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The Financialization of Digital Clinical Trials

Tensions between Efficiency and Scientific Evidence Accessibility

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19.1 INTRODUCTION

Over the past two decades, the use of digital technology in clinical trials has proliferated, a shift that has been argued to reach a more diverse and representative trial population more efficiently. Also known as decentralized clinical trials, digital clinical trials (DCTs) saw a vastly increased use amid the COVID-19 pandemic, when remote methods were employed to reach trial participants who could not reach trial sites in person. While improving clinical trial accessibility through decentralized approaches is important, it is also crucial who is leading these efforts in the generation of scientific evidence. This essay re-centers the relationship between private equity (PE) and clinical trials in the analysis of DCTs and the social value of access in the for-profit, private production of scientific evidence. In a highly fragmented biotechnology industry, where PE firms are increasingly acquiring small firms that provide outsourced clinical research services, DCTs and PE firm unions might bring about additional opportunities to increase drug data opacity, compromising the access to the greater production of scientific evidence driving digital technology.

Structured in three parts, the essay examines the current state of DCTs and questions whether PE firms' investment in DCTs is convenient for data generation and access to quality medicine. The first section discusses the exponential growth of DCTs, particularly in the years following the pandemic, and their potential to address challenges of the traditional on-site clinical trial model. The second section examines PE firms' increasing interest in DCTs from a business, law, and policy perspective. The final section discusses the risks of generating scientific evidence through profit-driven models, with a special focus on the issues of publicity in the wider political economy of PE-funded medical research.

19.2 FROM IN-PERSON TO REMOTE CLINICAL TRIALS

Clinical trials are essential for generating the scientific evidence that regulators require to permit and ensure only safe and effective health care innovations leave the laboratory bench and eventually reach the market. In the past decade, private actors, including PE firms, have invested and managed the evidence production endeavor, critical to innovation access. Meeting the appropriate trial enrollment levels has been an important dimension of generating relevant and sufficient trial data that can be used to evaluate the efficacy and safety of medical treatments, drugs, and devices.[1] Yet, finding and recruiting trial participants can often be an operationally limiting and expensive task.

Traditionally, patients had to attend medical research sites in order to participate in clinical trials. This presented a series of problems to researchers. Consider that more than 70 percent of the US population lives at least two hours away from an academic medical research center and that only 50 percent of the US population participates in clinical research.[2] Bringing patients to a facility reduces generalizability[3] and generally implies mobility constraints that could make trial participation expensive or impossible.[4] These difficulties, in addition to participants' communication and the identification of operational constraints, tended to increase the participants' burden, considerably extending trial timelines and inflating costs, particularly in trials involving a large number of participants.[5]

Diversity in trial patient pools is another problem affecting clinical data generation. A recent study of sixty-four trials that led to fifty-nine FDA-approved cancer therapeutics between January 2012 and December 2017 showed an adequate representation of women (56 percent), older adults (24 percent), and racially and ethnically minoritized patients (16 percent).[6] If evidence for new medical interventions is "dominated by data from unrepresentative populations," as independent researchers argue, different disease severities, comorbidities, age groups, geographies, and other

[1] Nat'l Acads. of Scis., Eng'g, and Med., Federal Policy to Advance Racial, Ethnic, and Tribal Health Equity (2023).

[2] See Andy Coravos, Software-Enabled Clinical Trials, Medium (Sept. 4, 2017), https://blog.andreacoravos.com/software-enabled-clinical-trials-8da53f4cd271.

[3] E-mail from Srinivas Murthy to Author (Sept. 15, 2023, 18:33 EST) (on file with author).

[4] Dawn Anderson, Digital R&D: Four Ways to Maximize Patient Engagement in Clinical Trials, Deloitte (June 25, 2018), https://www2.deloitte.com/us/en/blog/health-care-blog/2018/digital-rd-four-ways-to-maximize-patient-engagement-in-clinical-trials.html.

[5] See, e.g., Thomas Moore et al., Estimated Costs of Pivotal Trials for Novel Therapeutic Agents Approved by the US Food and Drug Administration, 2015–2016, 178 JAMA Internal Med. 1451 (2018) (comparing US$6 million mean cost for a 100-patient trial versus US$77 million for a 1,000-patient trial).

