie, *The Web at 25 in the U.S.*, PEW RES. CTR., 5 (Feb. 27, 2014), http://www.pewinternet.org/files/2014/02/PIP_25th-anniversary-of-the-Web_0227141.pdf (stating 87 percent of adults use the internet).

189. Lee Rainie & D'Vera Cohn, *Census: Computer Ownership, Internet Connection Varies Widely Across U.S.*, PEW RES CTR, (Sept. 19, 2014), <http://www.pewresearch.org/fact-tank/2014/09/19/census-computer-ownership-internet-connection-varies-widely-across-u-s/>.

190. *Id.*

191. See Zickuhr & Smith, *supra* note 184, at 2 (Aug. 26, 2013), http://www.pewinternet.org/~media/Files/Reports/2013/PIP_Broadband%202013_082613.pdf (finding 70 percent of the U.S. population has access to a high speed internet connection at home).

192. See *id.* at 3 (finding 62 percent of Americans living in rural areas, 43 percent of those over the age of 65, 37 percent of people who did not graduate from high school, and 54 percent of those earning less than \$30,000 per year have access to a fast internet connection).

193. See Amneris E. Luque et al., *Barriers and Facilitators of Online Patient Portals to Personal Health Records Among Persons Living with HIV*, 2 JMIR RES. PROTOCOL. 1, 6 (2013) (finding that inadequate internet access made access to online medical research more difficult.).

to recruit these people for studies. Because historically disadvantaged populations often lack a fast internet connection, recruitment of subjects for clinical research that relies exclusively on an online framework would be inherently inequitable.

For example, in online clinical research trials such as Pfizer's REMOTE or Ivivi's EMF trial, there were issues of equitable selection of subjects because the trials required subjects to have access to an internet connection.¹⁹⁴ In online clinical trials, subjects complete informed consent forms online and constantly enter information on the trial's website.¹⁹⁵ For Ivivi's Osteoarthritis EMF study it can take up to 20 minutes for the subjects to complete the required data forms online.¹⁹⁶ Since the entire trial depends upon constant and reliable access to fast internet, the recruitment and enrollment of subjects for these trials would be inherently inequitable, disproportionately excluding disadvantaged populations such as the elderly or low-income earners.

If a potential subject is required to have a high-end smartphone to participate, only wealthier individuals will have access to the clinical trials. A 2013 Pew Research Center poll revealed that 91 percent of adults own a cellphone¹⁹⁷ and 56 percent of cellphone users own a smartphone.¹⁹⁸ Generally, research conducted using smartphones presents problems of equitable subject selection.¹⁹⁹ People over the age of 65, people who did not graduate from high school, and those with an income lower than \$30,000 per year are less likely to own a smartphone than the rest of the population.²⁰⁰

Using the iPhone's ResearchKit as the platform for virtual clinical trials presents even greater issues of equitable subject selection and sampling bias due to the difference in the demographics of people who use Apple's iPhone instead of smartphones with other operating systems. ResearchKit is an "open-source framework" which allows researchers to create medical apps to conduct research on iPhone users exclusively.²⁰¹ By utilizing the iPhone's internal instruments,

194. See Orri et al., *supra* note 28, at 191 (stating that REMOTE trial participants were enrolled and managed entirely remotely through internet and mobile-phone platforms); see also Amp Orthopedics, *supra* note 23 (listing daily access to the internet as one of the inclusion criteria).

195. Orri et al., *supra* note 28, at 191.

196. *Mytrus Ivivi Osteoarthritis Study*, *supra* note 70.

197. Lee Rainie, *Cell Phone Ownership Hits 91% of Adults*, PEW RES. CTR. (June 6, 2013), <http://www.pewresearch.org/fact-tank/2013/06/06/cell-phone-ownership-hits-91-of-adults/>

198. Aaron Smith, *Smartphone Ownership 2013; 56% of American Adults Are Now Smartphone Owners*, PEW RES. CTR. (June 5, 2013), <http://www.pewinternet.org/2013/06/05/smartphone-ownership-2013/>, at 2.

199. *Id.*, at 3 (describing a study that found that only about half of Americans are smartphone owners and those who own smartphones tend to be educated and wealthy).

200. *Id.* at 3–4.

201. See *ResearchKit and CareKit*, APPLE, <https://www.apple.com/researchkit/> (last visited Jan. 22, 2017); see also *ResearchKit for Developers*, APPLE, <https://developer.apple.com/researchkit/> (last visited Jan. 22, 2017).

such as the phone's accelerometer and gyroscope, and by using the information collected from HealthKit—a set of apps which allow the user to enter health information and which also collect data passively—researchers can conduct studies on subjects remotely and collect metrics at any time of the day.²⁰² Current ResearchKit initiatives include medical research studies on asthma, Parkinson's disease, and diabetes.²⁰³

The future of ResearchKit may also involve virtual clinical trials for pharmaceutical companies. In July 2015, GlaxoSmithKline announced that it was in the planning phases of using ResearchKit for drug research and development.²⁰⁴ The pharmaceutical company behind the painkiller OxyContin, Purdue Pharma, also told reporters that it was exploring the possibility of using ResearchKit for drug research and development.²⁰⁵ Apple's Senior Vice President of Operations said that the company would be open to for-profit efforts that are going to "make an impact on people's health" and that this is the reason why Apple made ResearchKit an open-source platform.²⁰⁶

According to a Pew Research Center poll conducted in 2013, 40 percent of people earning over \$75,000 a year own an iPhone compared to only 13 percent of those who earn less than \$30,000 per year.²⁰⁷ Also, while 38 percent of college graduate smartphone users own an iPhone, only 11 percent of smartphone users who did not graduate high school own one.²⁰⁸ The disparity in iPhone ownership is even greater in the African-American community, in which only 16 percent of smartphone users own an iPhone.²⁰⁹

By conducting medical research exclusively on a narrow segment of the population, ResearchKit—and virtual clinical trials in general—presents issues of equitable selection as well as sampling bias. The risks and benefits of research will not be distributed across a representative sample of the general population or even the general smartphone-owning population. For example, people who

202. *ResearchKit and CareKit*, *supra* note 201; *see also HealthKit*, APPLE, <https://developer.apple.com/healthkit/> (last visited Jan. 22, 2017) (stating that customers may provide permission for the app to passively collect data to be used in research).

203. *ResearchKit and CareKit*, *supra* note 201.

204. *See* Stephanie M. Lee, *Big Pharma Eyes iPhone for Drug R&D*, BUZZFEEDNEWS (last updated July 12, 2015, 1:31 PM), <http://www.buzzfeed.com/stephaniemlee/big-pharma-eyes-apples-researchkit-for-drug-development#.hfOa1GEnq>; *see also* GSK, TWITTER (July 10, 2015, 1:56 PM) <https://twitter.com/GSK/status/619565807325048832>; *Can an iPhone Transform the Way we Monitor and Improve Patient Health?*, GSK (July 8, 2016), <http://us.gsk.com/en-us/behind-the-science/innovation/can-an-iphone-transform-the-way-we-monitor-and-improve-patient-health/>.

205. *See* Lee, *supra* note 204 ("Purdue Pharma, the privately held, multibillion-dollar drug developer in Connecticut that's best known for OxyContin painkillers, told BuzzFeed News that it's in the early stages of exploring whether Apple's new tool for research data collection can be used as part of its own drug R&D efforts.")

206. *Id.*

207. Smith, *supra* note 198, at 7.

208. *Id.*

209. *Id.*

choose to participate in ResearchKit studies are not only likely to be representative of the average iPhone user demographic (high-income, college-educated individuals) but also include those who use the iPhone's HealthKit to keep track of their calorie intake or step count.²¹⁰ Any developments that result from the research—such as a new drug—will have been developed from a very narrow sample of people; as commentators point out, a section of the “richest 15 percent of the world”²¹¹ that is proactive about managing their conditions and improving their health.²¹²

At the same time, however, virtual clinical trials can test the most dangerous treatments on low-income and disadvantaged populations. Researchers in the past have recruited vulnerable subjects and performed risky research on them.²¹³ For example, research sites have recruited homeless people²¹⁴ and undocumented immigrants²¹⁵ to participate in drug trials. These participants enter the trial for the opportunity to earn desperately needed money.²¹⁶ Researchers have failed to ensure that a participant is not simultaneously participating in several trials, which can affect the results of the studies.²¹⁷ Virtual clinical trials create even more opportunities to target vulnerable populations. Online behavioral marketing studies have demonstrated how to identify vulnerable, easy-to-manipulate

210. *Id.* (finding that more than three times as many iPhone users made over \$75,000 per year, compared to iPhone users who made less than \$30,000 per year; and more than three times as many iPhone users were college-educated than did not graduate high-school); see also *ResearchKit*, APPLE, <http://researchkit.org/> (last visited Jan. 22, 2017) (“ResearchKit works seamlessly with HealthKit, researchers can access even more relevant data for their studies—like daily step counts, calorie use, and heart rate.”).

211. See Jim Edwards, *The iPhone 6 Had Better Be Amazing and Cheap, Because Apple Is Losing the War to Android*, BUS. INSIDER (May 31, 2014, 8:27 AM), <http://www.businessinsider.com/iphone-v-android-market-share-2014-5> (explaining that the high price of Apple smartphones may be limiting its market share to 15%).

212. See Arielle Duhaime-Ross, *Apple's New ResearchKit*, THE VERGE (Mar. 10, 2015), <http://www.theverge.com/2015/3/10/8177683/apple-research-kit-app-ethics-medical-research> (explaining that people who use ResearchKit are more likely to be engaged in monitoring and improving their health, and may not represent the entire population affected by the disease).

213. Susan Perry, *Recruitment of Homeless People for Drug Trials Raises Serious Ethical Issues*, U Bioethicist Says, MINNPOST, (Aug. 11, 2014), <https://www.minnpost.com/second-opinion/2014/08/recruitment-homeless-people-drug-trials-raises-serious-ethical-issues-u-bioet>; see also, Carl Elliott, *The Best-Selling, Billion-Dollar Pills Tested on Homeless People; How the Destitute and the Mentally Ill Are Being Used as Human Lab Rats*, MATTER (July 28, 2014), <https://medium.com/matter/did-big-pharma-test-your-meds-on-homeless-people-a6d8d3fc7dfe#.eoz7mpmb2>; David Evans, Michael Smith & Liz Willen, *Big Pharma's Shameful Secret*, BLOOMBERG MKT, (Special Report, Dec. 2005), http://www.journalism.columbia.edu/system/documents/523/original/2006_Evans_Big_Pharma_s_Shameful_Secret_MAG.pdf.

214. See Elliot, *supra* note 213 (stating that research organizations send employees to homeless shelters to recruit patients).

215. See Evans et al., *supra* note 213, at 37–38, 42 (quoting an undocumented immigrant who volunteered as a patient to earn desperately-needed money for his family).

216. See *id.* at 37 (noting that patients who are desperate for money will participate in trials specifically for the monetary compensation).

217. *Id.* at 39.

people.²¹⁸ Data aggregators actually sell email lists labeled “sucker lists” of gullible people.²¹⁹

As pharmaceutical companies harvest increasingly rich sources of consumer and patient data, they are likely to adjust their product development priorities.²²⁰ The profiles generated from online and offline data may reveal relationships between particular conditions and optimal consumer populations—those who are wealthier, more likely to adhere to brand-name drugs, more likely to influence prescribing practices, or more likely to accept stigmatized diagnoses.²²¹ In addition, extensive behavioral data available about people based on their activities across the web can enable researchers to identify and recruit subjects who typically do not complain, thus leading to approval of a drug that has undocumented side effects. The development of treatments based on inequitable recruitment in virtual clinical trials may thus undermine the social goal of developing safe and effective treatments for the entire population.