[6] Tanvee Varma et al., Metrics, Baseline Scores, and a Tool to Improve Sponsor Performance on Clinical Trial Diversity: Retrospective Cross-sectional Study, 2 BMJ Med. e000395 (2023).

profiling factors will be excluded and users harmed by disparate access to medical treatment.[7]

The decentralization of trials has thus been presented as a way to deal with recruitment and demographic representation obstacles while significantly reducing associated costs and time. Trials conducted entirely virtually can reach a larger, diverse population and their participants no longer need to travel to medical research centers and might not even meet with their study teams.[8] Remote monitoring and real-time oversight of participants can alleviate investigators' and participants' workloads while increasing the opportunities for assessments over extended periods of time.[9] This is expected to accelerate scientific evidence generation, with higher and faster data accuracy and cost controls, and, potentially, contribute to catapulting more products to the market sooner. Technology adds to decentralization improved recruitment, oversight, and the retention of a larger and diverse trial participant pool, data collection and aggregation, and data analytics. Huge growing trial data volumes will progressively be subject to sophisticated analytics and data-driven algorithms, with Artificial Intelligence and Machine Learning in clinical research reshaping drug development.[10]

Although running medical research studies remotely with the assistance of technology has been an ongoing practice for years now,[11] and even captured the attention of the government,[12] it was only by the end of the past decade, with the COVID-19 pandemic, that their decentralization and the use of research digital tools gained popularity. As a result of isolation-based public health measures for the risks of contracting the virus and clinical networks' priorities shifting from research to the treatment of COVID-19 patients, trial enrollment decreased by more than

[7] Jennifer Miller & Joseph Millum, Ethical Considerations in International Clinical Trial Site Selection, 7(4) BMJ Global Health e008012 (2022), at 1, 2, n.4.

[8] O. T. Inan et al., Digitizing Clinical Trials, 3 NPJ Digit. Med., n.101 (2020).

[9] Id. at 2; see also Effy Vayena et al., Decentralised Clinical Trials: Ethical Opportunities and Challenges, 5 Lancet Digit. Health e390 (2023).

[10] Greg Licholai, AI in Clinical Research: Now and Beyond, Forbes (Sept. 18, 2023), https://www.forbes.com/sites/greglicholai/2023/09/18/ai-in-clinical-research-now-and-beyond/?sh=2612b13830c85.

[11] See Tim McAlindon et al., Conducting Clinical Trials over the Internet: Feasibility Study, 327 Brit. Med. J. 484 (2003) (on knee osteoarthritis studies); Bradly P. Jacobs et al., An Internet-Based Randomized, Placebo-Controlled Trial of Kava and Valerian for Anxiety and Insomnia, 84 Medicine 197 (2005) (on anxiety and insomnia treatments' studies); Pfizer Conducts First "Virtual" Clinical Trial Allowing Patients to Participate Regardless of Geography, Pfizer (June 7, 2011, 5:30 AM), https://www.pfizer.com/news/press-release/press-release-detail/pfizer_conducts_first_virtual_clinical_trial_allowing_patients_to_participate_regardless_of_geography (on Pfizer's FDA-approved REMOTE).

[12] See Digital Clinical Trials Workshop: Creating a Vision for the Future, Nat'l Health, Lung & Blood Inst. (2019), https://www.nhlbi.nih.gov/events/2019/digital-clinical-trials-workshop-creating-vision-future.

two-thirds across all therapeutic areas.[13] Remote trials proliferated and the Food and Drug Administration (FDA) required research sites to adjust their safety procedures or switch to digital, waiving Institutional Review Boards (IRB) or FDA approval but still subjecting them to reporting.[14] Remote trials during the pandemic helped to assess the strengths and weaknesses of virtual trials – for example, that studying patients remotely can be safe as long as participants do not have a serious medical condition (e.g., infectious disease or progressive cancer)[15] – and became a regular practice.[16] Since 2021, DCTs have become a "major part of [the industry's] portfolios."[17] Several clinical research organizations (CROs)[18] and academic research and related public–private initiatives[19] have developed products across the decentralized trial spectrum.

19.3 PRIVATE EQUITY'S INTEREST IN DCTS

The US health care industry has been increasingly attractive to PE firms for some time now.[20] Distinctively, the United States reports an average of 2.3 PE health care transactions daily.[21] From hospital and nursing home buyouts in the 2000s, to medical practice acquisitions such as radiology and outpatient care, including

[13] Consolidation in Clinical Research Sites and COVID's Impact, Provident Healthcare Partners (Aug. 2020), https://www.providenthp.com/expertise/consolidation-in-clinical-research-sites-and-covids-impact/.