V. INFORMED CONSENT

Informed consent is an essential prerequisite to medical research.²²² People cannot be required to be guinea pigs. A basic human right exists to refuse to participate in research for whatever reason.²²³ In fact, the first principle of the

218. Nathan Newman, *How Big Data Enables Economic Harm to Consumers, Especially to Low-Income and Other Vulnerable Sectors of the Population*, 18 J. INTERNET L. 11, 14 (2014).

219. *Id.* at 14.

220. Jamie Cattell, et al., *How Big Data Can Revolutionize Pharmaceutical R&D*, MCKINSEY & COMPANY (Apr. 2013), <http://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/how-big-data-can-revolutionize-pharmaceutical-r-and-d>.

221. *Id.* (explaining that pharmaceutical companies can use data mining to identify new potential drugs and focus R&D resources on drugs that are likely to be successful). Researchers might themselves choose only the wealthiest subjects by using data from their choice of websites (such as high end shopping sites) or their use of expensive digital devices. This allows the recruitment of subjects who will be able to afford expensive treatments. The pricing of the resulting treatment might prevent others from having access to the benefits of the research.

222. NUERNBERG MILITARY TRIBUNALS VOL. II, *supra* note 29, at 181–182.

223. See generally World Medical Association, *Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects*, 5, [http://www.wma.net/en/30publications/10policies/b3/index.html.pdf?print-media-type&footer-right=\[page\]/\[toPage\]](http://www.wma.net/en/30publications/10policies/b3/index.html.pdf?print-media-type&footer-right=[page]/[toPage]) (last amended Oct. 2013) (explaining that all subjects must be notified of their right to refuse to participate in a study).

Nuremberg Code, the international standard for medical research, is that participation must be informed and voluntary.²²⁴ Similar provisions exist in U.S. federal research regulations, which apply to all federally-funded research²²⁵ and to research that will be used in efforts to obtain Food and Drug Administration approval for a drug or other product.²²⁶ The federal regulations, influenced by the Nuremberg Code, have extensive requirements regarding what must be disclosed to potential research subjects and what must be done to ensure that a person is not coerced into participating in research.²²⁷ The regulations also require that informed consent forms include a “statement that participation is voluntary.”²²⁸ The subject’s right to be informed about the risks and benefits of the proposed research before they are enrolled in a research study and the right to refuse to participate in research is also part of medical ethics codes²²⁹ and common law legal obligations.²³⁰ For certain vulnerable groups—such as children—additional protections are in place under the federal research regulations.²³¹ Because

224. See NUERNBERG MILITARY TRIBUNALS VOL. II, *supra* note 29, at 181–82. The first tenet of the Nuremberg Code is: “1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision. This latter element requires that, before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person, which may possibly come from his participation in the experiment.” *Id.*

225. See 45 C.F.R. § 46.122 (2009) (“Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.”); see also 45 C.F.R. § 46.116 (2009) (listing the general requirements for informed consent).

226. See 21 C.F.R. § 50.25 (2015) (explaining that informed consent includes a statement noting participation is voluntary); see also 21 C.F.R. § 50.1 (2015) (“Compliance with these parts is intended to protect the rights and safety of subjects involved.”).

227. See 21 C.F.R. § 50.20 (2015) (noting that research shall not be undertaken without informed consent and the representative must have a chance to consider whether to participate or not); see also 21 C.F.R. § 50 (2015) (instructing people to lie because they have gotten the evidence paper as well as assigned her extra); 21 C.F.R. § 25 (2015) (explaining that informed consent includes a statement noting participation is voluntary); 45 C.F.R. § 46.111(a)(4) (2009) (“Informed consent will be sought from each prospective subject.”); 46 C.F.R. § 46.116 (2009) (explaining that investigators must receive informed consent from the subject).

228. See 21 C.F.R. § 50.25(a)(8) (2015) (noting that participants must receive a statement that participation is voluntary); see also 45 C.F.R. § 46.116(a)(8) (2009) (explaining that investigators must receive informed consent from the subject).

229. *The AMA Code of Medical Ethics’ Opinion on Clinical Research*, 17 AM. MED. ASS’N J. ETHICS 1136, 1136–37 (Dec. 2015).

230. See *Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479, 483 (1990) (explaining that physicians who fail to disclose research or commercial motives will create a cause of action for performing a medical procedure without the patient’s informed consent).

231. See 45 C.F.R. §§ 46.404–46.409 (2015) (specifying categories of research that are not suitable for children and the requirements for proper assent by children to participate in a study); see also 21 C.F.R.

of concerns that children cannot meet the requirements of voluntary informed consent,²³² certain risky research on children is prohibited altogether.²³³

Consent collected online—often referred to as electronic consent or e-consent—does not adequately guarantee that the consent is informed or voluntary, which is problematic both for the individual and for ensuring the validity of the research.²³⁴ With online consent, the person signing the consent form may not be the person he or she claims to be.²³⁵ A reporter was able to lie about her age in one of the ResearchKit apps in order to qualify for a study.²³⁶ The team behind the Parkinson's ResearchKit app deliberately chose to allow the system to give a person more than one opportunity to become eligible for the study: "It's tough, you know—it's certainly possible to have a system where you only get one shot with the eligibility criteria in our studies; but we chose not to do that."²³⁷

Little is done to verify the identity of research subjects.²³⁸ One group of online medical researchers suggests that it may be prudent to require a photo ID to verify the age and identity of potential subjects.²³⁹ This might be possible using the same scanning technology that banks use for mobile check deposits,²⁴⁰ as well as the widely available barcode scanning technology for smartphones.²⁴¹ However, a teenager pretending to be an adult could easily scan a parent's ID to

§§ 50.52–50.54 (2016) (specifying what types of research are permissible by the Food and Drug Administration when children are the subjects in clinical investigations).

232. See, e.g., Teresa Hughes & Mary Kay Helling, *A Case for Obtaining Informed Consent From Young Children*, 6 EARLY CHILDHOOD RES. Q. 225, 227 (1991) ("Children's limited experiences and developmental level make it difficult for them to understand long-term goals of research, the concept of risk, and the meaning of self-determination.").

233. See 45 C.F.R. §§ 46.404–46.409 (specifying categories of research that are not suitable for children and the requirements for proper assent by children to participate in a study); see also 21 C.F.R. §§ 50.51–50.56.

234. See text accompanying *infra* at notes 235–257.

235. See Duhaime-Ross, *supra* note 212 (one reporter changed her age on ResearchKit to become eligible for a research study, illustrating the issue of minors being able to participate in research despite being unable to legally consent).

236. *Id.*

237. *Id.*

238. See *Considerations and Recommendations Concerning Internet Research and Human Subjects Research Regulations, with Revisions*, THE SEC'Y'S ADVISORY COMM. ON HUMAN RES. PROTS., HEALTH & HUMAN SERVS, at 14 (2013) (explaining that "identity verification is a major issue in Internet research."); see also *id.* (describing an online study where she was able to return to the previous page and change her age in order to become eligible).

239. See Duhaime-Ross, *supra* note 212.

240. See Jeffrey Kopchik, *Supervisory Insights*, FED. DEPOSIT INS. CORP., <https://www.fdic.gov/regulations/examinations/supervisory/insights/sisum09/primer.html> (last updated June 29, 2009) (explaining "remote deposit capture" technology in which users take a photo of the check, electronically submitting it to the bank, quickly adding credit to the user's bank account).

241. See Jesse Emspak, *Smartphone App Foils Would-Be Underage Drinkers*, MASHABLE, (July 11, 2013), <http://mashable.com/2013/07/11/barzapp-app-underage-drinkers/#CpmP8ISsGkqy> (describing a new smartphone app, BarZapp, which scans the barcode on the back of an ID and instantly verifies the age of a person).

meet the criteria. Furthermore, requiring participants to provide additional personal data increases the risk of identity theft.²⁴²

The online consent process also eliminates the role of an intermediary capable of evaluating patient capacity and voluntariness, which are requisite for informed consent.²⁴³ Can a software program adequately detect impairments in the functional abilities involved in subject comprehension of information and use of information to evaluate the desirability of the balance between the study's risks and potential benefits? Can software detect extreme influences on the patient's indicated preferences, such as overwhelming family pressure to participate in the study for the possible therapeutic benefit, compensated care, or even payments for participation?

Furthermore, by removing the informed consent process from an in-person setting, online research eliminates a crucial aspect of the process, which is the dialogue between a potential subject and an investigator.²⁴⁴ Is there sufficient dialogue and interaction to make the informed consent process meaningful when the subject is simply tapping through e-consent prompts on a tablet screen?²⁴⁵ Making the informed consent process entirely digital hinders opportunity for such dialogue to take place.²⁴⁶ In a virtual clinical trial, without in-person physician oversight, a participant's additional conditions or use of drugs may go unnoticed, and lead to increased risks during the experimental treatment.²⁴⁷

242. See, e.g., Lorenzo Franceschi-Bicchierai, *Uber Left Hundreds of Drivers' Licenses and Social Security Numbers Exposed*, MOTHERBOARD (Oct. 13, 2015, 6:52 PM), <http://motherboard.vice.com/read/uber-left-hundreds-of-drivers-licenses-and-social-security-numbers-exposed?111> (describing a data breach of Uber that exposed hundreds of drivers' licenses, tax forms, and social security numbers); see also Ted Samson, *Flaw in Popular Mobile Apps Exposes Users to Identity Theft*, INFOWORLD (Apr. 9, 2012), <http://www.infoworld.com/article/2617115/mobile-security/flaw-in-popular-mobile-apps-exposes-users-to-identity-theft.html> (describing a flaw in popular mobile apps such as Facebook, Dropbox, and LinkedIn, which exposed users to identity theft "by saving user authentication keys in easily accessible, unencrypted plain text files.").

243. See Umesh Chandra Gupta, *Informed Consent in Clinical Research: Revisiting Few Concepts and Areas*, 4 PERSP. IN CLINICAL RES. 26, 26–27, 29 (2013) (explaining that the three essential elements of informed consent are "voluntarism, information disclosure, and decision-making capacity"; researchers are responsible for ensuring patients are participating voluntarily, provided with information relevant to making an informed decision, and able to understand and appreciate the decision they are making).

244. See Duhaime-Ross, *supra* note 212 ("Despite some improvements to the informed consent process, one problem remains: many of these apps haven't figured out a way to let users ask a question during the process, which is what the one-on-one interaction allows."); see also INST. OF MED. OF THE NAT'L ACADS., RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS 120–23 (Daniel D. Federman et al. eds., 2003) (recommending that informed consent should consist of an "ongoing, interactive dialogue between research staff and research participants").

245. See Christine Coughlin, *E-Consent: Can Informed Consent be Just a Click Away?*, 50 WAKE FOREST L. REV. 381, 394–95 (2015), at 394 (explaining that subjects are far less likely to read consent forms "on a screen or a tablet versus a hard copy").

246. Duhaime-Ross, *supra* note 212; see also *supra* text accompanying note 243.

247. See Coughlin, *supra* note 245, at 395 (explaining that reducing in-person interactions "increases the likelihood that physicians would not recognize shifting patient vulnerabilities.").