[14] Conduct of Clinical Trials of Medical Products during the COVID-19 Public Health Emergency: Guidance for Industry Investigators, and Institutional Review Boards, U.S. Dep't of Health & Hum. Servs. (Mar. 2020), https://www.fda.gov/media/136238/download; see also Jacqueline Corrigan-Curay, Conducting Clinical Trials during the COVID-19 Public Health Emergency, U.S. Food and Drug Admin. (Apr. 30, 2020), https://www.fda.gov/media/137496/download.

[15] Podcast: Can Famotidine, a Heartburn Drug, Treat Covid? Health Talk with Tobias Janowitz, Northwell Health (Jan. 23, 2023), https://www.northwell.edu/news/insights/podcast-researcher-talks-famotidine-for-covid-trial.

[16] See also Matthew Libassi, Northwell, CSHL Open Virtual COVID-19 Clinical Trial for Non-hospitalized Patients, Northwell Health (Jan. 27, 2021), https://feinstein.northwell.edu/news/the-latest/-northwell-cshl-open-virtual-covid-19-clinical-trial-for-non-hospitalized-patients (referring to Northwell's post-pandemic trial recruitment strategies).

[17] Marcus A. Banks, In the Wake of COVID-19, Decentralized Clinical Trials Move to Center Stage, 118(47) Proc. Nat'l Acad. Scis. e2119097118 (2021), at 2.

[18] Coravos, supra note 2 (e.g., Science 37, Koneksa Health, Medidata).

[19] Andy Coravos, Decentralized Clinical Trials, Medium (Oct. 15, 2018), https://blog.andreacoravos.com/decentralized-clinical-trials-e9dbde90ea95 (Clinical Trial Transformation Initiative by Duke University and the FDA).

[20] See John Geyman, Private Equity Looting of U.S. Health Care: An Under-Recognized and Uncontrolled Scourge, 53 Int. J. Health Servs. 233 (2003); Anaeze C. Offodile II et al., Private Equity Investments in Health Care: An Overview of Hospital and Health System Leveraged Buyouts, 2003–17, 40 Health Affs. 719, https://www.healthaffairs.org/doi/10.1377/hlthaff.2020.01535.

[21] Data from PitchBook Data Inc., Healthcare Services Report (2022), https://pitchbook.com/news/reports/q4-2022-healthcare-services-report.

urgent care and ambulatory surgery centers and neonatal and trauma units in the 2010s, PE health care investments have increased twenty times their value in the past two decades.[22] PE has also been active in nonhospital-based dermatology, dental, orthopedics, and behavioral health specialties,[23] and medical debt collecting.[24]

Clinical trials, particularly those remote and digital, represent a new business opportunity for PE firms: If a drug can reach the market sooner and at a lower cost, manufacturers will make more profit. By outsourcing the performance of trials to CROs, manufacturers can reduce investment risks and separate the operational costs of running a trial; in turn, CROs can make revenues despite trials failing or if a drug is not approved.[25] The way in which PE firms operate, raising capital and investing it into various privately held companies, often grants them ownership or enough of a stake to gain operational control of their portfolio's companies, appoint company directors, and dictate every aspect of the companies' business and affairs.[26] The decentralization and digitization of trials require infrastructure outside of a research institution and technology tools that are often proprietary. This provides CROs – and the PE firms that finance and manage them – with more opportunity to grow, continue penetrating the space of trials, and build the infrastructure and technology required. Studies found substantial value in employing DCT methods in phase II and phase III of clinical trials, with high returns on investments.[27] Decentralization would be particularly more amenable for "general population drugs," which serve a category of patients with less hospital-based resourcing needs;[28] yet, the industry has expressed interest in the decentralization of trials for rare diseases, too.[29]

Financial stability would make trials a reliable investment for PE portfolios. Business strategies vary somewhat by type of private equity investment, but prioritizing short-term, high profits stays as a primary goal.[30] Unlike other technology-based

[22] Eileen Appelbaum & Rosemary Batt, Private Equity Buyouts in Healthcare: Who Wins, Who Loses? 93–94 (Ctr. for Econ. & Pol'y Rsch., Working Paper No. 118, 2020), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3593887 (from US$5 billion in 2000 to US$100 billion in 2018).

[23] Myths v. Facts: Private Equity and Nursing Homes, Am. Health Care Ass'n (Mar. 11, 2022), https://www.ahcancal.org/News-and-Communications/Blog/Pages/Myths-vs–Facts-Private-Equity-and-Nursing-Homes.aspx.

[24] Geyman, supra note 20, at 233–34.

[25] See Rachana Pradhan, The Business of Clinical Trials Is Booming. Private Equity Has Taken Notice, Kaiser Fam. Found. Health News (Dec. 2, 2022), https://kffhealthnews.org/news/article/business-clinical-trials-private-equity/; Provident Healthcare Partners, supra note 13, at 4.

[26] John Morley, Too Big to Be Activist, 92 S. Cal. L. Rev. 1407, 1449 (2019).

[27] Joseph A. DiMasi et al., Assessing the Financial Value of Decentralized Clinical Trials, 57(2) Therapeutic Innovation & Regul. Sci. 209 (2023).

[28] E-mail from Greg Licholai to Author (Sept. 18, 2023, 22:55 EST) (on file with author) (referring that oncology and rare disease drugs might be less amenable to decentralization).

[29] Mercedeh Ghadessi et al., Decentralized Clinical Trials and Rare Diseases: A Drug Information Association Innovative Design Scientific Working Group (DIA-IDSWG) Perspective, 18(1) Orphanet J. Rare Dis. 79 (2023).

[30] Geyman, supra note 20, at 234.

industries, trial demand is resilient to inflation and economic declines. Research and development (R&D) of new health technologies can largely be government-backed, which secures low debt levels once entering clinical trial phases. Although these are signs of stable cash flow, some high volatility suggests clinical trials to be risky investments, with already cautionary tales of valuation fluctuation and labor struggles.[31] Science 37, one of the first DCT startups, showed continued and massive share price drops after an oversubscribed offering in 2020 and a major public listing in 2021.[32] Nevertheless, overall, DCTs make financial sense to PE firms that tolerate volatility and can make huge returns provided timely, good planning.[33] The clinical trial space is attractive for businesses; valued at US$16 billion, with an estimated 6.8 percent compound annual growth rate through 2025.[34] Since January 2021, ten PE-backed trial platforms have been acquired or created,[35] yet mostly interested in late-stage trials.[36] No drug studied via remote trials (whether PE funded or not) has been approved yet to date.

From a legal and policy perspective, the outsourcing of pharmaceutical services has not spurred enough regulatory oversight. Generally, PE firms' transactions are not subject to rigorous scrutiny even though they can have large effects on competition.[37] About 90 percent of PE transactions – either buyouts or investments – are exempt from the federal mandatory antitrust reporting threshold,[38] with the

[31] Kyle LaHucik, Two Decentralized Trials Startups Prove They're Not Immune to Broader Wave of Biotech Layoffs, Endpoint News (Aug. 24, 2022), https://endpts.com/two-decentralized-trials-startups-prove-theyre-not-immune-to-broader-wave-of-biotech-layoffs/.

[32] See Science 37 Raises $40 Million to Extend Its Leadership in the Decentralized Clinical Trial Market, PR Newswire (Aug. 20, 2020), https://www.prnewswire.com/news-releases/science-37-raises-40-million-to-extend-its-leadership-in-the-decentralized-clinical-trial-market-301115398.html; Ben Adams, Science 37 Taps a SPAC to Go Public, with Siteless Trial Specialist Valued at a Cool $1B, Fierce Biotech (May 7, 2021), https://www.fiercebiotech.com/cro/science-37-taps-a-spac-to-go-public-siteless-trial-specialist-valued-at-a-cool-1b.

[33] E-mail from Greg Licholai to Author (Sept. 20, 2023, 10:28 AM EST) (on file with author).

[34] Harris Williams, Return on Innovation, Part 6: Clinical Trial Sites (Mar. 2023), https://www.harriswilliams.com/our-insights/hcls-return-innovation-clinical-trials#part-6-full-report.

[35] Id.

[36] See Randal Smith, The Private Equity Firm That Quietly Profits on Top-Selling Drugs, N.Y. Times (July 8, 2017), https://nytimes.com/2017/07/08/business/dealbook/drug-prices-private-equity.html (Royalty Pharma's investment in Soliqua's late-stage clinical trial); David H. Crean, Private Equity Is Making Venture-Style Bets in Drug Development, Cardiff Advisory (Feb. 1, 2023), https://www.linkedin.com/pulse/private-equity-making-venture-style-bets-drug-david-h-crean/ (Blackstone's acquisition of pharma companies with undergoing clinical trials).