To the extent that the companies have made the electronic consent forms available, it appears that the forms allow the participants' information to be used beyond the initial study in studies the person has not specifically consented to.²⁴⁸ This conflicts with the principle that people should be informed about the particular nature and risk of a study that they are being asked to participate in. It also runs afoul of the clear evidence, from studies²⁴⁹ and cases,²⁵⁰ that research subjects have strong feelings about the types of research they want to participate in. People's consent to one type of research does not imply consent to another type of research.²⁵¹ If information voluntarily provided for one study is used without

248. See Marianne Kolbasuk McGee, *Apple's ResearchKit: The Privacy Issues*, DATA BREACH TODAY (Mar. 16, 2015), <http://www.databreachtoday.com/apples-researchkit-privacy-issues-a-8018> (explaining that although Apple's ResearchKit provides informed consent to consumers prior to participating in clinical studies through an app, "[i]t's not clear how ResearchKit and end users determine which apps have access to what data, for what purposes, and for how long." Furthermore, once an entity has a consumer's personal information "there is no way to know what they do with it . . . It is also relatively easy for a "malicious developer" to create an app and divulge private information.). See Valerie Gutmann Koch, *PGTandMe: Social Networking-Based Genetic Testing and the Evolving Research Model*, 22, 51 HEALTH MATRIX 33 (2012) (noting that using a person's information in "studies that were not identified at the time of enrollment challenges current expectations of how research protocols are defined and what it means to participate in research."). The strength of research subjects' desire to determine what type of research is performed on their information or samples is evinced by the fact that research subjects have sued research institutions that have used their samples for studies beyond the initial consented-to research. See, e.g., *Havasupai Tribe of Havasupai Reservation v. Ariz. Bd. of Regents*, 204 P.3d 1063 (Ariz. Ct. App. 2008).

249. See M.L. Goodson & B.G. Vernon, *A Study of Public Opinion on the Use of Tissue Samples from Living Subjects for Clinical Research*, 57 J. CLINICAL PATHOLOGY 135, 136–37 (2004) (asserting that many participants seek control over their tissues and will only join types of research that allows that control); see also Åsa Kettis-Lindblad et al., *Perceptions of Potential Donors in the Swedish Public Towards Information and Consent Procedures in Relation to Use of Human Tissue Samples in Biobanks: A Population-Based Study*, 35 SCANDINAVIAN J. PUB. HEALTH 148, 155 (2007) (suggesting that research procedures should be specialized based on the preferences of the participant); Briana Mezuk et al., *Participant Characteristics That Influence Consent for Genetic Research in a Population-Based Survey: The Baltimore Epidemiologic Catchment Area Follow-up*, 11 COMMUNITY GENETICS 171, 173–76 (2008) (stating that their study shows that people are influenced into participating by many variables); Jeanette M. Trauth et al., *Public Attitudes Regarding Willingness to Participate in Medical Research Studies*, 12 J. HEALTH & SOC. POL'Y 23, 39–40 (2000) (focusing on what life experiences influence people the most to participate in certain research studies); Lori B. Andrews and Julie Burger Chronis, *A Pound of Flesh: Patient Legal Action for Human Research Protections in the Biotech Age*, in PATIENTS AS POLICY ACTORS 83 (2011); Lori B. Andrews, *Assessing Values to Set Policies for Consent, Storage, and Use of Tissue and Information in Biobanks*, in NEW CHALLENGES FOR BIOBANKS: ETHICS, LAW AND GOVERNANCE 31 (2009).

250. See *Washington Univ. v. Catalona*, 490 F.3d 667, 673 (8th Cir. 2006) (allowing research participants to intervene and attempt to direct the transfer of their biological samples); see also *Havasupai Tribe v. Ariz. Bd. of Regents*, 204 P.3d 1063 (Ariz. Ct. App. 2008) (tribe whose blood was collected for diabetes research objected to its use in other studies).

251. See *Greenberg v. Miami Children's Hosp. Research Inst. Inc.*, 208 F.Supp.2d 918, 921–22 (N.D. Ill. 2002) (involving participants who sued a research hospital and researcher when their biological samples were used to file for a patent rather than provide support on an affordable and accessible basis).

specific consent for a different study, the nature of the latter study may be objectionable to the participant.²⁵² The participant may have been drawn to the initial research because it focused on a disease that affected his or her family and may not wish to participate in other research.²⁵³ Also, the trust that the subjects have in the initial researcher may not carry over to unspecified future researchers.²⁵⁴

There is reason to suspect that the risks of participation are not adequately explained in a digital informed consent form.²⁵⁵ It is unlikely that such forms include disclosure of the risks of stigmatization or discrimination associated with the aggregation of data about an individual.²⁵⁶ The informed consent form may even fail to adequately disclose the risks of the drug being used in the research.²⁵⁷

Some of the research studies undertaken via virtual clinical trials involve drugs which have been approved by the FDA to treat one condition being used for another condition.²⁵⁸ Miguel Orri, then Senior Director at Pfizer said that in the original REMOTE trial, researchers used “*an approved drug, with a well-established safety profile* in a condition where patients don’t die” (emphasis

252. See Goodson & Vernon, *supra* note 249, at 136–37 (saying that many participants want some type of control over their tissues and want to be consulted when their tissues are used for a different study); see also Kettis-Lindblad et al., *supra* note 249, at 154–55 (suggesting that there should be informed consent every time there is a different study than was originally entered into); see also Marc D. Schwartz et al., *Consent to the Use of Stored DNA for Genetics Research: A Survey of Attitudes in the Jewish Population*, 98 AM. J. MED. GENETICS 336–341 (2001) (noting that people want researchers to get their informed consent each time their tissues are used for different research).

253. See Trauth et al., *supra* note 249, at 31–40 (finding that those with sick family members and friends were significantly more willing to participate in medical research trials).

254. See *Havasupai Tribe v. Ariz. Bd. of Regents*, 204 P.3d 1063 (Ariz. Ct. App. 2008) (explaining that the Havasupai Tribe agreed to participate in a study focused on diabetes after a researcher developed a strong relationship with the tribe, then sued when they found out that their blood samples were used for projects that were not related to diabetes).

255. See Coughlin, *supra* note 245, at 382, 393–95.

256. See Eric T. Juengst, *Human Genetics ‘98: Ethical Issues In Genetics, Group Identity and Human Diversity*, 63 AM. J. HUM. GENETICS 673, 673, 677 (1998) (explaining that research that finds a genetic propensity for alcoholism in a particular group could be misinterpreted and applied to all members of a the group in a discriminatory way and arguing that individuals should be informed of this risk); see also Schwartz et al., *supra* note 252, at 336, 341 (surveying Jewish individuals and finding that they were less willing to participate in research regarding stereotypical or potentially stigmatizing traits).

257. See I. N. Olver et al., *The Adequacy of Consent Forms for Informing Patients Entering Oncological Clinical Trials*, 6 ANNALS OF ONCOLOGY 867, 867–69 (1995) (discussing how many participants could not name the severe side-effects of drugs even after reading the consent form).

258. See Jean Fain, *A Miracle Drug For Binge Eating? Not So Fast, Says Therapist*, WBUR (Feb. 10, 2015), <http://www.wbur.org/commonhealth/2015/02/10/a-miracle-drug-for-binge-eating-not-so-fast-says-therapist> (the use of Vyvanse for binge eating disorder would have severe side-effects for the user, even though it has been approved for another condition).

added).²⁵⁹ Yet, just because a drug has been approved for a particular condition does not mean it is 100% safe or that it will be safe for another condition.²⁶⁰

Virtual clinical trials are used to study new uses of old drugs.²⁶¹ Pharmaceutical companies are rebranding some of their top-selling drugs and marketing them for a different condition either because the patent is running out or simply because they want to expand the market for the drugs.²⁶² The researcher undertaking a virtual clinical trial with a previously-approved drug might be tempted to say in the informed consent form that the drug is “safe” based on previous approval. But the researcher may be failing to take into consideration the risks and benefits of the drug in a different circumstance.²⁶³ While the risks of a drug

259. See Kai Langel, *Virtual Clinical Trials – “They’re Here to Stay”*, ECLINICALHEALTH BLOG (Mar. 18, 2013), <https://www.clinpal.com/clinpal-blog/virtual-clinical-trials-theyre-here-to-stay/>.

260. See Fain, *supra* note 258. The author explains that although the drug Vyvanse has been used to treat ADHD there may be numerous drawbacks to the use of the drug for the treatment of binge eating disorder. *Id.*

261. See Langel, *supra* note 259 (explaining that the regulators were likely more willing to approve the REMOTE virtual trial because the drug was already FDA approved).

262. See Mary Ebeling, *Beyond Advertising: The Pharmaceutical Industry’s Hidden Marketing Tactics*, PRWATCH (Feb. 21, 2008, 12:00 PM), <http://www.prwatch.org/news/2008/02/7026/beyond-advertising-pharmaceutical-industrys-hidden-marketing-tactics> (explaining that Eli Lilly rebranded Prozac, used to treat depression, as Sarafem, used to treat premenstrual dysphoric disorder, effectively extending the patent on Prozac); see also John Russell, *Humira: One Drug. Nine Uses. More on the Way?*, CHI. TRIB. (Sept. 18, 2015), <http://www.chicagotribune.com/business/ct-humira-swiss-army-knife-0920-biz-20150918-story.html> (stating that pharmaceutical companies are trying to repurpose old drugs in order to gain money by skipping phase one of clinical trials).

263. For example, Sarafem has the same exact chemical composition as Prozac, but Sarafem is intended for the treatment of premenstrual dysphoric disorder instead of depression. See Ebeling, *supra* note 262. (describing the severe side-effects of Prozac and why it may not be a good idea to use it for other conditions). Another example is a drug called Vyvanse—made by the pharmaceutical company Shire—which was originally used to treat attention deficit hyperactivity disorder (ADHD) but that is now being used to treat binge eating disorder because “there was no other drug treatment available for the disorder.” See Katie Thomas, *Shire, Maker of Binge-Eating Drug Vyvanse, First Marketed the Disease*, N.Y. TIMES (Feb. 24, 2015), http://www.nytimes.com/2015/02/25/business/shire-maker-of-binge-eating-drug-vyvanse-first-marketed-the-disease.html?_r=1 (stating that Vyvanse was approved without a committee because there was no other drugs available for binge-eating disorder). The FDA did not request review by an advisory committee because the drug’s “safety profile is well known.” *Id.* According to the Physician’s Desk Reference website “anaphylaxis/angioedema requiring hospitalization and emergency treatment occurred with 1st or subsequent doses” of Tolterodine tartrate (the drug used for the REMOTE trial). See *Tolterodine Tartrate—Drug Summary*, PDR.NET, <http://www.pdr.net/drug-summary/detrol-la?druglabelid=477> (last visited Jan. 22, 2017) (describing the effects and warnings of the drug Detrol.); see also Stuart Henochowicz, *Anaphylaxis*, MEDLINEPLUS (Mar. 20, 2016). Similarly, Sarafem contains a boxed warning of an increased risk of suicide as well as extensive warnings including possible allergic reactions, bleeding, hyponatremia and the potential to “precipitate mixed/manic episode in patients at risk for bipolar disorder.” See *Fluoxetine Hydrochloride—Drug Summary*, PDR.NET, <http://www.pdr.net/drug-summary/Sarafem-Tablets-fluoxetine-hydrochloride-1946.5777> (last visited Jan. 22, 2017) (summarizing the drugs warnings and why it might not be smart to use for different conditions); see also *Drug Advertising: A Glossary of Terms—Boxed Warning*, FDA, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072025.htm> (last updated June 19, 2015) (explaining the function of a black box warning for drugs). Also, according to the Physicians’ Desk Reference, as a stimulant, Vyvanse has a “high potential for abuse and dependence” and may produce anxiety, anorexia, increased

might be tolerable when applied to a particular disease, such as one that is particularly devastating or that has no other treatment, that does not mean there would be an identical risk calculus for another disease.²⁶⁴

The FDA authorized the REMOTE trial because it had been designed to test the feasibility and methodology of conducting clinical trials online,²⁶⁵ and the FDA wanted to determine how the informed consent process would work when done entirely online.²⁶⁶ Mytrus' electronic informed consent ("eConsent") system is called Enroll.²⁶⁷ Enroll provides the informed consent form and an accompanying video in a digital interactive format through an iPad.²⁶⁸ The process includes different interactive features and questionnaires to assess the comprehension of the participant.²⁶⁹ According to Mytrus, this system will make the clinical trial process more cost effective.²⁷⁰ A report indicates that most of the ten biggest pharmaceutical companies are using Mytrus' Enroll electronic consent system,²⁷¹ and according to Mytrus' website, 30 IRBs have approved use of its Enroll system.²⁷² Other electronic informed consent forms exist, such as one

heart rate, sudden death and stroke. See *Lisdexamfetamine Dimesylate—Drug Summary*, PDR.NET, <http://www.pdr.net/drug-summary/vyvanse?druglabelid=538> (last visited Jan. 22, 2017) (explaining the warnings of using Vyvanse and suggesting why it might not be smart to use for other conditions).