[37] Fred Schulte, Sick Profit: Investigating Private Equity's Stealthy Takeover of Health Care across Cities and Specialties, Kaiser Fam. Found. Health News (Nov. 14, 2022), https://kffhealthnews.org/news/article/private-equity-takeover-health-care-cities-specialties/.

[38] The Growth of Private Equity in US Health Care: Impact and Outlook, Nat'l Inst. of Health Care Mgmt. Found. (2023), https://nihcm.org/publications/the-growth-of-private-equity-in-us-health-care-impact-and-outlook (referring to Zirui Song on PE expansion policies); see Statement of Commissioner Rohit Chopra Regarding Private Equity Roll-ups and the Hart-Scott Rodino Annual Report to Congress, Fed. Trade Comm'n (July 8, 2020), https://www.ftc

exception of a few states, such as Oregon and Massachusetts, that monitor health care antitrust activity.[39]

Fragmentation also makes clinical trials a prime target for PE firms. The medical research market includes stand-alone clinics and physician practices performing studies on a part-time basis, commercial sponsors, and CROs. As fragmented as trial activities thus become, it is harder for policies to address trial challenges with specificity, which creates the risk of ignoring the secondary effects of a given policy choice and moving toward contradictory policy goals – like expanding DCTs through PE firms.[40] For PE firms, *fragmentation* also represents the opportunity to consolidate markets and reduce operational costs, which PE firms do to maximize profits.[41] Vertical integration of CROs' service offerings (e.g., recruitment, data collection) allows PE firms to gain operational control over trials.[42] As PE firms acquire independent sites, they become part of larger networks to be sold off once they are rolled up into a business.[43] Following a merger, acquirers tend to prioritize services that are operationally cost-efficient. Recruitment might be one of them. Additionally, former CEOs of pharmaceutical companies are occupying influential seats at PE firms,[44] suggesting new combinations of *small and big* pharmaceutical industry dominance that will demand new private law tools to ensure that consolidations receive increased scrutiny.

19.4 GREATER SCIENTIFIC EVIDENCE AT THE RISK OF MORE OPACITY

Allegedly, PE firms have targeted DCTs as a blooming business opportunity.[45] At least 65 percent of the total clinical research transactions reported until February of 2023 have involved PE firms.[46] Eleven of the twenty-five PE firms

.gov/legal-library/browse/cases-proceedings/public-statements/statement-commissioner-rohit-chopra-regarding-private-equity-roll-ups-hart-scott-rodino-annual.

[39] Robin L. Davison et al., A Step Forward for Health Care Market Oversight: Oregon Health Authority's Health Care Market Oversight Program, Milbank Mem. Fund (Mar. 13, 2023), https://www.milbank.org/publications/a-step-forward-for-health-care-market-oversight-oregon-health-authoritys-health-care-market-oversight-program/.

[40] Pradhan, supra note 25.

[41] Richard M. Scheffler et al., Soaring Private Equity Investment in the Health Care Sector: Consolidation, Accelerated, Competition Undermined, and Patient Risk, Petris Ctr. (May 18, 2021), https://petris.org/soaring-private-equity-investment-in-the-healthcare-sector-consolidation-accelerated-competition-undermined-and-patients-at-risk/.

[42] Provident Healthcare Partners, supra note 13.

[43] Pradhan, supra note 25.

[44] Data with author.

[45] Pradhan, supra note 25.

[46] Author's examination of Private Equity-Backed CROs Tracker database provided by the nonprofit Private Equity Stakeholder Project (PESP) for this research project. The database collects data from Pitchbook Data Inc. available until February 24, 2023 (on file with the author). Fifty-seven of the eighty-seven research site acquisitions deals reported since 2020 are

identified by PitchBook as health care sector top investors have bought stakes in CROs.[47] Is it beneficial for scientific evidence production that PE firms finance and manage clinical trials, their decentralization, and digitization?