264. See *Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics*, U.S. DEPT. HEALTH & HUM. SERV. (May 2014), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf> (stating that the FDA is willing to accept greater risks and side effects from treatment for serious diseases and therefore some trials should receive accelerated approval); see also *Understanding Unapproved Use of Approved Drugs “Off Label”*, U. S. DEPT. HEALTH. & HUM. SERV. (May 2017), <https://www.fda.gov/forpatients/other/offlabel/default.htm> (advising patients considering off label use of FDA approved drugs to weigh the risks and benefits).

265. See *Pfizer Conducts First “Virtual” Clinical Trial Allowing Patients to Participate Regardless of Geography*, PFIZER (June 7, 2011), <http://press.pfizer.com/press-release/pfizer-conducts-first-virtual-clinical-trial-allowing-patients-participate-regardless-> (stating that the goal of the virtual trial was to test this method compared to an on-site clinical trial).

266. See Mike Mitka, *Strategies Sought for Reducing Cost, Improving Efficiency of Clinical Research*, 306 JAMA 364, 365 (2011).

267. *Reinvent Consent with Enroll*, MYTRUS, <https://www.mytrus.com/en/products-services/enroll> (last visited Jan. 22, 2017).

268. See *id.* (denoting the Enroll app's operation through an iPad).

269. See *id.* (discussing the features Enroll uses to enhance a clinical trial participant's understanding).

270. See Kristen Schneider, *Mytrus Pioneers to Patient-Friendly Technologies for Clinical Trials Participation*, SARTA (May 9, 2014), <http://sarta.org/blog/mytrus-pioneers-to-patient-friendly-technologies-for-clinical-trials-participation/> (addressing the increased cost efficiency of the Enroll system).

271. *Id.*

272. *Reinvent Consent With Enroll*, *supra* note 267.

designed by Sage Bionetworks that uses icons and explanations²⁷³ and one designed by surgeons at the Medical College of Wisconsin.²⁷⁴

Enroll allows subjects to flag terms they do not understand and click through to obtain more information, and in some cases even call a person.²⁷⁵ The system also collects data regarding how long a patient looked at each screen of the electronic informed consent form on the iPad and regarding sections where a participant had trouble understanding a particular idea or word.²⁷⁶ However, this system cannot determine if the subjects' consent is either informed or voluntary.²⁷⁷ The system is not designed to eliminate someone who reads the informed consent disclaimer in just a few seconds or who genuinely does not understand certain aspects of the study.²⁷⁸ Furthermore, the eConsent model does not address the difficulty in ascertaining whether the person signing the eConsent form in an entirely online clinical trial is actually the subject participating in the research study.²⁷⁹

The FDA notes that although use of the electronic informed consent may make research easier for sponsors, they "must attend to privacy and confidenti-

273. See John Wilbanks & Erin Holve, *EDM Forum's Collaborative Network, PCOR, and Apple's Research Kit*, ACADAMYHEALTH (Apr. 14, 2015), <http://www.academyhealth.org/blog/2015-04/edm-forums-collaborative-network-pcor-and-apples-research-kit> (discussing the two tiers of Sage Bionetworks system, the first tier being "icon dominant" and the second tier being more text and detail dominant).

274. See Matthew J. Frelich et. al., *Research Electronic Data Capture (REDCap) Electronic Informed Consent Form (eICF) is Compliant and Feasible in a Clinical Research Setting*, 2 INT'L J. CLINICAL TRIALS 51, 52 (2015) (addressing the creation of an electronic informed consent by Vanderbilt University with partners such as the Medical College of Wisconsin).

275. See Ann Neuer, *Informed Consent Goes Digital*, CLINICAL INFORMATICS NEWS (Aug. 29, 2013), <http://www.clinicalinformaticsnews.com/cln/2013/8/29/informed-consent-goes-digital.html> (explaining that the subject has the option to select "I understand," or "I have a question" before getting to the next screen; if the subject selects the question option, a site staff then reviews the information with the subject and answers any questions).

276. *Id.*

277. See NUERNBERG MILITARY TRIBUNALS VOL. II, *supra* note 29, 181–182 (discussing the high standard for consent to be both informed and voluntary and allowing inference that the standard would be difficult to meet through Mytrus's electronic Enroll system).

278. See *Reinvent Consent With Enroll*, *supra* note 267 (noting Enroll's capabilities, which do not include the ability to screen out participants who read the informed consent too quickly or who are genuinely confused about a study).

279. See *Reinvent Consent With Enroll*, *supra* note 267 (highlighting Enroll's capabilities, which do not address imposters in clinical trials); see also Duhaime-Ross, *supra* note 212 (discussing the risk of imposters and false claims of identity in clinical trials).

ality concerns when considering techniques for monitoring informed consent remotely.”²⁸⁰ Although the FDA’s main concern seem to be the accuracy and quality of the data obtained from the trial,²⁸¹ equally important is the vulnerability of access to private health information. Data breaches involving protected health information have increased exponentially.²⁸² As a result of the expected expansion in the use of electronic health records and cloud storage services, data breaches of health information are expected to increase.²⁸³

Informed consent is a crucial component of research on human subjects because protection of an individual’s autonomy to make decisions for himself or herself is not only legally required, but widely recognized as a fundamental principle of medical ethics.²⁸⁴ The informed consent methodology used in virtual clinical trials does not adequately protect research participants.

VI. CONFIDENTIALITY AND PRIVACY

The disclosure of health information is a sensitive matter. The quality of health care is based primarily on information that physicians get directly from their patients.²⁸⁵ If patients withhold information from their physicians, it may lead to ineffective care or even to potentially unnecessary procedures leading to

280. See U.S. Dep’t Health & Hum. Serv. et al., *Guidance of Industry: Oversight for Clinical Investigations—A Risk-Based Approach to Monitoring*, FDA GUIDANCE DOCUMENTS (Aug. 2013), at 9, <http://www.fda.gov/downloads/Drugs/.../Guidances/UCM269919.pdf>.

281. See *id.* at 1, 11 (explaining that the “nonbinding recommendations” provided by the FDA center around ensuring that a site’s records are complete, that the information regarding subjects be accurate, and that there is a low frequency of protocol violations).

282. See Vincent Liu et al., *Data Breaches of Protected Health Information in the United States*, 313 *JAMA* 1471, 1472 (2014). A study in the April 14, 2015 *JAMA* issue reported that “between 2010 and 2013, breaches of protected health information reported by HIPAA-covered entities increased and involved approximately 29 million records, with most data breaches resulting from overt criminal activity.” The study focused on a U.S. Department of Health and Human Services database which listed “data breaches of unencrypted protected health information.” The authors noted that most of such breaches (67%) occurred through the use of electronics—such as computers. They further noted that due to the fact that they used data pertaining to reported breaches only “[their] study likely underestimated the true number of health care data breaches occurring each year.”

283. See *id.* (predicting that data breaches are likely to increase because of increased use of “cloud based services provided by vendors supporting predictive analytics, personal health records, health-related sensors, and gene sequencing technology”).

284. 21 C.F.R. § 50.20 (2016); 45 C.F.R. § 46.116; THE NAT’L COMM’N FOR THE PROT. OF HUM. SUBJECTS OF BIOMED. AND BEHAV. RESEARCH, *supra* note 176, at 10.

285. See, e.g., Kevin McCarthy, *Study: 50 Percent of Patients Withhold Information from their Doctor*, NUEMD (Sept. 21, 2016), <http://www.nuemd.com/news/2014/12/19/study-50-percent-patients-withhold-information-their-doctor> (“Patients who withhold information about their medication use are increasing their chances of experiencing an adverse drug event, and individuals who lie about their diet or activity level may be withholding valuable diagnostic clues.”).

higher health care costs.²⁸⁶ Therefore, it is vital to ensure that an individual's health information remains private so that patients are willing to answer sensitive questions honestly.²⁸⁷ Furthermore, unwanted disclosures of private health information may lead to discrimination, stigmatization, embarrassment, denial of services and benefits, as well as other serious adverse consequences.²⁸⁸

Various federal laws have been adopted to protect health information specifically, such as the privacy regulations²⁸⁹ adopted under the Health Insurance Portability and Accountability Act²⁹⁰ and the federal research regulations, which state that Institutional Review Boards must determine whether a research plan contains adequate safeguards to protect the subjects' privacy and confidentiality prior to approving a study.²⁹¹ Some states have also enacted measures to protect people's health information.²⁹²

However, many of the federal and state legal protections fail to protect medical information online. For example, the privacy regulations²⁹³ adopted under HIPAA²⁹⁴ only apply to specifically-defined "covered entities," which include health care providers and plans, but not internet sites where researchers conduct online medical research. State laws are also limited in the type of health information that they protect²⁹⁵; for example, Rhode Island's law related to the privacy and confidentiality of medical information prohibits "any person" from disclosing a patient's "confidential health care information" without the patient's

286. See, e.g., Sally E. Thorne et al., *Is There a Cost to Poor Communication in Cancer Care?: A Critical Review of the Literature*, 14 *PSYCHO-ONCOLOGY* 875, 879–80 (2005) (reviewing empirical literature of communication between cancer patients and their doctors and finding that poor communication leads to higher healthcare costs).

287. See Katherine M. Woods & Regis McNamara, *Confidentiality: Its Effect on Interviewee Behavior*, 11 *PROF. PSYCHOL.* 714, 719 (1980) (describing a study in which interviewees who were told their answers might not be confidential disclosed less information).

288. *INST. OF MED, BEYOND THE HIPAA PRIVACY RULE: ENHANCING PRIVACY, IMPROVING HEALTH THROUGH RESEARCH* 77 (Sharyl J. Nass et al. eds., 2009).

289. The HIPAA Privacy Rule, 45 C.F.R. § 160 (2016); 45 C.F.R. § 164.102–106 (2016); 45 C.F.R. § 164.500–534 (2016).

290. The Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104-191, 100 Stat. 1936 (codified as amended in scattered sections of 26, 42 U.S.C.).

291. See 45 C.F.R. § 46.111(a)(7) (2015) ("In order to approve research covered by this policy the IRB shall determine that [among other things] . . . [w]hen appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.").

292. See, e.g., R.I. GEN. LAWS § 5-37.3-4 (2016) (requiring written consent of the patient prior to the release or transfer of confidential health care information); see also CAL. CIV. CODE § 56.06 (a), (b) (West 2016) (requiring that businesses that offer software or hardware for maintaining medical information be held to the same standards of confidentiality as health care providers).

293. See 45 C.F.R. § 160.103 (2015) (defining covered entities as a health plan, a health clearing house, or a health care provider who transmits health information electronically).

294. The Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104-191, 100 Stat. 1936 (codified as amended in scattered sections of 26, 42 U.S.C.).

295. 45 C.F.R. § 160.103 (2015).

consent.²⁹⁶ This law, however, only protects confidential health care information related to “health care history, diagnosis, condition treatment or evaluation obtained from a health care provider who has treated the patient.”²⁹⁷ Such narrow protections ignore the high risks associated with the collection of exactly the same types of information by different entities merely because those entities are not involved with treating the patient.

Some states have begun to express concern about health care information disclosure online. California and Delaware, for example, require that websites that collect personally identifiable information post a privacy policy about the type of information they collect.²⁹⁸ An additional California law requires that “any business that offers software or hardware to consumers” with the purpose of allowing consumers to “maintain medical information” or for “the diagnosis, treatment, or management of a medical condition” be considered as “a provider of healthcare” for purposes of requiring such entity to maintain “the same standards of confidentiality required of a provider of health care with respect to medical information disclosed to the business.”²⁹⁹ This means that disclosures of health information by such medical apps or websites for the purpose of recruitment would be considered actionable as a breach of confidentiality. In addition, unauthorized disclosure of health information to marketers or third parties that was collected during the study through the app designed to monitor health would be actionable.³⁰⁰

Researchers who conduct virtual clinical trials may inadvertently violate their subjects’ privacy. This can happen in a variety of ways—from accessing and combining private data to determine who should be recruited into a study,³⁰¹ to passively collecting data without consent (such as measuring a person’s speech pattern through an app’s use of a phone’s microphone³⁰² or the person’s gait

296. R.I. GEN. LAWS § 5-37.3-4 (a)(1)–(2) (2016).

297. R.I. GEN. LAWS § 5-37.3-3 (3)(ii) (2016).

298. CAL. BUS & PROF. CODE § 22575 (a), (b)(1) (West 2013); DEL. CODE ANN. 6, § 1205C (a), (b)(1) (2016).

299. CAL. CIV. CODE § 56.06(a)–(c) (West 2009).

300. See CAL. CIV. CODE § 56.36 (b)(1)–(2) (West 2007) (providing penalties for the violation of the confidentiality provision in the form of a private cause of action); see also, CAL. CIV. CODE § 56.36 (a), (c) (West 2007) (providing for further penalties in the form of criminal charges and administrative fines).

301. See, e.g., Walker, *supra* note 104 (highlighting how an individual may have been targeted for an arthritis clinical trial based off of innocuous web-browsing and/or credit card spending).

302. See, e.g., Zoe Kleinman, *Is Your Smartphone Listening to You?*, BBC (Mar. 2, 2016), <http://www.bbc.com/news/technology-35639549> (highlighting how an android-platform based mobile-phone application can be easily created to listen in on conversations in the presence of the device that the application is installed in).

when a phone is in the person's pocket),³⁰³ to storing research data with inadequate cyberprotection,³⁰⁴ to aggregating data in a way that puts subjects at risk of disclosure of private facts leading to stigmatization and discrimination.³⁰⁵

Virtual clinical trial researchers have created a market for privacy violations, incentivizing data aggregators' collection of data in much the same way they originally created the market that encouraged physicians to enroll their own patients in clinical trials. Commentators criticized this earlier system because it incentivized physicians to behave in unscrupulous ways in order to get large sums of money from pharmaceutical companies in exchange for enrolling their patients.³⁰⁶ Now, researchers are encouraging data aggregators to invade people's privacy through the surreptitious collection of data, thereby creating this new market.³⁰⁷ Because the HIPAA Privacy Rule does not cover online medical data that is not in the control of health care institutions or health care providers, entities that sell consumers' private data to researchers can violate people's privacy in their attempt to identify research subjects.³⁰⁸ Data can be legally collected about people's private web searches, social media posts and even their private email messages to friends, and can be used to recruit subjects based on inferred characteristics.³⁰⁹ These technically legal practices that researchers use

303. See, e.g., *Apple Announces New ResearchKit Studies for Autism, Epilepsy & Melanoma*, APPLE (Oct. 15, 2015), <http://www.apple.com/pr/library/2015/10/15Apple-Announces-New-ResearchKit-Studies-for-Autism-Epilepsy-Melanoma.html>; see also *ResearchKit and CareKit; Empowering Medical Researchers, Doctors, and Now You*, APPLE, <http://www.apple.com/researchkit/> (last visited Jan. 22, 2017) (discussing how the "mPower" app is helping researchers understand Parkinson's disease by using iPhone features to measure, along-side of other features, gait).

304. See, e.g., *Improper Disclosure of Research Participants' Protected Health Information Results in \$3.9 Million HIPAA Settlement*, U.S. DEPT. HEALTH & HUM. SERV. (Mar. 17, 2016), <http://www.hhs.gov/about/news/2016/03/17/improper-disclosure-research-participants-protected-health-information-results-in-hipaa-settlement.html> (detailing how the Feinstein Institute for Medical Research was fined for, among other things, storing research data without appropriate cyber-protection which led to a breach of that data).

305. See Leslie Wolf et al., *Certificates of Confidentiality: Protecting Human Subject Research Data in Law and Practice*, 14 MINN. J.L. SCI. & TECH. 11, 16–17 (2013) (demonstrating how research data collected may be exposed through litigation, exposing participants to stigmatization).

306. See generally Trudo Lemmens & Paul B. Miller, *The Human Subjects Trade: Ethical and Legal Issues Surrounding Recruitment Incentives*, 31 J.L. MED. & ETHICS 398, 401 (2003) (discussing how "financial pressures may bring physicians to stretch the inclusion and exclusion criteria [of a clinical trial testing a new medication] to enroll as many patients as they can, thereby compromising the trial's validity").

307. See generally *Sorrell v. IMS Health Inc.*, 564 U.S. 552 (2011) (health data miners prevailed in a First Amendment challenge to a Vermont statute that protected the privacy of information about doctors' prescribing patterns); also see generally Erika Check Hayden, *Mobile-Phone Health Apps Deliver Data Bounty*, 531 NATURE 422 (2016), <http://www.nature.com/news/mobile-phone-health-apps-deliver-data-bounty-1.19622> (noting that researchers are realizing the value of collecting health data through apps and the scope of such programs is expanding).

308. See generally Nicholas P. Terry, *Big Data Proxies and Health Privacy Exceptionalism*, 24 HEALTH MATRIX: J.L.-MED. 65, 84–87 (2015) (describing "medically infected data," data that although is not strictly medical, can be collected to infer medical status yet fall outside the scope of HIPAA's reach).

309. Walker, *supra* note 104.

to collect people's data are nonetheless particularly intrusive and violate people's privacy.³¹⁰

Targeted advertisements to recruit clinical trial participants also raise privacy concerns.³¹¹ For example, if a person Googles a disease, a clinical trial ad can appear related to that disease³¹² on another Google service. Imagine watching a YouTube video with your child when an advertisement appears asking you to participate in a clinical trial about cancer or sexually-transmitted diseases because you have searched for information about the condition online.

Once researchers identify a potential subject, new privacy risks arise. Virtual clinical trials collect data online, often through medical apps.³¹³ However, computers and cell phones are riddled with surreptitious tracking mechanisms such as cookies.³¹⁴ Medical and clinical trial apps are sometimes designed to send private health information to data aggregators.³¹⁵ A study conducted at IIT Chicago-Kent College of Law about diabetes apps found that over 80% of the apps sent user health information to third-party data aggregators.³¹⁶

The virtual clinical trial model also presents unique privacy issues because of the nature of digital information and storage. Because the information for such trials is stored and transmitted exclusively online through computers or mobile devices, any party besides the subject of an online clinical trial can potentially gain access to the information by using the device without the subject's authorization.³¹⁷ Since trial information—including informed consent forms and

310. Terry, *supra* note 308 at 84–85 (providing examples of where data are collected including “web-browsing trails, exhaust data from online transactions, web scrapers, social media interactions, mobile phone usage, smartphone sensors, mobile health apps, and both medical and non-medical networked devices”).

311. See, e.g., Brenda L. Curtis, *Social Networking and Online Recruiting for HIV Research: Ethical Challenges*, 9 J. EMPIRICAL RES. HUM. RES. ETHICS 58, 59–60 (2014), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4316828/pdf/nihms576496.pdf> (describing privacy issues associated with targeted online recruiting for HIV research).

312. See *Privacy Policy*, GOOGLE, <https://www.google.com/policies/privacy/#nosharing> (last visited Jan. 22, 2017).

313. Maged N. Kamel Boulos et al., *Mobile Medical and Health Apps: State of the Art, Concerns, Regulatory Control and Certification*, 5 ONLINE J. PUB. HEALTH INFORMATICS 1, 4 (2014) (describing trials that use mobile apps to collect health information such as body weight, calorie loss and disease-symptoms).

314. See Jonathan R. Mayer & John C. Mitchell, *Third Party Web Tracking: Policy and Technology*, CTR. FOR INTERNET & SOC'Y (2012), https://jonathanmayer.org/papers_data/trackingsurvey12.pdf (discussing methods of tracking mechanisms such as “cookies”).

315. See Sarah R. Blenner et al., *supra* note 113 (finding that a majority of diabetes apps surveyed use tracking cookies to collect user information, and many shared their information with third party data aggregators).

316. *Id.*

317. Cf. Kesa Bond et al., *Electronic Health Records: Privacy, Confidentiality, and Security*, 14 VIRTUAL MENTOR 712, 714 (2012), <http://journalofethics.ama-assn.org/2012/09/stas1-1209.html> (noting that physicians with unencrypted mobile devices leave digitally transmitted information vulnerable to interception).

subjects' health information—are stored online for clinical trials such as Pfizer's REMOTE, there is the additional risk that a data breach can expose people's sensitive medical data.³¹⁸

Some commentators argue that collecting information from websites and social media does not constitute an invasion of privacy because such sources are generally considered public places.³¹⁹ However, privacy scholars have argued in various contexts that privacy extends to otherwise public places when people have a reasonable expectation of privacy about the acts happening in the public setting.³²⁰ Should it be considered a violation of privacy to use a sound amplifier to listen to two people's conversation in a café? How about recording such a conversation without their consent? The fact that the internet may be a "public place" for some does not mean that traditionally private information put on the internet should lose its private nature, especially if it is private health information, which has historically been considered amongst the most private information about a person.

In addition, much of the data collected by data aggregators comes from online sources that the users themselves view as private—email, password-protected websites and so forth.³²¹ When people realize that data aggregators are collecting extensive information about them, many want legal change. A 2016 Pew Research Center study asked participants whether they would join a free social media website to communicate with old acquaintances about a class reunion if the website collected information about them to show them targeted advertisements.³²² Most of the participants said they would not find that scenario acceptable.³²³ Similarly, a Gallup poll found that 67 percent of adult Americans opposed being targeted by behavioral advertising and believe that advertisers

318. See, e.g., James Paul et al., *The Internet and Clinical Trials: Background, Online Resources, Examples and Issues*, J. MED. INTERNET RES. (2005), <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1550630/?report=printable> (asserting that security is a "central issue" when housing trial information online, as well as describing ways in which that security can be breached); see also Orri et al., *supra* note 28 at 193–97 (noting that, in a virtual clinical trial, all the study data collected was transferred to an electronic database).

319. See Solberg, *supra* note 114 (explaining that courts have found no reasonable expectation of privacy in posts on a social media site).

320. See, e.g., Carlos A. Ball, *Privacy, Property, and Public Sex*, 18 COLUM. J. GENDER & L. 1, 33 (2008) (arguing that the 4th Amendment protections of individuals beyond private residences allows for a sexual act occurring in public to take on a private dimension by the nature of the act itself).

321. Cf. Blenner et al., *supra* note 113, at 1051 (finding that a large percentage of diabetes apps, with a presumption of privacy, were sold to third party data aggregators).

322. See Lee Rainie & Maeve Duggan, *Privacy and Information Sharing*, PEW RES. CENT., at 31–32 (Jan. 14, 2016), <http://www.pewinternet.org/2016/01/14/privacy-and-information-sharing/> (finding that, while many Americans are willing to disclose information for a tangible benefit, they are cautious about doing so and are often unsatisfied when they know what a company will do with it).