This essay frames this question not as one of ownership but of governance, motivated by concerns around access to scientific evidence produced by private sector actors. PE firms' interest in DCTs is in tension with the original sponsor role of the industry. The FDA first coined the term drug "sponsor" in the 1960s to differentiate research tasks from development, when the labor of clinical investigations was conceived divorced from the industry. The role of drug manufacturers was to promote the merits of a novel product to the regulatory agency until it reached approval for commercialization.[48] The Bayh-Dole Act of 1980[49] opened the door for financialized actors to venture into drug development.[49] In the 1980s and 1990s, pharmaceutical firms underwent a corporate strategy transformation under the rise of the idea of shareholder value maximization (SVM), which distorted the way in which larger, publicly traded pharmaceutical companies generate growth for their shareholders – not on their current profitability but on their potential to deliver future earnings.[50] Although the expansion of financial actors, like venture capital, in the US health care system[51] and biotechnology particularly is not new,[52] as PE firms get more involved in the decentralization and digitization of research, the industry's original sponsor role reaches – yet again – new extremes. It also reinforces the supply-driven approach that has shaped biopharmaceutical innovation, which aligns biopharmaceutical innovation priorities with market demand over the social value of science, leaving the end goal of access to scientific evidence and resulting medicine at the periphery.[53]

private equity-backed. See also PESP 2023 Report, Private Equity in U.S. Healthcare: Trends in 2023 Deal Activity (2023), https://pestakeholder.org/private-equity-healthcare-2023-trends/ (reporting thirty-eight PE-backed deals in 2023).

[47] Headlands Research Sites Chosen for Crucial COVID-19 Vaccine Trials, Globe NewsWire (July 16, 2020), https://www.globenewswire.com/news-release/2020/07/16/2063568/0/en/Headlands-Research-Sites-Chosen-for-Crucial-COVID-19-Vaccine-Trials.html.

[48] Daniel Carpenter, Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA (2014).

[49] Arti K. Rai & Rebecca S. Eisenberg, Bayh-Dole Reform and the Progress of Biomedicine: Allowing Universities to Patent the Results of Government-Sponsored Research Sometimes Works against the Public Interest, 91(1) Am. Scientist 52, 52–59 (2003).

[50] Victor Roy, A Crisis for Cures? Tracing Assetization and Value in Biomedical Innovation, in Assetization (Kean Birch & Fabian Muniesa eds., 2020).

[51] Joseph D. Bruch et al., The Financialization of Health in the United States, 390(2) N. Engl. J. Med. 178 (2024).

[52] Gary P. Pisano, Can Science Be a Business, 84(10) Harv. Bus. Rev. 114, 114–24 (2006).

[53] Ariel Katz, Pharmaceutical Lemons: Innovation and Regulation in the Drug Industry, 14 Mich. Telecomm. & Tech. L. Rev. 1, 8 (2007).

Scholars have raised concerns about PE firms' investment in health care based on negative outcomes in the delivery of medical care: decline in safety and efficacy[54] and higher prices.[55] Clinical trials bring forth their own set of risks, too. Two areas of concern are the ethics of trial participants' engagement (including data privacy protections, inclusivity, and participants' rights and safety)[56] and the opportunities to skew or produce faulty data in uncontrolled environments.[57] In these cases, private law tools like torts are available to enforce data privacy obligations. But having new financialized actors like PE firms, private by nature, directly involved in a considerable and rising number of trials that generate critical scientific evidence that supports the release of new health technologies into the market, might affect *all and everyone* as potential science users, beyond trial participants, and subject to less transparency regulations.

Crucially, DCTs are expected to generate greater data volume and data diversity. As PE firms engage in ambitious DCTs, they will gain access to a larger number of patient data sources, leverage data management tactics with sophisticated digital tools, and be able to obtain more critical clinical data. For instance, a 2021 Tuft CSDD report evidenced that phase III clinical trials already generated an average of 3.6 million data points, three times the data collected by late-stage trials ten years ago.[58] These numbers are expected to continue to grow as trials are digitized. Now, more data has not always led to better scientific evidence for quality drugs. The clinical evidence that the industry currently produces and delivers to the FDA in order to assess the safety and efficacy of drugs is either incomplete or not as transparent and accessible as needed. There is no indication that PE firms' involvement in the generation of scientific evidence will fix the information problem clinical trials face – to the contrary, the risk of opacity may even increase under PE leadership due to their opportunistic business model.

PE firms generate scientific evidence that is essential for regulators to exercise oversight over drug development, improve treatment guidelines, incentivize better

[54] See Robert T. Braun et al., Association of Private Equity Investment in US Nursing Homes with the Quality and Cost of Care for Long-Stay Residents, 2 JAMA Health F. e213817 (2021), https://doi.org/10.1001/jamahealthforum.2021.3817.