323. *Id.* at 32.

should not be allowed to match advertisements to their particular interests according to the websites they have visited.³²⁴ The same poll found that 61 percent of Americans believe that the use of targeted advertisements is not justified even if reduces costs because free access to websites is not worth the invasion of privacy involved.³²⁵ A 2012 Pew poll found that 73 percent of Americans interviewed said they would not be okay with a search engine keeping track of their online searches and subsequently using this information to personalize search results in the future because it is an invasion of privacy, and 68 percent of participants in the same poll said “they are not okay with targeted advertisements because they do not like having their online behavior tracked and analyzed.”³²⁶

A breach of privacy in the virtual clinical trial context can exacerbate psychological harms evidenced in other online contexts.³²⁷ A teenager who searches for a size 14 prom dress or looks up a diet online may be emotionally devastated if the subsequent sites that she visits advertise weight loss trials for overweight teenagers. The target of an online advertisement might also face a physical risk, if she is lured into an inappropriate clinical trial and subsequently takes medication when she does not have the target condition. She may also face a risk if she avoids medical care due to the quick fix the “novel” therapy offered through participation in a research trial. Or she may lose the chance to benefit from an online support group if she withdraws due to privacy concerns after her name has “leaked” to recruiters.

Surreptitious data collection from social networks for medical research may also interfere with patients’ use of the web to gain information or learn from other patients.³²⁸ A triumph of social networks has been the way people isolated

324. See Lymari Morales, *U.S. Internet Users Ready to Limit Online Tracking for Ads*, GALLUP (Dec. 21, 2010), <http://www.gallup.com/poll/145337/Internet-Users-Ready-Limit-Online-Tracking-Ads.aspx>.

325. *Id.*

326. See Kristin Purcell et al., *Search Engine Use 2012*, PEW INTERNET & AM. LIFE PROJECT, 18–23 (Mar. 9, 2012), http://www.pewinternet.org/files/old-media/Files/Reports/2012/PIP_Search_Engine_Use_2012.pdf (finding that a majority of Americans surveyed do not like having their online behavior tracked and analyzed).

327. Tom Garrubba, *5 Ways Health Data Breaches Are Far Worse Than Financial Ones*, HEALTHCAREIT NEWS (Nov. 10, 2014), <http://www.healthcareitnews.com/news/5-ways-health-data-breaches-are-far-worse-financial-ones> (noting that data breaches may have deadly consequences in the health care context); see Charles Ornstein, *Small Violations of Medical Privacy Can Hurt Patients and Erode Trust*, NPR (Dec. 10, 2015), <http://www.npr.org/sections/health-shots/2015/12/10/459091273/small-violations-of-medical-privacy-can-hurt-patients-and-corrode-trust> (providing an analogous example of the emotional and psychological harm that can result from a breach of medical privacy); see also INSTITUTE OF MEDICINE ET AL., *BEYOND THE HIPAA PRIVACY RULE* 89 (Nass et al.eds. 2009) (explaining that a breach of private health information can result in a financial harm because it may lead to discrimination in health insurance and employment).

328. See Maged N. Kamel Boulos & Steve Wheelart, *The Emerging Web 2.0 Social Software: An Enabling Suite of Sociable Technologies and Health Care Education*, 24 HEALTH INFO. & LIBR. J. 2, 13 (2007) (noting that some users are wary about posting their personal information online because of data mining).

by distance—or medical conditions—can share intimate information.³²⁹ Patients who live in remote areas or suffer from rare diseases can come together in a seemingly private space to augment their medical care through hearing from others with similar symptoms or concerns.³³⁰ Social networks and online forums are powerful tools to help people kick smoking habits,³³¹ cope with chronic diseases,³³² overcome depression,³³³ monitor their health, and express their frustration about their condition.³³⁴ However, the intrusion of third parties (whether advertisers or medical researchers) without the patients' consent can cause them to flee social networks, denying them these potential benefits.³³⁵

A targeted subject also might suffer financial harm if her health information is leaked by third parties. Because of cookies and tracking programs on computers and cell phones, user information about health concerns and symptoms can readily be transmitted to insurance and credit card companies, without the research subject's knowledge or consent.³³⁶

329. See, e.g., Jae Eun Chung, *Social Networking in Online Support Groups for Health: How Online Social Networking Benefits Patients*, 19 J. HEALTH COMM.: INT'L PERSP. 639, 651–53 (2014) (explaining that online support groups provide access to emotional and informational benefits that might otherwise be unavailable due to geographic limitations or the rarity of a particular disease).

330. *Id.*

331. See Neill Bruce Baskerville et al., *Effect of a Digital Social Media Campaign on Young Adult Smoking Cessation*, 18 NICOTINE & TOBACCO RES. 351, 355–57 (2015) (reporting that young adults had greater cessation rates when using social media).

332. H. Alan Scott, *How Instagram Helps Young People Cope with Cancer*, VICE (Mar. 4, 2016), <http://www.vice.com/read/how-instagram-helps-young-people-cope-with-cancer>.

333. See Tim Anstiss, *How Social Media Is Supporting People with Depression*, GUARDIAN (Apr. 26, 2012), <http://www.theguardian.com/social-care-network/2012/apr/26/social-media-depression-support> (describing how social media provides an empathetic community to assist those suffering with depression).

334. See Felicity Morse, *How Social Media Helped me Deal with My Mental Illness*, BBC NEWSBEAT (Feb. 18, 2016), <http://www.bbc.co.uk/newsbeat/article/35607567/how-social-media-helped-me-deal-with-my-mental-illness> (explaining how Yik Yak has provided a platform for patients to express their frustrations anonymously).

335. See Purcell et al., *supra* note 326, at 23 (explaining that the majority of people strongly disfavor having their online behavior analyzed); see also Bernard Lo & Lindsay Parham, *The Impact of Web 2.0 on the Doctor-Patient Relationship*, 38 J.L. MED. & ETHICS 17, at 21 (2010) (explaining how companies that sell health products extract information from websites that do not have to abide by HIPPA Health Privacy Rule). In addition to the benefits aforementioned in this article, other benefits that authors Lo and Parham mention include better access to health information, better access to health care services, enhancement of patient decision-making, psychosocial benefits, and improved doctor-patient relationships. *Id.* at 19–20. There are also risks, such as that of receiving information that is inaccurate and the psychological and social risks of learning of a diagnosis over the Internet instead of from a health care professional. *Id.* at 20–21.

336. See Michael McFarland, *Ethical Implications of Data Aggregation*, SANTA CLARA U.: MARKKULA CTR. FOR APPLIED ETHICS (June 1, 2012), <https://www.scu.edu/ethics/focus-areas/internet-ethics/resources/ethical-implications-of-data-aggregation/> (warning that aggregated data can be transferred to a wide variety of marketers and may cause some people to be denied health insurance).

VII. VIRTUAL CLINICAL TRIALS AND THE INTEGRITY OF THE RESEARCH
PROCESS AND ENTERPRISE

Virtual clinical trials may be beneficial for people who live in rural areas or people who have a debilitating condition that inhibits them from traveling to research facilities.³³⁷ They may also be beneficial to patients who feel they spend enough time in medical settings and do not want to make additional trips to a hospital or doctor's office or who have conditions that cause them to feel embarrassed in public.³³⁸ However, online medical studies do not provide the most robust research results.³³⁹ It may be difficult to verify the accuracy and authenticity of the data.³⁴⁰ It may be difficult to verify that, for example, the person entering the data is in fact the person participating in the trial, or that the person is entering accurate and complete information. Monetary incentives increase the possibility that people who do not suffer from the condition being studied will attempt to participate in the trial.

Virtual clinical trials open the door for people to game the system. For example, if an unqualified individual is rejected from a clinical trial initially based on the answers he or she provides in a questionnaire, it is possible for that person to create a new email address and therefore create another opportunity to be selected. For a clinical trial that utilizes questionnaires to verify a participant's identity, the participant would need to know enough information about another person in order to be able to answer the questions. This would be fairly simple for anyone with access to a public record database, the individual's Facebook page, or if the person is a close friend or a family member (such as a teenage child) with access to the intended participant's information.

For a trial that requires medical records such as X-rays or that requires a preliminary blood test—such as the REMOTE trial—it would be more difficult to create a second opportunity to be selected, especially if the lab required the participant to show identification before conducting the blood test. This extra safeguard, however, would not work for virtual clinical trials developed for the treatment of conditions which are difficult to measure physiologically, such as depression and sleep apnea. In such trials, where no medical documentation of

337. See Sujay Jadhav, *Virtual Clinical Trials: The Future of Patient Engagement?*, APPLIED CLINICAL TRIAL, at 1 (July 12, 2016), <http://www.appliedclinicaltrials.com/virtual-clinical-trials-future-patient-engagement> (explaining the benefits of virtual clinical trials for patients with mobility issues).

338. See *id.* at 1 (identifying the ability of the patient to participate in the clinical trial from home as a key advantage associated with virtual clinical trials); see also Richard G. Heimber, *Cognitive-behavioral Therapy for Social Anxiety: Current Status and Future Direction*, 51 BIOLOGICAL PSYCHIATRY 101, 102 (2002) (explaining how patients with social anxiety disorder may feel humiliated or embarrassed in public).

339. See text *infra* accompanying note 341.

340. See Allison, *supra* note 9, at 898 (regarding self-reporting in the context of online medical research generally).

the illness is required, it would be easy to create a false profile matching the description of the condition—a person may simply search online for the symptoms associated with the condition.

When a research subject is not only recruited online, but also participates in the study without the involvement of a traditional research facility, there is an increased likelihood of physical harm and inaccurate conclusions about the experimental treatment. People who do not actually suffer from the conditions at issue—or who are minors participating without their parents' knowledge or consent—and are lured by monetary payment or a free smartphone, may be tempted to take an inappropriate drug which might be harmful to them. If a serious side effect or problem occurs, the person may report to their primary care physician or local emergency room, instead of the trial investigators who might then be unable to evaluate the potential dangers of the drug. On the other hand, a research subject may simply flush the drugs down the toilet and complete the online form reporting no side effects, when serious side effects actually exist. If pharmaceutical companies begin marketing treatments based on the results of clinical trials completed entirely remotely, dangers arise not only to the research subjects, but also to patients taking the drug after it receives approval as being “safe and effective” based on misrepresentations by deceptive participants.³⁴¹

Online medical research conducted with social network information may also lead to flawed conclusions and can serve as the basis for protocols or therapeutics that are ineffective or unduly harm patients because the assumptions made about an individual based on her or his social media profile may be wrong.³⁴² A person may lie about his or her age or weight on a social network profile or use a decade-old photo; a person may post a status update minimizing or exaggerating a health problem. If, for example, a biotechnology company was doing research about the impact of alcohol use on people with diabetes, it might choose to collect data on people who have searched the term “diabetes” on Google or maybe “liked” the American Diabetes Association page on Facebook. The biotechnology company might gauge this person's use of alcohol based on whether—and how many times—she or he checked in at a bar on Facebook, or had a photo of himself online with a red cup in his hand (a common depiction which police routinely use to show that someone under the age of 21 is drinking illegally).³⁴³ However, such assumptions about a person could be completely

341. See Ashwaria Gupta, *Fraud and Misconduct in Clinical Research: A Concern*, 4 PERSP. IN CLINICAL RES. 144, 146 (2013) (explaining how fraud can cause harmful medical products to be introduced).

342. See Naone, *supra* note 157 (describing a study that found that social networking data is not a reliable source of data).

343. See Rupa S. Valdez et al., *Beyond Traditional Advertisements: Leveraging Facebook's Social Structures for Research Recruitment*, 16 J. MED INTERNET RES. 10 E243 (2014), https://www.jmir.org/article/viewFile/jmir_v16i10e243/2 (explaining that researchers target individuals based on the information posted and provided on their social media page); see also KJ Lang, *Facebook Turns into Big Brother*,

wrong: this person may have been going to a bar with friends and abstained from drinking alcohol or could have been drinking a non-alcoholic beverage from the damning red cup. Or the person who “liked” the American Diabetes Association may be expressing solidarity for a friend and might not suffer from diabetes at all.

With the financial incentives for participation and the reliance on self-reporting about the effects of the drug or device, there is the probability that participants will declare the intervention as beneficial without even taking the drug or using the device.³⁴⁴ This may lead to FDA approval of dangerous interventions.³⁴⁵

Moreover, through the use of data aggregators that collect and sell thousands of pieces of information about people, researchers may be able to identify and use a particular research pool—such as healthier people with a particular medical condition—that makes their research results look better than if the research had been undertaken on a more diverse or random sample of individuals.³⁴⁶ This may lead to the marketing of treatments that pose more risks to the end users than the researchers admit.

VIII. ISSUES REGARDING IRBS IN ONLINE MEDICAL RESEARCH

Some commentators may argue that the problems raised by online research could be assuaged by an Institutional Review Board (IRB) evaluation of the research proposal.³⁴⁷ However, much of the research conducted online is not even reviewed by an IRB.³⁴⁸ Also, a growing body of literature suggests that IRBs

LACROSSE TRIBUNE, Nov. 19, 2009, http://lacrossetribune.com/news/local/facebook-friend-turns-into-big-brother/article_0ff40f7a-d4d1-11de-afb3-001cc4c002e0.html.

344. See Christine Grady, *Payment of Clinical Research Subjects*, 115 J. CLIN. INVEST. 1681, 1684–85 (2005) (noting concerns that subjects may deceive researchers in order to receive financial incentives).

345. See Gupta, *supra* note 243, at 146 (noting that the FDA plays a major role in preventing and detecting fraud). And as Valerie Koch points out in the context of self-reporting for studies (which also occurs in virtual clinical trials), “[w]ith no one to screen participants for eligibility, the possibility of selection and attrition-bias and mis-or over-reporting of symptoms and traits will likely increase, undermining the integrity of the data generated from such studies.” See Koch, *supra* note 248 at 53.

346. See Terry *supra* note 308 at 85–86. (explaining that data mining has become so sophisticated that researchers can use it to reveal medical attributes based on web browsing history).

347. See Heidi Ledford, *Death in Gene Therapy Trial Raises Questions About Private IRBs*, 25 NAT. BIOTECH. 1067 (2007) (noting that lack of oversight by IRBs can lead to botched clinical trials); U.S. GOV’T ACCOUNTABILITY OFF., HUMAN SUBJECTS RESEARCH: UNDERCOVER TESTS SHOW THE INSTITUTIONAL REVIEW BOARD SYSTEM IS VULNERABLE TO UNETHICAL MANIPULATION, 3 (Mar. 26, 2009) (explaining the importance of the IRB review board in their role of assuring patient safety and trial reliability).

348. See John Carberry, *Media Statement on Cornell University’s Role in Facebook ‘Emotional Contagion’ Research*, CORNELL U. MEDIA REL. OFF. (June 30, 2014), <http://mediarelations.cornell.edu/2014/06/30/media-statement-on-cornell-universitys-role-in-facebook-emotional-contagion-research/> (explaining that a professor who conducted a study on Facebook was not engaged in human research that would require review by the Cornell Human Research Protection Program because he only had access to the aggregated results of the study, and not individual identifiable data); see also Inder M.

are not doing an appropriate job of assessing the risks associated with proposed research projects, assuring the attainment of adequate informed consent, and protecting subjects from the risks.³⁴⁹ Online clinical trials present additional challenges for IRBs since they involve new processes (such as use of online health information, electronic consent forms, and so forth) that have not been specifically addressed in the federal research regulations that IRBs are supposed to follow.³⁵⁰ In addition, IRBs may not appreciate the novel types of harms presented by online recruitment, especially given the lack of transparency about data collection and use.³⁵¹

There are two types of IRBs. Traditional, not-for-profit IRBs are generally based at research institutions³⁵² and universities.³⁵³ However, in the past these traditional IRBs were unable to keep up with the increasing number of research trial proposals resulting from an exponential growth in biotechnological and pharmaceutical innovations,³⁵⁴ thus opening the door to private, for-profit IRBs

Verna, *Editorial Expression of Concern and Corrections*, 111 PROC. NAT'L ACAD. SCI. 10779, 10779 (2014) (expressing concern about the lack of institutional review board and the lack of an opt-out option in the emotional contagion Facebook study).

349. See Ezekiel J. Emanuel et al., *Should Society Allow Research Ethics Boards to be Run as For-Profit Enterprises?*, 3 PLOS MED. 0941, 0941 (2006) (discussing the problems with IRBs and how they are no longer properly reviewed and administered as they should be); see also Peter C. Williams, *Success in Spite of Failure: Why IRBs Falter in Reviewing Risks and Benefits*, 6 IRB: ETHICS & HUM. RES. 1 (1984) (stating that IRBs often avoid weighing the risks and benefits of a trial and when they do, they are often biased in favor of the trial moving forward); see also Sharona Hoffman, *Regulating Clinical Research: Informed Consent, Privacy, and IRBs*, 31 CAP. U. L. REV. 71, 84, 87, 89 (2003) (finding that most informed consent forms do not provide useful explanations and recommending that IRBs require the forms to be written in simple language); see also Donna Shalala, *Protecting Research Subjects—What Must Be Done*, 343 NEW ENG. J. MED. 808, 809 (2009) (warning that many IRBs are not doing enough to protect human subjects because the workload is excessive and they do not have enough resources); see also U.S. GOV'T ACCOUNTABILITY OFF., *supra* note 347, at 1 (explaining the importance of the IRB Review Board and their role of assuring patient safety and trial reliability).

350. See Stephanie Harriman & Jigisha Patel, *The Ethics and Editorial Challenges of Interest-Based Research*, 12 BMC MED. 124 (July 15, 2014), <http://bmcmmedicine.biomedcentral.com/articles/10.1186/s12916-014-0124-3> (noting that there is a lack of national standards for IRBs regarding internet based research in the UK and USA); see also CONSIDERATIONS AND RECOMMENDATIONS CONCERNING INTERNET RESEARCH AND HUMAN SUBJECTS RESEARCH REGULATIONS, WITH REVISIONS, SEC'Y'S ADVISORY COMM. ON HUM. RES. PROTS., HEALTH & HUM. SERVS, at 14 (2013) (recommending that the human subjects regulations be revised to address issues regarding internet research).

351. FTC, *DATA BROKERS: A CALL FOR TRANSPARENCY AND ACCOUNTABILITY* 57 (2015) (reporting that overall transparency in the data collection industry is lacking and making recommendations to enhance transparency and consumer control).

352. See Ledford, *supra* note 347, at 1067.

353. U.S. GOV'T ACCOUNTABILITY OFF., *supra* note 347, at 1.

354. See Obasogie, *supra* note 47 at 72–73 (discussing that there were approximately six times more clinical trials in the period of time between 2001 and 2004 than in the period of time between 1981 and 1985).

to fill in the demand for faster review and approval of studies.³⁵⁵ These private IRBs are organized either independently to review research studies or function within private companies to review the companies' own research studies.³⁵⁶ Research trials in traditional academic settings are now a minority when compared to the growing number of trials in private pharmaceutical companies.³⁵⁷

Despite the crucial function that IRBs could play in protecting human research subjects, scholars have criticized both the traditional and external IRB models as inadequate to ensure that research participants are adequately protected.³⁵⁸ On one hand, traditional IRBs are generally situated in the same research institution as the studies that are being conducted.³⁵⁹ Therefore, the researchers' colleagues are often sitting on the IRB and are responsible for approving or denying the studies.³⁶⁰ This raises the issue of whether or their evaluations of studies are impartial.³⁶¹ Similarly, an IRB that is funded by a private company conducting a research study necessarily has an interest in making sure that studies are approved in order to increase profits.³⁶² Even when reviewing studies for another entity, for-profit IRBs are interested in approving research quickly because for them it is a business transaction with the researchers conducting the study.³⁶³

Scandals and investigations surrounding the inadequacy of the IRB model have surfaced regarding both for-profit and traditional IRBs.³⁶⁴ Prestigious research institutions have had their studies and IRBs shut down due to gross inadequacies and lack of compliance with the relevant regulations.³⁶⁵ Investigative

355. See Ledford, *supra* note 347, at 1068 (addressing that researchers who also serve on non-profit IRB boards are evaluating their colleagues' research protocols which may increase the likelihood that they will not perform critical evaluations).

356. Emanuel et al., *supra* note 349, at 942.

357. See *id.* (explaining that between 1994 and 2004, the number of clinical research trials conducted in a traditional academic setting decreased from 63% to 26%).

358. See *id.* at 941 (explaining that not for profit IRBs are also subject to conflicts of interest that may compromise the integrity of their evaluation); see also U.S. GOV'T ACCOUNTABILITY OFF., *supra* note 347 at 1 (investigating the IRB system and finding that independent IRBs are subject to unethical manipulation).

359. See Emanuel et al., *supra* note 349, at 941; see also *Institutional Review Boards Frequently Asked Question—Information Sheet*, FDA (Jan. 25, 2016), <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm>.

360. Emanuel et al., *supra* note 349, at 941.

361. *Id.*

362. See *id.* at 942 (explaining that commercial IRBs have a financial interest in approving trials, creating a conflict of interest); see also Ledford, *supra* note 347, at 1067 (raising the concern of a system in which the regulated is the sole funder of its regulator and the regulated has the power to change its committee members to approve protocols to please customers).

363. Emanuel et al., *supra* note 349, at 942.

364. *Id.* at 942; Ledford, *supra* note 347.

365. See Emanuel et al., *supra* note 349, at 942 (discussing research institutions whose IRBs were shut down after the death of research participants); see also Ledford, *supra* note 347, at 1067 (discussing non-profits such as Hopkins, Duke, and the University of Colorado that have had their IRBs shut down).

groups have been able to submit and obtain IRB approval for fake research studies purposely designed as posing a potential safety threat to research participants.³⁶⁶

Because of the problems inherent in the current IRB model, it is questionable whether IRBs can truly ensure the protection of research subjects in virtual clinical trials. The Mytrus REMOTE trial underwent the review of two IRBs, one a traditional academic IRB at the University of California, San Francisco (UCSF) and the other a for-profit IRB, Western IRB (WIRB).³⁶⁷ However, it is questionable whether they were able to adequately protect the REMOTE subjects due to the issues commonly associated with IRBs and the novel nature of online trials. For example, WIRB's history of approving risky studies is troubling.³⁶⁸ Although UCSF's IRB was also involved in the review and approval process, it is questionable whether its faster-than-usual approval process could have truly taken into consideration all of the factors at play in the risk-benefit analysis and protection of research subjects in a trial with unprecedented methodology.³⁶⁹

With scholars questioning the adequacy of the current IRB model to review and approve traditional studies, it is unlikely that the added challenges to subject protection inherent in the online research model will be given the consideration they should receive when deciding to approve a study. In addition to the challenges posed by subjects being absent from a physical trial site—which could, for example, provide immediate medical assistance in case of an adverse reaction to a trial drug—the IRBs are ill-equipped to deal with the issues of electronic informed consent, as well as the increased threats to privacy and confidentiality of information arising from the online setting.³⁷⁰

IX. RECOMMENDATIONS

Virtual clinical trials present risks to participants and to the research process. Given the risks, several policy changes should be made.

366. See generally U.S. GOV'T ACCOUNTABILITY OFF., *supra* note 347.

367. Lisa Henderson, *An Idea Whose Time Came: Patient-Facing Clinical Trials Are Finally Implemented a Decade Later* <http://www.appliedclinicaltrials.com/idea-whose-time-came> (last visited Sept. 10, 2016).