[55] Yashaswini Singh et al., Association of Private Equity Acquisition of Physician Practices with Changes in Health Care Spending and Utilization, 3(9) JAMA Health F. e222886 (2022), https://jamanetwork.com/journals/jama-health-forum/fullarticle/2795946.

[56] See Vayena et al., supra note 9; Pradhan, supra note 25; Tessa I. van Rijssel et al., Ethics Review of Decentralized Clinical Trials (DCTs): Results of a Mock Ethics Review, 27(10) Drug Discovery Today 103326 (2022); Carlo Petrini et al., Decentralized Clinical Trials (DCTs): A Few Ethical Considerations, Front Public Health (2022), https://pubmed.ncbi.nlm.nih.gov/36590004/.

[57] Banks, supra note 17, at 2.

[58] Tuft Ctr. for the Study of Drug Dev., 23 Rising Protocol Design Complexity Is Driving Rapid Growth in Clinical Trial Data Volume (2021), https://f.hubspotusercontent10.net/hubfs/9468915/TuftsCSDD_June2021/pdf/Rising+Protocol+Design+Complexity+is+Driving+Rapid+Growth+in+Clinical+Trial+Data+Volume++++++++++.pdf.

innovation, and shed light on and correct bad industry practices. Data publicity is also important to bioethicists, who aim to reduce risks to trial participants and drug users; to health economists, to better direct health care spending to safe and effective treatments; and to independent researchers, advocates, and citizens at large for data reevaluation and accountability.[59] The FDA, which "houses the largest known repository of clinical data" in the world,[60] plays a gatekeeping role, with a primary function of information generation and validation.[61] This function is essentially frustrated when all information about drugs obtained in clinical trials is not made available or a part of it remains secret. *All* information includes both the positive and the negative data generated at trials. The burden to provide evidence of any negative effects is on firms.[62] However, drug developers have insufficient incentives to generate and share negative information as they want drugs to be approved, affecting validation.[63] A free rider problem leads to an information production and data publicity problem that PE firms could hardly overcome due to their appetite for maximizing profits in line with their fiduciary duty to create value for their investors in return for their entrusted money. This transactional PE–investor relationship silences other stakeholders' interests (e.g., developing science for the benefit of the community) and makes more socially oriented goals, such as making complete drug evidence accessible, be perceived with disbelief.[64]

Different trials produce different types of data. Metadata is essential for interpreting clinical trial results.[65] They include the study protocols that set forth investigators' statistical analysis plans and the endpoints a clinical study will evaluate. The FDA requires metadata for drug assessment and approval;[66] independent researchers use them to run a reanalysis of studies and identify probable misleading studies generating flattering results.[67] Summary data include clinical trial summaries,

[59] Christopher J. Morten & Amy Kapczynski, The Big Data Regulator, Rebooted: Why and How the FDA Can and Should Disclose Confidential Data on Prescription Drugs and Vaccines, 109 Calif. L. Rev. 506, 506–09.

[60] U.S. Food and Drug Admin., Driving Biomedical Innovation: Initiatives to Improve Products for Patients 22 (2011).

[61] Amy Kapczynski, Dangerous Times: The FDA's Role in Information Production, Past and Future, 102 Minn. L. Rev. 2357, 2357–58 (2018); Jorge L. Contreras, Leviathan in the Commons: Biomedical Data and the State, in Governing Medical Knowledge Commons 19–45 (Katherine J. Strandburg et al. eds., 2017).

[62] W. Nicholson Price II & Timo Minssen, Will Clinical Trial Data Disclosure Reduce Incentives to Develop New Uses of Drugs?, 33(7) Nature Biotech. 685, 685–86.

[63] Id. at 2363–64; Morten & Kapczynski, supra note 59, at 509.

[64] Jeanne A. Markey & Raymond M. Sarola, Private Equity, Health Care, and Profits: It's Time to Protect Patients, STAT News (Mar. 24, 2022), https://www.statnews.com/2022/03/24/private-equity-health-care-profits-time-to-protect-patients/.

[65] Morten & Kapczynski, supra note 59, at 512.

[66] See, e.g., 21 C.F.R. §314.50(d)(6) (2019) (requiring nondisclosure agreements to contain a statistical section).

[67] See, e.g., Yale Collaboration for Rsch. Integrity & Transparency, Promoting Transparency in Clinical Research: Why and How 9 (2017) (referring to the Paxil case).

prepared by manufacturers and submitted to the FDA, that highlight key trial results. Although not routinely disclosed by the FDA, summary data can jeopardize medicines' permanence in markets.[68] Another set of valuable data for reanalysis is individual patient-level data. On a voluntary basis, raw and granular data collected per trial participant is made available in analyzable form and used to identify discrepancies, for example, in summary data.[69] A drug is safe only if its known therapeutic benefits outweigh its known risks;[70] thus, because "safety can only be understood in relation to efficacy and vice versa,"[71] and the safety and efficacy of drugs must be determined together, it is absolutely necessary that all trial data – metadata, summary data, individual patient-level data, and others – are not omitted, but disclosed and shared. The hidden data and existing opacity practices over privately produced evidence have already translated into grave examples of unsafe medicine. Vioxx led to tens of thousands of cardiac deaths,[72] whereas Paroxetine (Paxil) caused suicidal thoughts in a substantial portion of young patients who used the antidepressant during pediatric treatment, despite studies showing their risks clearly.[73]

PE firms' profit incentive schemes continue to put the prioritization of safety maximization at risk. The absence of PE-backed trials and approved drugs to date makes it hard to run a comparative analysis between trials with and without PE support. During the pandemic, the New York-based private equity firm Headlands Research established in 2018, which provided outsourced COVID-19 vaccine decentralized trials to pharmaceutical firms (such as Pfizer, Moderna, AstraZeneca, and Johnson & Johnson), grew by buying established trial sites and opening new ones in the United States and Canada under the promise of boosting underrepresented racial and ethnic minority trial representation.[74] Many of their acquired locations promptly closed, and it remains unclear whether the enrollment targets set for

[68] Id. at 12–13 (referring to the Avandia case and the 2007 independent reanalysis of data that was possible due to a high-profile litigation settlement).

[69] Joshua D. Wallach et al., Updating Insights into Rosiglitazone and Cardiovascular Risk through Shared Data: Individual Patient and Summary Level Meta-Analyses, 368 Brit. Med. J. 1 (2020).

[70] FDA's Drug Review Process: Continued, U.S. Food and Drug Admin. (2015), https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-continued.

[71] Morten & Kapczynski, supra note 59.

[72] David J. Graham et al., Risk of Acute Myocardial Infarction and Sudden Cardiac Death in Patients Treated with Cyclo-Oxygenase 2 Selective and Non-Selective Non-Steroidal Antiflammatory Drugs: Nested Case-Control Study, 365 Lancet 475, 280 (2005); Harlam Krumholz et al., What Have We Learnt from Vioxx?, 334 Brit Med J. 120 (2007).

[73] Joanna Le Noury et al., Restoring Study 329: Efficacy and Harms of Paroxetine and Imipramine in Treatment of Major Depression in Adolescence, 351 Brit. Med. J. h4320 (Aug. 3, 2015).

[74] Pradhan, supra note 25 (some of these sites were in McAllen, Texas; Houston, Texas; Metro Atlanta; and Lake Charles, Louisiana).

COVID-19 vaccine trials were ever met. The drug company sponsor was the only entity that had access to the multisite aggregated clinical data.[75]

Considering the growing risks of clinical data opacity, PE firms should voluntarily commit to not only advocate for-profit maximization but simultaneously pursue the social value of generating scientific data. Different mechanisms to pursue social value may include targeting socially conscious executive compensation and multiple stakeholder board representation.[76]

19.5 CONCLUSION

PE investment in remote, digitized clinical trials promises to improve operational, technological, and financial trial inefficiencies. Securing trial participant safety can be ensured by demanding PE firms have higher standards of care, enforced by private law tools. Yet, leaving the production of substantial scientific evidence to PE-backed trials deserves greater scrutiny. It is access to evidence that allows safe and effective health technologies to reach the market. The publicity concerns present today in drug development already indicate a free rider problem and low incentives to generate and disclose all and necessary privately generated evidence. As PE firms with financial opportunistic interests encroach upon DCTs, the tension between profit maximization and evidence and drug safety and efficacy maximization will only become greater. Resolving this tension requires greater moral responsibility from the industry and closer monitoring and critical analysis of PE activity from regulators.

[75] Id.
[76] Emilie Aguirre, Beyond Profit, 54 U.C. Davis L. Rev. 2077 (2021).