368. See, e.g., Evans et al., *supra* note 213, at 39, 54, 56 (documenting WIRB's accountability for approving trials in which physicians were convicted in criminal investigations for putting the lives of research subjects in danger and for making false statements to the FDA); see also Ledford, *supra* note 347, at 1067 (noting that bioethicists were concerned about WIRB following the death of a research participant in a WIRB approved trial).

369. See Henderson, *supra* note 367. In an interview, then Mytrus' Chief Operating Officer, Anthony Costello, explained that the approval process for the trial was rather fast, despite the amount of information the IRBs had to review, and despite the fact that IRBs usually operate slowly. *Id.*

370. James C. Hamilton, *The Ethics of Conducting Social Science Research on the Internet*, 46 CHRON. HIGHER EDUC. B6 (1999) (reporting that many IRBs had reviewed proposals for online research but few of them had guidelines or the technical knowledge necessary to evaluate the proposals properly).

A. Online Health Information Should Be Treated as Confidential

Confidentiality laws should be adopted by the states to ban the unauthorized collection, marketing or use of health information that a person discloses on the web. The federal regulations adopted under HIPAA, should be extended similarly to cover any online health information, even if it is not in the hands of a health care provider or a health care institution.

B. Recruitment Should Be Exclusively Consumer-Initiated

Authorization for participation in research should be by an explicit opt-in.³⁷¹ Recruitment for medical research should not be based on health information revealed through a person's online activities or the imputation of health status through non-health data (such as posting about going to fast food restaurants or watching cable television). Instead, a clinical trial website should be created that people can go to on their own to express interest in receiving information about clinical trials, including virtual clinical trials. In order to strike a balance with researcher's legitimate need to enroll subjects into research trials, models such as the one developed by TrialX (where people can use Twitter to indicate that they would like to receive information about clinical trials) would be acceptable.³⁷²

Furthermore, people who wish to keep their medical conditions confidential should not be subject to the anxiety-inducing process of suddenly being solicited for a virtual or in-person clinical trial for those medical conditions.³⁷³ Therefore, the Federal Trade Commission should investigate more broadly instances of unsolicited recruitment for studies through the surreptitious collection of people's medical information and consider the marketing of health information or inferred health status a form of consumer fraud.

C. Researchers Should Be Treated as Fiduciaries of Research Subjects

Research subjects in virtual clinical trials currently lack the legal protections afforded to subjects in traditional research trials conducted by doctors in

371. Research suggests that people are largely in favor of an opt-in consent process, for example in research undertaken on biobank samples. See Christian M. Simon et al., *Active Choice but Not Too Active: Public Perspectives on Biobank Consent Models*, 13 GENETICS IN MED. 821, 826 (2011) (presenting a survey that found that a majority of focus group participants preferred an opt-in method).

372. @TrialX, TWITTER, <https://twitter.com/trialx> (last visited Dec. 9, 2016); see also *A New Twitter Application by TrialX Lets You Find Clinical Trials That Match Your Health Conditions*, FIERCE BIOTECH (Apr. 24, 2009, 10:16 am), <http://www.fiercebiotech.com/biotech/a-new-twitter-application-by-trialx-lets-you-find-clinical-trials-match-your-health>.

373. See StopCorp.Crap, Comment to *Acurian, Inc: Unsolicited Mail*, COMPLAINTS BOARD, <http://www.complaintsboard.com/complaints/acurian-inc-pennsylvania-c574582.html> (last visited Jan. 22, 2017) (showing examples of solicitation from clinical trials to persons who did not know that their medical conditions, or their child's medical conditions, were known).

medical institutions.³⁷⁴ This could be addressed by a legal policy holding researchers to be fiduciaries. Researchers have several things in common with doctors which would justify considering them fiduciaries.³⁷⁵ Those factors include the research subject's ignorance of the research and their need to entrust their well-being to researchers, the researcher's superior knowledge of the subject matter and the consequences of research,³⁷⁶ and the fact that the research subject may consider his or her relationship with the researcher the same as that of his or her relationship with a doctor.³⁷⁷ Holding researchers to be fiduciaries would allow subjects to have legal recourse against researchers on a fiduciary duty basis, for example, as a result of harm caused to the subject from his or her participation in an unduly risky virtual clinical trial.³⁷⁸

D. The Electronic Informed Consent Process Should Include Additional Information and Safeguards

Electronic informed consent should not be used without access to a person to answer questions. In addition, the process should have a means of assuring the identity of the person who is signing the form and also of the person participating in the study.

The consent process should also provide the subject with the ability to limit the sharing of information gathered from the study. Electronic informed consent forms should give subjects full control over the sharing of study data, that is, whether they want their data to be used only by the researchers conducting the

374. U.S. DEPT. HEALTH & HUMAN SERV., SEC'Y'S ADVISORY COMM. ON HUMAN RESEARCH PROT., *supra* note 147 (recommending revisions to the federal regulations because they do not adequately address internet research issues); *see also* Valerie Gutmann Koch, *A Private Right of Action for Informed Consent in Research*, 45 SETON HALL L. REV. 173, 176 (2015) (stating that research subjects often do not have a private right of action because most jurisdictions do not recognize a legal relationship between the researcher and the research subject).

375. *See* Richard S. Saver, *Medical Research and Intangible Harm*, 74 U. U. CIN. L. REV. 941, 990, (2006); *see also* Andrew Fichter, *The Law of Doctoring: A Study of the Codification of Medical Professionalism*, 19 HEALTH MATRIX: J. L.-MED. 317, 365–368 (2009) (arguing that researchers owe fiduciary duties to their subjects in a way that is similar to what is required of a doctor); *see also* Paul B. Miller & Charles Wijer, *Fiduciary Obligation in Clinical Research*, 34 J. MED. & ETHICS 424, 424, 428, 437 (2006) (arguing that the researcher-subject relationship should be considered fiduciary as a matter of law).

376. *See* Fichter, *supra* note 375, at 367 (stating the gap in knowledge investigators and participants possess inevitably exists, and that participants should not be responsible for their own protection). Whereas some legal commentators argue that researchers should be held to owe fiduciary duties to research subjects, other legal scholars are more skeptical, arguing that fiduciary duties are not compatible with the need for researchers to adhere to the research protocol; *see, e.g.*, E. Haavi Morreim, *The Clinical Investigator as Fiduciary: Discarding a Misguided Idea*, 33 J.L. MED. & ETHICS 586, 588 (2005) (maintaining that researchers are not fiduciaries, as many research trials do not involve medical care and each role in research must be individually considered).

377. *See* Saver, *supra* note 375, at 941–1012, 967–71, 990–92.

378. *See* Moore v. Regents of the Univ. of Cal., 793 P.2d 479, 483 (Cal. 1990) (finding that the doctor-researcher breached his fiduciary duty patient-participant and holding the doctor liable).

study, or if they would also consent to the use of their data in an additional specific study that is explained in detail.³⁷⁹ There should be no blanket consent for unspecified future research.

Informed consent policies for virtual clinical trials should also address the issues of data security inherent when conducting the clinical trial process entirely online and should disclose to subjects the consequences that can result from a data breach. It should clearly inform the subject of the potential issues that can arise as a result of the use of trial drugs—regardless of whether such drugs had been previously approved for the same or another condition.

E. Data Security Measures Should Be Taken by Virtual Clinical Trial Developers to Ensure the Protection of Sensitive Metrics and Personal Information of Research Participants

Not only is medical information collected, but some medical apps used in research can turn on a subject's microphone and track geolocation.³⁸⁰ As virtual clinical trials adopt smartphone platforms, more sensitive information about research subjects will be collected, demanding strict data security protocols.³⁸¹

F. Drugs Should Not Be Approved Based Only on the Results of a Virtual Clinical Trial

Because the virtual clinical trial's data is self-reported, there is no way to assure the accuracy of such data. Even the inventors who patented the virtual clinical trial process believe that "the internet based trial method is most suitable when the intervention is safe, the medical disorder can be confirmed by remote means and the outcome measures can be applied by using electronically transmissible technologies."³⁸² Also, to prevent potentially dangerous drugs from entering the market, some type of in-person clinical trial should follow the virtual clinical trial to validate the virtual trial's results.

379. Sage Bionetworks has developed an electronic informed consent form for ResearchKit's mPower Parkinson's disease app for iPhone. Although the app has an option for the sharing of study data with "Sage Bionetworks and its partners and qualified researchers worldwide" or to "only share [the] data with Sage Bionetworks and its partners" it does not specify who the partners are (their affiliations, whether they have any financial interests in the study, etc.) and it does not provide for an option to only let the researcher conducting the study (Sage Bionetworks) use the data. See Brian M. Bot et al., *The mPower Study, Parkinson Disease Mobile Data Collected using ResearchKit*, 3 SCIENTIFIC DATA 1, 2 (2016), <http://doi.org/10.1038/sdata.2016.11>.

380. See Blenner et al., *supra* note 113, at 1051 (reporting the results of a study that found that some diabetes apps could activate the microphone, track locations, and turn on the camera).

381. See *id.* (stating that the sharing of sensitive information from most medical apps is not currently prohibited by the Health Insurance Portability and Accountability Act).

382. McAlindon et al., *supra* note 65 at 487.

G. IRBs Should Be Given Explicit Directives in the Federal Research Regulations for Dealing with Virtual Clinical Trials

As technology changes the way in which research is conducted, IRB oversight will have to be implemented in a way that addresses novel challenges—such as the need for proper identification of the user-subject and protecting the confidentiality of the electronic data, and ensuring that subjects' health will be protected. In addition, IRBs should be required to analyze whether privacy has been breached in recruitment or data analysis and to determine that adequate measures have been taken to protect cyber-security. The IRBs should also be trained to recognize the novel psychological, physical and financial risks posed by virtual clinical trials.

H. Any Federal or State Law Protecting Subjects in Virtual Clinical Trials Should Include a Private Cause of Action

The current federal research regulations do not provide a private cause of action, thwarting recourse for even egregious violation of the regulations.³⁸³ A preferable model could be the California approach which gives research subjects the possibility of suing for violation of law regulating research, including inadequate informed consent.³⁸⁴

X. CONCLUSION

The purpose of research regulations is to: (1) protect people's choice of whether or not to participate in research; (2) assure that subjects will not be harmed by the research and that the benefits outweigh the risks; (3) protect research subjects' confidentiality; (4) protect the public by assuring that the research is adequate; and (5) ensure trust in the research enterprise so that people will continue to participate in research. However, the current conduct of online researchers fails to meet these goals and instead circumvents the very protection the regulations were meant to offer. Informed consent is likely to be overlooked and is difficult to obtain in the online setting, privacy is likely to be breached, and the study methodologies may not adequately assure the safety of treatments investigated in the digital milieu.

The internet has transformed relationships and social institutions in profound ways. Dating, education, marketing, and communicating are all stunningly different in the post-Facebook era than they were a decade ago. Physicians, pharmaceutical companies, and biotechnology companies are all taking

383. See 45 C.F.R. § 46.113 (1991) (stating that violation of the regulations warrants suspension of institutional review board approval rather than a private cause of action for the research subjects).

384. In California, the Protection of Human Subjects in Medical Experimentation Act makes researchers who conduct research on human subjects without informed consent liable to the subjects for damages. CAL. HEALTH & SAFETY CODE § 24176 (West 2003).

advantage of social networks and the web to pursue online medical research.³⁸⁵ Such research has risks as well as benefits, and it is important to employ traditional research protections for prior review, voluntary and un-coerced consent, assurances that the benefits of the research outweigh the risks, and protection of confidentiality.

385. See Allison, *supra* note 9, at 895 (detailing dozens of companies who are using social media to recruit patients and conduct clinical trials).